

JSS Medical College & Hospital, Mysuru



COVID Research & Publication Compendium

May 2020 to July 2021

Message



Dr Basavana Gowdappa H
Principal
JSS Medical College,
JSS Academy of Higher
Education & Research
Mysore

COVID-19 Pandemic has posed major challenges to all the sectors of society. Health care and medical education are among the worst hit sectors among all. JSS Medical College and Hospital have been in forefront in controlling and reducing the impact of COVID-19 pandemic since its beginning. Adapting to the needs of community in this critical health situation, the hospital has saved lives of thousands of sick through determined health care staff. Apart from taking care of patients suffering from COVID, the institution has kept the medical education ongoing through online teaching platforms. A matter of great pride is that the faculty and students of the institution have involved in conducting good quality research at the same time and published several research papers in various national and international journals.

I am extremely happy to note that JSS Medical College is coming out with the COVID-19 research and publication compendium. The present compendium demonstrates the research credentials of the staff and students of our institution at various domains of COVID-19 like, understanding the disease, its pathogenesis, epidemiological determinants, risk factors, preventive strategies, impact of disease on various dimensions of health, therapeutic interventions in line with sustainable development goals (SDG).

The compendium not only acts as a source of inspiration for the faculty and students in medical science for the years to come but also acts as a torch bearer for future research and innovations in the field of COVID-19 and other infectious diseases.

I congratulate all the faculty members and students for conducting the research on various aspects COVID-19 and converting their research into impactful publications. I wish them the best for their future endeavours in this regard. I would also like to express my sincere regards to the editorial team consisting of Dr Suma M N, Dr Praveen Kulkarni, Dr Anil S Bilimale and Smt. Shalini and Mr Vijaykumar for their constant efforts in publishing this document.

Dr H Basavanagowdappa
PRINCIPAL



Message



I am very happy to learn that the JSS Medical College is³ bringing out a compendium of Research & Publication on COVID-19 theme.

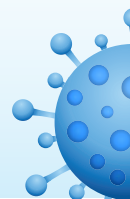
We have had many challenges and learnt numerous lessons throughout the journey of COVID-19 pandemic.

This endeavour will add value and contribute further to our knowledge base which we can share with among fellow healthcare professionals and administrators.

Recording all these experience and actions is of utmost importance and I am sure this will become a good source of reference for the future clinicians.

I am delighted to know that 104 publications have been categorised on various themes. This will be a fantastic effort from JSS Medical College and I congratulate the team and wish them all success.

DIRECTOR



INDEX

Sl No	Category	Number of Research projects	Page Number
1	Research Projects Related to COVID	07	6
2	Analysis of publication releated to covid		8

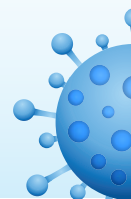
PUBLICATIONS ON COVID - BASED ON THE THEMES

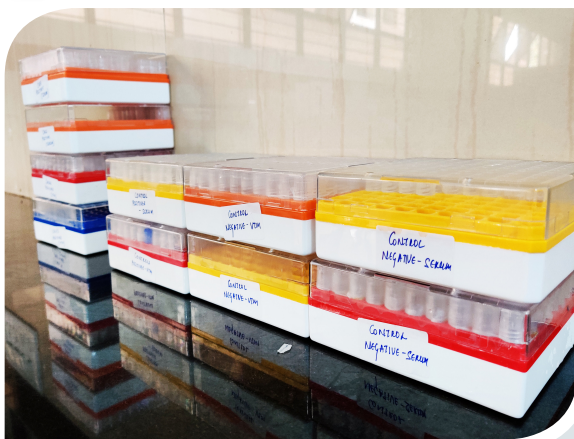
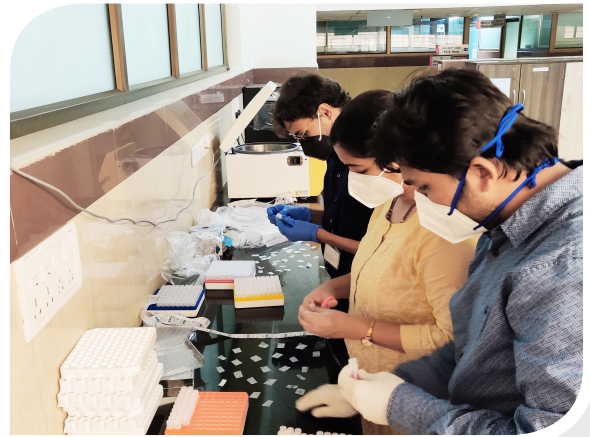
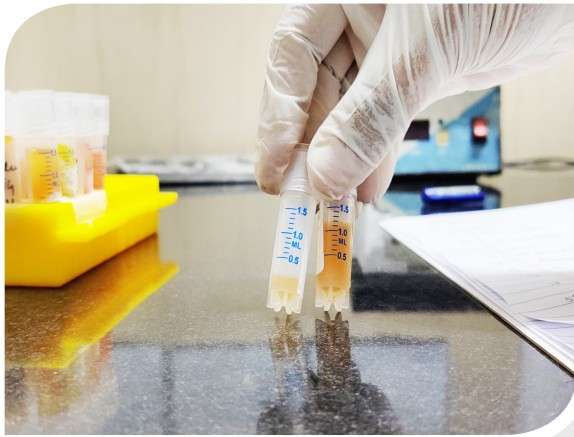
Sl No	Theme	No. of Publications under the theme	Page Number
1	Health Impact of COVID-19	12	9
2	Digital interventions for COVID-19 Pandemic	02	101
3	Learning never stops amidst Pandemic: Educational research	12	113
4	Impact of pandemic on health care delivery sector	02	167
5	Mental Health in Pandemic	23	175
6	Infodemic of pandemic	05	331
7	Diagnostic modalities	01	361
8	Therapeutic Dimension	10	367
9	Social Impact of Lockdown	16	449
10	Preventive strategies	06	583
11	Perception and practices related to COVID-19	08	635
12	Miscellaneous	04	689



RESEARCH PROJECTS RELATED TO COVID

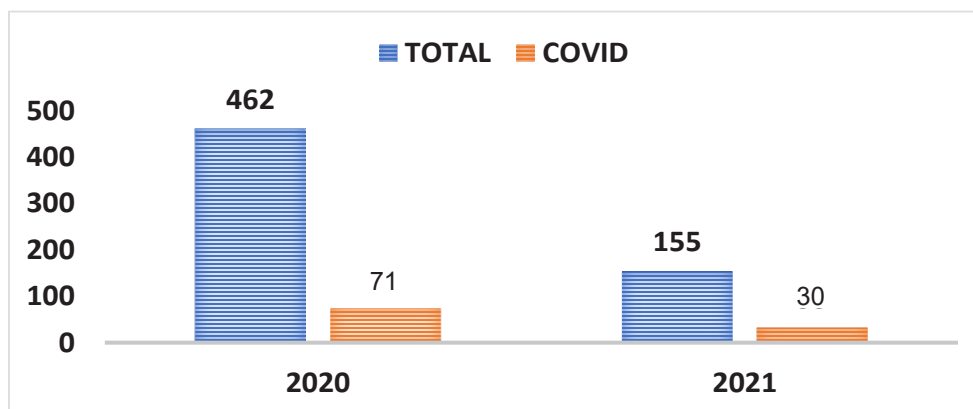
SI No	Project	Name and Designation of PI
1	Mission COVID Suraksha	Dr H Basavanagowdappa Principal, JSS Medical College
2	Efficacy of BCG Vaccine on COVID-19 among elderly	Dr Pratibha Pereira, Professor and Head, Dept of Geriatrics
3	Covishield- Phase 2/3 Vaccine Trial	Dr Praveen Kulkarni Associate Professor, Dept of Community Medicine
4	Sputnik V- Phase 2/3 Vaccine Trial	Dr Shilpa Avarebeel, Assistant Professor, Dept of Geriatrics,
5	Covovax: Phase 2/3 Vaccine Trial	Dr Praveen Kulkarni Associate Professor, Dept of Community Medicine
6	Risk factors for SARS-CoV-2 infection among healthcare workers	Dr.Anil S Bilimale Assistant Professor, Dept of Community Medicine
7	Effectiveness of Covaxin and Covishield vaccines in the community	Dr.Anil S Bilimale Assistant Professor, Dept of Community Medicine
8	13 Drug trials on COVID	Dr. Prathiba Pereira, Dr. Subhash Chandra, Dr. Jayaraj B.S. Dr. Tejaswini, Dr. Srinath, Dr. Shilpa Avarebeel, Dr. Ashok P Dr. Akshay



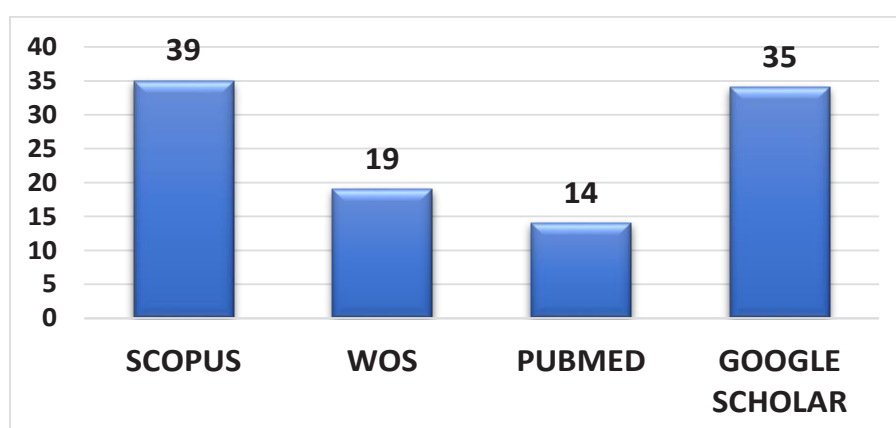


Analysis of publication releated to covid

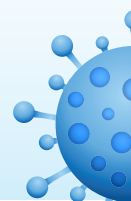
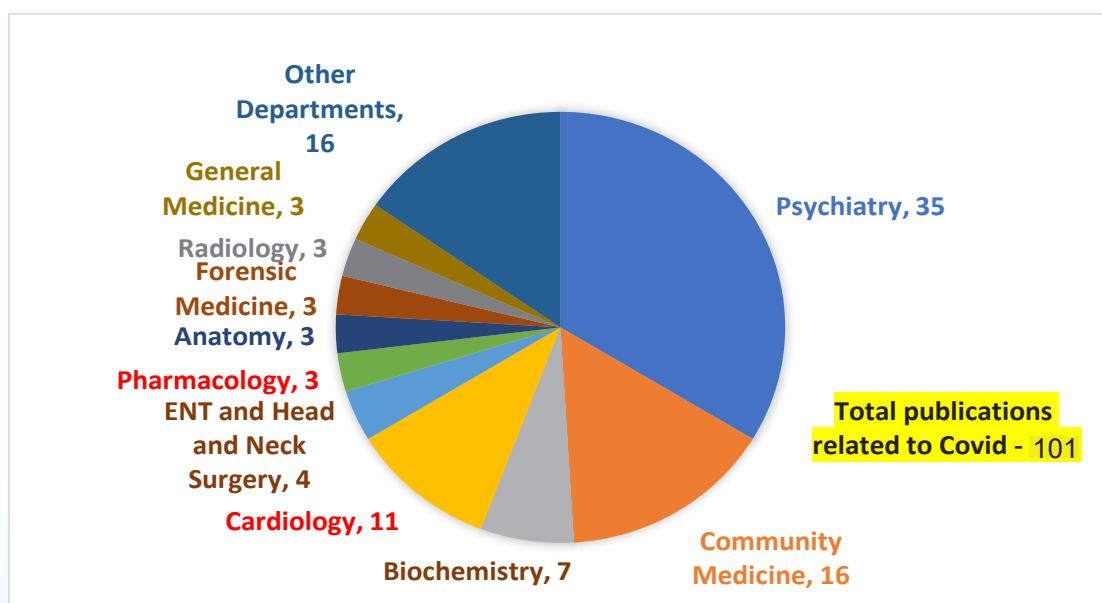
Publications



Indexing of Covid publications



Department wise publications

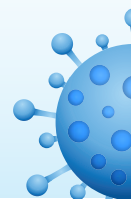


1. Health Impact of COVID-19






SI No	Title	SDG IMPACT
1	Does COVID-19 contribute to development of neurological disease?, Arehally M Mahalakshmi , Bipul Ray , Sunanda Tuladhar, Abid Bhat, ShastharaPaneyala, DuraisamyPatteswari, Meena Kishore Sakharkar, Hamdan Hamdan, David M Ojcius, Srinivasa Rao Bolla, Musthafa Mohamed Essa, Saravana Babu Chidambaram, M Walid Qoronfleh, Immunity, inflammation and disease	Goal 3: Good health and wellbeing
2	COVID-19 and gastrointestinal system: A brief review, Akhil Pola., Karnam S Murthy., Dr. Prasanna K. Santhekadur, Biomedical Journal, 2319-4170	Goal 3: Good health and wellbeing
3	Hearing Loss-a Camouflaged Manifestation of COVID 19 Infection, Dr Sandhya D., Dr Bharathi M.B., Kavya Sivapuram., Dr Prakash B.G., Sriram Madhan ., Ashima Madhu ., G Nivetha Devi ., Shaik Ayesha Aliya., S B Ramya, Indian Journal of Otolaryngology and Head and Neck Surgery, 1 -5, 0019-5421	Goal 3: Good health and wellbeing
4	Impact of COVID-19 pandemic on the dimensions of health and well-being: Time to widen our gaze, Dr Praveen Kulkarni., Dr BasavanaGowdappa H., Dr Prashant M.Vishwanath, International Journal of Health and Allied Sciences, 9, 97-100, 2278-4292	Goal 3: Good health and wellbeing
5	COVID-19 pandemic and the reduction in ST-elevation myocardial infarction admissions, Prashanth Kulkarni., Dr Manjappa M., Postgraduate Medical Journal, 96, 436-437, 0032- 5473	Goal 3: Good health and wellbeing



6	COPD Management during the COVID-19 pandemic, Sundeep Santosh Salvi., Raja Dhar., Dr Mahesh P.A., Zarir Farooq Udwadia., Digambar Behra, Lung India, 0970-2113	Goal 3: Good health and wellbeing
7	The COVID-19 Pandemic and Impact on the Cardiovascular Disease Patient: Special Emphasis on Rheumatic Valvular Heart Disease Care, K Prashanth., Dr Manjappa M., SRINIVAS A, European Journal of Molecular and Clinical Medicine, 7, 10-13, 2515-8260	Goal 3: Good health and wellbeing
8	COVID-19 Pandemic and the Impact on the Cardiovascular Disease Patient Care, Prashanth Kulkarni., Dr Manjappa M., SRINIVAS ALLURI Current Cardiology Reviews, 1- 5, 1573-403X	Goal 3: Good health and wellbeing
9	Extrapulmonary manifestations of COVID-19 pneumonia – An institutional experience, Sachin T., Dr Gurumurthy B., Dr Sudha Kiran Das., Dr Anupama C., DivyaVishwanathaKini, Journal of Medical and Scientific research, 8, 11-18, 2321-1326	Goal 3: Good health and wellbeing
10	Spectrum of atypical pulmonary manifestations of COVID-19 on computed tomography, Dr Gurumurthy B., Dr Sudha Kiran Das., Dr Rudresh Hiremath., Dr Sachin P.Shetty.,Aniketh Hiremath., Thasmai Gowda, Egyptian Journal of Radiology and Nuclear Medicine, 52, 0378-603X	Goal 3: Good health and wellbeing
11	COVID-19 Induced Cytokine Storm and the Impact of Obesity and Vitamin D Deficiency, Dr. Shobha C.R., Dr Akila Prashant., Dr Prashant M. Vishwanath, Journal of Krishna Institute of Medical Sciences University, 10, 1-14, 2231-4261	Goal 3: Good health and wellbeing
12	Predictors of mortality in patients with severe COVID-19 pneumonia—a retrospective study, M Mahendra, A Nuchin, R Kumar, S Shreedhar, PA Mahesh, Advances in Respiratory Medicine, 89, 135-142	Goal 3: Good health and wellbeing



Does COVID-19 contribute to development of neurological disease?

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 Abid Bhat^{1,2} | Shasthara Paneyala³ | Duraisamy Patteswari⁴ |
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Abstract

Background: Although coronavirus disease 2019 (COVID-19) has been associated primarily with pneumonia, recent data show that the causative agent of COVID-19, the coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can infect a large number of vital organs beyond the lungs, such as the heart, kidneys, and the brain. Thus, there is evidence showing possible retrograde transmission of the virus from the olfactory epithelium to regions of the brain stem.

Methods: This is a literature review article. The research design method is an evidence-based rapid review. The present discourse aim is first to scrutinize and assess the available literature on COVID-19 repercussion on the central

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nervous system (CNS). Standard literature and database searches were implemented, gathered relevant material, and extracted information was then assessed.

Results: The angiotensin-converting enzyme 2 (ACE2) receptors being the receptor for the virus, the threat to the central nervous system is expected. Neurons and glial cells express ACE2 receptors in the CNS, and recent studies suggest that activated glial cells contribute to neuroinflammation and the devastating effects of SARS-CoV-2 infection on the CNS. The SARS-CoV-2-induced immune-mediated demyelinating disease, cerebrovascular damage, neurodegeneration, and depression are some of the neurological complications discussed here.

Conclusion: This review correlates present clinical manifestations of COVID-19 patients with possible neurological consequences in the future, thus preparing healthcare providers for possible future consequences of COVID-19.

KEYWORDS

ACE2, COVID-19, glial cells, immune mediated demyelination, memory impairment, neurodegeneration, neuroinflammation, neurological circuits, neurology, SARS-CoV-2

1 | INTRODUCTION

Coronavirus disease-19 (COVID-19) was first identified in Wuhan, China, in early December 2019. In the past few months, this pandemic disease had spread all over the world and caused over 38,925,204 confirmed infections, with 1,098,378 fatal cases globally as of 16 October 2020, according to the Johns Hopkins University dashboard.

Coronaviruses (CoVs) are not new. The first described coronavirus was isolated from chickens in 1937. Human coronaviruses (HCoVs) were first found to be pathogenic in the mid-1960s by Tyrrell and Bynoe.^{1,2} HCoVs received more attention globally during the 2002-2003 outbreak of severe acute respiratory syndrome (SARS) by SARS-CoV, and the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012. Until then, HCoV strains were only known to cause mild upper respiratory tract infections.

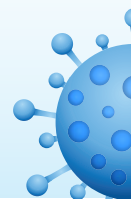
Infections by HCoVs (229E, OC43) are known to cause 15%–29% of common cold-like conditions³ with mild upper respiratory infections. The epidemic of SARS-CoV in 2002-2003 showed their potential for high virulence. Since the SARS outbreak, five new HCoV strains (SARS-CoV, NL63, HKU1, MERS-CoV, and SARS-CoV-2) have been identified. Of these, NL63 and KHU1 cause mild upper respiratory tract infections, with fever and very few fatalities. SARS-CoV, MERS-CoV, and SARS-CoV-2 are highly contagious and pathogenic and cause lower respiratory tract infection in the elderly and in

the immunocompromised.⁴ Interestingly, HCoVs like SARS-CoV, MERS-CoV, and SARS-CoV-2 have been reported to cause respiratory, enteric, hepatic and neurological disease, with variable clinical severity.⁵ This review is an attempt to gather data from isolated reports and elaborates on the potential of COVID-19 to cause neurological complications like immune-mediated demyelinating disease, cerebrovascular damage, neurodegeneration, and depression.

2 | CORONAVIRUSES AND THE BRAIN

Reports from preclinical studies show that SARS-CoV can access the brain through the olfactory bulb, and from there it reaches the brain via trans neuronal spread resulting in significant neuronal infection in SARS-CoV-receptor transgenic mice.⁶ Recent studies also show that SARS-CoV-2 is more transmissible than SARS-CoV.⁷ The high homology between SARS-CoV-2 and the previous generations of SARS and MERS coronaviruses suggests that SARS-CoV-2 could potentially damage the neurological system.⁸

Genomic analysis reveals similarity between SARS-CoV-2 and SARS-CoV, and this is consistent with the similarity in symptoms and pathogenesis of both viruses. SARS-CoV and SARS-CoV-2 also have a high affinity for the angiotensin-converting enzyme 2 (ACE2)



receptor through which they can gain access to respiratory alveoli.⁹

The extent of SARS-CoV-2 infection of the brain might be influenced by various factors, including environmental and genetic. Some patients with COVID-19 infection also have chronic diseases, which might have increased their risk to infection and decreased their immune-mediated responses. Limited information is available on how this virus induces immunologic responses to infection in the brain or the related neuropsychiatric outcomes. Neural and immune cells serve as reservoirs of latent SARS-CoV-2, which may contribute to the delayed neurodegenerative events.^{10,11}

Interestingly, other than respiratory distress as a major symptom of COVID-19, patients also experience headache, nausea, dizziness and vomiting, which suggests a probable involvement of the nervous system.¹² Furthermore, out of 214 SARS-CoV-2 patients in one study, 78 patients had neurological symptoms. Severely sick patients exhibited neurological symptoms such as cerebrovascular disease, impaired consciousness and skeletal muscle injury.¹³ Reports also suggest that some SARS-CoV-2 coronavirus can also spread from lungs and lower respiratory tract to cardiovascular and respiratory centers in the medulla of the brain via mechanoreceptors and chemoreceptors through synaptic routes. The brain stem is the most affected SARS-CoV-2 target area of the brain in both experimental animals and patients.⁸

Although the ACE2 receptor is expressed by different tissues in the body, and the cells expressing ACE2 receptors are targets for the SARS-CoV-2 infection,¹⁴ their expression in the oral cavity and tongue creates a possible gateway to the organism.¹⁵ SARS-CoV-2 docking studies to ACE2 receptors revealed that lungs, heart, kidneys, intestines, brain and testicles are the major targets.¹⁶ In the brain, besides neurons, the ACE2 receptors are also present on glial cells.¹⁷ Thus, glial cells might be a route for SARS-CoV-2 infection of the brain. Gene sequencing of cerebrospinal fluid shows the presence of SARS-CoV-2, which adds to the evidence that the coronavirus has the ability to invade the central nervous system.¹⁸

In addition, studies have demonstrated increased expressions of ACE2 receptors in ischemic brains, diabetes and in smokers, suggesting increased susceptibility to SARS-CoV-2 infection.¹⁹ ACE2 null mice have been reported to show decreased amino acid tryptophan uptake from the gut, resulting in lower levels of the amino acid in the blood. It is speculated that this could possibly influence kynurenine pathway.^{20,21} Upregulated or downregulated ACE2 receptors are expressed in many disease groups like depression, diabetes and ischemia. Hence, they are more vulnerable to infection by SARS-CoV-2.

Similarly, many reports describe central nervous system (CNS) infections by neurotropic viruses like cytomegalovirus, herpes simplex viruses, varicella-zoster virus, West Nile virus (WNV), henipavirus, Japanese encephalitis virus, chikungunya virus, Ebola virus and rabies virus.^{22,23} HIV-1 can also cross the blood-brain barrier (BBB) either paracellularly or transcellularly, and invade the CNS through a “Trojan horse” mechanism via the infected blood cells. Here, the infected monocytes cross the BBB via the production of pro-inflammatory mediators like CCL2, which compromise the BBB.²⁴ Rabies virus binds to nicotinic acetylcholine receptors at neuromuscular junctions, and travel into motor and sensory neurons.²⁵ WNV is also reported to cause associated encephalitis by disrupting the BBB, and resulting in microglia activation, inflammation and loss of neurons.²⁶

3 | POSSIBLE ACCESS OF CORONAVIRUS TO THE NERVOUS SYSTEM

The possible mechanistic pathway of penetration of the coronavirus into the nervous system could be either hematological or through peripheral nerves.²⁷ In the hematological route of entry, the coronavirus either enters the leukocytes and enters the blood stream or enters the blood through mucosa. Many viruses can breach the BBB. The BBB in the healthy state prevents the breach by pathogens. However, if there is immunosuppression and inflammation, invasion of viruses can occur. Clinical and experimental animal studies reports that the neuro-invasive potential of coronavirus spread from the respiratory tract to CNS occurs via retrograde axonal transport from peripheral nerves, such as olfactory nerve or through the hematogenous pathway²⁸ (Figure 1). Substantiating this, a recent report presents the magnetic resonance imaging of COVID-19 patient brain, demonstrating anosmia.²⁹

4 | CORONAVIRUS INFECTION AND IMMUNE-MEDIATED DEMYELINATING DISEASES

Brain autopsy of multiple sclerosis patients showed the presence of antibodies for coronavirus.³⁰ The presence of coronavirus antigen and RNA in active demyelinating plaques also suggests the possible involvement of coronaviruses in the etiology and pathogenesis of multiple sclerosis.³¹ The neurovirulence of the coronavirus depends on its ability to induce proinflammatory signals



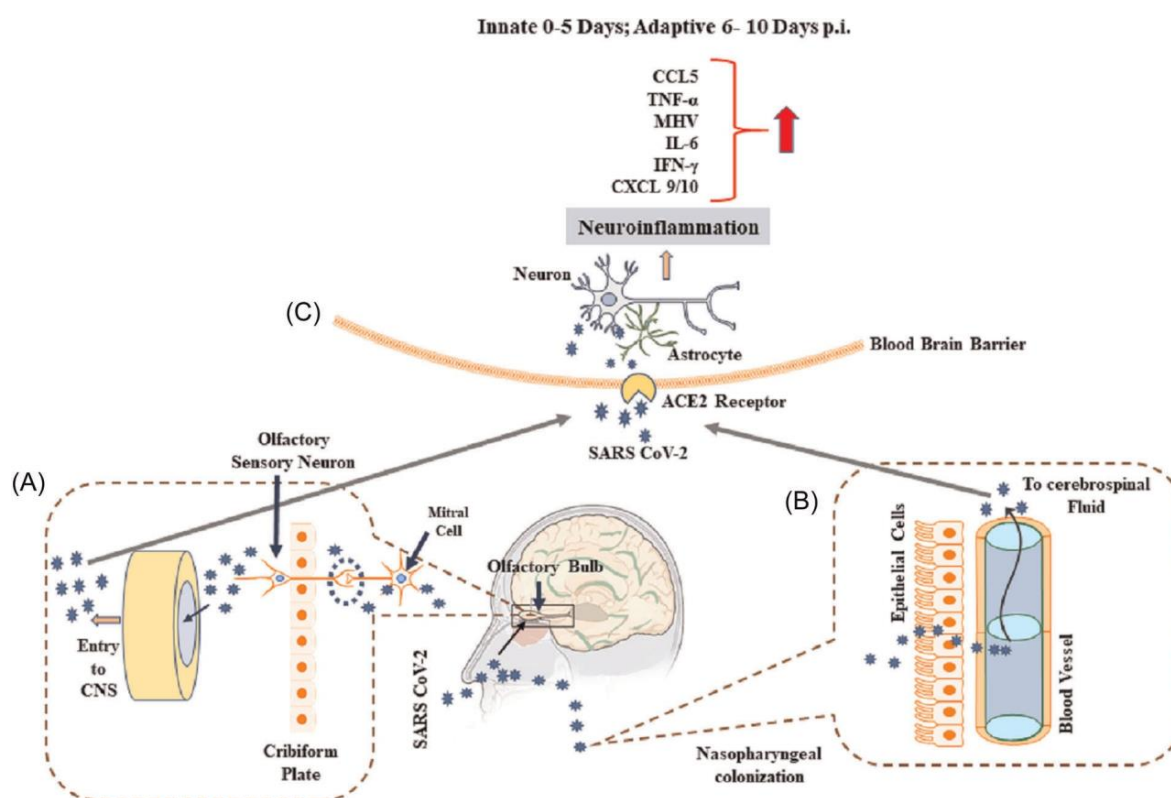


FIGURE 1 Possible entry routes of SARS-CoV-2 into brain. (A) Describes entry of SARS-CoV-2 from nasal epithelium to olfactory bulb entering CNS. (B) Explains entry of SARS-CoV-2 from the nasopharyngeal region to cerebrospinal fluid, thus gaining access to CNS. (C) Describes binding of SARS-CoV-2 to ACE-2 receptors on the endothelial cells of BBB thus invading CNS and stimulating the cytokine storm by binding to ACE-2 receptors on the glial cells and neurons. ACE-2, angiotensin-converting enzyme 2; BBB, blood-brain barrier; CNS, central nervous system; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

from brain cells for the recruitment of blood derived inflammatory cells. Viruses with varying neurovirulence infecting brain astroglia and microglia cultures (primary brain immune cell cultures) show variable capability to induce proinflammatory cytokines like interleukin 2 (IL-12), p40, tumor necrosis factor α (TNF- α), IL-6, IL-15, and IL-1 β in both astrocytes and microglia of mouse brain and spinal cords.³² Infection of the human astrocytic cell lines U-373MG with the OC43 strain of human coronavirus led to increased transcription of IL-6, TNF- α , and MCP-1, altered matrix metalloproteinases-2 and 9 activity, and upregulation of nitric oxide production in both U-373 cells and CHME-5 human microglial cell lines.³³ These results suggest a possible role of coronavirus-induced glial cell mediated inflammation leading to conditions such as immune mediated demyelination of neurons. The 229-E coronavirus strains could also infect fetal astrocytes, adult microglia, astrocytes and oligodendrocytes in cell culture.³⁴ A unique domain at the N-terminus of spike protein conferring its ability to bind to ACE2 receptors is absent in the 229-E strain. However, C-terminal parts

of the spike protein in conjunction with specific amino acids bind to CD13.³⁵

Experiments confirmed the ability of the coronavirus strain HCV-OC43 to persistently infect astrocytic cell lines U-373 MG and U-87, suggesting the possible role of human coronaviruses to persist in CNS by targeting astrocytes.^{36,37} Further intracerebral infection of rats with coronavirus results in initial downregulation of transcription of myelin protein proteolipid protein, leading to infected oligodendrocytes, followed by necrosis of the demyelinating lesions; whereas oligodendrocytes without detectable virus antigen levels were observed to undergo apoptosis. Although minimal remyelination was observed after clearance of virus antigen in oligodendrocytes, the destruction of oligodendrocytes continued due to apoptosis.³⁸ Coronavirus-induced encephalomyelitis in Lewis rats is reported to result in necrosis of infected oligodendrocytes followed by formation of demyelinated plaques. The central area of the plaques shows no virus antigen, while the peripheral regions of the plaques displayed virus antigen. Also, the virus-induced inflammatory demyelination displayed increased expression of interferon γ (IFN- γ), IL-2, TNF- α ,

iNOS and a novel cytokine, endothelial monocyte activating polypeptide II along with increase in the messenger RNA (mRNA) levels of regulatory calcium binding S₁₀₀ proteins MRP8, MRP14, and CP10.³⁹ Parra et al.⁴⁰ reported that inhibition of IFN- γ signaling reduces coronavirus replication; however, demyelination, axonal damage and infection of oligodendrocytes continued. Human coronavirus OC43 inoculation in mice resulted in infection of the CNS as a whole and the devastating effects of the virus were mostly attributed to the microglial reactivity and inflammatory reactions. Apparently microglial reactivity was due to direct neuronal injury.⁴¹

A murine coronavirus produced upregulation of Class I major histocompatibility complex antigens in oligodendrocytes and astrocytes. Induction of H-2 antigen causes glial infection and triggers glial-immune reactions.⁴² These data strongly suggest that the pattern of virus-induced demyelination involves immune glial cells, which causes tissue destruction during the course of the disease. Indeed, the status of oligodendrocyte precursor cells, oligodendrocyte differentiation, axonal contact and myelin regeneration need to be studied further in coronavirus infections. Similar pathophysiological circumstances involving glial cells (being primary target) and oligodendrocytes, hence demyelination, may be expected in SARS-CoV-2 infection.

5 | CORONAVIRUS AND CEREBROVASCULAR HEALTH

SARS-CoV-2 may reach the cerebral vasculature through the general circulation, possibly by breaching the BBB and affecting the parenchyma.¹⁷ A possible risk for stroke in respiratory virus infections was demonstrated by Warren-Gash et al.⁴³ One of the clinical studies reported four patients positive for stroke who were also positive for COVID-19. All of the four cases displayed cerebrovascular accidents at early stages of illness.⁴⁴ Interestingly, another study reported a 3% incidence of thrombotic complications in the COVID-19 patients with critical illness.⁴⁵ Oxley et al.⁴⁶ reported five cases of large vessel stroke in COVID-19 patients. Cases of large vessel strokes were also reported in the SARS-CoV-2 outbreak in Singapore.⁴⁷ Reports propose that coagulopathy and vascular endothelial dysfunctions are also complications of SARS-CoV-2 infection.⁴⁸ The etiopathological reasons for COVID-19 induced stroke may range from inflammation induced venous and arterial thromboembolism, and hypoxia to diffused intravascular coagulation.⁴⁵ A case study of a COVID-19 patient reported ischemic stroke attributed to infection-induced hypoxia and excessive secretion of inflammatory cytokines.⁴⁹ Another study found higher D-dimer or fibrin degradation product

levels predisposing to a hypercoagulable state, and lower platelet count-induced cerebrovascular hemorrhage in SARS-CoV-2 positive cases.^{50–52} Coagulopathy and anti-phospholipid antibodies were also observed in critically ill COVID-19 patients.⁵³ A correlation was observed between cytokines released, encephalopathy and stroke symptoms in a COVID-19 patient with cortical stroke.⁵⁴ Reports show the ability of SARS-CoV to induce poly-neuropathy, encephalitis and aortic ischemic stroke.⁵⁵ Data also shows influenza virus triggering a cytokine cascade and thereby exacerbating ischemic brain damage and intracerebral hemorrhage after treatment with tissue plasminogen activator.⁵⁶ Interestingly, SARS-CoV-2 infections also result in cytokine storms.⁵⁷ These similarities suggest that viral infection-induced cytokine release mediated cerebrovascular dysfunctions may be one possible mechanism leading to stroke.⁵⁸

6 | CORONAVIRUS AND NEURODEGENERATION

Upregulation of the SARS-CoV open reading frame, ORF-6, leads to enhanced apoptosis via caspase-3 mediated ER-stress and JNK-dependent pathways.⁵⁹ SARS-CoV ORF-9b is localized on host cell mitochondria and disrupts mitochondrial functions to suppress host innate immunity.⁶⁰ SARS-CoV infection is also reported to induce mRNA levels of several UPR proteins like GRP78, GRP94, and C/EBP homologous protein, along with the accumulation of viral spike proteins in the endoplasmic reticulum.⁶¹ Coronaviruses affect some of the host proteases like endosomal cathepsins, cell surface transmembrane protease or serine proteases, furin, and trypsin.⁶² Most of these proteases are known for their involvement in the pathogenesis of various neurodegenerative diseases. Cathepsin D plays an important role in degrading altered neuronal proteins like alpha-synuclein, amyloid precursor and huntingtin, whose abnormal degradation by altered protease could lead to accumulation of these proteins, which are prominent in neurodegenerative diseases like Parkinson's disease (PD) and Alzheimer's disease (AD).⁶³ Some reports also show possible interactions of SARS-CoV with the CNS, resulting in signs of PD.⁶⁴ Also intracerebral injection of influenza virus A shows its virulent effect on substantia nigra and hippocampus, causing formation of Lewy body like structures and suggesting a role for this viral infection in neurodegenerative diseases.⁶⁵ Furthermore, mice expressing Parkinson's disease linked to p.G2019s LRRK2 mutation exhibit reovirus-induced encephalitis, resulting in increased mortality; and brains from these mice also show increased accumulation of alpha synuclein.⁶⁶



The findings so far on SARS-CoV-2 infection show similarity with pathogenesis due to infection with SARS-CoV and H1N1 in multiple aspects, including the effects on mitochondrial function, proteases, and ER stress responses. These pathways are strongly correlated with pathogenesis of various neurodegenerative diseases.

7 | CORONAVIRUS-INDUCED AMYLOID BETA AGGREGATION AND MEMORY LOSS

Emerging evidence indicates that MERS-CoV and SARS-CoV can promote neurological complications.^{67,68} Neuronal death, especially in the medulla of mice infected with SARS-CoV, has been reported.⁶ Respiratory syncytial virus (RSV) and herpes simplex virus type 1 (HSV-1) trigger the accumulation of a distinctive protein corona in different biological fluids, which represents the initial phase of viral–host interactions. HSV-1 infects peripheral sensory neurons.⁶⁹ Several studies have reported that HSV-1 contributes to the progression of AD.⁷⁰ HSV-1 infection has also been found to promote the deposition of neurotoxic amyloid beta ($A\beta$) in brains of infected mice.⁷¹ HSV-1 DNA was found to be localized within $A\beta$ plaques in AD patients.⁷² Similarly RSV have been found to accelerate the deposition of $A\beta$ in mice.⁷³ Infection with RSV and HSV-1 demonstrated that viruses can physically act as nano-surfaces capable of catalyzing amyloid nucleation, leading to accelerated fibril formation. Increased levels of Apo-E, which is a well-known risk factor for AD, have been observed in the HSV-1 corona.⁷³ Accumulation of $A\beta$ plaques results in memory impairment and synaptic dysfunction.⁷⁴ Accumulation of $A\beta$ downregulates the expression of synapse associated proteins like synaptophysin, SNAP-25, PSD-95, and p-GluR1 at Ser 845 in the mouse hippocampus. These proteins are necessary for maintaining the synapse and intercommunication between the neurons.⁷⁴ $A\beta$ -induced synaptotoxicity may be critical in inducing memory dysfunction. Reduced synaptophysin, SNAP-25, PSD-95, and p-GluR1 expression in the hippocampus is associated with cognitive dysfunction and memory loss in AD patients.⁷⁵

8 | CORONAVIRUS ISOLATION-INDUCED ANXIETY AND DEPRESSION, AND RELATIONSHIP WITH SEROTONIN

Most viral infections begin in the peripheral tissues. Despite protective barriers and the immune systems, viruses can invade the CNS through the bloodstream or

by infecting the nerves connecting to peripheral tissues.⁷⁶ A recent study reported SARS-CoV-2 infection of the brain, causing disturbances in the mental health of the patients with COVID-19.⁷⁷ At the same time, an increase in symptoms like anxiety and depression were expected during the circumstances and restrictions of the global pandemic.

In terms of pathophysiology, a closely related coronavirus (SARS-CoV) is reported to be neurotoxic and affect mental health.^{78–80} A HCoV strain (HCoV-NL63) is also reported to be associated with a mood disorder.⁸¹ Thus, there is a possibility that SARS-Cov-2 could induce some of the neurotoxic states and symptoms of SARS-CoV infection.

In a recent retrospective study of 214 COVID-19 patients in Wuhan, China, 36%–45% reported CNS-related disorders like dizziness, headache, loss of smell, impaired consciousness, loss of taste, and muscle pain.¹³ In another study involving 144 COVID-19 patients in Wuhan, 34.72% and 28.47% of the patients reported to have symptoms of anxiety and depression, respectively.⁸² Furthermore, among the survivors of SARS infection, patients were reported to have persistent elevated stress, and over 64% of the survivors are reported to have a combination of stress, anxiety, and depression.⁸³ But it is still not known if the symptoms can be attributed to the viral infections.

Many studies suggest that downregulation of serotonin (5HT) plays a significant role in conditions like depression.^{84–86} Other studies show that viral infection can lead to production of cytokines that impair neuronal firing, causing depression-like symptoms.⁸⁷ Summarizing the clinical symptoms reported in SARS virus infection, there is thus the possibility that SARS virus infection affected mood by altering the serotonin system. Hence, targeting the serotonin system could be considered as a potential option in therapies being developed for treating depression and anxiety induced by the COVID-19 infection.

Moreover, the World Health Organization is concerned about the psychological impact of COVID-19 on health workers, and people are anxious about the risk of infection and adapting to protective measures such as social isolation.⁸² However, there is concrete evidence showing that social isolation and loneliness are negatively correlated with mental health.⁸⁸ In a study among 1210 cases from the general population in China, during the initial outbreak of COVID-19, 16.5% reported severe depression, 28.8% anxiety, and 8.1% severe stress.⁸⁹ The levels of anxiety and depression were also high among medical staff in Wuhan who treated the COVID-19 patients, in comparison to healthy people.⁹⁰ In another similar study in Wuhan,



China, with 1257 responding doctors, 50.4%, 44.6%, 34.0%, and 71.5% reported symptoms of depression, anxiety, insomnia, and distress, respectively.⁹¹

9 | PERSPECTIVE FROM THE NEUROLOGIST'S CLINIC

The impact of COVID-19 is affecting all ages of life.^{92–}

⁹⁷ Both neurotropic and neuro-invasive properties of SARS-CoV-2 infection are increasing. A broad spectrum of neurological manifestations including demyelinating, vascular and degeneration have been cited, making it imperative for clinicians to maintain a holistic approach in tackling the complications of COVID-19. Cytokine-mediated inflammation can cause both encephalopathy and stroke, along with altered protease-mediated neurodegeneration and neurotransmitter alteration, resulting in depression and anxiety. Neurologists should be aware of the multitude of manifestations of this viral infection, which can manifest itself even in the absence of prominent respiratory symptoms, which are the primary reported diagnostic criteria used by most healthcare providers.

10 | CONCLUSION

Extensive reports of the pathogenesis of SARS-CoV-2 infection present a complex picture of the etiological factors involved, the intricate causes of disease, and their consequences. It is noteworthy that although the major clinical manifestations of the disease involve the respiratory system, the key mediator of the pathogenesis is related to the immune system. Retrograde transmission of virus into the CNS is clear from the available literature. Hyper-induction of chemokines and cytokines and a compromised cellular immune response caused by direct infection or indirect injury of immune cells in the CNS may contribute to COVID-19-related neurotropism. A compromised immune response may further lead to aggravation of SARS-CoV-2-induced CNS disorders alongside respiratory distress. Advances made in our understanding of the pathology and pathogenesis of COVID-19 could potentially serve as a guide for neurologists in the diagnosis, prevention, and treatment of post-COVID-19 neurological effects. As the world is still combating the pandemic, the present review provides neurologists some directions on treating the post-pandemic effects.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Arehally M. Mahalakshmi, Bipul Ray, Sunanda Tuladhar, Abid Bhat, Shasthara Paneyala, and Duraisamy Patteswari performed literature research, gathered and analyzed information, and generated short preliminary write-ups. Meena Kishore Sakharkar, Hamdan Hamdan, and David M. Ojcius provided research insight, content examination, and supported wide ranging aspects of the manuscript development process. Saravana Babu Chidambaram, Srinivasa Rao Bolla, Musthafa Mohamed Essa, and M. Walid Qoronfleh completed the conceptual work, framework, final draft write-up, critical reading, and editing. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT


Data sharing is not applicable to this article as no new data were created or analyzed in this study. All information generated or analyzed during this study are included in this published article.

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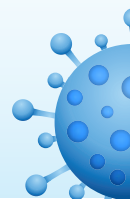
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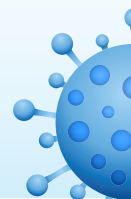
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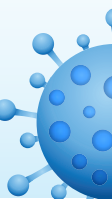


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Review Article

COVID-19 and gastrointestinal system: A brief review

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ABSTRACT

COVID-19 is a recent pandemic that is still a major health problem of modern times and already more than 17.5 lakhs people succumbed to this deadly disease. This disease is caused by novel coronavirus which is named SARS-COV-2 by the International Committee on Taxonomy of Viruses. This virus originated from Wuhan city in Hubei province of China in December 2019 and within a short period spread across the many countries in the globe. There are a lot of basic as well as clinical research is going on to study the mode of transmission and the mechanism of action of SARS-COV-2 infection and its therapeutics. SARS-COV-2 is not only known to infect lungs, but it also infects other organs in the human body including the gastrointestinal (GI) tract, the liver, and the pancreas via the angiotensin-converting enzyme (ACE) 2, an important component of the renin-angiotensin system. In this short review, we are mainly discussing the mode of SARS-COV-2 transmission, physiological counterbalancing roles of ACE2 and ACE and the tissue patterns of ACE2 expression, and the overall effect of COVID19 on human gastrointestinal System. Therefore, this review sheds light on the possible mechanism of SARS-COV-2 infection in the GI system and its pathological symptoms raising a potential possibility of GI tract acting as a secondary site for SARS-CoV-2 tropism and infection. Finally, future studies to understand the fecal-oral transmission of the virus and the correlation of viral load and severity of GI symptoms are proposed to gain knowledge of the GI symptoms in COVID-19 to aid in early diagnosis and prognosis.

The novel coronavirus (nCoV) identified in 2019 belongs to a strain of human coronaviruses (CoVs) which include 229E, NL63, OC43, HKU1, Middle East respiratory syndrome (MERS-CoV), severe acute respiratory syndrome (SARS-CoV) [1]. Coronaviruses belong to the family Coronaviridae and further subdivided into alpha, beta, gamma, and delta genera

coronaviruses. SARS-CoV, MERS-CoV, and SARS-CoV-2 belong to the genus beta-coronaviruses [1]. The International Committee on Taxonomy of Viruses named nCoV as SARS-CoV-2 because it shares more than 80% identity in nucleotide with the original SARS-CoV, and the disease caused by SARS-CoV-2 as COVID-19 [2]. Of the seven strains, SARS-CoV, MERS-CoV,

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and SARS-CoV-2 have a zoonotic origin and proven to be highly pathogenic: SARS in 2003 and MERS in 2012 and COVID-19 in 2019 [3]. The SARS outbreak of 2002 caused by the SARS-CoV lasted until 2004. SARS was first identified in Foshan in the Guangdong province of China in November 2002. The major phase of this outbreak lasted for about 8 months until July 2003 when WHO declared that the virus has been contained. Cases were continued to be reported until May 2004 [4]. 8422 people were infected with the virus and 916 people died worldwide [5]. A total of 29 countries were affected. China had the greatest number of cases and deaths with 5329 and 336, respectively [6]. The Middle Eastern respiratory syndrome (MERS) outbreak of 2012 caused by MERS-CoV was first originated in Saudi Arabia was mostly contained after it had caused 2521 cases and 866 deaths [7]. Most of the cases of MERS were confined to the Arabian Peninsula. The first case of COVID-19 was originated in the Hubei Province in the city of Wuhan in China in late 2019 [8]. Since then, the virus has spread at a rapid rate with more than 79.72 million infections and 1,749,340 fatalities globally as of December 25, 2020.

Mechanism of transmission

The genomics, epidemiology, and pathogenesis of SARS-CoV and SARS-Cov-2 are also similar [9]. In addition to the animal to human transmission, human to human transmission has been reported with SARS-CoV, MERS-CoV, and SARS-CoV-2. Akin to SARS-CoV, the transmission of SARS-CoV-2 is through droplet infection (respiratory secretions) and close person-to-person contact [10e12]. Transmission through asymptomatic cases appears to play a critical role in the transmission of SARS-CoV-2. The primary infection of coronaviruses involves the respiratory tract, and the infection causes the common cold, pneumonia, bronchiolitis, pharyngitis, sinusitis, and other symptoms such as diarrhea [13]. Coronaviruses (CoVs) are either pleomorphic or spherical and derive their name by the presence of characteristic club-shaped projections on the membrane envelope that contains a single-stranded RNA genome (size range between 26.2 and 31.7 kb, positive sense) that is packed in the nucleocapsid protein [14]. The RNA genome of CoV is the largest among all RNA viruses [15]. The genetic material of CoV is susceptible to frequent recombination processes resulting in new strains with altered virulence [16]. The spike (S) protein (trimeric), membrane (M) protein, envelop (E) protein, and the nucleocapsid (N) protein are the important structural proteins of SARS-CoV-2 [Fig. 1]. The surface S proteins play an important role in infecting the host cell [17,18].

It was established that the angiotensin-converting enzyme (ACE2) was the host receptor for the SARS-CoV-1 virus [19]. It was also found that the many viruses belonging to coronavirusidae also used ACE2 as a host receptor. The spike (S) proteins containing an S1 subunit and S2 subunit on the envelope of coronaviruses promote the entry of the virus into the host cells [20]. Similar to SARS-CoV, the receptor-binding domain (RBD) within the S1 protein in SARS-CoV-2 binds to the ACE2, albeit with much higher affinity and this correlates with greater infection rates and efficient spread of SARS-CoV-2 among humans [21]. Unlike SARS-CoV, the S protein of

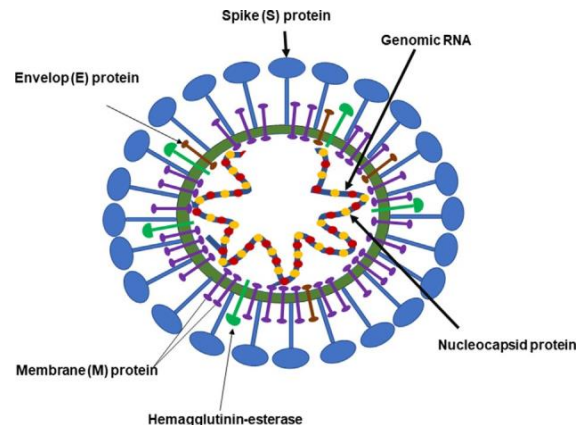


Fig. 1 Schematic representation of the SARS-CoV-2. The major structural proteins of SARS-CoV-2 consists of a spike (S), membrane (M), and envelop proteins that are embedded in the lipid bilayers and nucleic capsid (N) proteins covering single-stranded RNA. The spike proteins of the SARS-CoV-2 for which they derived the name 'corona' are the key structures that attach to host cell receptor proteins angiotensin-converting enzyme 2 (ACE2). The S proteins consist of S1 and S2 subunits that attach to the ACE2 and the cell membrane, respectively. The membrane envelops a large single-stranded positive-sense RNA.

SARS-CoV-2 has a site that is activated by host cell protease furin that is found in several tissues including the lung [22]. The entry of the virus causes internalization of ACE2 thus reducing the availability of enzyme for cleavage of Angiotensin II, the main physiological function of ACE2 [23]. Upon entry of the virus via ACE2, the viral RNA that is released intracellularly manipulates the cellular programs of the host for viral replication. Open reading frames of viral RNA are translated resulting in RNA polymerase complex that is responsible for replication and transcription of viral RNA. Viral nucleocapsids, after assembly and budding off from the lumen of ER-Golgi complex encase viral RNA to produce new virions and that undergo exocytosis [24].

Physiology of ACE and ACE2

The Renin-Angiotensin-Aldosterone System (RAAS) plays a major in the control of blood pressure and electrolytes in the body [25]. Renin secreted from kidney converts angiotensinogen that is produced and secreted by the liver to angiotensin I (Ang I). Angiotensin-converting enzyme (ACE) converts Ang I to angiotensin II (Ang II) [26]. The major effects of Angiotensin II, acting mainly via its cognate AT1 receptor (AT₁R), are vasoconstriction, reabsorption of sodium and excretion of potassium in the kidney, aldosterone synthesis, elevation of blood pressure and induction of pro-inflammatory pathways [27]. The octapeptide Ang II is cleaved by the peptidase activity of ACE2 to a heptapeptide called angiotensin (1e7) (Ang (1e7)) which has vasodilating, anti-inflammatory and anti-fibrotic effects acting mainly via

its cognate Mas Receptor (MasR) [28]. There is also another pathway, which ACE2 participates where it converts Ang II to Ang (1e9) and later, under the action of ACE, it forms Ang (1e7), but this pathway is considered to be of less significance physiologically [29]. ACE2 is considered as a homolog of ACE, but they have opposite actions in the body, ACE2/Ang (1e7)/MasR pathway is considered anti-inflammatory and anti-fibrotic whereas ACE/AngII/AT1R pathway is pro-inflammatory and pro-fibrotic [Fig. 2]. The eventual function of RAAS activation depends on the balanced activities of ACE/AngII/AT1R and ACE2/Ang (—7)/MasR pathways. This balance is influenced by a lot of factors like the blockade of the RAAS using certain pharmacological drugs like ACE inhibitors for certain diseases. Studies have shown that increased dietary intake of sodium, fat, and fructose which are major risk factors for cardiovascular conditions distort the ACE/ACE2 balance and shift the curve more towards the ACE/Ang II/AT1R-mediated pro-inflammatory and pro-fibrotic effects [30e33].

ACE2 expression

Since ACE2 is the target protein of SARS-CoV-2, clinical symptoms of COVID-19 may be related to distribution and abundance of ACE2, which is ubiquitous in its expression in the body. The tissue distribution of ACE2 in the human body may also suggest potential infection routes and targets of SARS-CoV-2. ACE2 is predominantly expressed in the respiratory tract lining on the alveolar epithelial cells (type II alveolar cells) [34]. In the lungs, ACE2 acts as the entry point of the SARS-CoV-1 and SARS-CoV-2 viruses [29,35,36]. This makes a strong case for the respiratory tract as a route of transmission of SARS-CoV-2 virus and the GI tract being another possible route of transmission because it is also present on the small intestinal epithelial cells in the

gastrointestinal tract (GI Tract) in the duodenum, jejunum, and ileum but not the colon [37,19,38]. In a study conducted by Hamming et al. it was found that ACE2 was present in endothelial cells from small and large arteries and veins in all the tissues studied in arterial smooth muscle cells [38]. ACE2 is also present in organs like the kidney, more so in the brush border of proximal tubular cells, and weakly in other areas like the epithelia in distal tubules and collecting ducts [38]. In the skin, ACE2 was present in the basal layer of the epidermis, and in the nasal and oral mucosa and nasopharynx, ACE2 was expressed in the basal layer of the epithelium [38]. GI manifestations are often associated with respiratory disorders in COVID-19 patients. Although the evidence for the involvement of the respiratory tract in the pathogenesis of COVID-19 is evident, the direct evidence for the involvement of GI in the pathogenesis is not clear. The GI manifestation could be due to the response of the immune system to viral infection. Recent studies using the rhesus monkey model demonstrated the relationship between GI dysfunction and lung infection induced by SARS-CoV-2. Intranasal inoculation with SARS-CoV-2 caused both lung infection and GI dysfunction that is associated with detectable viral RNA in the contents of swabs from nose, throat, and anus, and in the fecal samples. Intra-gastric inoculation with SARS-CoV-2 also caused both lung infection and GI dysfunction. These results indicate that both the GI tract and respiratory system play important roles in SARS-CoV-2 pathogenesis. The dysfunction of the GI tract with intranasal inoculation and dysfunction of the lung with intragastric inoculation could be due to the release of viruses from the infected tissue and/or via inflammatory cytokines. The bidirectional ‘gut-lung axis’ is also possible due to microbial metabolites and endotoxins resulting from the virus-induced changes in respiratory tract flora and the gut microbiome. Further studies are not needed to understand the variation in the GI symptoms, the relationship between

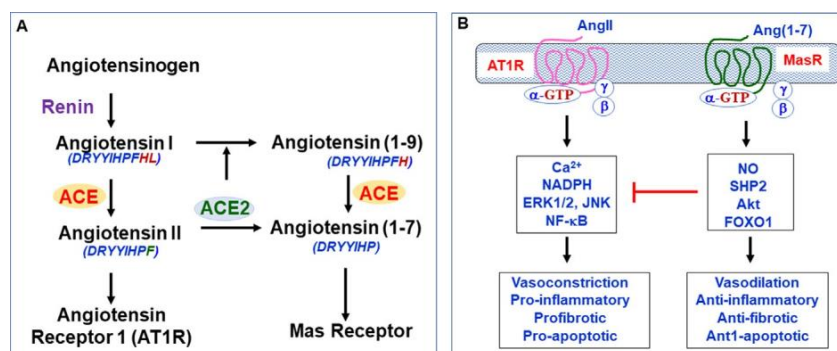


Fig. 2 Simplified scheme of the renin-angiotensin system, and ACE/AngII/AT1R and ACE2/Ang (1e7)/MasR pathways. A. Renin derived from kidney converts angiotensin to decapeptide angiotensin I (Ang I). Angiotensin-converting enzyme (ACE) converts Ang I to octapeptide angiotensin II (Ang II). ACE2 converts Ang II to a heptapeptide Ang (1e7). ACE2 also acts on Ang I to form Ang (1e9) which then yields Ang (1e7) upon further cleavage by ACE. B. The effects of Ang II are mediated via activation of its cognate G protein-coupled receptor AT1 (AT1R), whereas the effects of Ang (1e7) are mediated via activation of its cognate G protein-coupled Mas receptor (MasR). The ACE2/Ang1-7/MasR pathway acts as a counter-regulatory pathway to the ACE/Ang II/AT1R pathway. The effects of ACE/Ang II/AT1R pathway involves an increase in Ca^{2+} and activation of NAD(P)H oxidase, extracellular regulated kinase1/2 (ERK1/2), Jun kinase (JNK) and the transcription factor NF- κ B. The effects of the ACE2/Ang (1e7)/MasR pathway involves an increase in nitric oxide (NO) formation, and activation of Akt and the phosphatase SHP-2 and the transcription factor FOXO1.

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severity of symptoms and route of infection, use of antibiotics and antiviral drugs on the gut microbiome and the role of microbiomes in the manifestation of GI dysfunction, the effect of COVID-19 on underlying chronic GI dysfunctions such as inflammatory bowel disorder, liver disorders, etc., and to define the importance of fecal testing for initial diagnosis and during discharge [39]. In the oral mucosa, ACE2 was highly expressed on the tongue and this could explain why COVID-19 patients experience altered taste sensation and a theory was suggested that it may be due to the binding of the virus to sialic acid receptors [40]. A hypothesis as to how COVID-19 causes an altered sense of smell was that it could directly damage the olfactory pathway [41]. It was present in the endothelial and smooth muscle cells in the brain and, ACE2 was absent in the spleen, thymus, lymph node, and the cells of the immune system [38].

ACE2 in GI tract and GI symptoms of COVID19

Abundant expression of ACE2 in the epithelial cells of the GI tract is also reported and the expression levels are higher than lung [37,39]. The role of ACE2 in amino acid transport underscores the importance of ACE2 in the GI tract [42]. The C-terminal domain of ACE2 is a homolog of renal transmembrane glycoprotein which plays a role in the regulation of neutral amino acids. It is discovered that ACE2 shares about nearly 50% of its domains with collectrin [43]. Since both collectrin and ACE2 are 50% similar, it is suggested that they might have a similar function as well. Later, it is discovered that ACE2 does indeed play an important role in the transport of amino acids and this had a profound impact on the gut microbiota [44]. These studies have shown that ACE2 knockout animals had reduced levels of neutral amino acids in the serum and tryptophan is more significantly reduced compared to the other neutral amino acids [44]. This lack of tryptophan leads to decreased expression of antimicrobial peptides which altered gut microbiota. The gut microbiota is successfully restored following the administration of tryptophan [44]. An important study recently hypothesized that coronary artery disease (CAD) patients with decreased tryptophan levels were found to have a reduced life expectancy which could mean that ACE2 in the gut has a cardioprotective impact [45].

Expression of ACE2 on the luminal epithelial cells of the GI tract suggests the possibility of a secondary site for enteric SARS-CoV-2 infection [39]. Gastrointestinal symptoms such as nausea, vomiting, and diarrhea are common with infection of SARS-CoV and MERS-CoV [46]. Similarly, although, SARS-CoV-2 infection is manifested by respiratory symptoms suggesting droplet transmission, gastrointestinal manifestations such as vomiting, abdominal pain, and diarrhea are also reported [47]. The GI symptoms seem to precede the typical respiratory symptoms of COVID-19. SARS-CoV-2 RNA is identified in anal/rectal swabs and stool specimens of COVID-19 patients, suggesting also the fecal-oral route of transmission [48]. Immunohistochemical studies showed viral nucleocapsid protein in the cytoplasm of gastric, duodenal, and rectal epithelial cells [49]. Interaction of SARS-CoV-2 with ACE2 in the GI tract may lead to damage to the barrier function via disrupting barrier proteins ZO-1, occludin, and claudins, and increase in

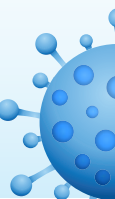
inflammatory cytokine production, which in turn may lead to dysbiosis and exacerbation of intestinal inflammation [50,51]. Besides, intestinal inflammation may augment dysbiosis and damage to the intestinal mucosal barrier function, and the intestinal lymphocytes, dendritic cells, and macrophages may perpetuate the cytokine storm. In animal models, leaky gut can be mitigated or exacerbated with either the gain or loss of ACE2 expression [51]. Co-morbid conditions such as diabetes, obesity, and hypertension may have adverse effects on gut microbiome [52], and infection with SARS-CoV-2 and decrease in ACE2 function may worsen the gut microbial dysbiosis [44]. Augmentation of diabetes-induced dysbiosis by ACE2 deficiency was reported [53].

ACE2 in the liver and liver symptoms of COVID19

In the liver, ACE2 was mainly expressed on the cholangiocytes rather than the hepatocytes [54]. The classical ACE/AngII/AT₁R pathway of RAAS contributes to the development of nonalcoholic fatty liver disease (NAFLD) [55,56]. The non-conventional ACE2/Ang (1e7)/MasR pathway of RAAS shows effects opposite to that of the classical axis. The loss of ACE2 seemed to worsen liver fibrosis in chronic liver injury models. Importantly, the consequences of loss of the ACE2 gene in the liver become apparent only after chronic injury [57]. In a study conducted by Cao et al. it was discovered that the deletion of ACE2 aggravates the development of hepatic steatosis, oxidative stress, and inflammation. It was reported that overexpression of ACE2 decreased the hepatic steatosis in db/db mice [57,58]. These studies suggest that ACE2 has a protective role against inflammation. These studies also raise the possibility that COVID-19 patients with co-morbid liver dysfunction, the decrease in ACE2 expression and function due to infection may lead to exacerbated liver dysfunction. Impairment in liver function has been reported in patients infected with both SARS-CoV and MERS-CoV [59]. Liver impairment was also noted in several COVID-19 patients. Biochemical markers were elevated in these patients which signified mild-moderate hepatic dysfunction [60,61]. Markers like liver function tests (AST, ALT, GGT, and ALP) were elevated along with hypoalbuminemia, prolonged prothrombin time, and increased CRP, LDH, and hyperferritinemia which may indicate acute inflammation [60]. Patients with severe COVID-19 seem to have higher rates of liver dysfunction [61]. The exact mechanism by which liver injury occurs in COVID-19 is not clear, but it could involve direct infection or secondary infection due to prior liver injury and/or drug-mediated hepatotoxicity. Future studies on direct infection of liver and secretion of the virus into the bile are necessary to reveal see its route of presence in the GI tract. Studies on the replication of the virus in the hepatocytes or cholangiocytes and liver organoids are also important.

ACE2 in the pancreas and pancreatic symptoms of COVID-19

A protective role for ACE2 was also reported in the pancreas. Wang et al. in a cell culture model of pancreatic damage



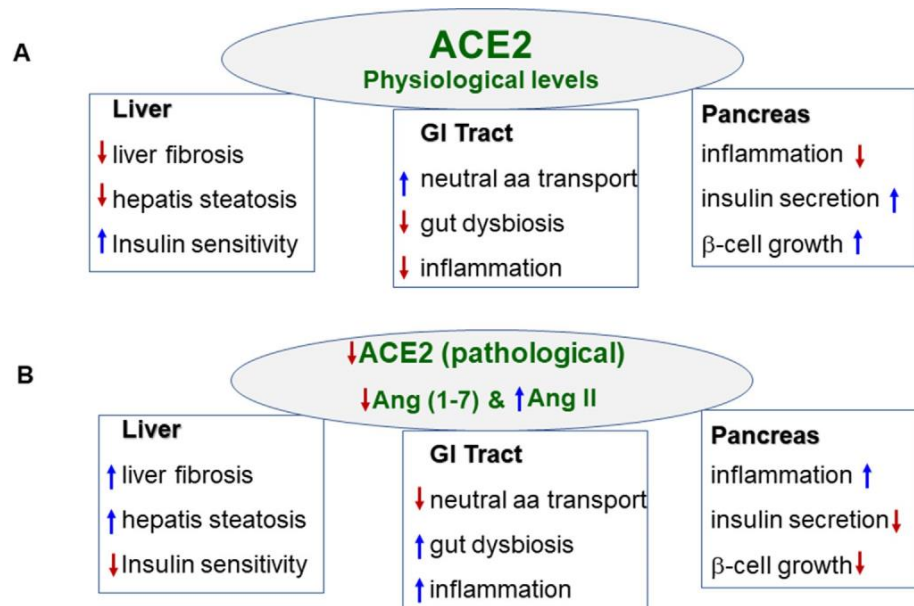


Fig. 3 Schematic diagram summarizing the role of ACE2/ANG-(1e7) in GI systems in normal physiology and presumably its involvement in SARS-CoV-2 infection. A. Physiologically, ACE2/Ang (1e7) mediates neutral amino acid transport and facilitates the release of antimicrobial peptides to decreases gut dysbiosis and prevent inflammation in the gastrointestinal (GI) tract, promotes insulin sensitivity and decrease fibrosis and steatosis in the liver, and promotes b cell growth and insulin secretion and decreases inflammation in the pancreas. B. Decrease in ACE2 function during SARS-Cov-2 infection may lead to an increase in Ang II and a decrease in Ang (1-) levels resulting in a decrease in neutral amino acid transport and an increase in gut dysbiosis and inflammation in the GI tract, decrease in insulin sensitivity and an increase in fibrosis and steatosis in the liver, and an increase in inflammation and decrease in b cell growth resulting in insulin secretion in the pancreas. A decrease in ACE2 expression and function of ACE2/Ang (1e7) may play a key role in the pathogenesis of SARS-CoV-2. A decrease in ACE2 expression and activity and loss of protective effects of ACE2/Ang (1e7) due to co-morbid conditions such as old-age, diabetes, liver diseases (e.g., NAFLD) and pancreatic inflammation may exacerbate the symptoms associated with SARS-CoV-2 infection. Arrows indicate an increase or a decrease.

showed that the non-conventional ACE2/Ang (1e7)/MasR pathway inhibits pancreatitis significantly by increasing the anti-inflammatory IL-10 cytokine and decreasing IL-6 and IL-8 which are pro-inflammatory [62]. Liu et al. showed that the expression of ACE2 was higher in the pancreas than lungs [63]. The expression of ACE2 was observed in both the exocrine glands and islets. These studies suggest that entry of SARS-CoV-2 into the pancreas may lead to b-cell dysfunction and glucose metabolism. Besides, in a subset of COVID-19 patients elevated levels of serum amylase and lipases were reported [64]. It was reported that patients who were positive for SARS-CoV-1 which caused SARS had elevated blood glucose levels [65,66] and this could be due to impairment of ACE2-mediated protective mechanism in energy metabolism. A study was done by Chhabra et al. where mice were infused with Ang II [67]. After 7 days of infusion with Ang II, it was seen that these mice had a significantly increased fasting blood glucose (FBG) compared to before the infusion of Ang II. And after 14 days, the effect of Ang II on FBG was more pronounced compared to after 7 days. The infusion of Ang II was shown to have significantly reduced the ACE2 expression in the islets and the pancreas. This shows that reduced ACE2 activity may adversely affect glycemic control. To test this relationship, on the 7th day of Ang II infusion, the mice were injected with

intrapancreatic ACE2 and there was a significant improvement in glycemic control which does show that ACE2 does play an important role in glycemic control by improving insulin secretion and reversing the insulin resistance due to Ang II [67]. Future studies in COVID-19 patients involving imaging will provide insights into pancreatic inflammation in COVID-19 patients.

Conclusion

With the current COVID-19 pandemic taking center stage in the form of an unprecedented health crisis, we are learning new things about the SARS-CoV-2 daily. Although the infection with SARS-CoV-2 mostly affects the respiratory tract, the manifestation of gastrointestinal symptoms is common in many COVID-19 patients. Expression of SARS-CoV-2 receptor ACE2, presence of viral proteins in the cytoplasm, and presence of SARS-CoV-2 in the anal swabs and feces provided insights into the receptor-mediated entry into the host cells and basis for its possible transmission route through the fecal contents. The presence of ACE2 proteins in the GI tract, liver, and pancreas, the protective function of ACE2 in these organs against inflammation, the manifestation of GI symptoms in

COVID-19 patients, and the possibility of possible fecal-oral transmission has important implications in understanding disease transmission, infection control, and disease management. Studies also suggest that patients with co-morbidity are likely to present severe symptoms. Imbalance in ACE/AngII/AT1R and ACE2/Ang (1e7)/MasR pathway to a predominant ACE/AngII/AT1R pathway due to the binding of SARS-CoV-2 to ACE2 resulting in attenuation of ACE2-mediated protective effects may augment morbidity and mortality in patients with co-morbid conditions associated with GI tract [Fig. 3]. Further studies on gut involvement and exit of SARS-CoV-2 in the feces and duration of virus viability in the environment are necessary to investigate the possibility of fecal-oral transmission of the virus, which is particularly relevant in regions of poor sanitation. Equally important are studies on the correlation between the amounts of fecal virus and the severity of GI symptoms. Establishing that GI symptoms precede respiratory symptoms in COVID-19 may improve early detection.

Conflicts of interest

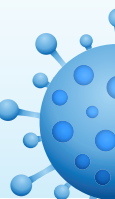
Authors do not have any conflicts of interest.

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Hearing Loss-a Camouflaged Manifestation of COVID 19 Infection

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Abstract The symptomatology of novel Severe Acute Respiratory Syndrome Corona virus type 2 infection runs the entire gamut of mild to moderate and serious illness among the affected individuals. As listed in recent literature, respiratory, cardiovascular, gastrointestinal, olfactory and gustatory systems are commonly involved. With the growing knowledge about the disease, varied manifestations have been identified and lately, otorhinolaryngology dysfunctions in COVID 19 have been described. Hearing loss in COVID era is one of the emerging areas of concern and calls for further research in the field for the better understanding and treatment of this entity. This study was designed to assess the audiological profile among 100 mild to moderately affected COVID-19 individuals, so as to make a contribution to the emerging literature on otologic manifestations in COVID 19. In our case series, high frequency hearing loss and referred OAE was noted among significant number of COVID 19 positive patients. This was even observed in patients without any otologic symptoms. Hence, early identification and intervention if required helps to give a better quality of life to the patient.

Keywords Hearing loss · COVID 19 · Pure tone audiometry · Oto acoustic emissions

Introduction

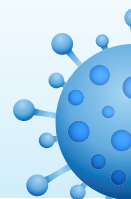
The outbreak of novel Severe Acute Respiratory Syndrome Corona virus type 2 (nSARS-CoV-2) infection in Wuhan, China in December 2019 has had a catastrophic impact on the world, resulting in over 2.2 million deaths globally [1, 2]. The world envisioned sufferings of unprecedented proportions as mankind endured losses in terms of health, finances and importantly, life. The symptomatology of COVID 19 runs the entire gamut of mild to moderate and serious illness among the affected individuals. As listed in recent literature, it commonly involves respiratory, cardiovascular, gastrointestinal, olfactory and gustatory systems [3–5]. With the growing knowledge about the disease, varied manifestations have been identified and lately, otologic dysfunctions in COVID 19 have been described [6].

Viral infections have been implicated in causing hearing loss, the reasons being direct or indirect inner ear damage [7–9]. Hence, the prospects of involvement of the auditory system following COVID 19 has been under scrutiny, the frequently reported otologic symptoms being tinnitus and hearing loss [6, 10]. Sensorineural hearing loss has been more commonly implicated in these patients although a few have exhibited conductive hearing loss as well [6, 10–14]. Various theories explaining the involvement of the ear following SARS CoV-2 infection have been postulated, which include immune mediated damage, haematogenous spread, ischaemia theory, inflammation of auditory pathway components, presence of angiotensin converting enzyme receptors (ACE2) receptors in neurons and glial cells [6–9].

Hearing loss in COVID era is one of the emerging areas of concern and calls for further research in the field for the better understanding of this entity. This study was designed to assess the audiological profile among 100 mild to

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moderately affected COVID-19 individuals, so as to make a contribution to the emerging literature on otologic manifestations in COVID 19.

Materials and Methods

Study Design

A cross sectional observational study of audiological assessment was done among the patients admitted with SARS COV 2 infection in a tertiary care hospital designated for COVID 19 patients. This study was carried out over a period of 3 months from September 15th 2020 to December 15th 2020.

Study Population

This study included 100 patients admitted in our hospital COVID 19 wards who met the inclusion criteria as follows:

- (1) Age 21–60 years
- (2) COVID 19 RTPCR Positive
- (3) No prior history of any ear symptoms (hard of hearing, ear discharge, tinnitus, ear pain, giddiness)

Exclusion criteria:

- (1) Age \geq 60 years
- (2) History of previous ear symptoms, tympanic membrane perforations or ear surgeries
- (3) Patients with history of Diabetes mellitus, Renal disease, patients on ototoxic drugs.
- (4) Patients not maintaining saturation and requiring O₂ support
- (5) Intensive care unit patients

Methodology

Patients admitted to our Hospital COVID wards with mild to moderate symptoms were enrolled in the study after obtaining prior consent from them. The particulars pertaining to each patient were compiled through a structured proforma (Table 1). After a thorough history taking as well as clinical examination which included otoscopic examination of the ears, these patients were then subjected to audiological evaluations by Pure Tone Audiometry and Oto Acoustic Emissions in a sound proof room. Pure tone thresholds were measured in both ears at 500, 1000, 2000, 4000 and 8000 Hz. Transient Evoked Oto Acoustic Emissions (TEOAE) were measured in all the patients and the results obtained were documented.

Results

A total of 100 patients were included in the study. Among these 58 were male patients and 42 were female patients. There were 23 patients in the age group of 20–30 years, 31 in 31–40 years and 28 patients in 41–50 years age and 18 patients between 50 and 60 years. Of the 100 patients, 27 patients had hypertension, 6 patients had history of ischemic heart disease. Only one patient had history of using propranolol. 22 patients in total received remdesivir injections for their symptoms.

31 among the 100 patients had ear symptoms, the most common being tinnitus (39%) and the least complained symptom as giddiness (10%) (Fig. 1).

Otoscopic examination showed normal external auditory canal and tympanic membrane in 95 patients, 4 patients had retracted tympanic membrane and 2 had dull TM.

Pure tone audiometry measured in both ears at 500, 1000, 2000, 4000 and 8000 Hz revealed high frequency hearing loss among these patients and the most common pattern of hearing loss was sensorineural hearing loss (SNHL). 6 patients had conductive hearing loss (CHL) (Fig. 2).

Sensorineural hearing loss was present in 53 patients in total. Among 53 patients, 11 patients had symptoms of hearing loss whereas rest 42 patients did not report hard of

hearing as a symptom. Sensorineural hearing loss was present in all the individuals who received remdesivir in their treatment. Age wise distribution of patients and sensorineural hearing loss is shown in Fig. 3a, b respectively.

Among the 100 patients, a total of 49 patients had a referred OAE in both the ears, with majority of the patients having high frequency hearing loss.

Among the 31 patients who complained of ear symptoms, 18 had a referred OAE, so did 31 among the 69 patients who never had any ear symptoms (Fig. 4).

Discussion

Growing evidence among the COVID 19 positive subjects mandates the hearing assessment in subjects tested positive for the virus. Early identification of hearing loss in these individuals would have a far-reaching impact when looking at the quality of life post COVID, as it is often a much neglected symptom. In our case series, hearing loss was noted in 11% of the patients who had symptom of hearing loss and 48% of the patients who did not have any symptom of hearing loss (42%—SNHL, 6%—CHL). Sriwijitalai et al., reported the first case of SNHL in a COVID 19 positive patient in april 2020 [11]. Following this few other reports also have been published relating SNHL in COVID 19 positive patients [10, 12–14].



Table 1 Proforma

S.No	Domains	Details
1	Name	
2	Age/Sex	
3	Contact number	
4	Tested positive on	
5	Date of admission	
6	Date of evaluation	
7	Ear complaints	
8	Pre-existing ear conditions	Ear pain/discharge, hard of hearing, tinnitus, aural fullness, giddiness
9	New onset of ear symptoms	Ear pain/discharge, hard of hearing, tinnitus, aural fullness, giddiness
10	Co-morbidities	Type 2 DM, HTN, Renal disease, Cardiovascular diseases
11	Drug history	Furosemide/ Amikacin/ Streptomycin/ Propranolol/ Indomethacin
12	Use of Remdesivir	Yes/No

Ear–Right Left

External auditory canal–

Tympanic membrane–

Pure tone audiometry: Average thresholds Type of hearing loss

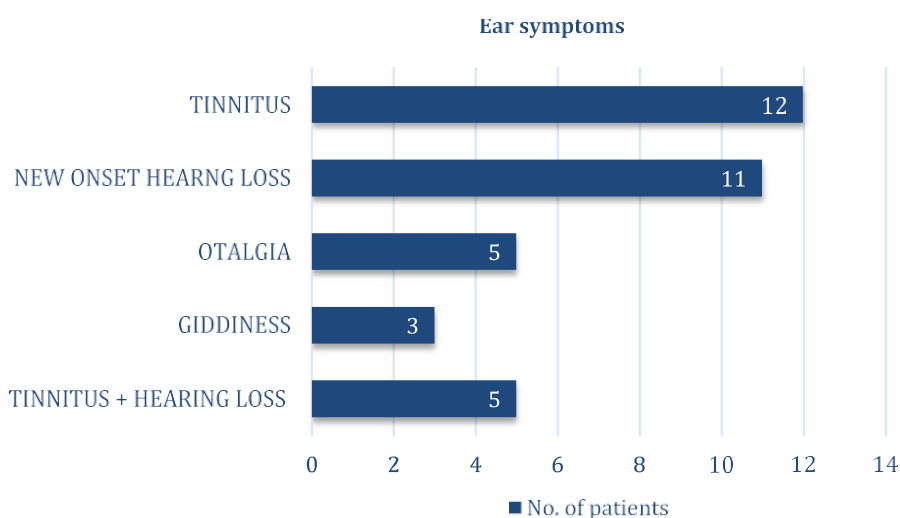
Right–

Left– OAE–

Pass/Referred

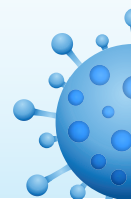
If referred–High frequency/ low frequency

Fig. 1 Most common ear symptoms



Hearing loss could be viral induced, immune complex mediated, vascular occlusion or cellular stress response [7, 8]. Literature shows various reports of viral mediated hearing loss most commonly implicated viruses being herpes virus and cytomegalovirus [6, 12, 15, 16]. SARS COV 2 virus is also thought to be responsible in causing sensorineural hearing loss through inflammatory response on cochlear hair cells. Presence of ACE2 receptors in brain, medulla oblongata, temporal lobe has facilitated the entry of SARS CoV2 affecting the brainstem and hearing centres

leading to inflammatory response through cytokine release. This could lead to neurologic and otologic manifestations in COVID 19 affected patients [17]. Samir et al., reported a case report of SSNHL in a patient who presented with complaints of sudden onset of left side hearing loss and gradually worsening tinnitus on day 3 of COVID 19 infection. Patient was managed with 3 doses of intra-tympanic methyl prednisolone and repeat audiogram after recovery showed significant improvement in hearing loss [13].



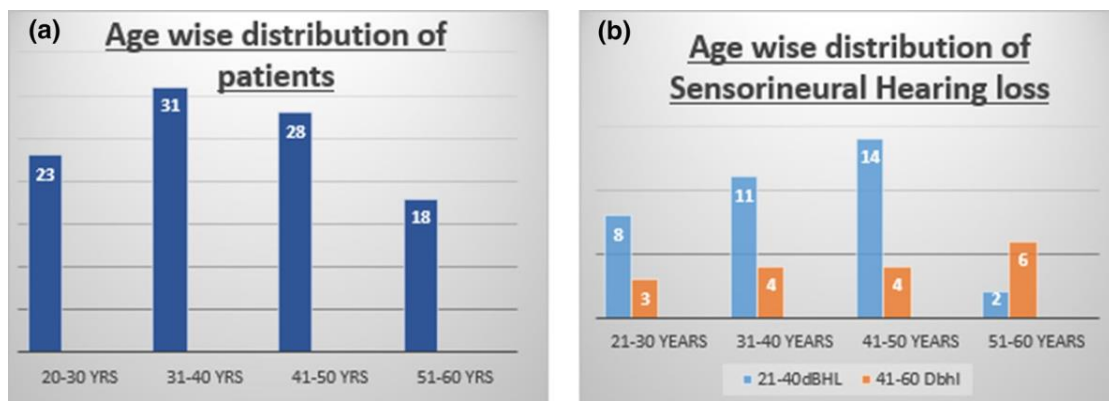


Fig. 2 Pure tone average thresholds

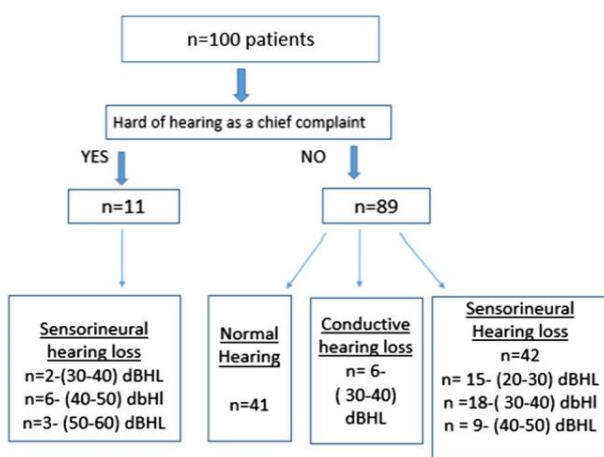


Fig. 3 Age wise distribution of patients and sensorineural hearing loss

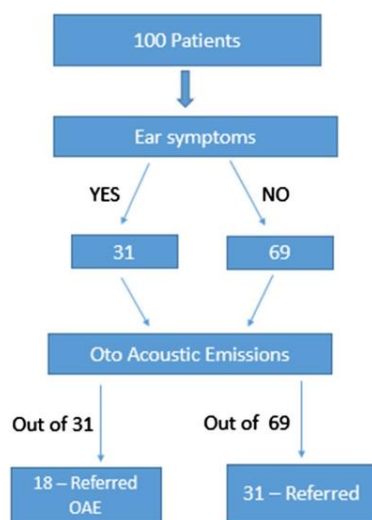


Fig. 4 Transient Evoked Oto Acoustic Emissions (TEOAE)

Chantal et al., reported a case of 60 year old male patient, a confirmed case of COVID 19 infection with severe symptoms under ICU care for 13 days complained of hearing loss and tinnitus. Audiological evaluation showed complete deafness on right side and profound sensorineural hearing loss on left side and MRI brain revealed pronounced contrast enhancement in right cochlea, decreased fluid signal in basal turn showing an inflammatory process in cochlea. Patient was managed by cochlear implantation in right ear and intratympanic triamcinolone in the left ear [14]. This study showed the importance of audiological evaluation and radio-imaging as and when required when COVID 19 positive patients present with severe hearing loss and emphasized the need for prompt management for better quality of life of the patient.

Recent systematic review of 5 case reports and 2 case series by Maharaj et al., on otological dysfunction in COVID 19 patients showed hearing loss as the most common presenting symptoms followed by tinnitus, vertigo and otalgia. They concluded that there is significant association of otological disorders, hearing loss in specific in COVID-19 patients [6]. Hearing loss can be part of the clinical spectrum of COVID-19 and may in some cases signal the onset of the disease.

A comparative study of audiological evaluation between 20 asymptomatic COVID-19 positive patients and 20 normal hearing patients by Mustafa et al., revealed significant high frequency pure tone thresholds hearing loss and referred TEOAE in asymptomatic COVID 19 patients indicating inimical effects of COVID 19 infection on cochlear hair cell functions [12]. In our study, high frequency pure tone threshold sensorineural hearing loss and referred TEOAE was noted even in many patients without symptoms of hearing loss. 6 of our patients had conductive hearing loss probably due to the presence of middle ear effusion caused by the infection in nasopharynx.



This shows the possibility that SARS CoV2 infection has detrimental effects on cochlear function. Hearing assessment through audiometry in patients with COVID19 infection will aid us in early identification of any otological adverse effects. As per this case series, it can be illustrated that mere absence of symptoms does not rule out auditory involvement and hence early intervention will help in improving the quality of life of the patient.

Our case series includes 100 patients which is a high number among the publications till date. High frequency hearing loss and referred OAE was noted among significant number of COVID 19 positive patients. All the patients received intravenous steroids as per the institution COVID 19 treatment protocol. So far, new onset hearing loss has been documented in COVID 19 positive individuals. But whether this hearing loss is transient or permanent is yet to be established. We present this case series as an initial work up. These patients will be followed up at regular intervals of 3 and 6 months for repeat audiometric evaluation. A detailed remark can be made after a follow up period of 6–9 months.

Conclusion

Otologic disorders among COVID19 affected individuals is becoming increasingly evident day by day. Assessment of hearing loss is of utmost importance to safeguard the cochlear function and prevent the progressive deterioration of cochlear hair cells [13, 14]. High frequency hearing loss and referred OAE was noted among significant number of COVID 19 positive patients in our case series. Early identification and intervention will help to give a better quality of life to the patient. This case series is an initial work up on COVID 19 positive individuals. A detailed review of whether this hearing loss is transient or permanent in nature can be specified only after regular follow up of these individuals.

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Data Availability Data transparency has been maintained.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval Appropriate ethical clearance has been obtained from the institute.

Human or Animal Rights It was an observational study done on the human participants after obtaining the informed consent from all the individuals.

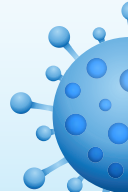
Consent for Publication Appropriate consent for publication taken.

Informed Consent Informed consent was obtained from all individual participants included in this study.

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Perspective

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Impact of COVID-19 pandemic on the dimensions of health and well-being: Time to widen our gaze

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Abstract:

Novel coronavirus disease termed as nCOVID-19 by the World Health Organization has posed serious threat to the health and well-being of humankind. The pandemic has caused unprecedented disruption of life and impacted almost all the sections of the society. Health-related emergencies and urgencies due to COVID-19 have drawn major attention of all the stakeholders involved in ensuring the well-being of the society. On the other hand, the pandemic has impacted the mental, emotional, social, educational, nutritional, and vocational dimensions of health. Nationwide lockdown, a measure taken toward achieving social distancing, thereby flattening the curve has resulted in a rise of mental health issues, emotional disturbances, migrant exodus, poverty, deficient food supply, hunger, academic stagnation, learning crisis, unemployment, and job insecurities among people. All these problems have the potential to impact the health and well-being of the society in the long run and hamper the attainment of sustainable development goals.

Keywords:

Dimensions of health, impact, nCOVID-19, sustainable development goals

COVID-19 is a dreaded emergency, bothering the humanity, which initiated its journey from a small province of China in the last week of December 2019. The disease has spread like a wildfire involving more than 210 countries and territories in the world.^[1] Apart from the previous pandemics of the century such as H1N1 and Middle East respiratory syndrome, the one due to COVID-19 has caused an unprecedented impact on medical, political, administrative, financial, education, industries, and business sectors.

India reported the first confirmed case of COVID-19 on January 30, 2020, in the state of Kerala after a gap of almost a month of the emergence of the infection in its neighboring country.^[2] Even though the spread of infection was sluggish at the initial days, it took a major surge after some socio-religious

gatherings in the country, which, in turn, resulted in local spread among close contacts and secondary contacts, taking a shape of public health emergency.

India being the second most populous country in the world with tremendous demographic, sociocultural diversities took major decisions in a preemptive manner to curb the spread of the infection. Public health education on the prevention of the spread of disease, screening and strict quarantine on deployment for international passengers, establishing fever clinics, strengthening hospital infrastructure to manage COVID patients, establishing nationwide public as well as private labs to conduct tests, active surveillance for symptomatic cases, contact tracing, elaborating cluster containment plans, involving private medical establishments in clinical care, risk communication through social media and websites, and bringing amendments in the Epidemic Disease Act-1987 are the few

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S97

notable ones.^[3] In the absence of vaccine and specific medicines and higher contagiousness of disease, social distancing is the only effective strategy to prevent the spread of infection.^[4] In order to achieve this, a three-phase nationwide lockdown was implemented in the country with varying degree of success and distress expressed in some regions.

Undoubtedly, the current pandemic has posed serious risk on the health and well-being of the population across the globe. An exponential increase in the number of cases, varying level of severity of disease, unpredictable case fatality rates, unpredictable spread in spite of the containment measures, etc.,^[5] exhaustion of hospital beds and medicines, shortage of health-care staff, insufficient number of intensive care units and ventilators, and nonavailability of personal protective equipment for frontline health-care workers are the matters of serious concern.^[6] Apart from the direct impact on the physical dimension of health, other domains such as mental (psychological), emotional, social, educational, nutritional, and vocational dimensions are equally affected by the pandemic [Figure 1]. In this article, we would be discussing the impact of the current pandemic on nonphysical dimensions of health which can have long-lasting effects on the well-being and hinder the attainment of sustainable development goals set by the United Nations.^[7]

Nationwide lockdown is the biggest psychological experiment. Fear of infection, lack of knowledge related to disease and its transmission, information overload, spread of misinformation through news rooms/social media platforms, fear of loss of job, closure of schools/colleges, fear of salary deductions, loss of wages, emotional isolations, stigma, and familial conflicts pose risk for the development of an array of psychosocial problems among people. Mental health problems such as depression, anxiety, stress, substance abuse, domestic

violence, child abuse, insomnia, irritability, anger, and frustration are increasing in their magnitude and are expected to expand furthermore in the days to come.^[8] There are reports suggestive of higher risk of relapse and deterioration among people who were already diagnosed to have these conditions in the pre-pandemic period.^[9]

The impact of the COVID-19 pandemic on the emotional dimension of health cannot be fully separated from that of psychological dimensions as they go hand in hand. Vicarious traumatization caused by the pandemic on the general public and health-care professionals has resulted in emotional distress, suicidal ideation, and suicidal tendencies.^[10] Stigmatization associated with quarantine and isolation is related with emotional disturbances, fear of falling sick, staying away from the close ones, helplessness, and a sense of being responsible for spreading infection to family members, which will further add to the emotional deterioration.^[11,12]

The COVID-19 pandemic has emerged as a major contributor to the already-existing social pathologies. Economic crisis associated with the pandemic is pushing the families to poverty, hunger, unemployment, migration, and xenophobia. People who do not have shelters to lead their life (homeless), refugees, displaced populations, and destitute stand to suffer disproportionately both from the pandemic and its socioeconomic consequences.^[13] Children who are largely spared by the direct health-related effects of COVID-19 till date are expected to be the biggest victims. The economic emergencies arising from the pandemic along with the school closure may force children to dropout from schools and indulge in child labor. Street children and orphans who have no homes and parental care are at risk of exploitation and other negative coping measures.^[14] Older persons are at the risk of double trouble. The discourse around COVID-19, in which it is perceived as a disease of older people, exacerbates

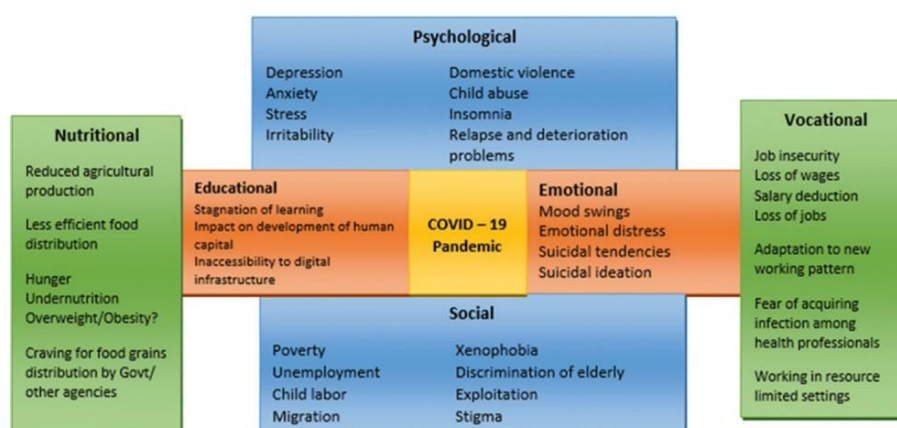
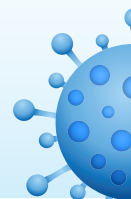


Figure 1: Impact of COVID-19 on nonphysical dimensions of health



negative stereotypes about them who may be viewed as weak, unimportant, and a burden on the society. This may lead to discrimination of older persons which has a direct impact on the seeking of health care and well-being. Other vulnerable sections of the society such as unemployed youth, people with disabilities, and indigenous people are also at the potential risk of being victims of the social consequences of this pandemic.^[13]

Learning crisis among children and youth is another important outcome of the current pandemic. The unprecedented closure of educational institutions in more than 180 countries and territories across the world has resulted in stagnation of academics. The potential losses that may accrue in learning children and youth of today, and for the development of their human capital, are hard to fathom. In order to minimize these losses, few academic institutions have started distance education through online learning platforms. Availability of android phones/supportive devices, accessibility to the Internet, and residence in remote settlements/inaccessible areas with limited web infrastructure are the major barriers for the online education in low- and middle-income countries.^[14]

Food security has emerged as one of the major issues in the current pandemic, which deserves due attention. Impact (reduced) agricultural production, exhaustion of stock, delays in transportation, and less efficient distribution of food grains to the beneficiaries are the root causes behind food insecurity. People who reside in the urban slums, informal settlements, and difficult-to-reach areas are at higher risk of suffering with hunger. These are the ones who rush to get the food packets and rations offered by the governments, philanthropists, and civil societies without caring much for social distancing and end up becoming either the victims or persons responsible to transmit the disease in the community.^[15] Governments have taken several steps to ensure food security through public distribution systems, but there are still large numbers of people who crave for food and sleep with hunger. If we do not give due attention to this dimension, we may face undernutrition and related complications in the days to come. There appears to be another extreme of this problem, where people have ample of food to eat, but due to lockdown and social distancing, they may not practice physical activities/exercises and end up with overweight and obesity.

Vocational well-being is another important dimension of health. The lockdown has resulted in serious job insecurities among people working in unorganized sectors. Loss of daily wages, deduction in salaries, changed working patterns such as work from home and disrupted division of labor, etc., have posed a tremendous impact on people.^[6]

Health-care professionals including paramedics are facing major vocational consequences due to the current pandemic. At one end, they are at extremely high risk of acquiring COVID infection due to their close proximity with active/suspected cases and at the other end, they are at a tremendous stress of working in resource-limited health-care settings with insufficient personal protective gears.^[16] Grassroot level health-care workers involved in contact tracing are receiving backlash from people in communities and having hard time in convincing people for testing and quarantine.

Conclusion

The COVID-19 pandemic has stretched its tentacles toward all the dimensions of health and well-being. Thus, we need to adapt a comprehensive, multidimensional, and multipronged strategy to combat the menace and exigencies created by the present pandemic. Along with quality medical care, we also should give emphasis on reducing its impact on mental, social, emotional, nutritional, educational, and vocational dimensions of health to achieve holistic well-being and attain sustainable development goals.

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Conflicts of interest

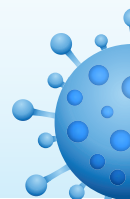
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COVID-19 pandemic and the reduction in ST-elevation myocardial infarction admissions

Since its initial description in December 2019, the COVID-19 infection caused by severe acute respiratory syndrome coronavirus 2 has rapidly spread across the globe and according to WHO this pandemic has caused 311 847 fatalities as on 18 May 2020.¹ With lockdown imposed in most countries of the world causing unfathomable social and economic disruption, there is palpable anxiety in the society and uncertainty in the scientific community and healthcare facilities.

The clinical presentation of COVID-19 is quite variable and still not fully elucidated. Observational studies from China revealed that 81% of the patients had mild symptoms, 14% experienced severe symptoms and 5% were critical. It has also been observed that COVID-19 infection is more likely to have poor prognosis and increased mortality in patients with advancing age, co-morbidities like obesity, chronic obstructive pulmonary disease, diabetes mellitus, hypertension, coronary artery and cerebrovascular diseases.^{2,3}

Recent reports suggest that presentation of COVID-19 infection mimicking ST-elevation myocardial infarction (STEMI) with an elevation of cardiac biomarkers, electrocardiographic and echocardiographic abnormalities is highly prevalent, and is associated with more severe disease and worse prognosis.⁴ This overlapping atypical presentation of COVID-19 with STEMI has compounded the management of the infected patients and has overstretched the healthcare resources, and in some instances fatally exposed the medical personnel such as cardiologists to this contagion.

Paradoxically in cardiac centres across the world, it is observed that there has been a significant reduction in presentations of STEMI. In Spain the interventional cardiology working group of the Spanish Society of Cardiology conducted a retrospective survey at 71 cardiac service centres across the country during this ongoing COVID-19 pandemic and found out that there was a significant reduction of 40% in the admissions for STEMI. The survey also revealed reductions in the number of diagnostic procedures (57%), coronary therapy (48%), structural therapy (81%) and COVID-19 infection was diagnosed in 17 interventional

cardiologists (5%).⁵ In the Lombardy region, which is the epicentre of the COVID-19 outbreak in Italy, STEMI cases are down by an estimated 70%.⁶ The Minneapolis Heart Institute Foundation real-time data analysis from nine large US STEMI centres during the COVID-19 pandemic shows a 38% reduction in US cardiac catheterisation laboratory STEMI activations. This finding is consistent with the reduction reported in Spain.⁷ The reduced STEMI hospital admissions during the current COVID-19 outbreak are also being palpably felt in the Indian subcontinent.

This sudden reduction in STEMI presentations during the pandemic has intrigued cardiologists across the world. Many plausible theories are being flouted for this phenomenon. One possible explanation is that patients are too anxious to visit the hospital for fear of contracting the COVID-19 infection. Alternatively, it is also being speculated that patients with less symptoms or stable coronary artery disease (CAD) are being overlooked at the already overwhelmed hospitals that are now preferentially triaging the COVID-19 patients. These stable patients will possibly end up later in aggravated underlying CAD or delayed complications of STEMI. Other reasons proposed for a sudden reduction in STEMI admission are less exposure of the individuals to stresses like pollution, which is now substantially reduced due to lockdown imposed, no annoyance of daily commute in traffic to the workplace, less physical strain, more family time and relaxation. Also probably there is less smoking, alcohol consumption and better medication adherence leading to adequate control of hypertension and diabetes mellitus.⁸ A retrospective analysis of acute coronary syndrome (ACS) admissions in 15 Italian hospitals during the early days of COVID-19 pandemic, revealed a decrease in ACS admissions but also an increase in death rate unrelated to COVID-19 infection. This has led to doubts that few patients with ACS died without seeking medical attention.⁹

However, as STEMI is a medical emergency that forces the majority of patients to seek immediate medical help, this unusual trend is worth noticing and needs to be explored further for possible causes.

There is growing concern among cardiologists that once the COVID-19 pandemic abates there could be a sudden spurt of cardiovascular cases due to late presentation of the earlier hidden or stable patients to the hospital, and this might overwhelm the healthcare institutions leading to burnout of the medical

staff.¹⁰ There are also apprehensions that as a consequence of this crisis, in the immediate future there could be a surge of patients with delayed mechanical complications of STEMI, reinfarctions, heart failures and arrhythmias.

The reasons for the sudden decrease in STEMI admissions need to be vigorously pursued and analysed. If this trend is genuinely due to a reduction in the daily stresses as mentioned above, it is worth the attention of policymakers, healthcare providers and cardiologists to implement preventive measures in decreasing STEMI cases and related morbidity and mortality.

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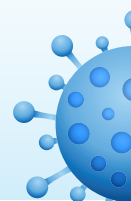
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Commentary

COPD Management during the COVID-19 pandemic

INTRODUCTION

The COVID-19 pandemic caused by the SARS-CoV-2 virus started in December 2019 in the city of Wuhan, from where it spreads to over 188 countries in the world. An estimated 22.5 million people are reported to be infected so far with 0.79 million deaths globally. The COVID-19 disease largely affects the respiratory tract causing pneumonia in around 20%–25% cases, some of which further progress to develop severe acute respiratory syndrome. The mortality rates vary from 2% to 15% and are higher among the elderly and those with associated comorbid conditions such as hypertension, ischemic heart disease, diabetes, and chronic obstructive pulmonary disease (COPD).^[1,2]

In the middle of this ongoing COVID-19 pandemic, there are an estimated 300 million cases of COPD in the community worldwide who are more vulnerable to not only catch the infection but also develop the more severe form of the COVID-19 disease and have an increased likelihood of dying from it.^[3] There are an estimated 55 million cases of COPD in India, which is already the second leading cause of death and disability-adjusted life years. Physicians in India need to be well prepared to not only manage the COVID-19 pandemic but also safeguard the vulnerable population of COPD.^[4]

In this manuscript, we discuss 10 important clinical issues related to COPD and COVID-19, the evidence that is currently available so far for each of these and then offers our specific recommendations. We believe that this discussion will offer practicing physicians' adequate knowledge to manage their patients of COPD better in the ongoing COVID-19 pandemic.

ARE PATIENTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AT A HIGHER RISK OF CATCHING THE COVID-19 INFECTION? IF THEY ARE, DO THEY DEVELOP A MORE SEVERE FORM OF COVID-19 DISEASE?

Description of the available evidence

The SARS-CoV-2 virus that causes the COVID-19 disease uses the angiotensin-converting enzyme receptor-2 to enter inside the cells to cause the infection.^[5] ACE-2 receptors are expressed on the apical surfaces of the polarized lung epithelial cells of both the upper and lower airways. Their numbers are significantly increased in patients with COPD compared to those who do not have COPD,^[6] and this has been suggested that this accounts for not only having a greater risk of catching the COVID-19

infection but also for developing the more severe form of the disease.

A single-center, case-series study^[7] reported that COPD patients were more vulnerable to develop the more severe form of COVID-19 disease than those who do not have COPD. A large case-series of COVID-19 patients from China reported a higher prevalence of COPD among patients with severe COVID-19 presentation with worse outcomes, compared to patients who did not have COPD.^[8] A couple of meta-analyses have shown that patients with preexisting COPD have greatly aggravated symptoms and a 4–5.9-fold greater risk of developing severe form of COVID-19 compared to patients without COPD.^[9,10]

The clinical symptomatology of COVID-19 and acute exacerbations of COPD (AECOPD) are difficult to differentiate and may potentially result in delayed or inappropriate medical intervention. Hence, there are chances of increased risk and worse prognosis of COVID-19 in patients with COPD.

Summary and recommendations

Patients with COPD are at a high risk of catching the COVID-19 infection, developing a more severe form of COVID-19 disease, and a greater risk of dying from it. COPD patients should therefore be encouraged to adopt more restrictive measures to minimize potential exposures to COVID-19 and every effort must be made to reduce their contacts with suspected or confirmed cases of COVID-19. Staying at home, proper hand hygiene, and wearing a mask are crucial to reduce the risk of catching the COVID-19 disease. It is important to ensure that COPD is managed well with appropriate pharmacotherapy, vaccination (influenza and pneumococcal), and rehabilitation, and all measures must be undertaken to prevent the development of any acute exacerbation. COPD patients should not be admitted for acute exacerbations in COVID hospitals.

IN THIS COVID-19 PANDEMIC, HOW CAN YOU DIAGNOSE NEW CASES OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN THE ABSENCE OF SPIROMETRY?

Description of the available evidence

Spirometry is the gold standard diagnostic test for COPD and must be undertaken in all patients to confirm the diagnosis. However, because of the effort required to perform the test, it is an aerosol-generating procedure and therefore comes with a substantially increased risk of transmitting the infection to and from other patients



and the clinic/hospital staff. The GINA 2020 guidelines for asthma have recommended avoidance of spirometry in patients with confirmed/suspected COVID-19^[11] and also postponement of spirometry within health-care facilities, unless there is an urgent need.

Summary and recommendation

Spirometry is an aerosol-generating procedure and should be avoided in all patients with either confirmed or suspected COVID-19 and more so in regions where community transmission of COVID-19 has already taken place. Although GOLD has not yet issued any advisory on restrictions for the use of spirometry in patients with COPD for either diagnosis or management, it seems prudent to avoid this test until the pandemic is over.

Taking a good history and conducting a short and quick clinical examination will be necessary to arrive at a diagnosis of COPD. While taking a history from the COPD patient, both the patient and the physician should wear a surgical or a reliable cloth mask. The patient should be encouraged not to speak loudly and certainly not shout. The physician should sanitize his/her hands with 70% alcohol disinfectant before and after every patient and must wear gloves while examining the patient, which should be discarded immediately after the examination is over. Patients should preferably be seated on a steel round chair that can be easily disinfected with 1% sodium hypochlorite. The outpatient clinic should be well ventilated. Wherever possible, air conditioning should be avoided, as it reduces the air exchange ratio. A good history can help in differentiating COPD from other respiratory or cardiovascular causes.

HOW SHOULD YOU MANAGE A PATIENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH AN ACUTE EXACERBATION IN THIS CURRENT PANDEMIC OF COVID-19?

Description of the available evidence

AECOPD are crucial events that occur in the natural course of COPD and respiratory viral infections are an important cause of COPD exacerbations.^[12] In general, viral infections may facilitate subsequent bacterial infection or increase the number of bacteria already present in the lower airways.^[13] It is likely that the SARS-CoV-2 virus causes AECOPD.

Breathlessness in patients with COPD observed during an acute exacerbation, apart from microbial infections, could also be because of pulmonary thrombosis, which seems to be common in patients of COVID-19 with severe disease. One observational study showed a cumulative incidence of venous and arterial thrombotic complications of 31% during intensive care unit (ICU) admission of patients with COVID-19 pneumonia, with pulmonary embolism being the most common thrombotic complication.^[14]

COPD exacerbations are often associated with an increased risk of myocardial infarction, stroke, all-cause mortality, and cardiovascular mortality, especially among those with an associated pneumonia.^[15]

Oral corticosteroids impair induction of antiviral Type-I interferon responses to a range of respiratory viruses, effects that are likely to also occur in the context of COVID-19.^[16]

Recommendations

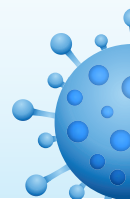
When a COPD patient develops a new/increased productive cough or breathlessness, it should be evaluated and treated as an acute COPD exacerbation. Presence of pneumonia, pneumothorax, pleural effusion, pulmonary embolism, pulmonary edema, and cardiac arrhythmias should all be ruled out using appropriate investigations. A chest X-ray may prove to be a very valuable tool in this diagnosis. Sometimes, a high-resolution computed tomography (HRCT) gives a lot more information than chest X-ray, and therefore where ever available and necessary, HRCT should be done. Manage the patients as per the hospital protocol and/or GOLD 2020 guidelines.

Start the treatment with short-acting inhaled beta₂-agonists with or without short-acting anticholinergics. Do not start blanket antibiotic treatment for all patients. If the patient has any signs of super-added infections, pyrexia, X-ray infiltrates, and/or increase in inflammatory markers, antibiotics can be initiated considering the risk versus benefit, although systemic steroids should be used with caution but should certainly not be avoided in the context of an acute COPD exacerbation.

Although antithrombotic drugs are routinely used in the management of severe COVID-19 infection, the evidence supporting its use is weak. In a multicenter, observational study in Italy, treatment with antiplatelets or anticoagulants did not reduce the risk of ARDS or death during hospitalization (clinical impacts of preadmission antithrombotic therapy in hospitalized patients with COVID-19). We need more evidence to support the use of antithrombotic drugs in COVID-19.

Patients with AECOPD and COVID-19 may be at a high risk of cardiovascular events and mortality following the acute phase of the disease. It has been recommended that in this vulnerable period, patients be closely followed with a management plan that pays special attention to the prompt recognition of cardiovascular complications, especially in the 30 days following the resolution of the acute phase.^[17]

In case of worsening of symptoms, the patient should have a discussion with the health care provider. Telemedicine/teleconsulting platforms can be used to get in touch with the patients.



ARE THERE ANY PRECAUTIONS THAT NEED TO BE UNDERTAKEN WHILE USING NONINVASIVE VENTILATION OR HIGH-FLOW NASAL OXYGEN DURING CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATIONS?

Description of the available evidence

The application of noninvasive ventilation (NIV) in patients with COVID-19 in the ICU is controversial. Studies of NIV during the SARS outbreak (2003) are not necessarily applicable today due to improvements in mask design and measures to increase patient tolerance of NIV. In clinical practice, leakage (around the mask) is common and contributes to increased dispersion of droplets. NIV is generally not recommended for patients with viral infections complicated by pneumonia because, although NIV temporarily improves oxygenation and reduces the work of breathing in these patients, it does not necessarily change the natural course of the disease.^[18] Considering the above factors, clinicians might not use NIV for critically ill patients with ARDS due to COVID-19 until further data from the COVID-19 epidemic are available. However, NIV can be used in patients with “mild” or “moderate” ARDS as a temporary measure under close observation monitoring for any worsening which might require invasive ventilation.

There are insufficient data to indicate whether high-flow nasal oxygen (HFNO) is as safe. Theoretically, because HFNO circuits are “leaky”, they may pose a higher risk compared to NIV (especially if the latter is used with full-face or helmet masks or with double-limbed circuits ± filters over expiratory vents/ports).

In general, in terms of disease transmission, NIV and HFNO may be similar, but the safety signal (more evidence based) is stronger for NIV.

Recommendations

In general, if invasive mechanical ventilation (IMV) is necessary, its use is preferred over NIV. Clinical need should determine the use of NIV and HFNO. NIV is preferred over HFNO in relation to the risk of disease transmission.

A patient with COPD presenting in Type 2 respiratory failure with their exacerbation should be considered for NIV if indicated as per the current COPD treatment guidelines (even though NIV is not recommended for COVID alone as a bridge to IPPV). There are no grounds for an indiscriminate ban on the use of NIV or HFNO.

NIV should be delivered by a nonvented mask followed by a viral/bacterial filter followed by a circuit with an expiratory port. NIV is preferred over HFNO because of its lower risk of disease transmission and lower consumption of oxygen supplies. If a patient is failing to respond to noninvasive support, early transfer from NIV (or HFNO) to

IMV is advisable to prevent delay in intubation (with the exception of patients with a ceiling of care on noninvasive respiratory support).

Health-care workers looking after patients on NIV should wear full PPE (eye protection, N95 or higher respirators, gloves, and long-sleeved gowns). Patients on NIV should be managed in negative pressure facilities whenever possible. If required, patients on NIV may be managed in side-rooms, with the door closed.

WHAT IS THE ROLE OF SMOKING CESSATION IN THE CURRENT PANDEMIC OF COVID-19?

Description of the available evidence

It has been recently reported that the gene expression for ACE2 receptors is higher in smoker samples as compared to never-smokers.^[6] In a multivariate logistic analysis, the single modifiable host factor associated with progression of COVID-19 pneumonia was current smoking (odds ratio [OR] = 14.3, 95% confidence interval [CI]: 1.6–25.0).^[19] In a study comparing the severe ($n = 173$) to nonsevere ($n = 926$) COVID-19 cases, the percent of current and former smokers were higher among the severe cases: 17% and 5%, respectively, than among the nonsevere cases (12% and 1%, respectively).^[20] More smokers as compared to nonsmokers (26% vs. 12%) were admitted into the ICU, required mechanical ventilation, or died. Middle East respiratory syndrome coronavirus (MERS-CoV) that caused a small coronavirus epidemic in 2012–2015 presented with similar clinical features as the current COVID-19, and reports also indicated an association between smoking status and fatality rate with current smoking also more frequent among cases than among controls (37% vs. 19%, OR = 3.14, 95% CI: 1.10–9.24, $n = 146$).^[21]

Recommendations

Smoking is a strong predictor of COVID-19 severity. COPD patients who smoke should be strongly encouraged to stop smoking completely during the entire course of the COVID-19 pandemic. This could involve telephone, video, or e-mail consultation support. The help of a counselor, respiratory therapist of a respiratory specialist nurse, might be sought in this endeavor.

WHAT IS THE ROLE OF INHALED CORTICOSTEROIDS, ORAL CORTICOSTEROIDS, NEBULIZERS, AND ANTIBIOTICS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE MANAGEMENT DURING THE COVID-19 PANDEMIC?

Description of the available evidence

While there is some evidence that use of ICS in COPD may increase the overall risk of pneumonia (both viral and bacterial), it has been recommended by the NICE Guidelines (UK) that



this risk alone cannot be a reason to change treatment in those COPD patients who are on regular ICS.^[22]

Systemic corticosteroids were widely used during the outbreaks of severe acute respiratory syndrome (SARS)-CoV and Middle East respiratory syndrome (MERS)-CoV.^[23,24] However, current interim guidance from WHO on clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected (released January 28, 2020) advises against the use of corticosteroids unless indicated for other reason.^[25]

No clinical data exist to indicate that net benefit is derived from corticosteroids in the treatment of respiratory infection due to RSV, influenza, SARS-CoV, or MERS-CoV. The available observational data suggest increased mortality and secondary infection rates in influenza, impaired clearance of SARS-CoV and MERS-CoV, and complications of corticosteroid therapy in survivors.^[26]

The University of Oxford's RECOVERY trial reported that low-dose dexamethasone reduced mortality only among COVID-19 patients requiring IMV (11.7% absolute reduction) or oxygen supplementation (3.5% absolute reduction).^[27] However, the effect was only modest and the number needed to treat was large.

Recommendations on use of inhaled corticosteroids in chronic obstructive pulmonary disease

COPD patients on inhaled corticosteroids (ICS) should not discontinue ICS because of the fear of developing viral or bacterial pneumonias during the COVID pandemic.

Patients on long-term oral corticosteroids should continue to take them at their prescribed dose because stopping them can be more harmful. There is no indication for starting new oral steroids, except low-dose dexamethasone among those put on invasive ventilation or requiring supplemental oxygen.

Patients already prescribed prophylactic antibiotics should continue taking them as prescribed, unless there is a new reason to stop them (for example, side effects or allergic reaction). Avoid routine use of prophylactic antibiotics in COVID-19 infection.

Avoid nebulizers where ever possible. Pressurized metered dose inhaler via a spacer is the preferred route of drug delivery during severe exacerbations, with a mouthpiece or tightly fitting face mask if required. Best practice at all times is that inhalers or spacer devices should not be shared. Keep the inhalers and spacers in a safe place when not in use. Standard hygienic practice should be sufficient.

The quality of management of stable COPD should be upgraded to the highest standards, especially during the COVID-19 pandemic. Apart from keeping them away from potential COVID-19 infected patients, ensure adherence to appropriate pharmacotherapy (inhaled bronchodilators ± steroids), vaccination (influenza and

pneumococcal), pulmonary rehabilitation, and smoking cessation program whenever required.

WHAT SHOULD WE ADVISE PATIENTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON LONG-TERM OXYGEN THERAPY DURING THE COVID-19 PANDEMIC?

Recommendations

In the absence of any specific evidence, patients currently receiving long-term oxygen therapy should continue with the same. The patient should monitor the SpO₂ using a pulse oximeter and maintain the same in the range prescribed by the health-care provider. In case of worsening breathlessness and declining SpO₂, the patient should be advised to reach out to the health-care provider.

SHOULD A PATIENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE CONTINUE PRACTICING AIRWAY CLEARANCE TECHNIQUES DURING THE COVID-19 PANDEMIC?

Recommendations

In the absence of any evidence so far, it would be prudent to advise patients currently practicing airway clearance to continue as they were. However, several precautions need to be taken. The patient should perform airway clearance techniques in a well-ventilated room, away from other family members if possible. Other family members should be advised not to enter the room until enough time has passed for aerosols to clear.

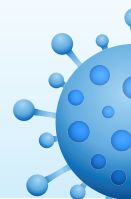
WHAT ADVICE SHOULD WE GIVE PATIENTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE REQUIRING HOME NONINVASIVE VENTILATION AND CONTINUOUS POSITIVE AIRWAY PRESSURE?

Description of evidence

There is no evidence that using continuous positive airway pressure (CPAP) increases the risk of COVID-19 infection and nothing to suggest that CPAP will worsen COVID-19. As of now, there are no data to suggest whether CPAP increases viral spread within a household. Stopping home NIV risks the return of symptoms (lethargy, headache, dyspnea, and confusion), increased patient and family anxiety, and may precipitate life-threatening acute hypercapnia, which is likely to result in hospital admission, patient exposure to COVID-19, and other infections.

Recommendations for chronic obstructive pulmonary disease with obstructive sleep apnea^[28]

People with obstructive sleep apnea (OSA) should continue to use their CPAP at home as before. Stopping CPAP during the COVID-19 pandemic is not recommended, especially



for key workers, such as those with safety critical jobs and those with increased workload during the pandemic. If a CPAP user develops symptoms (or has asymptomatic proven COVID-19), then self-isolation and a discussion with their health-care provider regarding stopping the CPAP for about 2 weeks (risks versus benefit) need to be considered.

Sleeping more upright, avoiding alcohol, weight loss, and using a mandibular advancement device if available may help as alternatives to CPAP in reducing OSA a little during the period CPAP is not used. Routine hygiene is adequate for infection control including changing machine filters routinely, cleaning surfaces, cleaning mask, and tubing with hand-hot soapy water (washing up liquid) and washing hands regularly. Masks and machines should not be shared. Patients with decompensated obesity hypoventilation or COPD/OSA overlap should be provided with a nonvented mask, viral filter, and a circuit with an exhalation port, in a side room with a hospital CPAP machine.^[29]

Recommendations for chronic obstructive pulmonary disease patients on home noninvasive ventilation

Home NIV patients often have limited mobility or are housebound. Hence, they can be asked to self-isolate. There is therefore a higher risk of a carer to patient transmission. NIV does generate droplets, but using a nonvented mask with a viral filter reduces the spread significantly.^[30] Patients with domiciliary NIV should bring in their machines if requiring hospitalization.

WHAT ADVICE SHOULD WE GIVE PATIENTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON PULMONARY REHABILITATION?

Not much is known about the long-term sequelae of COVID-19, especially in patients with COPD.

Recommendations

Pulmonary Rehabilitation remains an important component of COPD management. Although we do not know the long-term consequences of COVID-19 on COPD, pulmonary rehabilitation should be continued as it was being practiced before. Encourage patients to undergo on-line or web-based programs and as far as possible avoid hospital visits.

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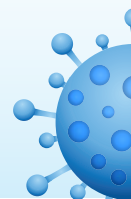
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The COVID-19 Pandemic and Impact on the Cardiovascular Disease Patient: Special Emphasis on Rheumatic Valvular Heart Disease Care

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ABSTRACT

The COVID-19 crisis has surged worldwide putting immense stress on the health care services, leading to institutions deferring elective procedures and struggling to triage the emergency care of the cardiac patient. This has affected the management of the rheumatic valvular heart disease patient especially in Asia and other developing countries, potentially placing these patients at enormous risk for complications like congestive cardiac failure, stroke and death. In this current review, we explore the COVID-19 pandemic and its impact on the cardiovascular disease patient with special emphasis on rheumatic valvular heart disease care. We try to provide a framework that address the procedural considerations of interventions like percutaneous transluminal mitral commissurotomy (PTMC) and mitral and aortic valve surgeries. We also highlight the implications for the outpatient valve clinic and address the safety issues of the patient and health care workers during this on-going COVID-19 pandemic.

Keywords: COVID-19, Cardiovascular, ARF, RHD, PTMC

INTRODUCTION

The COVID-19 infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first identified in Wuhan, China in December 2019, was declared a global pandemic of concern by World Health organization (WHO) on March 11th 2020 (WHO 2020). To stem the spread of the virus nations have imposed lockdowns and social distancing, affecting the daily life, leading to hardships and economic slowdown.

The COVID-19 infection presentation can range from mild symptoms like that of a common cold to severe acute respiratory distress syndrome (ARDS) leading to difficulty in breathing, fatigue, fever, and dry cough. Studies emerging from China reveal that majority of the patients i.e. around 80% have mild form of COVID-19 viral infection and the remaining 20% have severe to critical disease requiring intensive care unit (ICU) admission and invasive ventilation, and the fatality rate was 4.3% (Wang et al., 2020).

The cardiovascular involvement and manifestations in COVID-19 infection ranges from viral myocarditis, and myocardial ischemic injury as a result of hypoxemia and hemodynamic instability caused by severe pneumonia. Acute cardiac injury is present in 7% of the virus infection with an elevation of troponins and arrhythmias were seen in 16.7% and shock in 8.7% of the patients respectively (Wang et al., 2020). Since the risk factors for COVID-19 infection are similar to that for myocardial ischemia, namely age more than 60 years with comorbidities like hypertension and diabetes mellitus, there is a potential for Type 1 myocardial ischemia due to atherosclerotic plaque rupture caused by the stress of pneumonia and resultant inflammation

and shock. The thromboembolic risk is increased in this viral infection due to the resultant inflammation and immobilisation in severe cases (Libby 2020). A retrospective analysis done in China showed that the incidence of cardiovascular disease in patients who were admitted to ICU with COVID-19 infection was higher compared to those who were not admitted to the ICU i.e. 23% vs. 11% (Huang et al., 2020).

Rheumatic heart disease (RHD) is characterized by immune mediated destruction of cardiac valves in the setting of episodes of acute rheumatic fever (ARF) after exposure to strains of group A streptococcus bacteria. Most episodes of ARF occur in children between age 5 and 14 years, but they may well occur in adulthood, and an Indian study done revealed that RHD was prevalent even in the elderly population aged more than 60 years (Lawrence et al., 2013, Manjunath et al. 2014). RF and RHD are global problems but are most prevalent in developing countries. In these countries, RF accounts for up to 60% of all cardiovascular disease in children and young adults in their most productive years, and it has the potential to undermine national productivity and puts additional burden on the economy (Githang'a 1999, Joint WHO/ISFC meeting on RF/RHD control with emphasis on primary prevention, Geneva 1994). A large proportion of the individuals with CHF required cardiac valve surgery within 5–10 years (Murray et al., 1996). The reported prevalence of RHD in the world varies between 0.2 to 77.8 per 1000 population and the estimated annual mortality from RHD was 332000 in the year 2000 (Report of a WHO Expert Consultation Geneva 2001).

Mitral valve is the most commonly affected valve in RHD (60%) followed by combined mitral and aortic involvement (29%), tricuspid (10.7%) and pulmonary valve (0.04%) (Manjunath et al. 2014).

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EJMCM



Percutaneous transluminal mitral commissurotomy (PTMC) is done for mitral stenosis with favourable anatomy and the risk of restenosis is 40% after seven years (Farhat et al., 1998). Surgical procedures performed are closed mitral commissurotomy, valve repair, and valve replacement surgeries with both mechanical and bioprosthesis in mitral, aortic, tricuspid and pulmonary positions respectively. The patient having atrial fibrillation, and with mechanical valves need anticoagulation and this is an independent determinant of long-term survival (Butchart et al., 2002).

Percutaneous mitral valve repair with Mitraclip system for rheumatic mitral regurgitation is a feasible option in appropriately selected patients with suitable mitral valve anatomy and no co-existing mitral stenosis or severe valve calcification (Wong et al., 2019). Transcatheter mitral valve repair and replacement are yet to be proven effective treatment modalities for primary rheumatic mitral regurgitation. On-going trials will reveal the future directions and usefulness of these technologies in RHD patients (Overtchouk et al., 2020). Rheumatic aortic stenosis is typically characterised by valve thickening and commissural fusion, rather than the calcific degeneration encountered in the degenerative aortic valve disease.

A single-center TAVR study done in the United Kingdom for rheumatic aortic valve disease showed similar procedural and clinical outcomes compared to conventional TAVR patients, and the results reveal that for high risks patients with severe rheumatic aortic valve disease TAVR could be a viable alternative (Brennan et al., 2019). Transcatheter tricuspid interventions currently are in the infancy and further studies are needed to recommend the use of these procedures in rheumatic tricuspid valve disease.

During an outbreak like COVID-19, delivery of cardiovascular services becomes a challenge especially for those suffering from valvular heart disease and elective cardiac procedures are invariably postponed. Due to the vast number of coronavirus patients presenting to the hospital and beds in hospital preferentially earmarked for them, other clinical services are bound to suffer. Patients with underlying cardiovascular conditions have high risk of adverse outcomes and strategies have to be put in place to prioritise those who require critical cardiac interventions and at the same time reduce the chances of virus infection to them and the health care professionals.

COVID-19 AND THE IMPLICATIONS FOR THE RHD PATIENT

Cardiac Interventional Procedure Considerations

All elective structural heart interventions should be postponed until the pandemic recedes. In the hospital triage systems favour COVID-19 patients and intensive care unit (ICU) beds would be needed to treat these patients. Scheduling a non-urgent interventional procedure at this stage will put more strain on the hospital resources and also potentially expose the patient and the caregivers to the viral infection in the

hospital environment. Few cases of structural heart interventions need anaesthetist back-up for intubation and also require trans-oesophageal echocardiography (TEE), thus exposing the healthcare professionals to high risk situations, requiring personal protection equipment (PPE) to prevent the virus contagion. The symptomatic rheumatic valvular heart disease requiring interventional procedure would be a high risk for complications like cardiac failure and postponing interventions in them could be fatal.

Percutaneous transluminal mitral commissurotomy (PTMC)

PTMC with Inoue balloon is the preferred intervention for patients with New York Heart Association (NYHA) class III-IV symptoms with moderate to severe mitral stenosis (Mitral valve area $<1.5 \text{ cm}^2$ and or valve area index $<0.6 \text{ cm}^2/\text{m}^2$) and suitable anatomy based on Wilkins scoring system (Wilkins et al. 1988).

PTMC has excellent hemodynamic and long-term results with low rate of complications. After the procedure, patients experience significant improvement in symptoms and this procedure is a viable alternative for those who are high risk for mitral valve surgery (Feldman et al. 1991) Patients with mild symptoms of NYHA class I-II and moderate to severe mitral stenosis (MS) should be optimised on medications and closely followed up by telehealth clinic for any deterioration in symptoms that warrant emergency PTMC.

It is not uncommon especially in the Indian subcontinent to come across overt or silent MS during the second or third trimester of pregnancy. The combination of physiological changes of pregnancy and the pathological impact of MS over pregnancy and labour can lead to cardiac decompensation and pulmonary oedema, and if untreated carry significant maternal and foetal mortality (Kannan et al., 2010).

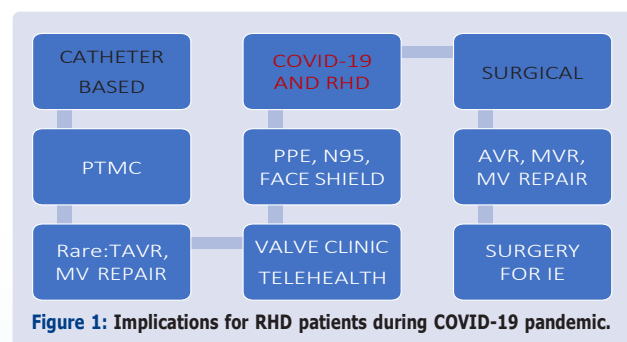
In symptomatic MS with pregnancy, the second trimester is the preferred period for PTMC which provides reduction in symptoms and has good success rate (Sutton et al., 2005). Mitral valve replacement (MVR) surgery in pregnancy is reserved for severe calcified MS with mural thrombus but this carries high maternal mortality of 1.5–5% and the reported foetal loss is 16–33% (Sharma et al., 1994). A pregnant patient with symptomatic MS requiring PTMC should not be denied the intervention during this pandemic and appropriate institutional triage system should be created to manage these patients. Also, adequate hospital infection prevention protocols should be followed to negate the risk of contagion to the patient and the healthcare professionals.

Other structural intervention considerations

In RHD patient procedures like TAVR, transcatheter mitral valve repair and replacement are not the common therapeutic options and instead surgical valve repair and replacements are the first choice. Nonetheless in rare selective symptomatic patients when these emergency procedures are considered, appropriate guidelines should be followed, minimising the risk to the patient and the heart care team (Shah et al., 2020).

Cardiac Surgery Considerations

The symptomatic RHD patient not amenable for cardiac catheter intervention should be considered for cardiac surgery on a case to case basis, after the heart team discussion. To sustain hospital services all elective surgeries should be deferred and the patients followed up closely via telehealth for any escalation of symptoms. Each service providing centre should develop a case triage protocol for emergency cardiac surgeries and minimise the risk of COVID-19 infection to the patient and healthcare staff. Before considering an emergency surgery, the availability of hospital resources like ICU beds, ventilators, cardiopulmonary bypass (CPB) machine, extracorporeal membrane



oxygenator (ECMO) and operation room supplies like valves, blood products and sutures should be taken into account (Mavioglu et al., 2020).

The indications for surgical treatment are as follows (Bonow 1998):

- In the presence of MS, patients with moderate or severe MS (mitral valve area 1.5 cm^2) and NYHA class II/IV symptoms.
- In the presence of MR, patients with NYHA functional class symptoms II/III/IV with:
 - normal left ventricular (LV) function (ejection fraction $>60\%$ and end-systolic dimension $<45 \text{ mm}$);
 - mild dysfunction (ejection fraction $50\text{--}60\%$ and end-systolic dimension $45\text{--}50 \text{ mm}$);
 - moderate dysfunction (ejection fraction $30\text{--}50\%$ and end-systolic dimension $50\text{--}55 \text{ mm}$);
 - severe LV dysfunction and chordal preservation, or normal LV function and pulmonary hypertension.
- In the presence of AS, symptomatic patients with severe AS or in the presence of LV dysfunction, ventricular tachycardia, $>15 \text{ mm}$ LV hypertrophy, valve area $<0.6 \text{ cm}^2$.
- In the presence of AR, with NYHA functional class symptoms II/ III/ IV with:
 - NYHA functional class III/IV and preserved LV function (ejection fraction $>50\%$);
 - preserved LV function (ejection fraction $>50\%$), but LV dilation or declining ejection fraction at rest or at functional studies;
 - mild dysfunction (ejection fraction $50\text{--}60\%$ and end-systolic dimension $45\text{--}50 \text{ mm}$);
 - moderate dysfunction (ejection fraction $30\text{--}50\%$ and end-systolic dimension $50\text{--}55 \text{ mm}$).

The emergency surgeries for RHD that can be considered during the pandemic are (Matt et al. 2020):

1. Mitral valve replacement:
 - (a) Symptomatic severe mitral stenosis with valve anatomy not favourable for PTMC.
 - (b) Symptomatic severe mitral regurgitation.
2. Aortic valve replacement in symptomatic severe aortic stenosis or severe aortic regurgitation.
3. Infective endocarditis involving the left sided valve causing a severe valve defect and/or large mobile vegetation.

Implications for the Healthcare Personnel

Healthcare workers are at a heightened risk for getting infected during this pandemic especially when operating on a suspected or COVID-19 positive patient (Adams et al., 2020). The staff should be equipped with PPE including a N95 respirator mask, goggles, face shield and adhere to meticulous hand washing and personal hygiene measures (Adams et al., 2020). They should be well versed with the PPE donning and doffing protocols, and avoid contaminating or touching the surfaces in the hospital environment which could harbour the coronavirus (Adams et al., 2020). The institution and the stakeholders could devise and constitute multiple units of different cardiac professionals and post them on rotation for emergency services, so that in case of an exposure

to the virus, quarantine issues can be applied to the individual unit rather than the entire group (Matt et al. 2020).

Outpatient Valve Clinic Considerations

During this pandemic outpatient clinic visit for the RHD patient would be adversely affected due to lockdown and sparse transportation availability. In this context virtual consultation, telehealth and video counselling are becoming the favoured mode of interaction between the physician and the patient. Many institutions are rapidly ramping up the telehealth facilities to address this sudden transition in the outpatient clinic services. The virtual clinics are important for the uninterrupted follow-up of the recently operated patients and this will help them avoid making multiple trips to the hospital and minimize the risk of virus transmission among the patients, and health care personnel (Adams et al., 2020). Many of the RHD patients having atrial fibrillation and or those who have undergone valve replacement surgeries will be on anticoagulants like warfarin and will require test of international normalised ration (INR). This testing may be hampered or unavailable as most of the health services are working with less capacity. Till the time INR tests become available, asymptomatic patients should continue to take the anticoagulants especially if the preceding INR values were stable and in the therapeutic range. Some clinics are providing home testing of INR to avoid patient needing to visit the hospital (COVID-19/Coronavirus Illness and Heart Valve Disease 2020). As secondary prophylaxis to prevent recurrent attacks of RF, RHD patients are required to take intramuscular injection of benzathine benzyl penicillin every three or four weeks (Lue et al. 1986). Due to limited stock supplies and curtailed hospital services during this pandemic, the patient might face difficulties to take this injection. Oral penicillin may be used as an alternative in secondary prophylaxis if penicillin injection is not available.

CONCLUSION

The present COVID-19 pandemic has led to disruption of hospital systems and severely affected the RHD patient management. The heart care team needs to harness its skills and continue to provide telehealth services and optimal emergency care to the patients. With the hospital triage under increasing strain from burgeoning number of critically ill COVID-19 patients, institution-based protocols are to be devised to provide a safe environment for the health care professionals and the patients seeking the cardiac services.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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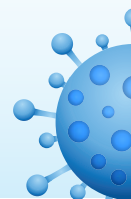
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COVID-19 Pandemic and the Impact on the Cardiovascular Disease Patient Care

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Abstract: The COVID-19 pandemic has emerged as a serious global threat causing a large number of fatalities and putting enormous strain on the health care resources across the world. This has resulted in preferentially triaging the coronavirus infected patients and placing others, especially cardiovascular patients at increased risk for adverse complications. The effective management of cardiac patients in the hospital environment during this COVID-19 pandemic has emerged as a real challenge. We try to address this issue and also highlight the interplay between COVID-19 and cardiovascular diseases. We hereby review the available literature and emerging guidelines about cardiovascular implications related to COVID-19 which will have a bearing on the patient care, health care professionals and cardiac centres.

Keywords: COVID-19, Cardiovascular, Myocarditis, Acute Coronary syndrome, Primary PCI.

1. INTRODUCTION

The COVID-19 infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in Wuhan, China in December 2019. This viral pandemic since then has rapidly disseminated across the globe and according to the World Health Organization (WHO) it has infected more than 2 million individuals in 213 countries and has resulted in about 357 688 fatalities as on May 19, 2020 [1, 2]. To contain the spread of this highly contagious infection, many nations have imposed lockdowns, restricted travel, and advocated social distancing, leading to disruption of daily lives, causing anxiety and hardships in the society.

The individuals infected with COVID-19 have a varied clinical presentation. A retrospective single-centre study done in China revealed that of the confirmed cases: 81% were mild, defined by no or mild pneumonia, 14% were severe with significant lung infiltrates or signs of respiratory compromise and 5% were critical with respiratory failure requiring mechanical ventilation (47% of the total cases), shock or multi-organ system failure. Those requiring intensive care unit (ICU) care were predominantly older (median age 66 years) with a higher prevalence of co-morbidities like diabetes mellitus, hypertension, cardiovascular and cerebrovascular diseases than in those not needing ICU care. The acute cardiac injury was observed in about 7% and the overall mortality was 4.3% [3].

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The myocardial involvement in coronavirus infection is direct in the form of viral myocarditis and indirect injury to myocardium can occur due to increased oxygen demands caused by fever and tachycardia, and reduced oxygen delivery caused by hypotension and hypoxemia. During the acute infection cytokines released can augment thrombotic risk leading to acute coronary syndromes [4]. Anecdotal reports suggest that presentation of COVID-19 infection mimicking ST-elevation Myocardial infarction (STEMI) with an increase in the levels of cardiac biomarkers especially the troponins, electrocardiographic and echocardiographic abnormalities is frequently encountered, and is associated with more severe disease form and worse prognosis[5]. This overlapping of COVID-19 presentation with STEMI which is being termed as “STEMI mimics” has compounded the diagnostic challenges of the coronavirus infection.

In cardiac centres around the world surprisingly there is a significant reduction in presentations of STEMI during the coronavirus pandemic. In a retrospective analysis at nation's cardiac service centres conducted by the Spanish society of cardiology revealed a significant reduction of 40% in the admissions for STEMI and a reduction in the number of diagnostic procedures by 57%, coronary intervention procedures by 48% and structural heart interventions by 81% [6]. A similar reduction in STEMI admission numbers by 70% is observed in Italy's Lombardy region [7]. A real-time data analysis done by the Minneapolis heart institute foundation from nine large USA STEMI centres shows a 38 % reduction in the cardiac catheterization laboratory STEMI procedures [8].

The vast number of COVID-19 infected patients being prioritised in-hospital triage and ICU has a direct impact on cardiovascular disease patient care and may hinder in providing optimal treatment for them. Cardiac care clinicians and healthcare workers amid this pandemic can become vulnerable to coronavirus infection and inadvertently become vectors of virus transmission. Clinicians and healthcare systems must be aware of the dynamic changes occurring during this crisis and judiciously use the resources for patient care. The objective of this review is to address these vital issues arising during this pandemic and to optimize cardiovascular patient care outcomes.

2. IMPACT ON CARDIOVASCULAR DISEASE PATIENT CARE

2.1. Outpatient Clinic Considerations

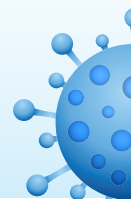
To mitigate the spread of COVID-19 infection lockdowns and physical distancing imposed across nations has interrupted the daily life in the community. This has a direct bearing on the patient's visit to the doctor's office and has drastically transformed the physician practices from physical to virtual consultation. Many hospitals are turning to telehealth to address this transition and are ramping up their capabilities to include video consultations, telephone calls and electronic messaging. This is advantageous to both the patients and healthcare workers as there would be no potential risk of exposure to COVID-19 infection by avoiding in-person consultation [9]. In this crisis by adopting virtual practices the strain on emergency departments is reduced and the healthcare workers can be optimally utilised in the management of COVID-19 patients.

2.2. Inpatient Care and Catheterization Laboratory Considerations

The telehealth services under the present circumstances are a convenient solution for patients with chronic and stable cardiac ailments seeking physician consultation. Patients presenting with acute coronary syndrome will require emergency medical attention and appropriate strategies should be adopted by hospitals to provide optimal care for them. Given the ongoing pandemic and overlapping of presentations of both COVID-19 and STEMI, the cardiac health care providers are at a heightened risk of contracting the virus infection. Hence institutions must develop protocols of infection prevention, control and adhere to treatment guidelines in the care of these patients [10].

The American college of cardiology's (ACC) interventional council and the Society of cardiovascular angiography and intervention (SCAI) have issued a joint statement of catheterization laboratory considerations during the coronavirus (COVID-19) pandemic [12] and the summary is enumerated below and in Table.1 [13].

ST-elevation myocardial infarction (STEMI) patient: During this pandemic, China adopted protocols of its Sichuan provincial people's hospital that followed the principles of maximum protection for health care professionals. When dealing with patients of STEMI having fever, and respiratory symptoms, and presenting within 12 hours of symptoms, this protocol advocates rapid nucleic acid testing and fibrinolytic therapy [11]. For those with a delayed presentation of STEMI beyond 12 hours, the risk of infection versus PCI should be weighed. If such patients are stable, serial echocardiograms should be performed and they should be treated conservatively and followed up closely for deterioration of symptoms [11]. However, worldwide for those suffering from STEMI primary percutaneous coronary intervention (PPCI) is the gold standard treatment and hence offering thrombolytic therapy should be carefully considered especially in unstable patients. Also, COVID-19 rapid testing kit may not be readily available in most centres, and thrombolytic therapy can be riskier in COVID-19 infection with STEMI, as patients with a severe infection have deranged coagulation parameters and prone for bleeding [14]. However, given the pandemic and the strain on health care systems, a stable active COVID-19 patient presenting with STEMI thrombolysis can be considered, carefully gauging the patient benefit and staff risk of exposure to the virus. In patients with active COVID-19 and unstable STEMI requiring Primary PCI, appropriate personal protective equipment (PPE) including an N95 mask should be worn by all the members of the cardiac team involved in the care of these patients [12]. Additionally, all the personnel should be trained and well versed with proper techniques for doffing and donning of the PPE. Ideally, cardiac intervention procedure on a COVID-19 positive patient should be performed in a negative pressure catheterization laboratory [12, 15]. In most



hospitals, operating rooms and catheterization laboratories use positive ventilation systems, and in normal circumstances, these steps help to protect the equipment and patients from surrounding airborne contaminants like viruses, bacteria and fungi [16]. In these positively pressured rooms, the air inflow is designed specifically in such a way that airborne contaminants disperse downwards away from the patient to the other end of the room [17]. However, in the current pandemic for enhanced safety of the patients, these rooms will require conversion to an air neutral or negative-pressure area so that infectious transmission originating within the room while operating on a COVID-19 patient does not occur [16]. A positive-pressure operating room can be converted into a negative-pressure zone by establishing an anteroom within this area and additionally by sealing off other access points and reversing the airflow design in the room [16, 18, 19]. In the non-availability of a negative-pressure catheterization laboratory or operating room, terminal cleaning protocols should be adopted after the end of each procedure [20].

Table 1: COVID-19 pandemic and the cardiovascular disease patient care considerations

OUTPATIENT CLINIC CARE	INPATIENT /ICU CARE	CARDIAC CATHETERISATION LABORATORY CONSIDERATIONS	CARDIAC SURGERY CONSIDERATIONS
<ul style="list-style-type: none"> • Telehealth • Virtual consultation 	<p>STABLE PATIENTS</p> <ul style="list-style-type: none"> • Telehealth <p>ICU CARE</p> <ul style="list-style-type: none"> • Use PPE during procedures where appropriate in COVID-19 patient (as per guidelines) 	<ul style="list-style-type: none"> • Avoid elective procedures • Negative pressure labs for emergency procedures • PPE for staff during emergency interventional procedures in COVID-19 patients (as per guidelines) • Thrombolysis for STEMI if PCI not feasible 	<ul style="list-style-type: none"> • Cancel elective surgeries • Negative pressure operating rooms for emergency surgeries • PPE for staff in operating rooms during emergency surgeries in COVID-19 patient(as per guidelines)

Non ST-elevation myocardial infarction (NSTEMI) patient: In an NSTEMI patient with suspected COVID-19, diagnostic testing for COVID-19 should be performed before taking up for the cardiac catheterization procedure. If unstable NSTEMI patients undergo coronary revascularization, they should be discharged early to prevent exposing them to the viral infection and followed-up by telehealth [12, 13]. In a COVID-19 patient presenting with features suggestive of type 2 myocardial infarction or myocarditis, these patients could be treated conservatively and if possible invasive management should be deferred.

Elective cardiac catheterization procedures should be deferred to avoid patient exposure to potential COVID-19 infection and preserve precious resources like hospital beds, which can be utilised to manage the coronavirus infected patients especially in locations with high case volumes.

2.3. Cardiac Surgery Considerations

The COVID-19 pandemic has put enormous strain on the global health care services. Optimal utilisation of the hospital resources is the need of the hour and in this context, elective cardiac surgeries should be postponed. Emergency cardiac surgeries not amenable by medical management or interventional procedures should be undertaken after adhering to infection prevention and control protocols of the hospital. Examples of emergency surgeries include severe left main coronary artery stenosis or symptomatic severe triple vessel disease, left-sided infective endocarditis with severe valve defects or large mobile vegetation, acute type A aortic dissection and symptomatic valvular heart disease [21]. Cardiac surgeries should be preferably carried out in a negative pressure operating room and all personnel should wear PPE if operating on a COVID-19 patient.

2.4. COVID-19 Drug therapy and Cardiovascular Considerations

Currently, there are no definitive treatment regimens for the COVID-19 infection and experimental therapies are constantly evolving.

Antivirals like ribavirin, lopinavir and ritonavir have shown in-vitro effectiveness against SARS-CoV-2 and have been included in clinical trials for COVID-19 [22, 23]. Lopinavir and ritonavir may cause prolongation in QT and PR intervals and should be monitored especially in those on QT-prolonging drugs [23]. Ribavirin, lopinavir and ritonavir have potential interactions with anticoagulant warfarin and hence warfarin dosing should be closely monitored [24]. Lopinavir and ritonavir may be avoided with CYP3A mediated novel anti-coagulant drugs such as rivaroxaban and apixaban [25, 26].

Lopinavir and ritonavir through CYP3A4 inhibition can decrease serum concentrations of anti-platelet drugs like clopidogrel and prasugrel and increase the serum concentrations of ticagrelor leading to increased bleeding risk [27, 28] and hence should be monitored in concomitant therapy of these drugs.

Lopinavir and ritonavir can interact with statins and can increase their levels leading to myopathy. Concomitant therapy of statins like simvastatin and lovastatin with these anti-virals should be avoided as there is a risk of rhabdomyolysis. Low doses of atorvastatin and rosuvastatin should be administered when they are used concomitantly with lopinavir and ritonavir [23].

Antimalarial drugs Chloroquine and hydroxychloroquine have shown in-vitro inhibitory activity against SARS-CoV-2 [29, 30]. These drugs on long term usage can cause myocardial toxicity leading to restrictive or dilated cardiomyopathy [31, 32]. These drugs are also associated with a risk of inducing torsade des pointes in patients with electrolyte abnormalities, those who are on QT-prolonging drugs or have underlying cardiac ailments especially channelopathies. Chloroquine and hydroxychloroquine can potentiate concentrations of beta-blockers and hence should be monitored closely when on concomitant therapy with both these drugs.

Steroid drugs such as methylprednisolone are being used in COVID-19 associated acute respiratory distress syndrome (ARDS) and were extensively used in Chinese hospitals involved in coronavirus patient care [33]. This drug can cause electrolyte derangement, fluid retention and hypertension and should be closely watched for side effects, especially in patients with a pre-existing cardiac condition.

CONCLUSION

The COVID-19 pandemic has caused enormous crisis impacting lives, health care systems and economy across continents. Until this pandemic mitigates and newer therapies and vaccines are discovered against the coronavirus, preventive measures like social distancing and personal hygiene should be vigorously practised. Relatively stable cardiovascular patients can make use of telehealth and virtual physician consultations for follow-up care and health-related queries. Health care systems should defer elective procedures, make the judicious utilisation of scarce resources, including PPE and continue to provide optimal emergency cardiovascular services.

CONSENT FOR PUBLICATION

All authors have participated in the work and have reviewed and agree with the content of the article.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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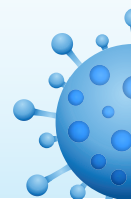
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Extrapulmonary manifestations of COVID-19 pneumonia – An institutional experience

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Abstract

Background: The purpose of this article is to provide insight into the varied extrapulmonary manifestations associated with the novel corona virus disease 2019 (COVID-19). This study mainly focuses to identify the most common extrapulmonary manifestations encountered in patients with COVID-19 pneumonia as noted in the Indian subcontinent.

Materials and methods: A total of 145 hospitalized patients with COVID-19 disease were retrospectively evaluated for extrapulmonary imaging findings or complications. These patients had undergone various imaging examinations during the course of hospital stay. Images were reviewed using the institutional PACS database system over a period of three months (August to October 2020).

Results: Among the 145 patients (91 males and 54 females), 54 patients (37.2%) had extrapulmonary findings or complications on imaging. Various extrapulmonary findings observed are as follows: ischemic brain infarcts (n=12), intracranial hemorrhage (n=5), viral encephalitis (n=1), perinephric fat stranding (n=3), small bowel ischemia (n=1), acute pancreatitis (n=2), splenomegaly (n=15), pericardial effusion (n=2), mediastinal lymphadenopathy (n=9), and pneumomediastinum (n=4).

Conclusion: With increasing spread of COVID-19 infection worldwide, it is important to identify the spectrum of extrapulmonary manifestations related to COVID-19 pneumonia in the long run. A clear understanding of the extrapulmonary imaging findings in COVID-19 pneumonia is essential so that the radiologist can make a timely and accurate diagnosis to aid in patient management.

Keywords: severe acute respiratory syndrome (SARS); COVID-19 pneumonia; extrapulmonary manifestations; viral encephalitis, renal dysfunction; pneumomediastinum

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Introduction

In March 2020, the World Health Organization (WHO) declared novel corona virus disease 2019 (COVID-19) as a pandemic, declaring the same as a public health emergency of great international concern [1]. With a reproduction rate of 2.5 as estimated by the WHO, the world has witnessed a rapid and widespread infection affecting patients of all age groups. Various researches have shown that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) shares a homologous sequence with SARS-CoV and MERS-CoV (family of coronaviruses), and is characterized by similar pathogenesis and manifestations [2]. The cellular entry of SARS- Cov-2 follows similar mechanism as that of SARS- CoV with ACE-2 (angiotensin-converting enzyme 2) as functional entry receptor. TMPRSS2, a cellular serine protease helps in priming of the spike protein and entry into the target cells [3]. This leads to dysregulation of RAAS (renin-angiotensin-aldosterone system) causing endothelial damage and thromboinflammation. This suggests that organs with ACE-2 receptors are at risk of COVID-19 related complications.

COVID-19 infection is more common among the elderly (>60 years) and patients with comorbidities. Patients generally become symptomatic after an incubation period of approximately 5.2 days [4]. Fever, cough, and fatigue are the most common symptoms during the initial phase of COVID-19 illness with gradual development of severe pneumonia at later stages. Other less common clinical manifestations include sore throat, headache, myalgia, arthralgia, nausea or vomiting, anosmia, nasal congestion, ageusia, diarrhea, hemoptysis, and conjunctival congestion [5, 6]. According to WHO report on COVID-19 infection, the disease has no specific disease manifestation, clinical presentation can vary from asymptomatic carriers to severe pneumonia and death [2]. Due to wide range of clinical manifestations, studies regarding multiorgan dysfunctions will help to take necessary precautions in the future.

The genetic sequence of the COVID-19 showed more than 80% identity to SARS-CoV and 50% to the Middle East respiratory syndrome (MERS) coronavirus (MERS-CoV) [7]. Research on previous SARS and MERS infections has shown multiorgan dysfunctions involving renal, hepatic, neurological,

gastrointestinal and hemodynamic abnormalities [8, 9]. Since the genomic sequences and clinical manifestations between SARS, MERS, and COVID-19 are identical, the possibility of extrapulmonary manifestations and complications in COVID-19 must be evaluated for future therapeutic management of the patients.

Materials and methods

This was a retrospective observational study conducted at JSS Medical College and Hospital (JSS AHER), for a period of 3 months. The study included 145 patients who were positive for COVID-19 infection by RT-PCR test and were admitted to the hospital. The patient records between August-2020 and October-2020 were retrieved. CT was performed using a 128- slice Philips MDCT scanner (Ingenuity, Netherlands) and MR images were obtained using a 3T Philips MRI scanner (Ingenuia, Netherlands). Images were evaluated using the institutional PACS database system to assess the incidence of extrapulmonary findings in COVID-19 positive patients. The clinical characteristics and incidence of extrapulmonary findings were described as frequency rates and percentages.

Table 1: Various extrapulmonary findings among the study group.

<i>Patient characteristics (n=145)</i>	<i>Number (percentage)</i>
Male	91 (62.7%)
Female	54 (37.2%)
Imaging studies (n=145)	
CT Brain	18 (12.4%)
CT Chest	120 (82.7%)
CT Abdomen	6 (4.1%)
MRI Brain	1 (0.7%)
Extrapulmonary findings(n=54)	
Ischemic infarct	12 (22.2%)
Intracranial hemorrhage	5 (9.2%)
Encephalitis	1 (1.8%)
Mediastinal lymphadenopathy	9 (16.6%)
Pneumomediastinum	4 (7.4%)
Pericardial effusion	2 (3.7%)
Perinephric fat stranding	3 (5.5%)
Splenomegaly	15 (27.7%)
Bowel ischemia	1 (1.8%)
Acute pancreatitis	2 (3.7%)



Results

A total of 145 COVID-19 positive patients (91 males and 54 females) were included in the study. CT and MRI were performed as per the clinical indications. Eighteen patients underwent CT brain who had presented with hemiparesis, headache, and loss of consciousness. Plain CT chest was performed for 120 patients. Six patients who had presented with acute abdomen underwent CT of the abdomen. MRI brain without contrast was done in one patient who had presented with altered sensorium and seizures. Out of 145 patients, 54 patients showed various extrapulmonary imaging findings as depicted in Table 1. Most common extrapulmonary manifestations include splenomegaly (27.7%) followed by ischemic brain infarcts (22.2%).

Discussion

Neurological abnormalities

Neurological manifestations in COVID-19 can involve both the central and the peripheral nervous system. Pathophysiology of neurological complications has been attributed to direct viral invasion, immunological reaction or hypoxic metabolic changes.

Common clinical manifestations are insomnia, headache, metabolic or hypoxic encephalopathy and cerebrovascular accidents, to less common features such as seizures, encephalitis, acute hemorrhagic necrotizing encephalopathy, ADEM, PRES like features, cerebral venous thrombosis and myelitis. Other common features involving the peripheral nervous system include, myalgia, anosmia, ageusia, vision loss and neuralgic pain. Rare but reported would be isolated cranial nerve palsies, Guillain-Barre syndrome, Miller-Fisher syndrome and others [10].

Radiologically, the most common occurrences were of acute and subacute infarcts (Figure 1). Other common findings included a spectrum of leukoencephalopathy, presence of micro hemorrhages, leptomeningeal contrast enhancement, cortical FLAIR signal abnormalities, and rarely is necrotizing encephalopathy [11].

Acute hemorrhagic necrotizing encephalopathy as a neurological complication in a patient with SARS-

CoV-2 infection was reported in a recent study [12]. Similarly, few studies have reported the occurrence of acute ischemic stroke in COVID-19 patients [13, 14].

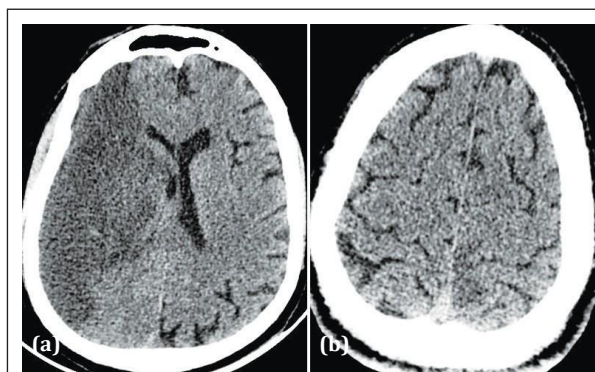
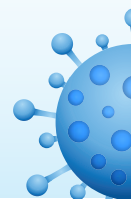


Figure 1: 60-year-old male patient with severe COVID pneumonia and left hemiparesis: (a) Axial non contrast CT of the brain shows hypodensity in the right cerebral hemisphere suggestive of right MCA territory infarction; (b) 42-year-old male patient with moderate COVID pneumonia and right hemiparesis – axial non contrast CT of the brain shows subtle hypodensity in the left parasagittal parietal cortex suggestive of ischemic changes.

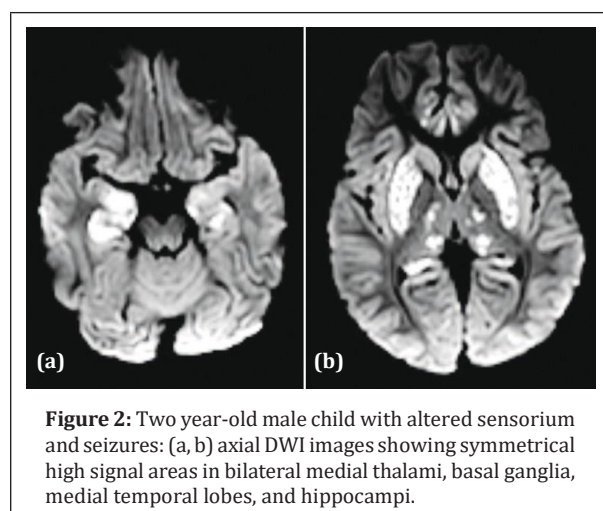
Cytokine storm syndrome (CSS) is a major complication in severe COVID-19 patients which can lead to acute cerebrovascular disease [15]. Further, high levels of D-dimer and thrombocytopenia in severe COVID-19 patients increases the risk of acute cerebrovascular events [16].

Viral encephalitis in COVID-19 patient scan manifest as altered mental status, abnormal behavior or speech, abnormal motor movement and focal neurological abnormalities such as flaccid paralysis, paresthesia, hemiparesis, or seizures [17]. Previously it was shown that corona virus nucleic acid was found in CSF of patients with SARS [18]. Relying on remarkable similarities between manifestations of these groups of viruses, a possibility for SARS-CoV-2 neuroinvasion should also be documented [19]. Other possible route of transmission of corona virus was found to be across the cribriform plate of the ethmoid bone and subsequently cause neuronal damage by interacting with ACE2 receptors. Additional symptoms, such as hyposmia or anosmia were found to be due to high expression of ACE-2 in nasal epithelial cells. 3D T2 FLAIR signal intensity involving olfactory bulb was greater in the patients with COVID-19 and neurologic symptoms.



Possibility of cerebrovascular endothelial rupture leading to bleeding and fatal complications was also mentioned [20]. Imaging of critically ill patients have shown microbleeds involving the corpus callosum, microbleeds in juxtacortical regions, gray-white matter interface and occasionally involving the middle cerebellar peduncles and cerebellum [21].

Acute hemorrhagic necrotizing encephalopathy on imaging presented as symmetric areas of hypoattenuation within the bilateral medial thalami on CT and hemorrhagic rim enhancing lesions within the bilateral thalami, medial temporal lobes, and sub insular regions on MR imaging [12]. Symmetric areas of diffusion restriction in bilateral medial thalami, basal ganglia, medial temporal lobes, and hippocampi without hemorrhagic transformation was seen in the present study (Figure 2).



Renal involvement

Renal dysfunction in COVID-19 disease appears to be multifactorial and secondary to sepsis, comorbidities, rhabdomyolysis, treatment-related interstitial nephritis, and altered immune response [22]. Significant co-expression of ACE2 and TMPRSSs genes in podocytes and proximal convoluted tubules which makes them a potential host for SARS-CoV-2 and resulting in glomerulopathy, acute tubular necrosis, and protein leakage in the Bowman's capsule [23, 24]. Various reports from China and USA have reported the occurrence of AKI in critically ill COVID-19 patients [25, 26]. Patients with both chronic kidney disease (CKD) and hypertension have an increased risk of severe COVID-19 infection [27].

CT images in patients with AKI showed reduced parenchymal density with perinephric fat stranding suggesting edema and inflammation (Figure 3). Such patients should be cautiously monitored and might require early therapeutic management to prevent further damage. Need for contrast-enhanced imaging (CT and MRI) in such patients should be avoided to prevent contrast induced nephropathy.



Figure 3: 56-year-old male patient with severe COVID pneumonia: Axial non contrast CT of the upper abdominal section shows mildly reduced renal parenchymal density with perinephric fat stranding (Arrow pointed away).

Gastrointestinal and abdominal manifestations

A significant number of patients with COVID-19 disease have presented with gastrointestinal symptoms. The overall incidence varies from 3-70% [28]. The presence of ACE-2 receptors in the enteric epithelial tissue presumed to result in gastrointestinal symptoms such as diarrhea, nausea, vomiting, and abdominal pain [29-31]. Many patients with COVID-19 disease have presented with isolated gastrointestinal manifestations without fever or respiratory symptoms [32]. There is excretion of viral particles in feces in up to 50% of COVID-19 patients and the stool samples remain positive for as much as 4 weeks [33]. This suggests a possibility of fecal-oral route of transmission.

Few studies have reported bowel abnormalities such as bowel wall thickening and findings of bowel ischemia (pneumatosis and portal venous gas) [34]. A 58-year-old male patient with COVID-19 pneumonia presented with acute abdomen and contrast CT of the abdomen showed findings of small bowel ischemia (Figure 4). Few isolated case reports have raised the suspicion that there may be an association between COVID-19 disease and acute pancreatitis (Figure 5).





Figure 4: 58-year-old male patient with COVID pneumonia: Axial contrast CT of the abdomen revealed mildly dilated small bowel loops with intramural air (arrow) and mild interloop free fluid.



Figure 5: 21-year-old female patient with COVID pneumonia: Axial non contrast CT of the abdomen revealed bulky pancreas with hypodense areas and peripancreatic inflammatory changes (Dengue serology was negative in this patient).

Low levels of ACE-2 receptors are found in cholangiocytes resulting in direct damage to biliary ducts [35]. Further, cytokine storm syndrome (CSS) and hypoxia associated metabolic derangements also result in liver injury [36]. Various investigational drugs currently used to treat COVID-19 result in drug-induced liver injury, particularly remdesivir and tocilizumab [37]. Wide ranges of other histopathologic changes are observed which include hepatic steatosis, portal fibrosis, lymphocytic infiltrates and ductular proliferation, lobular cholestasis, and acute liver-cell necrosis [38]. This warrants long term follow up of these patients with routine liver function tests.

Mild splenomegaly has been observed as an additional finding in patients with COVID-19 disease

during routine ultrasound of the abdomen and in the upper abdominal sections of the CT thorax (Figure 6). The cause appears to be non specific and similar to other viral infections [39]. Patients with severe COVID-19 infection can present with rare hyperinflammatory syndromes such as cytokine storm syndrome, secondary haemophagocytic lymphohistiocytosis (sHLH) or macrophage activation syndrome. Such patients can present with unremitting fever, cytopenias, hyperferritinaemia, and hepatosplenomegaly [40]. Few patients with COVID-19 infection presented with co-existent dengue fever. Such patients with chest symptoms should be evaluated for COVID-19 disease.

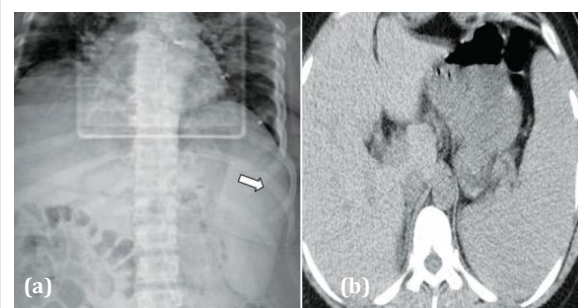
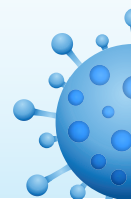


Figure 6: 42-year-old female patient with moderate severity COVID-19 pneumonia: (a) enlarged splenic shadow on scout image (arrow); (b) axial NCCT of the upper abdominal sections showing mildly enlarged spleen.

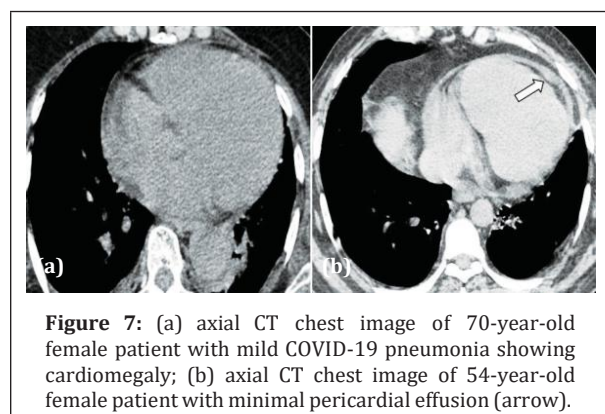
Cardiac complications

Significant higher expression of the ACE-2 in cardiac tissues such as cardiac myocytes, fibroblasts, endothelial cells, and smooth-muscle cells appears to be the likely cause of cardiovascular complications [41]. Most common manifestations include myocarditis, acute coronary syndromes (ACS), cardiomyopathy, acute cor pulmonale (ACP), arrhythmias, and cardiogenic shock [42]. Myocardial injury was indicated by increased levels of cardiac bio-markers such as cardiac troponin I (cTnI), creatine kinase (CK), α -hydroxybutyrate dehydrogenase (HBDB), and lactate dehydrogenase (LDH) [43]. Apart from myocardial ischemia, cardiac arrhythmias have been observed in COVID-19 patients without a previous history of cardiac diseases. These patients might remain asymptomatic or present with palpitations [42]. Most patients with arrhythmias show some type of ECG changes including sinus tachycardia, sinus bradycardia, QTc prolongation (often drug induced), torsades



de pointes and paroxysmal atrial fibrillation [44]. Routine electrocardiogram monitoring is needed in all critically ill patients and especially with a previous history of ischemic heart disease or cardiovascular risk factors. The mortality rate is found to be higher in patients with CVS comorbidities [45]. Cardiomegaly and pericardial effusion are the most common incidental cardiac imaging findings in patients with COVID-19 disease (Figure 7).

Long term follow up of these infected patients (cardiac biomarkers and echocardiogram) are needed to assess the changes in cardiac functional parameters.



Mediastinal complications

Mediastinal lymphadenopathy is not a typical imaging feature in COVID-19 disease as described in previous studies [5]. However, enlarged mediastinal nodes was a common finding in patients with more severe infection [46]. Lymphadenopathy could be due to secondary infections or reactive phenomenon to viral disease (Figure 8a).

Spontaneous pneumomediastinum is another rare mediastinal complication observed in COVID-19 patients. Various case reports have been described regarding development of spontaneous pneumothorax and pneumomediastinum in COVID-19 patients without assisted ventilation [47, 48]. The rupture of alveoli secondary to diffuse alveolar injury in patients with severe COVID-19 pneumonia could be the cause for spontaneous pneumomediastinum (Figure 8b). An increase in the intra-alveolar pressure results in the alveolar rupture and migration of free air into the mediastinum which is referred as Macklin effect [49].

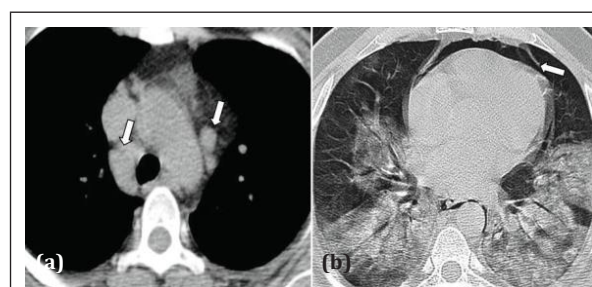


Figure 8: (a) 55-year-old male patient with mild COVID-19 pneumonia and enlarged mediastinal lymph nodes (arrows); (b) 36-year-old male patient with severe COVID-19 pneumonia complicated with pneumomediastinum (arrow).

Hematological manifestations

COVID-19 angiopathy or vasculopathy appears to be an emerging hematological complication in patients recovering from COVID-19 pneumonia. Elevated levels of D-dimer and fibrinogen are markers of COVID-19-associated vasculopathy [50]. Severe thromboinflammation results in hypercoagulability, endothelial damage, complement activation and other mechanisms which increase the risk of venous thromboembolism [51]. CT pulmonary angiography and ultrasound imaging can be used in patients with elevated levels of D-dimer and high suspicion of pulmonary thromboembolism (PTE) and deep vein thrombosis (DVT). The pulmonary involvement in COVID-19 pneumonia has been attributed to microvascular thrombosis [52]. Lymphopenia, neutrophilia and thrombocytopenia are other markers of COVID-19 infections [53].

Ocular and dermatological manifestations

Ocular involvement in COVID-19 patients is uncommon and has low prevalence [54]. The presentation is similar to follicular conjunctivitis with increased secretions, chemosis, ocular irritation, and foreign body sensation. RTPCR test with conjunctival swabs of patients with ocular symptoms have shown positive results suggestive of viral replication in the conjunctiva [55]. A rare case report of central retinal artery occlusion has been described which needs to be substantiated with further studies [56].

Dermatological manifestations are of less significance in COVID-19 patients and do not correlate with disease severity. Major cutaneous manifestations include maculopapular rash, papulovesicular rash, urticaria, painful acral red-purple papules, livedo reticularis lesions, and petechiae [57].



Others

Recent studies have shown high ACE2 receptor expression in the testicular cells might result in reproductive disorders through abnormal activation of ACE2 pathway [58]. Scrotal ultrasound in COVID-19 patients with testicular pain might be useful in the detection of the viral orchitis which is the most common manifestation.

Conclusion with future implications

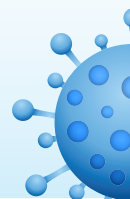
There is a substantial increase in the number of COVID-19 cases and associated extrapulmonary manifestations that need to be familiarized. The present study illustrates the incidence of neurological, renal, gastro-abdominal, hepato-biliary, cardiac, and mediastinal findings in COVID-19 patients. Further analysis of data from a larger patient cohort is necessary before the pandemic reaches a second peak. At present more attention is paid to the pulmonary manifestation of COVID-19 pneumonia. It is important for both clinicians and radiologists to understand and anticipate extrapulmonary complications in patients with COVID-19 disease to improve the clinical outcome.

Conflicts of interests

Authors declare no conflicts of interest.

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RESEARCH

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Spectrum of atypical pulmonary manifestations of COVID-19 on computed tomography

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Abstract

Background: The typical CT manifestations of COVID-19 pneumonia include ground-glass opacity (GGO) with or without consolidation and superimposed interlobular septal thickening. These are often rounded in morphology and frequently bilateral, multilobar, posterior, peripheral, and basilar in distribution. The various atypical CT features of COVID-19 are seldom described in the literature. The study aims to enumerate the atypical pulmonary CT features in patients with COVID-19 pneumonia in correlation with the disease severity.

Results: A total of 298 confirmed cases of COVID-19 pneumonia with positive reverse transcription polymerase chain reaction (RT-PCR) who underwent chest CT scans were retrospectively evaluated. The cohort included 234 (78.5%) men and 64 (21.5%) women and the mean age was 53.48 ± 15.74 years. The most common presenting symptoms were fever [$n = 197$ (66.1%)] and cough [$n = 139$ (46.6%)]. Out of 298 cases of COVID-19 pneumonia, 218 cases (73.1%) showed typical CT features while 63 cases (21.1%) showed atypical CT features with concurrent classical findings and the remaining 17 cases (5.8%) were normal. Among the atypical CT features, the most common was pulmonary cysts [$n = 27$ (9%)]. The other features in the order of frequency included pleural effusion [$n = 17$ (5.7%)], nodules [$n = 13$ (4.3%)], bull's eye/target sign [$n = 4$ (1.3%)], cavitation [$n = 3$ (1.0%)], spontaneous pneumothorax [$n = 2$ (0.6%)], hilar lymphadenopathy [$n = 2$ (0.6%)], spontaneous pneumo-mediastinum with subcutaneous emphysema [$n = 1$ (0.3%)], Halo sign [$n = 1$ (0.3%)], empyema [$n = 1$ (0.3%)] and necrotizing pneumonia with abscess [$n = 1$ (0.3%)].

Conclusion: CT imaging features of COVID-19 pneumonia while in a vast majority of cases is classical, atypical diverse patterns are also encountered. A comprehensive knowledge of various atypical presentations on imaging plays an important role in the early diagnosis and management of COVID-19.

Keywords: COVID-19 pneumonia, Atypical CT features, Pulmonary cysts, Bull's eye/target sign, Halo sign, Hilar lymphadenopathy, Necrotizing pneumonia

Background

Coronavirus disease 2019 (COVID-19) is caused by a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 is known to involve multiple organ systems with protean clinical and radiological manifestations, lungs being the most frequently involved [1].

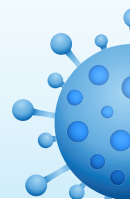
The imaging changes in COVID-19 pneumonia, though classical in a majority, a small subset of it can present with diverse pulmonary findings. Based on current literature, the typical imaging features of COVID-19 pneumonia on CT include bilateral, multilobar GGOs with/without consolidation and superimposed interlobar septal thickening [2, 3]. They show a peripheral, posterior and basilar distribution [2].

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Apart from anecdotal case reports, the various atypical CT features of COVID-19 are less clearly described. Anecdotal occurrence of atypical CT features has been reported till date. This study aims to enumerate the spectrum of atypical features and its incidence as observed at our institute in correlation with disease severity.

Methods

Study design and data collection

This was a retrospective observational study conducted during the period from 1 July till 31 October 2020. The study included reverse-transcriptase polymerase chain reaction (RT-PCR) confirmed 298 COVID-19 pneumonia patients who were admitted to the hospital and underwent chest HRCT scan. Images were evaluated using the institutional Picture Archiving and Communication Systems (PACS) database system to assess the various imaging features in COVID-19 pneumonia cases. This study was approved by the Institutional Ethics committee.

Selection criteria

Inclusion criteria

Reverse-transcriptase polymerase chain reaction (RT-PCR) confirmed COVID-19 pneumonia patients who underwent chest HRCT scans were considered.

Exclusion criteria

- Patients with negative RT-PCR results.
- Patients discharged to another facility during the course of illness.

CT imaging protocol

CT was performed using a 128-slice MDCT scanner (Ingenuity core 128 v3.5.7.25001; Philips healthcare). Patients were placed in a supine position with single breath hold. Scanning parameters were scan direction (cranio-caudally), tube voltage (120KV), tube current (250 mA), slice collimation (64×0.625 mm), width (0.625×0.625 mm), pitch (1), rotation time (0.5 s), and scan time (12.06 s). Images were reconstructed with a slice thickness of 0.5 or 1.5 mm and an interval of 0.5 or 1.5 mm, respectively.

CT imaging interpretation

The images were evaluated by two senior professors and a senior resident in radiology with experience of 17 years, 15 years, and 4 years, respectively. The evaluators independently assessed the CT features using both axial CT images and multiplanar reconstruction images. The scans were first assessed whether negative or positive for

Table 1 Age distribution of the cohort

Age (in years)	Total number (out of 298)	Percentage (%)
0–10	1	0.4
11–20	1	0.4
21–30	27	9
31–40	39	13
41–50	51	17.2
51–60	79	26.5
61–70	55	18.5
71–80	36	12
81–90	9	3

typical findings of COVID19 pneumonia (bilateral, multilobar, posterior peripheral ground glass opacities) as defined by the RSNA Consensus statement [4, 5]. Later the various atypical CT imaging features were noted. Severity was assessed using CT severity score (total score out of 25) and categorized into mild (score < 7), moderate (score 7–18) and severe (score > 18) as done by Saeed G A et al. [6]. The two senior professors were blinded to the outcome of the cases.

Statistical analysis

The analysis was performed using SPSS 21.0. Descriptive statistics of patients' demographics and clinical results were reported as numbers and relative frequencies. The mean differences between the groups with typical and

Table 2 Presenting symptoms of patients with COVID-19 pneumonia

Symptom	Total number	Percentage (out of 298)
Fever	197	66.1
Cough	139	46.6
Dyspnea	83	27.8
Generalized weakness	32	10.7
Myalgia	29	9.7
Hemoptysis	2	0.6
URTI symptoms	18	6.0
Diarrhea	16	5.3
Vomiting	8	2.6
Easy fatigability	33	11.0
Palpitation	1	0.3
Pain abdomen	8	2.6
Chest pain	12	4.0
Headache	10	3.5
Loss of smell/anosmia	5	1.6
Loss of taste	2	0.6
Hemiparesis	3	1.0
Loss of appetite	16	5.3



Table 3 Comorbidities/risk factors of patients with COVID-19 pneumonia

Co-morbidities	Total number	Percentage (out of 298)
Diabetes	100	33.5
Hypertension	94	31.5
Cardiovascular disease	23	7.7
Cerebrovascular disease	4	1.3
Chronic kidney disease	5	1.6
Hypothyroidism	9	3.0
Chronic pulmonary disease	14	4.6
Immunocompromised	2	0.6
Others	3	1.0

atypical CT features were subjected to Mann–Whitney *U* test to check for the statistical significance. The Spearman correlation coefficient test was used to investigate the correlation between the groups with typical/atypical CT features and mortality and also was used to investigate the correlation between the age and CT severity score among the patients with atypical CT features.

Results

A total of 298 reverse-transcriptase polymerase chain reaction (RT-PCR) confirmed COVID-19 pneumonia patients admitted between 1 July and 31 October 2020 were retrospectively evaluated. The demographics pertaining to age, gender, presenting symptoms, presence of comorbidities/risk factors, CT severity score, and disease outcome (alive or died) are as below.

The mean age in our cohort was 53.48 ± 15.74 years [range 9–90 years]. The age was further classified into 9 groups: (0–10), (11–20), (21–30), (31–40), (41–50), (51–60), (61–70), (71–80), and (81–90) as depicted in the Table 1. The age group (51–60) had highest cases with total of 79 cases (26.5%) There was predilection for males 234 (78.5%) when compared to female 64 (21.5%).

The most common presenting symptoms were fever [$n = 197$ (66.1%)] and cough [$n = 139$ (46.6%)]. Other symptoms were dyspnea, generalized weakness, myalgia and others with frequencies as depicted in the Table 2.

The comorbidities/risk factors considered were hypertension, diabetes mellitus, cerebrovascular diseases, and others as depicted in the Table 3. Comorbidities/risk factors were found in 161/298 patients (54.0%). The most common associations were diabetes mellitus [$n = 100$ (33.5%)] and hypertension [$n = 94$ (31.5%)].

Out of 298 cases of COVID-19 pneumonia, 218 cases (73.1%) showed typical CT features while 63 cases (21.1%) showed atypical CT features with concurrent classical findings and the remaining 17 cases (5.8%) were normal. Among the atypical CT imaging features, pulmonary cysts were the most common feature in our study. Other various atypical imaging features with their incidences in our study are as depicted in the Table 4.

In our cohort, the pulmonary cysts on HRCT were well defined, thin walled (2–4 mm) and of size < 2.5 cm. The most common pattern of distribution of pulmonary cysts was peripheral lung distribution [$n = 23$ (85.2%)]. Other patterns were random distribution [$n = 3$ (11.1%)] and perihilar distribution [$n = 1$ (3.7%)]. They showed lower lobe predominance ($n = 15$) when compared to upper lobe ($n = 9$) and middle lobe ($n = 2$).

The nodules on HRCT showed peripheral subpleural distribution [$n = 12$]. Only one case showed centrilobular distribution with tree in bud pattern. Both solid ($n = 6$) and GGO ($n = 7$) nodules were equally seen. No difference in the lobar predominance [upper lobe ($n = 6$) and lower lobe ($n = 7$)].

Out of 17 cases of pleural effusion, 13 cases showed bilateral effusion. A total of 15 cases showed mild effusion and two showed moderate effusion. In 10 cases, there was no presence of other co-existent diseases while 7 cases had co-existent diseases.

Table 4 Incidences of the atypical CT findings of COVID-19 among the study group

SL no.	Atypical CT imaging features	Number of cases	Percentage (out of 298 cases)
1.	Pulmonary cysts	27	9.0
2.	Pleural effusion	17	5.7
3.	Nodules	13	4.3
4.	Bull's eye/target sign	4	1.3
5.	Cavitation	3	1.0
6.	Spontaneous pneumothorax	2	0.6
7.	Hilar lymphadenopathy	2	0.6
8.	Spontaneous pneumo-mediastinum, subcutaneous emphysema	1	0.3
9.	Halo sign	1	0.3
10.	Empyema	1	0.3
11.	Necrotizing pneumonia with abscess	1	0.3

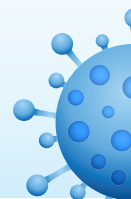


Table 5 Atypical features of COVID-19 cases and their CT severity score

CT severity score (out of 25)	Total number(out of 63)	Percentage (%)
Mild (< 7)	26	41.26
Moderate (8–17)	25	39.68
Severe (> 18)	12	19.04

All four cases with the bull's eye sign/target sign were all peripherally located in the lower lobes.

All cases with cavitation ($n = 3$) showed peripheral distribution with two cases involving the lower lobe and one in the upper lobe.

Two cases showed bilaterally enlarged hilar group of lymph nodes with short axis diameter of > 10 mm with more on right side compared to left. Loss of hilar fat pad was noted in both the case.

Correlation between atypical CT imaging features with age and severity

Significant positive correlation between CT severity score among atypical group and age was observed in our study ($\rho = 0.343$ and $p = 0.006$), indicating that with increase in age there was increase in the CT severity score and also of atypical CT features. Out of 63 patients with atypical features, CT severity score were as depicted in Table 5.

However, there was no statistically significant correlation ($p > 0.05$) between typical or atypical CT features and the severity of the disease (CT severity score).

In terms of clinical outcome, 289 patients (97%) were discharged after clinical improvement and 9 patients (3%) died in hospital at the time of the study. Out of 9 demises, CT severity was of moderate (score 8–17) and

severe category (score > 18). All cases were aged above the mean of 53.4 years and majority was associated with comorbidities ($n = 8$). Males [$n = 7(78\%)$] were affected more compared to females [$n = 2(22\%)$]. However, no statistically significant association between typical or atypical CT features and mortality was noted ($p > 0.05$).

Discussion

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This has rapidly resulted in a worldwide pandemic with significant increase in morbidity and mortality [1]. The imaging changes in COVID-19 pneumonia are diverse with the various atypical CT features being less clearly described. The study conducted herein explains the atypical CT features in COVID-19 pneumonia.

In our study, the most common presenting symptoms were fever and cough consistent with the study by Shi H et al. [7]. There was predilection towards males (78.5%) as seen in the study done by Huang C et al. [8]. The other predisposing conditions in our study were elderly patients (mean 53.4 years) and comorbidities which are consistent with the study by Shi H et al. [7]. The mortality rate in our study was 3%. All the deaths occurred in elderly patients who had comorbidities, consistent with

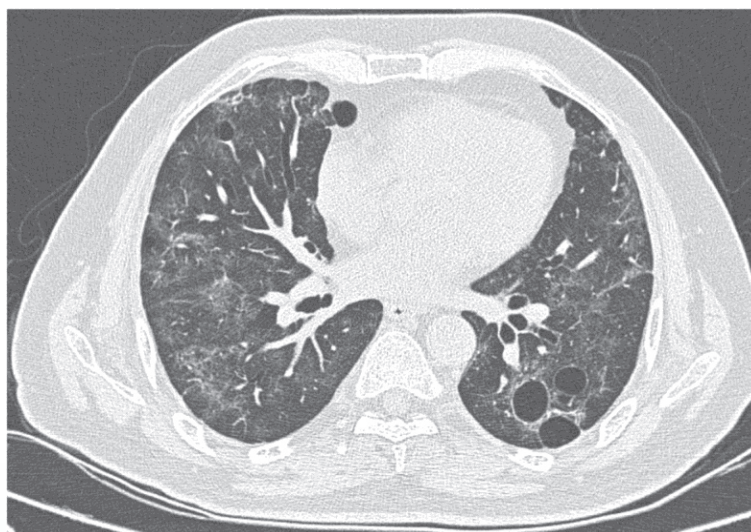


Fig. 1 Axial CT thorax of a 60-year-old COVID pneumonia patient showing multiple thin-walled air-filled cystic lesion in the bilateral lower lobes. Areas of GGOs with interlobular septal thickening are also seen



previous reports (8) and had moderate-severe CT severity score. Hence, advanced age, male sex, presence of comorbidities and higher CT severity score might be risk factors for poor prognosis.

Based on current literature, the typical imaging features of COVID-19 pneumonia on CT include bilateral, multilobar GGOs with/without consolidation, and superimposed interlobar septal thickening [2, 3]. They show a peripheral, posterior, and basilar distribution [2]. In our study, majority of the patients (73.1%) showed typical CT features and only 21.1% patients showed atypical CT features with concurrent above classical findings. Among the atypical CT features, the most common was pulmonary cysts. The other features in the order of

frequency included pleural effusion, nodules, bull's eye/target sign, cavitation, spontaneous pneumothorax, hilar lymphadenopathy, spontaneous pneumo-mediastinum with subcutaneous emphysema, halo sign, empyema, and necrotizing pneumonia with abscess.

The incidence of pulmonary cysts in our study was 9.0% which is consistent with the study by Shi H et al. [7]. Recent studies speculate that the pulmonary cystic change in COVID-19 might be secondary to ischemic parenchymal damage, lung fibrosis and low lung compliance [9]. Another explanation is blockage of the bronchioles by mucus and mucus plugs followed by the over-inflation of the alveoli and resultant rupturing of the alveolar septum with subsequent formation of small cysts

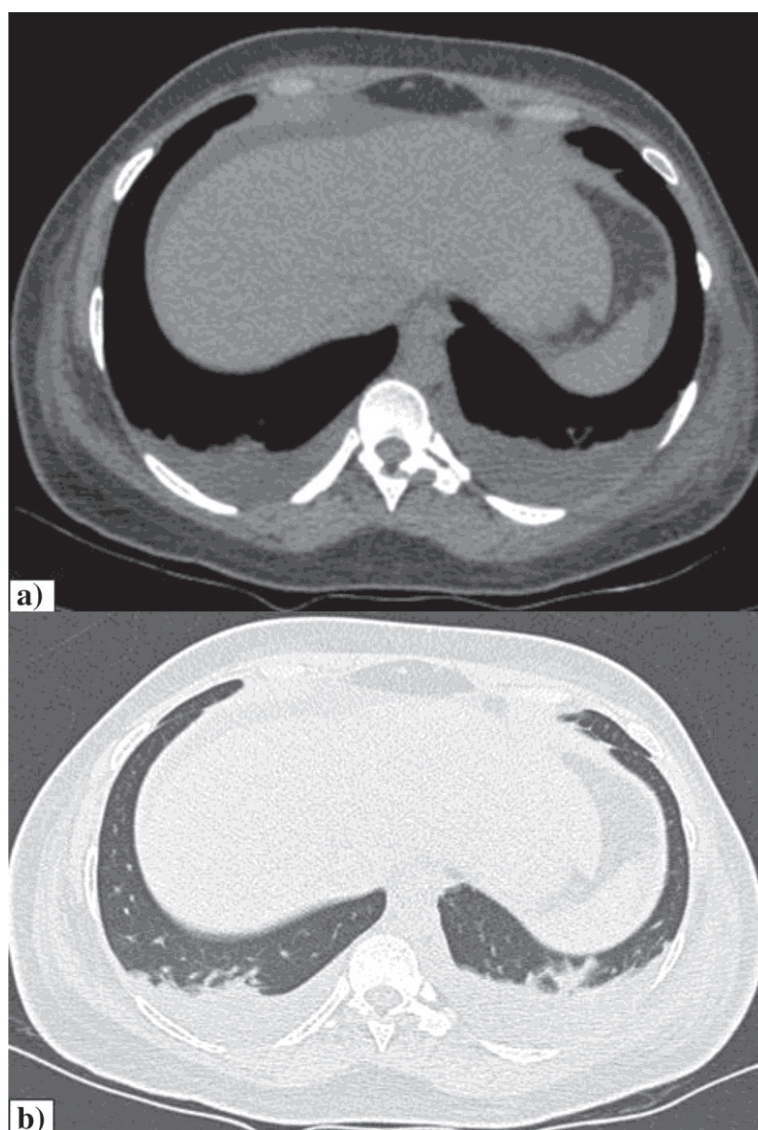
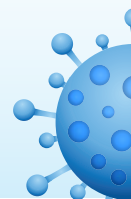


Fig. 2 Pleural effusion. a, b Axial CT thorax (mediastinal window and lung window) of a 38-year-old COVID pneumonia patient showing bilateral pleural effusion with underlying sub-segmental collapse



[10]. None of the patients in our study were on mechanical ventilation and hence ruling out barotrauma induced cystic changes [9]. The peripheral subpleural cysts are prone to rupture causing pneumothorax. Hence, in COVID-19 pneumonia, prominent identification of pulmonary cysts and close monitoring for complications are required. Figure 1 shows pulmonary cysts in a case of COVID-19 pneumonia.

The incidence of pleural effusion in our study was 5.7%. However the incidence of pleural effusion in COVID-19 has been reported to be varying as per the available literature [11]. According to the study by Shi et al., the prevalence of pleural effusion varies depending on the stage of the disease, with a reported prevalence of 13% in the third week after onset of symptoms [7]. Pleural effusion may also be predictive of worse prognosis [11]. The presence or absence of underlying medical conditions, study setting, disease stage, and concurrent superimposed bacterial pneumonia are to be considered in order to comment on the prevalence and etiology of pleural effusion in COVID-19 infection [12]. The presence of effusion in cases with no concurrent comorbidities can possibly be attributed to COVID-19 infection or superadded bacterial infection. Figure 2 shows bilateral pleural effusion in a case of COVID-19 pneumonia.

The bull's eye/target sign consists of central ground glass opacity surrounded by an inner ring of air and an outer ring of ground glass as shown in Fig. 3. It is presumed that bull's eye sign may be a variant of the reverse halo sign [13]. In our study, bull's eye sign accounted to 1.3% of the cases. Only few case reports on COVID-19 with bull's eye sign has been made in the literature [13–

15]. It has been theorized that they represent regions of organizing pneumonia, with perilobular involvement and a tendency to be located peripherally within the lung parenchyma [13]. The bull's eye sign/target sign in the presented cases likewise were all peripherally located in the lower lobes [13].

Lung cavitation due to COVID-19 pneumonia is an uncommon finding which usually is seen in the late stage [16, 17]. The incidence in our study was 1%. There are few reports of intrapulmonary cavities of COVID-19 infection [11, 16, 18, 19]. However majority of other reviews showed no cavitation in their study [7, 20–23]. The cavitation may be related to diffuse alveolar damage, intra-alveolar hemorrhage, and necrosis of parenchymal cells based on prior autopsy reports [24, 25]. Common causes of cavitory lung lesions must be investigated appropriately in all patients [26]. In our study, there was no laboratory evidence supporting bacterial infections. Hence, the possibility of COVID-19 independently resulting in cavitation is to be considered. Close monitoring is required for complications like hemorrhage within the cavity, rupture of peripheral cavity resulting in pneumothorax, and superadded bacterial infection resulting in an abscess. Figure 4 shows pulmonary cavity with clots in a case who presented with hemoptysis.

Spontaneous pneumomediastinum (SPM) refers to the presence of air in the mediastinum occurring in the absence of traumatic or an iatrogenic origin [2, 27]. In current limited research, only few case reports of SPM in COVID-19 have been made [2, 28–30]. The incidence of SPM in our study was 0.3% and isolated spontaneous pneumothorax was 0.6%. Chen N et al. showed

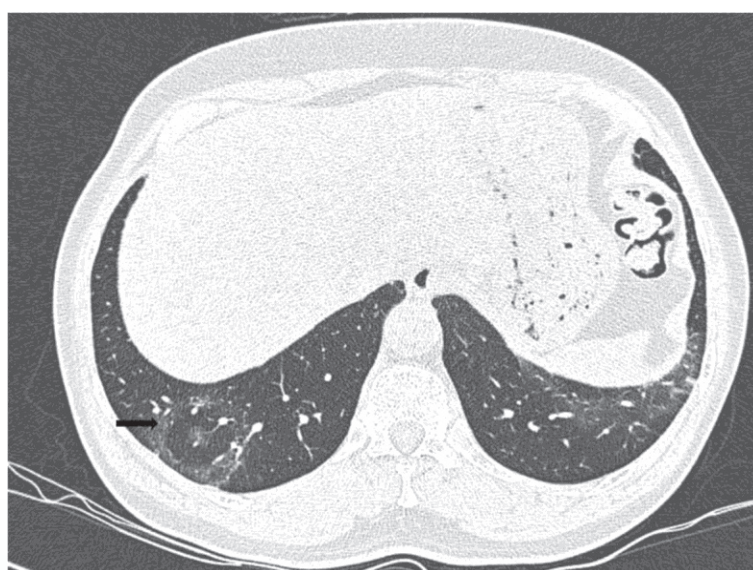


Fig. 3 Bull's eye sign. Axial CT thorax of a 55-year-old COVID pneumonia patient showing central ground glass opacity surrounded by an inner ring of air and an outer ring of ground glass in the right lower lobe



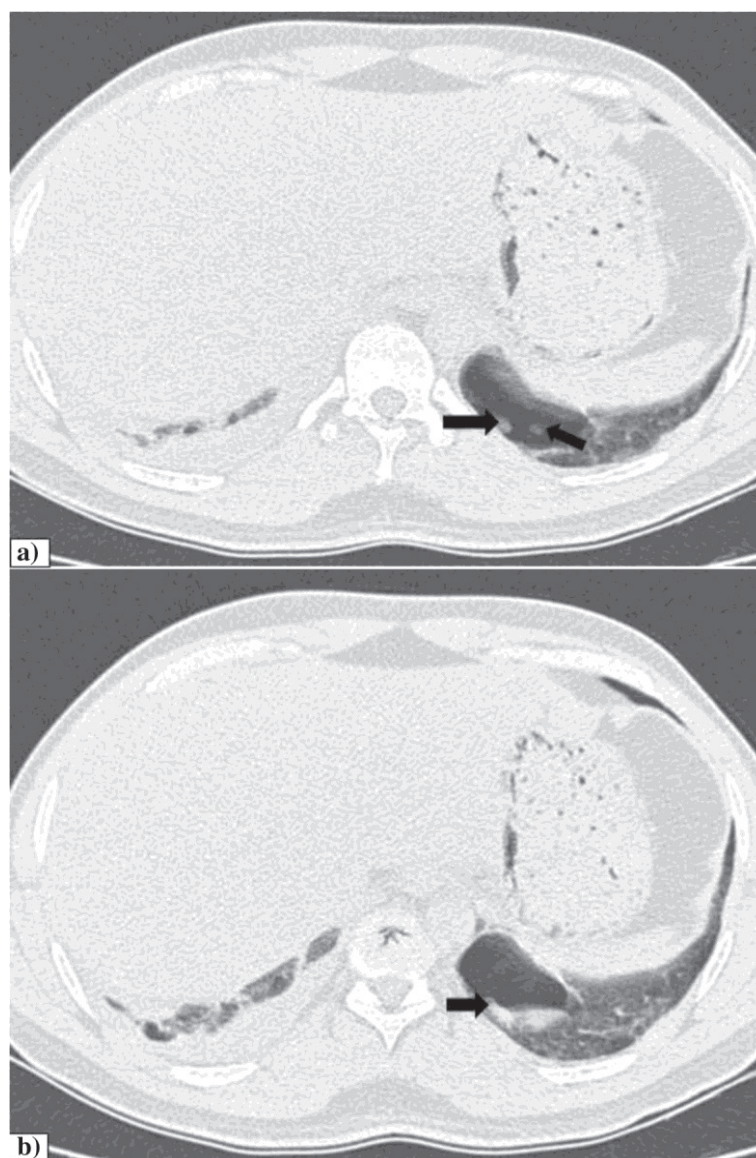
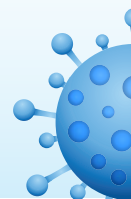


Fig. 4 Pulmonary cavity with clots. a, b Contiguous sections of axial CT thorax of a 35-years-old COVID pneumonia patient who presented with hemoptysis, showing thin wall cavity in the posterior basal segment of left lobe with soft tissue component of hemorrhagic density as indicated by the arrows. Right pleural effusion is also seen

incidence of isolated spontaneous pneumothorax of 1% in COVID-19 patients [20]. It is believed that the possible causes of SPM in COVID-19 were similar to those in SARS showing severe diffuse alveolar damage. This diffuse alveolar damage results in alveolar rupture which can be further precipitated by high interalveolar pressure caused by factors like artificial ventilation, coughing or straining. This results in air migration into the mediastinum through the Macklin effect [2, 31–33]. The SPM can lead to other complications such as pneumothorax, extensive subcutaneous emphysema, and an uncommon complication of lung infections [2]. In our study, none of

the cases were mechanically ventilated at the time of initial CT imaging. One case with emphysematous changes showed SPM with pneumothorax and extensive subcutaneous emphysema as shown in the Fig. 5, which we believe would have occurred due to progression of pre-existing lung lesions resulting in rupture of subpleural bulla or secondary to alveolar rupture as described above. Isolated spontaneous pneumothorax in our study might be secondary to rupture of subpleural pulmonary cysts or due to alveolar rupture.

The halo sign represents area of consolidation/pulmonary nodule/mass surrounded by ground-glass



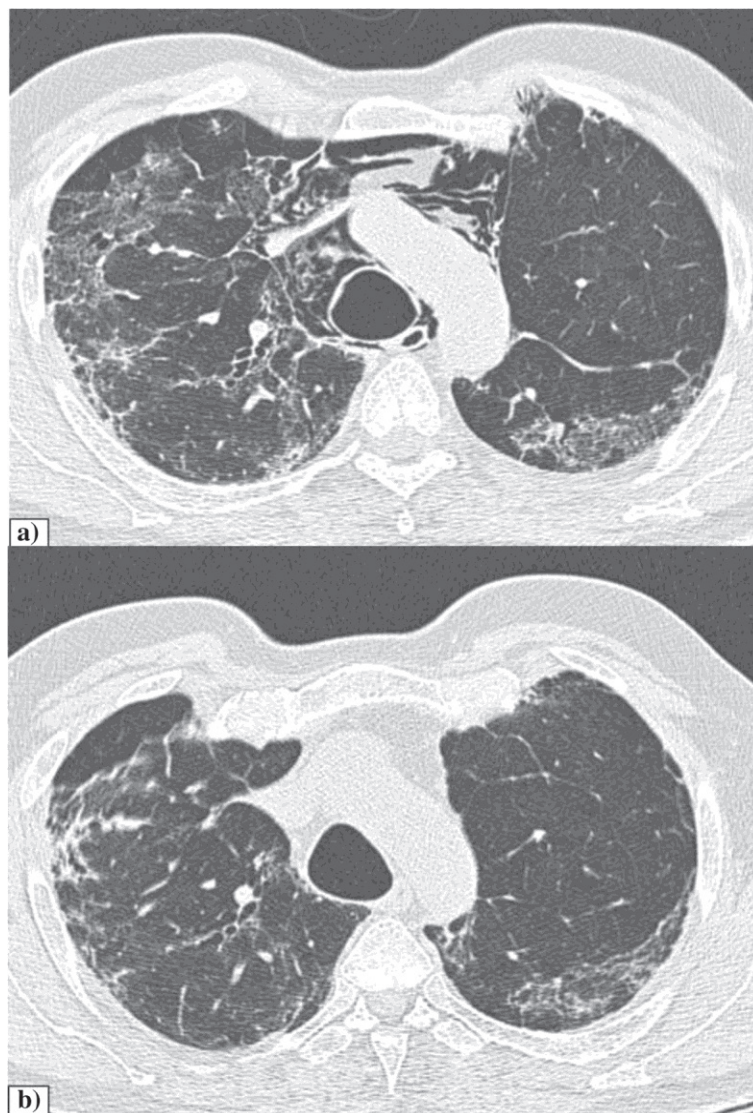


Fig. 5 Spontaneous pneumomediastinum. a Axial CT thorax of a 58-year-old COVID pneumonia patient showing pneumomediastinum in the pre-vascular space and around trachea and esophagus. Visualized lung shows peripheral GGOs with interlobular septal thickening. b Complete resolution of pneumo-mediastinum after 10 days

opacity [34–36] as shown in the Fig. 6. The incidence of halo sign in our study was 0.3%. In current limited research, only few cases reports on the halo sign has been made in COVID-19 [11, 37, 38]. Based on the pathological findings as seen in some recent studies, extensive thrombotic damage of the pulmonary microcirculation can explain the “halo sign” of consolidations [34].

The incidence of hilar lymphadenopathy in our study was 0.6%. In the available current literature, only one case report with hilar lymphadenopathy has been reported in COVID-19 [39]. Few studies showed no presence of hilar lymphadenopathy in COVID-19 [21, 40]. Thoracic lymphadenopathy includes hilar and mediastinal group of lymph nodes. Mediastinal

lymphadenopathy previously thought to be an atypical feature has been redefined as “not-atypical” feature of COVID-19 [7, 41]. However, hilar lymphadenopathy which is usually associated with fungal infections, mycobacterial infections, and sarcoidosis are seldom seen in COVID pneumonia [39]. Histopathological correlation was unavailable for our cases. Hence, bacterial or fungal co-infection cannot be ruled. Follow-up imaging is to be done to evaluate the persistence or resolution of hilar lymphadenopathy and is required to establish their clinical importance.

In our study, the incidence of pulmonary nodules was 4.3%. The reported incidence of nodules in COVID-19 has been found to be varying, 3 ~ 13% as per the



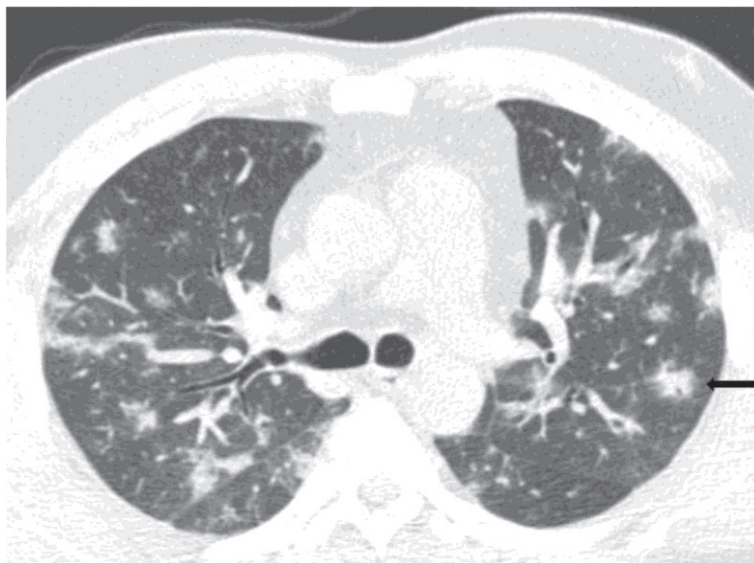


Fig. 6 Halo sign. Axial CT thorax of a 40-year-old COVID pneumonia patient showing multiple bilateral patchy consolidations with surrounding ground-glass opacities as indicated by the arrow

available literature [42, 43]. The relation between COVID-19 and nodules are not fully understood. Further studies are required to know whether these are incidental nodules or atypical manifestation of COVID-19 pneumonia. Figure 7 shows a case with GGO nodule.

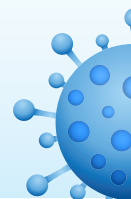
Empyema has significant clinical morbidity [44]. In our study, a case presented with loculated hydropneumothorax as shown in the Fig. 8. Later, pus-like pleural fluid was aspirated and sent for analysis which showed elevated glucose, protein, and chlorides with predominant

neutrophils (90%). This confirms the superadded bacterial infection in COVID-19 pneumonia resulting in empyema. Isolated empyema in COVID-19 is seldom reported in the literature.

Necrotizing pneumonia is a severe complication of lung infection characterized by necrosis and liquefaction of lung parenchyma, likely secondary to ischemia caused by thrombosis of intrapulmonary vessels [45]. In viral pneumonias, necrotizing processes with development of cavities and air-fluid level in the initial



Fig. 7 GGO nodule. Axial CT thorax of a 35-year-old COVID pneumonia patient showing small solitary GGO nodule in the left upper lobe as indicated by the arrow



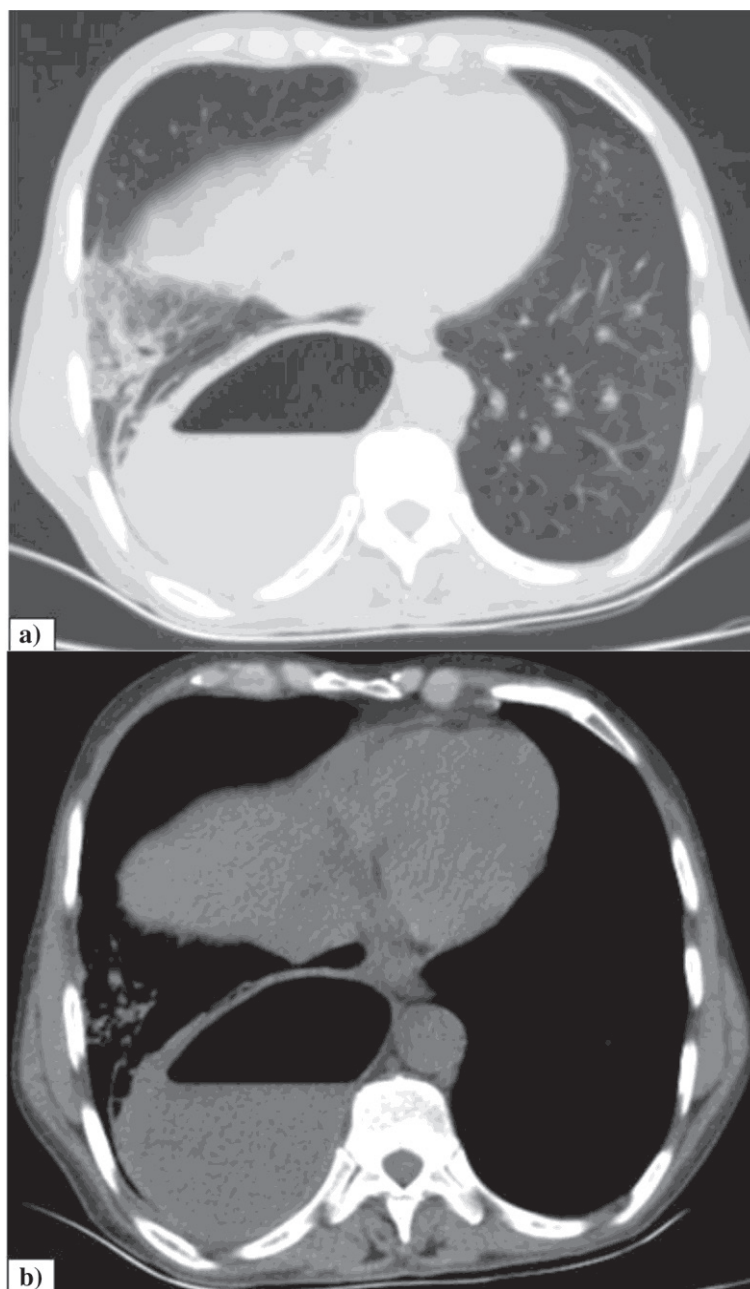


Fig. 8 Empyema. a, b Axial CT thorax (lung window and mediastinal window) of a 63-year-old COVID pneumonia patient showing right sided loculated empyema. Adjacent areas of consolidation are also seen

areas of consolidation have been described before in the literature [46]. Similarly, COVID-19 which causes small vessel microthrombi and severe dysregulation of the host immune reaction can result in necrotizing pneumonia. Although bacterial and fungal lung abscesses are known to occur in COVID-19 in up to 11% and 3%, respectively, which were presumed to have formed after hospital admission [47]. Our study showed an incidence of only 0.3%. This discrepancy

might be due to the differences in demographic features and hospital care. Figure 9 shows a case of necrotizing pneumonia with secondary cavitation and abscess formation.

Conclusion

During the course of the pandemic, much of the literature published describes the classical imaging features encountered in COVID-19, with anecdotal references



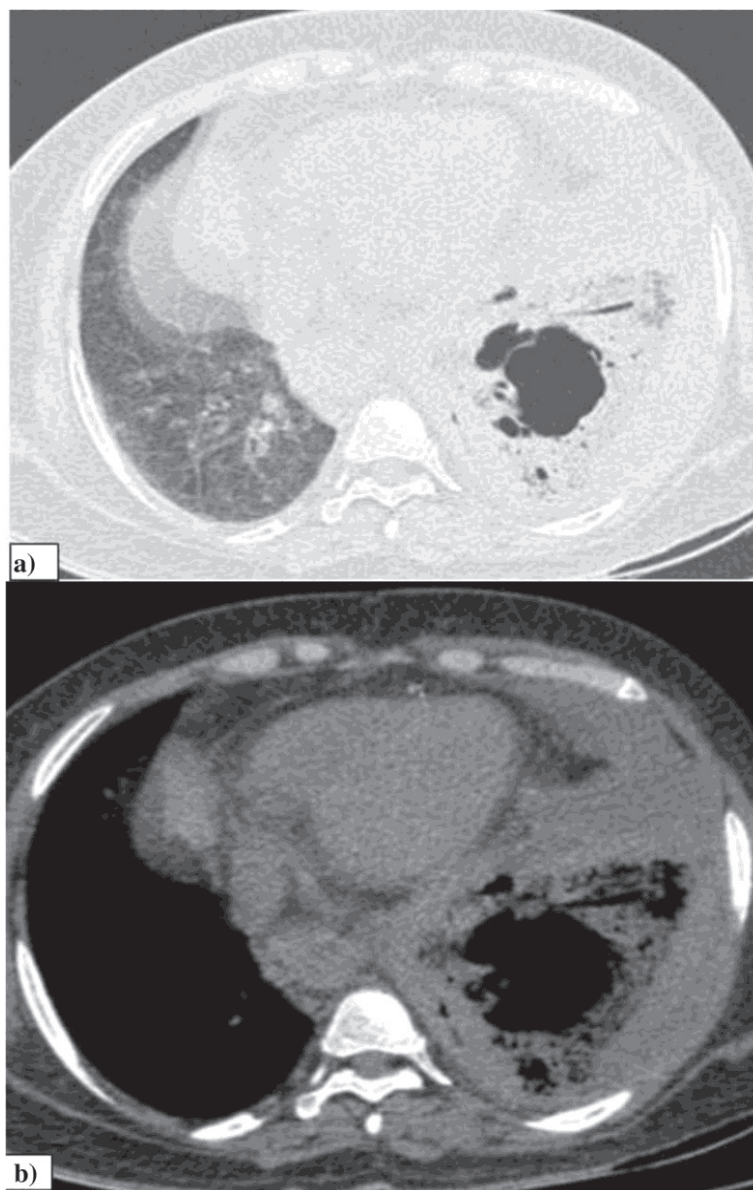


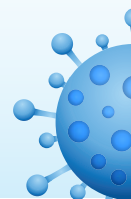
Fig. 9 Necrotizing pneumonia. a, b Axial CT thorax (lung window and mediastinal window) of a 51-year-old COVID pneumonia patient areas of cavitation in the background of consolidation in the left lower lobe. Left pleural effusion also noted

made to the atypical CT imaging features. A small subset of cases with COVID-19 pneumonia show diverse imaging manifestations, which if ignorant can confound the clinical approach to the patient leading to misdiagnosis. The present study aimed not only to illustrate the various atypical CT features in COVID-19 pneumonia but also correlated with disease severity. The atypical features observed includes pulmonary cystic changes, pleural effusion, nodules, bull's eye/target sign, cavitation, halo sign, hilar lymphadenopathy, spontaneous pneumothorax, spontaneous pneumo-mediastinum, empyema and necrotizing pneumonia with abscess.

Significant positive correlation between CT severity score among atypical group and age was observed in our study indicating that with increase in age there was increase in the CT severity score and also of atypical CT features. Thus, a comprehensive knowledge of these atypical pulmonary presentations and its complications on imaging plays an important role in the early diagnosis and management of COVID-19.

Abbreviations

CT: Computed tomography; Covid-19: Coronavirus disease 2019; GGO: Ground glass opacity; RT-PCR: Reverse-transcriptase polymerase Chain reaction; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2;



PACS: Picture Archiving and Communication Systems; HRCT: High-resolution computed tomography; MDCCT: Multidetector computed tomography; SPM: Spontaneous pneumo-mediastinum

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Authors' contributions

Dr BG—study conception and design, analysis, and interpretation of data, draft manuscript preparation. Dr SDK—study conception and design, analysis, and interpretation of data. Dr RH—supervision of the project, analysis, and interpretation of data. Dr SS—draft manuscript preparation. Dr AH—data collection. TG—data collection. All authors discussed the results and contributed to the final manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to privacy of the study participants.

Declarations

Ethics approval and consent to participate

This study is approved by the Ethics committee of the JSS Academy of Higher Education and Research, Mysore, Karnataka, India. Only anonymous patient details were used for data collection and analysis. No interventions were done. The Institutional Ethics committee's reference number—JSSMC/IEC/231220/04 NCT/2020-21 dated on 24 December 2020.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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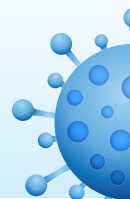
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REVIEW ARTICLE**COVID-19 Induced Cytokine Storm and the Impact of Obesity and Vitamin D Deficiency***Shobha Chikkavaddaragudi Ramachandra¹, Akila Prashant¹, Prashant Vishwanath^{1*}**¹Department of Biochemistry, Center of Excellence in Molecular Biology and Regenerative Medicine, JSS Medical College, JSS Academy of Higher Education & Research, Mysuru-570017 (Karnataka) India*

Abstract:

Recent studies on Coronavirus Disease 2019 (COVID-19) have shown that obesity and vitamin D deficiency increase the risk of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection and its complications. The levels of cytokines are increased in SARS-CoV-2 infection, obesity, and vitamin D deficiency aggravating the complications related to COVID-19. The Angiotensin-converting Enzyme 2 (ACE2), through which SARS-CoV-2 enters the host cell, is highly expressed in adipose tissue showing the vulnerability to the infection. In this review we have explained how obese individuals are more prone and contagious than lean to COVID-19, the role of adipose tissue as a reservoir of infection, vitamin D sequestration and deficiency in obese, and its association with COVID-19 and the combined release of cytokines in obesity, vitamin D deficiency and SARS-CoV-2 infection leading to cytokine storm both locally and systemically, hence leading to multi-organ failure in elderly and younger generations.

Keywords: COVID-19, SARS-CoV-2, Obesity, Vitamin D, Cytokines, ACE2, Cytokine Storm.

Introduction:

The risk of developing Coronavirus Disease 2019 (COVID-19) and its complications are common in

people with an impaired immune response or increased pro-inflammatory response. The low-grade chronic systemic inflammation is seen in people with overweight, obesity, and Vitamin D deficiency [1]. The cytokine storm leading to multiorgan failure seen in COVID-19 may get exacerbated by the pro-inflammatory cytokine seen in obesity and Vitamin D deficiency. Obese individuals are more contagious than lean leading to an increased rate of morbidity and mortality [2]. The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) enters the host cell through Angiotensin-Converting Enzyme 2 (ACE2), zinc-containing metalloenzyme, that is highly expressed in adipose tissue showing susceptibility to the infection. Calcitriol, the vitamin D agonist modulates the expression of members of Renin-Angiotensin-Aldosterone Systems (RAAS) such as ACE2 in lung tissue, protects from a lung injury, and shows that vitamin D deficiency acts as a pathogenic factor in COVID-19. Through this review, we have tried to explain how obesity and vitamin D deficiency in younger generations may act as a contributing factor in developing COVID-19 and its complications like cytokine storm leading to multiorgan failure.



COVID-19:

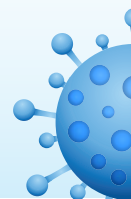
COVID-19 is an infectious disease caused by a newly discovered SARS-CoV-2. It was first reported in Wuhan, Hubei province of China in late December 2019, sequenced and isolated by January 2020 [3], and pandemic was declared in the mid of March 2020 by the World Health Organization (WHO) [4]. As of 15th March 2021, more than 119,220,681 cases have been reported globally, resulting in more than 2,642,826 deaths [5]. In India, 11,359,048 cases were reported positive with 158,607 deaths [6].

SARS-CoV-2 enters the host cell via ACE2 which is abundantly present in type 2 alveolar cells of the lungs. The surface glycoprotein present on the virus called spike attaches to the enzyme ACE2 and gains access to the host cell [7]. The entry into the cell may occur either by endocytosis or by proteolytic cleavage of the receptor. The coronavirus primarily spreads by close contact via small respiratory droplets produced during sneezing, coughing and talking. The virus primarily infects the upper respiratory tract leading to symptoms like cough, shortness of breath or difficulty in breathing, fever, chills, sore throat within 2-14 days after exposure and the disease may progress to pneumonia, multi-organ failure, and death in some. Elderly people and people with any underlying medical illness like lung disease, cardiovascular disease, diabetes, chronic kidney or liver disease, immunocompromised people, over-fat (overweight and obese) individuals, and vitamin D deficiency states are at increased risk of developing COVID-19 [8-9].

Burden of Obesity and COVID-19:

In 2016, as estimated by WHO, nearly 650 million

adults aged 18 years and above along with 340 million children and adolescents were reported to be obese globally. In India, 3.9% of adults were reported to be obese in the same year [10]. Increased calorie intake and decreased physical activity are the major factors for increasing the prevalence of obesity. For Asians, the cut-offs of $\geq 23.0\text{kg/m}^2$ and $\geq 25.0\text{kg/m}^2$ are defined as overweight and obesity respectively that are lower than WHO criteria due to tendency towards abdominal obesity and associated morbidities [11-12]. An ongoing study conducted by Sir Gangaram Hospital's Institute of Minimal Access, Metabolic and Bariatric Surgery, and the Department of Internal Medicine and Infectious Disease in 1000 patients who developed COVID-19, have shown that almost half of the patients in ICU are obese with less than 50 years of age [13]. A study conducted at COVID-19 ICU, at university hospitals at Johns Hopkins, New York University, University of Cincinnati, University of Washington, Florida Health, and the University of Pennsylvania showed an inverse correlation between age and Body Mass Index (BMI). The younger individuals admitted had a median BMI of 29.3 kg/m^2 , 25% of individuals had a BMI of less than 26 kg/m^2 , and 25% exceeding a BMI of 34.7 kg/m^2 . Hence it was concluded that not only the older generations, but COVID-19 also affects the younger population with a high prevalence of obesity [14]. Another retrospective analysis by Peng *et al.* showed that among the SARS-CoV-2 infected patients, the median BMI of the critical group was 25.5 kg/m^2 which was significantly higher than that of the general group with a median



BMI of 22.0 kg/m². Patients further were divided as non-survivors and survivors. 88.2% of patients among the non-survivors had a BMI > 25 kg/m² which was significantly higher compared to survivors (18.9%). Hence, it was concluded that obesity may be an aggravating factor for the development of complications and death from COVID-19 infection [15]. Table 1 depicts few other studies demonstrating the fact that obesity and overweight aggravate SARS-CoV-2 infection

[16-24]. These studies highlighted the fact that overweight and obesity may play an important role in the prognosis of SARS-CoV-2 infection not only in the elderly but also in the younger population.

Obesity, Adipocytes and Inflammation:

Well balance between calorie consumption and energy expenditure should be maintained for healthy weight and BMI. Any imbalance leads to the storage of intracellular triglyceride in

Table 1: Global Status of Obesity and COVID 19

Study conducted in	Type of study and number of participants	Results
Italy [16]	Retrospective cohort study of 482 patients	BMI ≥ 30 kg/m ² & BMI ≥ 35 kg/m ² increase the risk of severe illness & risk of death respectively
New York [17]	Retrospective study of 200 patients	Severe obesity, higher age, and males were associated independently with mortality of COVID-19
Italy [18]	Prospective cohort study of 233 patients	Obesity, older age, and severe illness are the associated factors to increase the risk of morbidity in hospitalized COVID-19 patients
New York [19]	Retrospective study of 3,406 patients	Younger patients younger than 50 years, who were hospitalized with severe obesity, are at increased risk to die of COVID-19.
China [20]	Retrospective study of 383 patients	Obese patients are prone to progress to severe COVID-19
Chicago [21]	Retrospective study of 238 patients	Among the inpatients with COVID-19, obesity is a major predictor of mortality after adjusting for gender, age, and other comorbidities
United States [22]	Retrospective cohort of 103 patients	COVID-19 with severe obesity was associated with ICU admission, and required aggressive treatment.
Spain [23]	Retrospective cohort of 2226 patients	COVID-19 with obesity are 51% more likely to have mortality
Brazil [24]	Retrospective study of 717 patients	Obese people require hospitalization more than twice following COVID-19 development.



adipocytes increasing the fat mass which evince both hypertrophy and hyperplasia in adipocytes. Obesity is the result of increased adipogenesis and increased basal rate of lipolysis. Accumulation of visceral white adipose tissue than subcutaneous adipose tissue leads to complications of obesity like insulin resistance and metabolic syndrome. Many factors like insulin, glucocorticoid, Tumor Necrosis Factor 1-Alpha (TNF1- α), Insulin-like Growth Factor-1 (IGF-1), and transcription factors like Peroxisome Proliferator-Activated Receptor- γ (PPAR- γ), CCAAT/Enhancer-Binding Proteins (C/EBPs), Sterol-Regulatory Element-Binding Protein (SREBP) play an important role in hypertrophy and hyperplasia of the adipocytes [25].

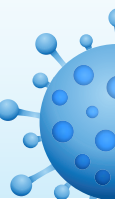
In obesity, there exists chronic low-grade sterile inflammation or inflammation in metabolic tissues along with increased levels of circulating pro-inflammatory factors without clinical signs of inflammation. The local and systemic cytokine levels, infiltrating immune cells and neutrophils are increased in the acute phase whereas macrophages are seen in the chronic phase [1]. Adipose tissue is involved in the regulation of physiological and pathological processes like immunity and inflammation by releasing a variety of adipokines like leptin, adiponectin, and resistin, pro-inflammatory cytokines like TNF- α , Interleukin (IL)-6, anti-inflammatory cytokines like IL-4 and IL-10, and both anti-inflammatory and pro-inflammatory cytokine-like interferon (IFN)- γ [26].

In a cross-sectional study, it has been shown that SARS-CoV-2 infected patients with a similar BMI as control patients had significantly higher levels

of serum leptin. Due to SARS-CoV-2 infection, ACE2- Angiotensin II disbalance occurs leading to local pulmonary inflammation which is enhanced by an increase in leptin production in visceral fat. Hence, it was concluded that visceral adipose tissue, leptin, and lung tissue have an interconnecting role in SARS-CoV-2 infection [27]. Michalakis *et al.* stated that SARS-CoV-2 and obesity (resistance to leptin and resistin) share common elements of the inflammatory process exacerbating SARS-CoV-2 infection in the obese [28]. A mild or highly acute respiratory syndrome caused by COVID-19 causes the release of pro-inflammatory cytokines like IL-6 and TNF- α . Thus, modification of the dietary regimen by adding ω -3 PUFA improves the adiponectin levels prevents the infection with COVID-19 and reduces the cytokine release [29].

Cytokines:

Cytokines are a group of proteins, glycoproteins, or peptides (~5–20 kDa), secreted by specific cells of the immune system that have a definite effect on the interactions and communications between cells. Cytokine may have autocrine action which acts on the cells from which it is secreted, endocrine action which acts on distant cells, or paracrine action which acts on nearby cells. Cytokines include lymphokine, interleukin, chemokine, and monokine. They are mainly produced by helper T cells and macrophages [30]. In case of severe immune reactions like severe infection and autoimmune diseases body responds by releasing various cytokines all at once which leads to multi-organ failure or death. This is known as a cytokine storm. Cytokine storm is a complication seen in respiratory diseases caused



by coronaviruses, SARS, and MERS, and few non-infectious diseases. There is a release of cytokines in inflammatory conditions like obesity. This along with the infections caused by coronaviruses may exacerbate cytokine storm. The cytokine storm is the systemic expression that results in the release of more than 150 inflammatory mediators including cytokines, oxygen-free radicals, and coagulation factors. In patients with severe infections, cytokine storm results in the release of both the pro-inflammatory cytokines like TNF- α , IL-1, and IL-6 and anti-inflammatory cytokines like IL-10 and IL-1 receptor antagonist. Such patients present with high fever, redness and swelling, severe fatigue and nausea [31].

Cytokine Storm:

After the primary exposure, the viruses replicate within the cell at the same time infecting other cells. Inflammatory responses are triggered when infected cells die by either necrosis or apoptosis. Initially, there is an acute inflammation that is characterized by increased blood flow, enabling plasma and leukocytes to reach the extra-vascular sites of injury, elevating local temperatures, pain, and activating pro-inflammatory cytokines or chemokines. These chemokines lead to the recruitment of inflammatory cells followed by increased expression of inflammatory, antiviral and apoptotic genes, immune cell infiltration, and tissue damage. The resolution of the damage and regenerative processes will be initiated at the same time and by this reparative process, functions can be completely rebuilt in most cases. In severe inflammation associated with cytokine storm, more serious pathological changes like immunopathologic injury and persistent organ dysfunction

occur. These severe inflammatory cytokines enter the circulation leading to systemic cytokine storms, resulting in multi-organ dysfunction [32-33].

The term Cytokine Release Syndrome (CRS) is interchanged occasionally with the term cytokine storm due to resemblance in clinical phenotype and biomarker signature [34]. The cytokines that are found to be raised in CRS include IL-6, IL-10, and IFN- γ . The activated T cell causes an enormous release of IFN- γ which triggers CRS. The released IFN- γ causes activation of macrophages, thus releasing more amounts of cytokines such as IL-6, IL-10 and TNF- α . TNF- α released is responsible for the synthesis of acute-phase proteins, watery diarrhea, vascular leakage, lung injury, and cardiomyopathy [35]. In the pathophysiology of CRS, the endothelium plays a crucial role by amplifying the inflammatory response and also as a target organ [36]. The endothelial cells of large adipose tissue, which are increased in obese individuals, secrete cell adhesion molecules, chemokines, adipokines, and inflammatory molecules playing a significant role in the promotion of both adipocyte alterations and inflammation [37].

Obesity and Vitamin D:

Vitamin D is inversely associated with overweight and obesity and it is said that for every 1 kg/m² increase in BMI, there is a decrease of 1.15% of 25-hydroxyvitamin D [25(OH)D] [38]. The possible mechanisms responsible for this could be: (A) decreased 25(OH)D due to negative feedback from the increased concentration of 1,25(OH)D: The increased demand in overweight and obese individuals leads to further hydroxylation of 25(OH)D to the active form,



1,25(OH)D, which further switches off the 25(OH)D production [39]. (B) The lower 25(OH)D concentration due to volumetric dilution: Vitamin D is fat-soluble, present in fat, muscle, liver, and serum, whose compartments are increased in volume in obesity. Hence, the lower vitamin D reflects the volumetric dilution effect even when the stores of vitamin D are adequate [40]. (C) Sequestration of vitamin D within adipose tissue: Vitamin D gets 'trapped' in adipose tissue because of adipose expansion due to insufficient lipolytic stimulation or tissue dysfunction/adaptation.

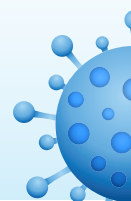
A study by Carrelli *et al.* showed that total body vitamin D stores measured by mass spectroscopy in subcutaneous and omental adipose tissues, were significantly greater in obese (2.3 ± 0.6 mg) than in lean (0.4 ± 0.8 mg) individuals. Hence, hypothesized that obese individuals with increased adipose tissue act as a reservoir for vitamin D and that the increased amount of vitamin D is needed to saturate this large depot, which may predispose obese individuals to low serum 25(OH)D. Thus, a high dose of vitamin D is required in overweight and obese. (D) Decreased sun exposure due to reduced outdoor activity, increased body surface area: a study has shown that regular exercise improves the function of adipocytes and mobilizes vitamin D from adipose tissue [41].

Effect of Obesity and Vitamin D Deficiency in COVID-19:

Hypertrophy of adipocytes seen in obesity triggers the release of adipokines and cytokines increasing the risk of complications related to cytokine storm (Fig 1). Obese individuals have an increased inflammatory response compared to lean. A study

by Muniz *et al.* showed that increased basal leptin expression in obese individuals led to chronic low-level inflammatory response making the obese individuals more susceptible to *Francisella tularensis* infection and exacerbated immunopathological cytokine storm [42]. A study by Easterbrook *et al.* showed that the antigen of influenza virus was more pronounced in the alveolar regions of the lungs of diet-induced obese mice than control mice due to interferon- β and proinflammatory cytokines in circulation. This has led to increased morbidity and mortality among H1N1 influenza-infected obese mice than non-obese mice [43]. The immunological response of adipocytes through leptin shows that altered leptin concentration leads to altered cell-mediated immune responses and insulin resistance [42]. A study by Zhang *et al.* to assess the role of leptin-mediated pathogenesis of influenza A (H1N1) pandemic showed that preexisting higher levels of serum leptin, a pro-inflammatory cytokine, and chemokine contributes to the development of complication like severe lung injury [44]. The adipokine (adiponectin) which is inversely related to BMI released from adipocytes too plays a role in an immune response by induction of interleukin 10 and suppression of nuclear factor-kB in macrophages [45]. A study by Kuwabara *et al.* showed that the Neutrophil Toll-like receptor 4 pathway was affected in the experimental models (obese and diabetes), resulting in altered production of cytokines and chemokines, migration and myeloperoxidase activity [46].

Human ACE2 is a recognized receptor for the entry of COVID-19 into host cells. The tissue expression of ACE2 differs in different organs like in lungs,



kidneys, and heart of healthy patients and coronavirus-infected patients. The adipose tissue shows higher level of ACE2 expression than in lung tissue, which shows adipose tissue may be vulnerable to infection. And also, treatment with ACE inhibitors for hypertension and angiotensin receptor blockers increases the expression of ACE and viral entry into the host [47]. Adipose tissue acts as a reservoir for certain viruses such as adenovirus, influenza virus, HIV, cytomegalovirus, etc [48]. Similarly, adipose tissue may be attributed to act as a reservoir of infection and may act as a research model for a better understanding of the pathogenesis of COVID-19 [49].

The severe vitamin D deficiency (<25 nmol/L) is associated with disease progression and increased mortality in patients with autoimmune liver diseases [50]. Vitamin D deficiency was seen in 63% of individuals with diabetes, 58% of individuals with prediabetes, and 80% of obese individuals, who are at high risk for COVID-19 [51]. Calcitriol, the vitamin D agonist modulates the expression of members of RAAS such as ACE2 in lung tissue, thus exhibiting the protective role against acute lung injury [52]. This may lead to the conclusion that vitamin D deficiency acts as a pathogenic factor in COVID-19. A study by Ilie *et al.* who investigated the role of vitamin D in the prevention of COVID-19 stated that there is a

severely low level of vitamin D in the aging population of Spain, Italy and Switzerland, who are most vulnerable to COVID-19 and vitamin D supplementation plays a significant role in reducing the mortality among them [53]. Based on the data of retrospective analysis, it was shown that vitamin D deficiency is associated with high CRP, a surrogate marker for cytokine storm, and vitamin D supplementation reduces the complications of unregulated inflammation and cytokine storm [9]. Calcitriol has a protective role against acute lung injury which modulates the expression of RAAS members like ACE2 [52]. VDRs are abundantly distributed in respiratory epithelial cells and immune cells such as B cell, T cell, macrophages, and monocytes. In the bronchial epithelium and immune cells, the dominant circulating form of vitamin D 25(OH)D is converted to 1,25-dihydroxyvitamin D, the active form of vitamin D with the help of the enzyme 1 α -hydroxylase. Thus, vitamin D may improve the immune response with an adequate amount of 25(OH)D to increase levels of 1,25-dihydroxyvitamin D [54-55]. Vitamin D also plays a significant role in the production of antimicrobial peptides and reducing the inflammatory response to COVID-19, that reduces the infection, mortality, and morbidity when infected with the virus [56].



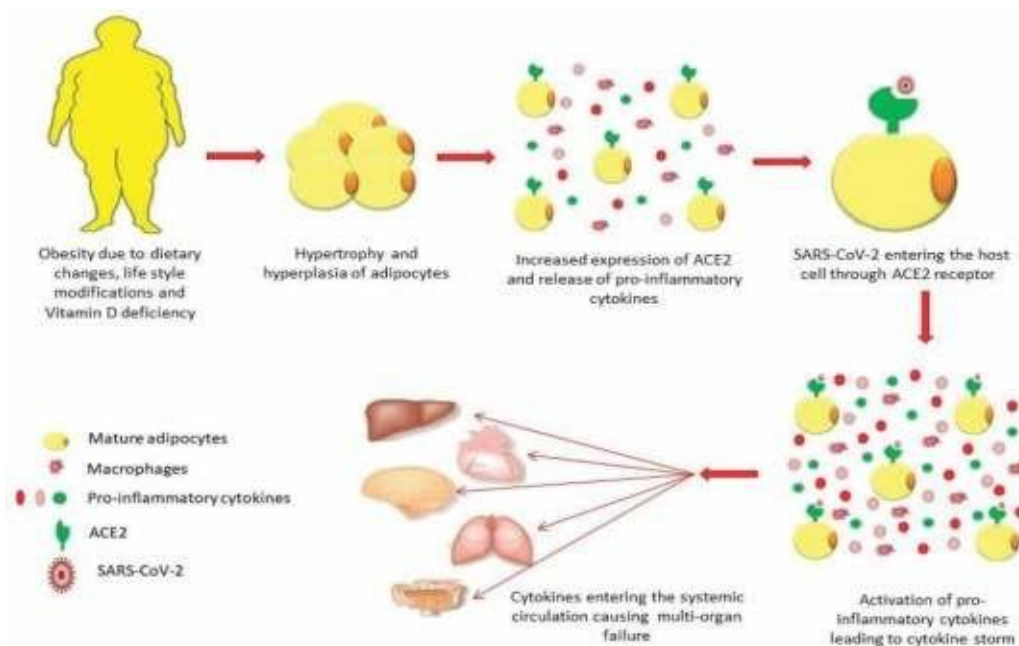


Fig. 1: Obesity, Vitamin D Deficiency, Cytokine Storm and SARS-CoV-2 Infection Leading to Multi-Organ Failure:

Overweight and obesity is a chronic low-grade inflammatory state caused by hypertrophy and hyperplasia of adipocytes and Vitamin D deficiency resulting in the release of pro-inflammatory cytokines and adipokines like leptin, adiponectin, and resistin. The SARS-CoV-2 gain entry into the host cell through ACE2 whose expression is higher in adipose tissue than compared to lungs. Once inside the host cell, the virus proliferates activating pro-inflammatory cytokines or chemokines and also infect the neighboring cells leading to overproduction of pro-inflammatory cytokines called a cytokine storm. These pro-inflammatory cytokines or chemokines enter the systemic circulation leading to multi-organ failure called systemic cytokine storms.

Vitamin D and Inflammation:

Vitamin D regulates intestinal, bone, and kidney calcium and phosphorus absorption, bone mineralization, and also plays a vital role in inflammation. There is an inverse relationship between 25(OH)D and markers of inflammation. The prolonged inflammatory microenvironment can lead to tumor production. Vitamin D influence this inflammatory microenvironment by mechanisms like: A. balancing the interaction between tumor cells and immune cells to regulate cytokines levels (inhibiting IL-6, 8,10 and TGF and

activating IL-17A), B. up-regulating MAP Kinase Phosphatase 5, a calcitriol responsive gene, C. inhibiting NF- κ B signaling pathway, D. inhibiting the prostaglandins pathway via reducing prostaglandins receptor, reduced COX-2 expression and increased 15-hydroxyprostaglandin dehydrogenase expression which is an antagonist of COX-2 and E. inhibiting immune cells via Vitamin D Receptor (VDR) [57]. Deficiency of vitamin D impairs the macrophages' ability to mature, to synthesize macrophage-specific surface

antigens, to synthesize the lysosomal enzyme acid phosphatase, and secretion of hydrogen peroxide which is their integral antimicrobial function [53]. The activity of matrix metalloproteinase in sputum cells during respiratory diseases like Chronic Obstructive Pulmonary Disease (COPD) is altered and also there is an increase in MMP-9 during acute exacerbations of COPD. MMP-9 is increased by TNF- α in alveolar macrophages and IL-10 reduces the ratio of MMP-9 to the MMP inhibitor. Vitamin D inhibits TNF- α and enhances IL-10 in immune cells of healthy individuals and supplementation of vitamin D in such patients may improve the condition [58]. A meta-analysis on vitamin D supplementation to prevent acute respiratory tract infections showed that vitamin D supplementation was safe and protected against acute respiratory tract infections and the patients with very low serum 25(OH)D (<25 nmol/L) concentrations, not receiving any prior vitamin D supplementation experienced the most benefit [59].

SARS-CoV-2, Inflammation, and Cytokine Storm:

Among the patients infected with SARS-CoV-2, 80% had mild disease, 14% had severe disease and 5% had critical disease as reported by the Chinese Center for Disease Control and Prevention [60]. The triggering factor which is responsible for severe disease in patients infected with SARS-CoV-2 is not only related to viral load but also because of the excessive inflammatory response which is associated with high levels of circulating cytokines, profound lymphopenia, and substantial mononuclear cell infiltration in the lungs, heart, kidney, spleen and lymph nodes [61-62]. Many studies have reported that higher the age and

the existence of comorbidities are the risk factors for severity of disease in patients with COVID-19, but later it was also seen that COVID-19 can also occur in younger age group people without any pre-existing medical comorbidities [62]. The pathophysiology of SARS-CoV-2 infection closely resembles that of SARS-CoV infection, with aggressive inflammatory responses. Hence the disease severity is not only due to the viral infection but also the host response [63].

Increased inflammatory markers such as C-reactive protein, ferritin, and D-dimers, neutrophil to lymphocyte ratio, and inflammatory cytokines and chemokines are associated with severity of disease and morbidity. These profiles of systemic cytokine were found to be similar to that in cytokine release syndromes, such as macrophage activation syndrome and increased production of cytokines such as IL-6, IL-7, and TNF. There is global T cell lymphopenia in the CD8 T cell compartment which is more pronounced in patients with the severe form of the disease. Hence, it can be concluded that COVID-19 is associated with hyper-inflammation [61-62,64].

ACE2 is predominantly present in airway epithelial cells, alveolar epithelial cells, vascular endothelial cells, and macrophages in the lung. ACE2 is a zinc-containing metalloenzyme and a homolog of ACE that acts as a transmembrane protein for the entry of the coronavirus into the host cell. ACE2 by converting Angiotensin II to Angiotensin 1-7, regulates the renin-angiotensin system negatively, by declining and opposing the angiotensin II, vasoconstrictor effect. The interactions of ACE, ACE2, angiotensin II, and other RAAS are quite complex, and paradoxical. ACE2 plays a major role

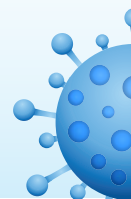


in maintaining blood pressure, fluid and electrolyte balance, and enhancing inflammation and vascular permeability in the airways. The viral load decreases the function of ACE2, hence altering the RAAS. The severity of lung injury are reduced by ACE inhibitors in certain viral pneumonia, and it has been argued that they could be advantageous in COVID-19 [38]. SARS-CoV-2 infects the cells which express the surface receptors ACE2 leading to active replication and release of the virus which triggers the host cell to undergo pyroptosis and release damage-associated molecular patterns. This process is recognized by the neighboring endothelial cells, epithelial cells, and alveolar macrophages, leading to the release of pro-inflammatory cytokines and chemokines. The released proteins attract monocytes, macrophages, and T cells to the site of infection, further assisting the inflammation and initiating the pro-inflammatory feedback loop. In the normal immune response, at the early stage of inflammation, T cell which is virus specific is attracted to the site of infection and neutralizing antibodies eliminate the infected cells and hence stop the virus spread. This neutralized virus is recognized by the alveolar macrophages which are cleared by phagocytosis and hence the lung damage is reduced. In the altered immune response, overproduction of pro-inflammatory cytokines in the lung results in a cytokine storm, further this cytokine storm spreads to other organs causing multi-organ damage [31, 63, 65].

Obesity and Its Infectious Nature:

An epidemiological study to investigate the duration of influenza viral shedding in obese and non-obese by Maier *et al.* showed that obese adults

infected with influenza A virus shed the virus for up to 104% longer period than non-obese adults [66]. A study by Honce *et al.* showed that an altered microenvironment in obesity contributes to the development of heterogeneous viral quasispecies due to decreased type 1 INF response in both obese mice and obesity-derived human bronchial epithelial cells implying that obesity allows the putative growth of pathogenic viral variants [67]. A study by Yan *et al.* to check the infectious seasonal influenza virus in exhaled breath of symptomatic individuals in a 30-minute breath sample and nasopharyngeal swab showed that BMI was positively associated with shedding the infectious virus in both fine and coarse aerosols with a stronger association in fine than coarse aerosols [68]. Hence, they came to the assumption that obese individuals are more contagious than lean [2]. The most important cause of obesity is a sedentary lifestyle and improper diet. Reduced physical activity alters the immune response against a viral load. Evidence from epidemiological studies has shown an inverse relationship between physical activity and markers of low-grade systemic inflammation [69]. Ertek *et al.* showed that moderate physical activity has anti-inflammatory effects in healthy adults and elderly subjects and also in patients with cardiovascular risk factors such as metabolic syndrome [70]. Similarly, Warren *et al.* showed that physical activity reversed the obesity-associated alterations in host-immune defense [71]. Obesity also restricts ventilation by impeding the diaphragm which is a necessary treatment for the severely affected patients admitted in ICU [14].



Conclusion:

The burden of overweight and obesity and its comorbidities like diabetes mellitus, cardiovascular disease, hypertension, etc. may increase the risk of acquiring the SARS-CoV-2 infection. By the information available till now it is not only elderly above the age of 60 who are at risk, even the younger generations are also at risk. This may be attributed to obesity, where there is a surge of cytokine storm and ACE2 levels. Overweight and obesity are associated with vitamin D deficiency which is a pathogenic factor involved in infections like COVID-19. Obesity may increase the risk of infection or its complications, hence increasing the mortality rate. Calcitriol modulates the expression of RAAS members such as ACE2 in lung tissue, hence vitamin D deficiency may act as a pathogenic factor in COVID-19. The combined

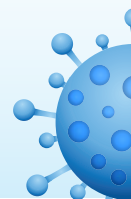
effect of both obesity and vitamin D deficiency may exacerbate the SARS-CoV-2 infection and its related complications. It is not clear what kind of people or what percentage of affected people will develop complications or die due to cytokine storm and to date no vaccine with 100% efficacy or definite treatment is available for the SARS-CoV-2. Knowing the fact, that regular physical exercise helps in desequstration of vitamin D from adipose tissue and aid in normal levels and its function, measures should be taken to do regular exercise. And other preventive measures like regular or frequent hand wash, use of mask, sneezing and coughing etiquette, social distancing, and proper diet should be followed to fight against the infection and obesity.

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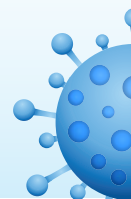
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Predictors of mortality in patients with severe COVID-19 pneumonia – a retrospective study

Abstract

Introduction: The novel coronavirus pandemic has caused significant mortality throughout the world. This study was done as there is scarce data on mortality predictors in severe COVID-19 pneumonia patients admitted to ICU in the Indian population.

Material and methods: A retrospective study was conducted on COVID-19 pneumonia patients admitted to tertiary care center during June–October 2020. The records of patients admitted to ICU were collected and data included demography, symptoms, comorbidities and vital parameters. Laboratory parameters included complete hemogram, random blood sugar, serum ferritin and LDH, renal function test, liver function test. Treatment-associated information such as the use of remdesivir, timing of initiating remdesivir after the symptom onset, the use of steroids, use of anticoagulants, use of HFNC, NIV, ventilator were collected. 30 days mortality data post-discharge was collected via telephonic interview.

Results: 4,012 confirmed cases of COVID-19 were admitted to hospital, of which 560 (13.95%) with severe pneumonia were included in the study. Mean age was 57.75 ± 13.96 years. The mortality rates were 54.64% among severe COVID-19 cases and 5% among mild to moderate COVID-19 cases. The Cox multinomial regression analysis identified $SpO_2/FiO_2 < 400$, age > 50 years, duration of symptom > 4 days, serum ferritin $> 450 \mu g/L$, respiratory rate $> 23/min$, the presence of comorbidities and non-usage of remdesivir were independently associated with increased mortality. Mortality rate at 30 days was 56.60%.

Conclusion: Severe COVID-19 pneumonia is associated with very high mortality, especially in a resource-constrained setting. The use of remdesivir may have to be considered early in the course of disease to prevent excess mortality related to COVID-19.

Key words: COVID-19, pneumonia, mortality, remdesivir

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Introduction

The novel coronavirus disease (COVID-19) has drew worldwide attention by causing the first pandemic by coronavirus leading to international public health emergency. On the 3rd November, 2020, the World Health Organization (WHO) declared coronavirus outbreak as pandemic and public health emergency of international concern [1]. SARS-CoV-2 infection has caused significant morbidity and mortality throughout the world leading to immense health care burden. Currently, worldwide around 55 million people have been infected with SARS-CoV-2, which has re-

sulted in around 1.35 million deaths [2]. In India, around 9 million people have been infected and approximately 132 thousand people have succumbed to SARS-CoV-2 infection [3]. Very little attention has been paid to clinical characteristics and outcomes of severe COVID-19 pneumonia patients in intensive care unit (ICU), data on whom are scarce but are of paramount importance to reduce mortality in a resource-constrained setting such as a government hospital. This study aimed to identify factors associated with mortality in patients with severe COVID-19 pneumonia admitted to a tertiary care COVID-19 hospital in South India.

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Material and methods

Study design

We conducted a retrospective study at a tertiary care teaching hospital in South India. The study was approved by institutional ethics committee (SIMS/IEC/503/2020-21).

Participants and eligibility criteria

We retrospectively analyzed consecutive patients with severe COVID-19 pneumonia who had been admitted to our hospital from June to October 2020. Individuals aged 18 years and above were included in the study. Diagnosis of COVID-19 was defined as the patient having a positive result on the oropharyngeal and nasopharyngeal swab for SARS-CoV-2 by reverse transcriptase polymerase chain reaction (RT-PCR). Our hospital used test kits provided by the government of Karnataka.

Classification of severity of SARS-CoV-2 infection was based on the revised national guidelines on clinical management of SARS-CoV-2 infection given by the Ministry of Health and Family Welfare, Government of India [4].

We defined severe COVID-19 pneumonia as an “adult with fever or suspected respiratory infection, plus one of the following; respiratory rate >30 breaths/min, severe respiratory distress, $\text{SpO}_2 < 90\%$ at room air”.

Data collection

The records of patients admitted to high dependency unit and intensive care unit were collected and evaluated for predictors of mortality. Data included demographic details, symptoms and the duration of symptoms, comorbidities like diabetes, hypertension, heart disease, obesity, chronic kidney disease, chronic liver disease, malignancy, chronic respiratory diseases like asthma and Chronic Obstructive Pulmonary Disease. Clinical parameters like pulse rate, heart rate, blood pressure, peripheral capillary oxygen saturation/fraction of inspired oxygen ($\text{SpO}_2/\text{FiO}_2$) on admission were collected. Laboratory parameters included complete hemogram (Sismex, 6 part differential cell counter), neutrophil-lymphocyte ratio, random blood sugar, serum ferritin (Beckman), Serum Lactate Dehydrogenase (LDH) (ERBA EXEL 640), renal function test, liver function test, arterial blood gas, chest radiography. Treatment details like the use of remdesivir, the day of starting remdesivir after the symptom onset, the use of steroids, use of anticoagulants, use of high-flow nasal cannula, noninvasive ven-

tilation, ventilator, incidence of hospital-acquired infections were collected. The outcome variables included the length of hospital stay and mortality.

The patients were managed with supportive care and specific pharmacological protocols created by the hospital's COVID-19 management guidelines committee in accordance with the government of Karnataka. Specific pharmacological treatments included systemic corticosteroids, low-molecular-weight heparin, oxygen and remdesivir. Data collected were cross-checked by the authors, and at the end of data entry - by an independent investigator. Any disagreement between two investigators was resolved by reaching a consensus.

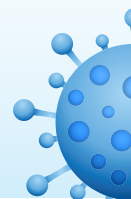
A total of 4,012 patients with laboratory-confirmed SARS-CoV-2 were admitted during the study period. We excluded from the final analysis patients who were still receiving care in the hospital at the time of preparation of this manuscript and those with incomplete information.

Statistical analysis

Descriptive data are presented as frequencies (percentages) of discrete variables and as means (SDs) of continuous variables. For comparisons between the two groups, ANOVA test with the Bonferroni correction was used. χ^2 -test was applied to evaluate categorical factors. Fischer's exact test was used in case of low cell frequency. The Cox regression univariate and multinomial analysis and Kaplan-Meier analysis were used for survival investigation. The receiver operating characteristic (ROC) curves were constructed for age, duration of symptoms, $\text{SpO}_2/\text{FiO}_2$, serum ferritin, respiratory rate and the cut-off value with the highest sensitivity and specificity selected as threshold. All statistical tests were 2-tailed, and factors were considered statistically significant at $p < 0.05$. IBM SPSS version 22 and CDC Epi Info version 7 were used for analysis.

Results

A total of 4,012 confirmed cases of COVID-19 were admitted to hospital, of which 560 (13.95%) with great severity were included in the study (Figure 1). Mean age of the study population was 57.75 ± 13.96 years. Three hundred sixty-five (65.17%) were men. Hypertension (41.25%) followed by diabetes (41%) was the most common comorbidity. Dyspnea (69.46%) was the most frequent symptom followed by fever (52.5%) and cough (46.78%) (Table 1). Mean duration of symptoms before admission



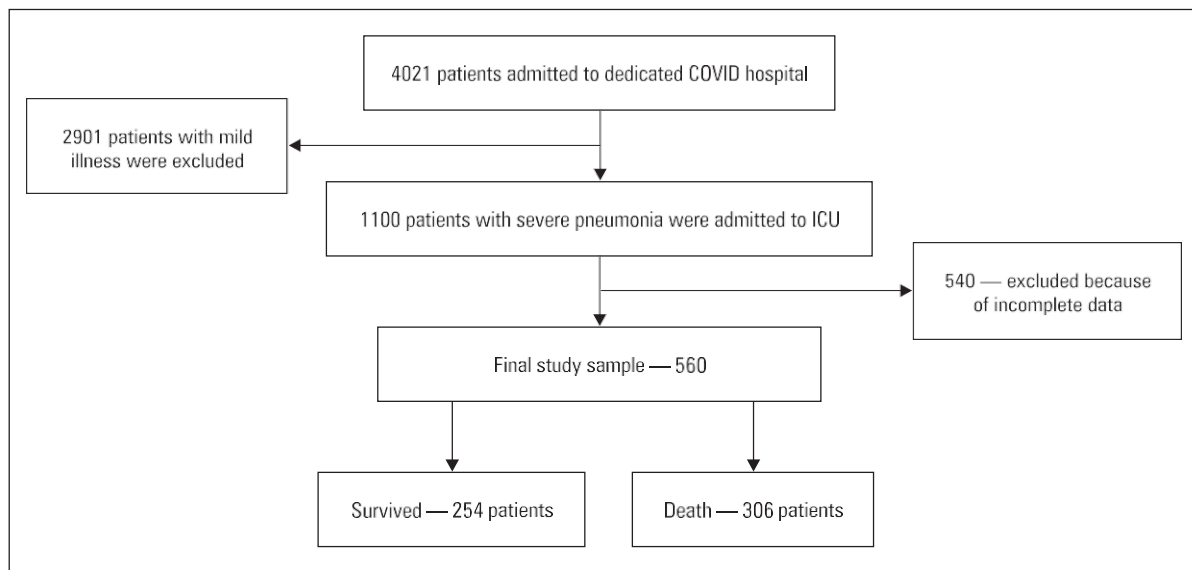


Figure 1. The flowchart depicting enrolment of COVID-19 patients into the study

was 4.11 ± 2.09 days. Remdesivir was given to 298 (53.21%) patients. Mean duration of starting remdesivir after the symptom onset was 5.58 ± 2.78 days. High-flow nasal cannula was given to 245 (43.7%) subjects. Ninety-one (16.25%) needed ventilatory support. A very high mortality, i.e. 306 (54.64%) cases was observed at our hospital. Among the patients who died, nearly quarter of them (82 patients) died within 24–48 hours from admission. Secondary bacterial infection was noted at a late stage of the disease in 8 patients, and organisms isolated were *Streptococcus pneumoniae*, *Klebsiella pneumoniae* and *Staphylococcus aureus*. In the Cox regression analysis, we observed age > 50 years, duration of symptoms more than 4 days, $\text{SpO}_2/\text{FiO}_2 < 400$ on admission, serum ferritin > 450 $\mu\text{g/L}$ on admission, respiratory rate > 23/min on admission, the presence of comorbidities and non-usage of remdesivir to be independent predictors of mortality in patients with severe COVID-19 pneumonia (Table 2). We observed an increased hazard of death by two days after the onset of symptoms which peaked on the 5th day of the symptom onset. The risk of death then decreased, but remained significant till the 8th day (Figure 2). We found steroid usage, use of mechanical ventilation and the day of starting remdesivir after the symptom onset to be independent predictors of prolonged hospitalization in patients with severe COVID-19 pneumonia (Table 3). The presence of chronic liver disease, use of mechanical ventilation, day of starting remdesivir after the symptom onset to be inde-

pendent predictors of prolonged ICU stay in patients with severe COVID-19 pneumonia (Table 4). The Kaplan-Meier analysis showed statistically significant mortality benefit in patients who received remdesivir and even better survival if used within 4 days of the symptom onset (Figure 3A and 3B). Only a small number of subjects (< 2%) succumbed post-discharge due to COVID-19-related complications with a final mortality rate at 30 days of 56.60%.

Discussion

In the present study, we found elderly patients with male predominance more commonly affected by moderate to severe pneumonia with very high mortality rates of more than 50%. We observed age > 50 years, duration of symptoms more than 4 days on admission, $\text{SpO}_2/\text{FiO}_2 < 400$ on admission, serum ferritin > 450 mcg/L on admission, respiratory rate > 23/min on admission, the presence of comorbidities and non-usage of remdesivir to be independent predictors of mortality in patients with severe COVID-19 pneumonia.

Elderly patients are commonly affected by severe pneumonia due to age-dependent decline in immunity. A Korean meta-analysis of COVID-19 pneumonia found old age to be the risk factor for increased mortality [5]. Old age is an established risk factor for various infections, including viral infections and by far most significant predictor of mortality in COVID-19 pneumonia [6, 7].



Table 1. Baseline characteristics of patients with severe COVID-19 pneumonia admitted to ICU

Variables	Total (n = 560)	Survived (n = 254)	Death (n = 306)	P-value*
Age [years], mean (SD)	57.75 (13.96)	54.39 (14.99)	60.54 (12.39)	0.004
Gender, n [%]	365 (65.17)	166 (65.35)	199 (65.03)	0.840
Symptoms, n [%]				
Cough	262 (46.78)	131 (51.57)	131 (42.95)	0.083
Dyspnea	389 (69.46)	140 (55.12)	249 (81.37)	0.001
Fever	294 (52.5)	161 (63.39)	133 (43.46)	0.0001
Myalgia	61 (10.89)	41 (16.14)	20 (6.54)	0.315
Duration of symptoms before admission, mean (SD) [in days]	4.11 (2.09)	3.27 (1.92)	4.79 (1.98)	0.0001
Comorbidities, n [%]				
Diabetes, n [%]	230 (41)	80 (31.50)	150 (49.02)	0.016
Hypertension, n [%]	231 (41.25)	72 (28.35)	159 (51.96)	0.009
Ischemic heart disease, n [%]	48 (8.5)	11 (4.33)	37 (12.09)	0.118
Chronic kidney disease, n [%]	32 (5.7)	4 (1.57)	28 (9.17)	0.043
Chronic liver disease, n [%]	9 (1.6)	1 (0.39)	8 (2.61)	0.171
Morbid obesity, n [%]	13 (2.3)	1 (0.39)	12 (3.92)	0.092
Vitals				
SpO2 at room air [on admission], mean (SD)	78.70 (18.72)	87.74 (12.17)	71.19 (19.87)	0.0001
Respiratory rate, breath/min, mean (SD)	21.37 (4.82)	19.94 (2.97)	22.5 (5.67)	0.003
Laboratory findings at the time of admission				
Hemoglobin [gm%], mean (SD)	12.35 (2.14)	12.42 (2.18)	12.34 (2.08)	0.121
Total white blood cell count, mean (SD)	9.87 (6.5)	9.04 (4.59)	10.56 (7.74)	0.071
Platelet count [lakh/mm ³]	2.10 (0.93)	2.24 (0.87)	2.03 (0.86)	0.081
Neutrophil Lymphocyte Ratio mean (SD)	8.02 (8.66)	5.87 (4.37)	9.80 (10.71)	0.029
Serum ferritin [µg/L], mean (SD)	539.66 (381.78)	367.2 (308.63)	632.29 (385.61)	0.0001
Serum Lactate dehydrogenase [LDH] [U/L], mean (SD)	845.73 (593.51)	788.1 (681.62)	866.39 (558.52)	0.160
Serum Creatinine, [mg/dl] mean (SD)	1.66 (2.08)	1.24 (1.33)	1.94 (2.51)	0.002
Random blood sugar [mg/dl] mean (SD)	215.49 (135.3)	181.32 (112.48)	239.92 (144.8)	0.002
Treatment				
Remdesivir usage n [%]	298 (53.21)	165(64.96)	133(43.46)	0.019
First dose of Remdesivir after symptoms onset, mean (SD)	5.58 (2.78)	5.06 (3.12)	6.01 (2.37)	0.0001
Low-molecular-weight heparin, n [%]	365 (65.17)	154 (60.63)	211 (68.95)	0.161
Steroid usage n [%]	454 (81)	185 (72.83)	269 (87.91)	0.023
First dose of steroid after admission [in days], mean (SD)	1.22 (1.19)	1.19 (1.25)	1.24 (1.03)	0.931
High-flow nasal cannula, n [%]	245 (43.7)	41 (16.14)	204 (66.67)	0.0001
Ventilator, n [%]	91 (16.25)	3 (1.18)	88 (28.76)	0.0001
No. of days in ICU, mean (SD)	4.48 (3.23)	5.48 (3.18)	3.64 (3.04)	0.0001
No. of days of hospital stay, mean (SD)	8.71 (7.54)	12.53 (8.76)	5.52 (4.28)	0.00001

*ANOVA test with Bonferroni adjustment for multiple comparisons

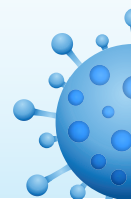
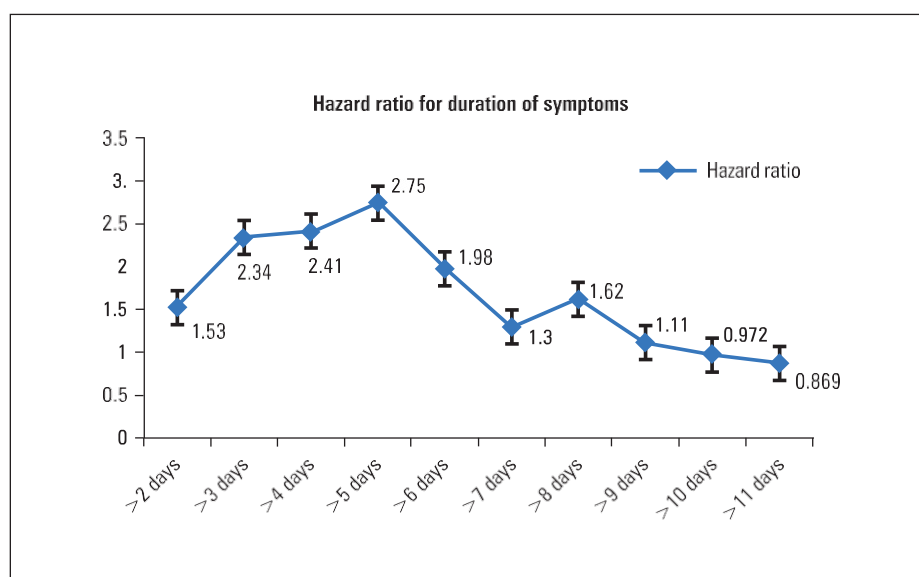


Table 2. Cox univariate and multivariate analysis of factors associated with mortality in patients with severe COVID-19 pneumonia

Variables	Hazard ratio (95% CI)	P-value	Adjusted hazard ratio (95% CI)	P-value
SpO ₂ /FiO ₂ < 400	3.35(2.631–4.264)	0.001	2.424 (1.869–3.145)	0.0001
Age > 50 years	1.01 (1.00–1.02)	0.0001	1.589 (1.132–2.228)	0.007
Duration of symptoms > 4 days	1.23 (1.18–1.28)	0.0001	2.410 (1.659–3.502)	0.0001
Serum ferritin > 450 µg/L	1.001 (1.001–1.001)	0.0001	2.134 (1.671–2.725)	0.0001
Neutrophil to lymphocyte ratio > 7	1.02 (1.01–1.03)	0.0001	1.122 (0.880–1.429)	0.354
First dose of remdesivir after symptom onset > 4 days	1.038 (1.003–1.075)	0.038	1.234 (0.747–2.036)	0.411
Respiratory rate > 23/min	1.08 (1.06–1.10)	0.0001	1.343 (1.046–1.725)	0.021
Diabetes	1.46 (1.16–1.83)	0.001	0.835 (0.635–1.097)	0.195
Hypertension	1.12 (1.02–1.23)	0.014	0.874 (0.754–1.012)	0.072
Ischemic heart disease	1.87(1.33–2.65)	0.001	1.233 (0.857–1.774)	0.258
Chronic kidney disease	2.35 (1.59–3.48)	0.0001	1.383 (0.886–2.158)	0.153
Presence of any comorbidity	2.32 (1.79–3.0)	0.0001	1.822 (1.286–2.581)	0.001
Remdesivir usage	0.75 (0.59–0.93)	0.013	0.453 (0.342–0.599)	0.0001
Steroid usage	1.73 (1.22–2.44)	0.001	1.097 (0.749–1.608)	0.633
Creatinine > 1.5 mg/dl	1.08 (1.04–1.12)	0.001	1.161 (0.884–1.524)	0.284

**Figure 2.** The graph depicting hazard ratio of mortality for each day from the symptom onset and duration of hospitalization

Elderly patients infected with SARS-CoV-2 tend to trigger hyper-activation of the immune system and hypercoagulation in small blood vessels leading to cytokine storm [8]. Though it is still unclear why the elderly are more prone to cytokine storm, possible mechanisms include an increase in activity and abundance of NLRP-3 (Nucleotide-binding oligomerization domain, Leucine rich Repeat

and Pyrin domain containing protein 3), a component of inflammasome in immune cells and alveolar macrophages in the lungs which upon chronic stimulation cause pulmonary fibrosis [9]. NLRP-3 activity is normally under control of Sirtuin-2 (protein implicated in longevity) which reduces with age. This decline in Sirtuin-2 is exacerbated by SARS-CoV-2 infection and might



Table 3. Cox univariate and multivariate analysis of factors associated with prolonged hospital stay more than 5 days in patients with severe COVID-19 pneumonia

Variables	Hazard ratio (95% CI)	P-value	Adjusted hazard ratio (95% CI)	P-value
Fever	0.72 (0.581–0.90)	0.004	0.804 (0.638–1.014)	0.066
Dyspnea	1.26 (1.01–1.58)	0.036	1.04 (0.806–1.356)	0.738
Comorbidities	1.28 (1.03–1.59)	0.025	1.17 (0.930–1.17)	0.177
First dose of Remdesivir after symptom onset > 4 days	0.959 (0.929–0.989)	0.008	0.932 (0.899–0.966)	0.0001
Steroid usage	1.29 (0.98–1.71)	0.06	1.42 (1.030–1.976)	0.032
Use of ventilator	2.38 (1.58–3.59)	0.0001	2.17 (1.428–3.313)	0.0001

Table 4. Cox univariate and multivariate analysis of factors associated with prolonged ICU stay more than 4 days in patients with severe COVID-19 pneumonia

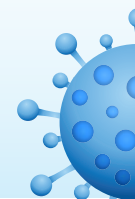
Variables	Hazard ratio (95% CI)	P-value	Adjusted hazard ratio (95% CI)	P-value
Fever	0.670 (0.520–0.864)	0.002	0.77 (0.588–1.008)	0.062
Dyspnea	1.38 (1.07–1.80)	0.014	1.18 (0.884–1.598)	0.254
Ischemic heart disease	1.59 (0.998–2.55)	0.05	1.45 (0.869–2.44)	0.154
Chronic kidney disease	1.91 (0.981–3.73)	0.05	1.50 (0.751–3.019)	0.249
Chronic liver disease	9.49 (2.97–30.35)	0.0001	6.58 (1.94–22.27)	0.002
Comorbidities	1.44 (1.12–1.86)	0.004	1.20 (0.904–1.614)	0.202
First dose of Remdesivir after symptom onset >4 days	0.956 (0.923–0.989)	0.015	0.940 (0.904–0.977)	0.002
Use of ventilator	3.35 (2.15–5.23)	0.0001	3.23 (2.031–5.152)	0.0001

promote hyperactivation of NLRP3 and trigger cytokine storm in elderly patients [10]. Another possible reason for increased susceptibility to COVID-19 infection in the elderly could be due to a decrease in T-cells and subsets, which reduces with aging [11]. Mahase *et al.* found that overall death rate from COVID-19 was 0.66% and was sharply rising to 7.8% in elderly people aged over 80 years [12].

Ferritin is an intracellular protein that stores iron and releases in a controlled fashion. Apart from the role of iron store, it has a potential capacity during inflammation following SARS-CoV-2 infection. Ferritin is found to be secreted by alveolar macrophages in the lungs and also stimulated by various cytokines, including IL-6 [13]. Active ferritin in turn stimulates the immune system and activates macrophages leading to an increase in inflammatory process [14]. Various single-center retrospective studies done in China found higher ferritin levels in patients who succumbed compared to survivors and discovered a decrease in ferritin levels with remission of the

disease [15–17]. We also found elevated ferritin levels in non-survivors (632.29 µg/L) compared to survivors (367.2 µg/L).

We noted SpO₂/FiO₂ (SF) ratio on admission < 400 to be an independent predictor of mortality in severe COVID-19 pneumonia patients. SpO₂/FiO₂ has been used as a surrogate prognostic marker of PaO₂/FiO₂ in acute respiratory distress syndrome (ARDS) patients with similar characteristics and the outcome in the previous study [18]. According to the Kigali modification, ARDS was defined without the need for positive end-expiratory pressure (PEEP), with the presence of bilateral opacities in the chest radiograph and hypoxia defined with a cut-off of SpO₂/FiO₂ less than or equal to 315 [19]. The study done by Rivello *et al.* using Kigali modification of the Berlin definition had good correlation with the diagnosis of ARDS [20]. SpO₂/FiO₂ is one of noninvasive parameters that might predict a poor outcome in patients with severe SARS-CoV-2 infection [21]. SpO₂/FiO₂ ratio could be used for correct estimation of ARDS in developing countries like India,



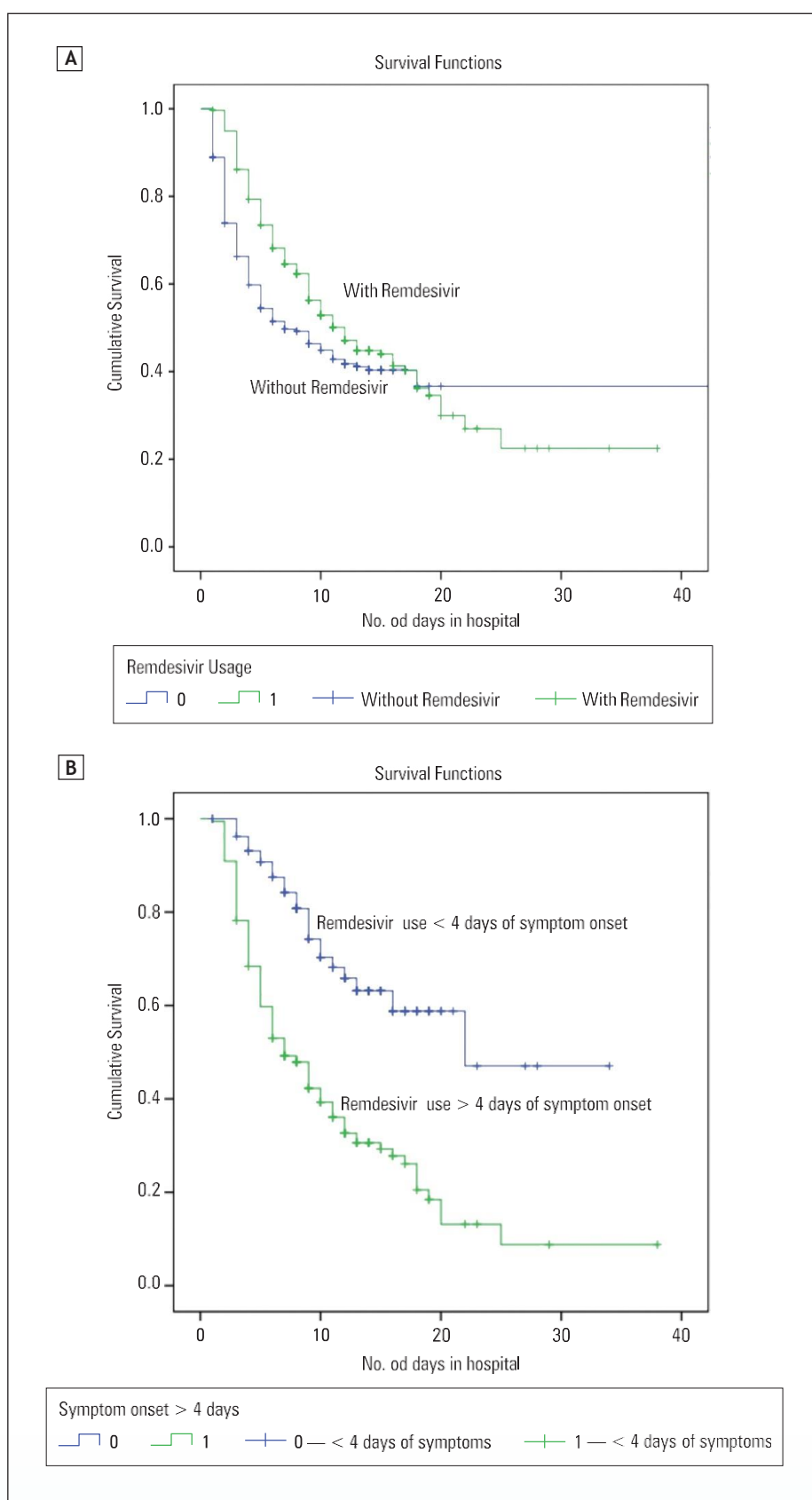


Figure 3. A. The Kaplan-Meier graph for survival with the use of remdesivir in patients with severe COVID-19 pneumonia; **B.** The Kaplan-Meier graph for survival with remdesivir use before and after 4 days of the symptom onset in patients with severe COVID-19 pneumonia



where there is scarcity of critical care specialist and intensive care in the periphery, especially in the COVID-19 pandemic situation.

Several antiviral drugs have been evaluated for the treatment of SARS-CoV-2 infection, but no antiviral agents have shown any mortality benefit. Remdesivir, a nucleoside analog with broad antiviral activity among RNA viruses, including Ebola, has been tried for treatment of SARS-CoV-2 infection. It acts by interfering with non-structural protein 12 polymerase (nsp12) which is a multisubunit of RNA synthesis complex that is responsible for viral RNA genome replication. Remdesivir has shown to decrease time to recovery in adults hospitalized with lower respiratory tract infection in an preliminary study of randomized control trial [22], and may prevent progression to more severe disease. The final report showed that remdesivir improved mortality rates for those receiving supplemental oxygen (4% with remdesivir versus 13% with placebo on day 29 of treatment) [23]. A Chinese study by Wang *et al.* showed numerical reduction in time to improvement with remdesivir compared to placebo, however, it was not statistically significant [24]. A randomized controlled trial (RCT) done by Spinner *et al.* also observed early clinical improvement in patients on remdesivir compared to standard care [25]. None of the RCTs has shown mortality benefit from usage of remdesivir.

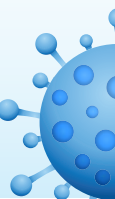
The median duration of starting remdesivir in our study was 5.50 days compared to studies done by Spinner *et al.*, Beigel *et al.*, Wang *et al.* which was 8 days, 9 days and 11 days, respectively [22, 24, 25]. In the above mentioned clinical trials, the benefit of remdesivir was larger when given earlier in the illness. Like other viral infections (eg.influenza), early use of antiviral drug is associated with improved clinical outcome [26]. Whether the use of remdesivir early in the course of disease when viral replication is the most active and complications have not yet occurred, would improve outcomes - remains to be confirmed by larger RCT studies.

The presence of comorbidities is an established risk factor for mortality in patients with COVID-19 pneumonia in various studies done across the globe [27–30]. We observed comorbidities in nearly 61% of patients. Hypertension (41.25%) and diabetes (41%) were the most commonly noted. Nearly 66.5% of patients with comorbidities succumbed to illness. A recent meta-analysis done in India found the prevalence of hypertension (22.9%) the highest among COVID-19 patients, and diabetes was more prev-

alent in the Indian population compared to other countries [30]. One of the largest Chinese studies (n = 72,314) found significantly increased mortality in COVID-19 patients with comorbidity [31]. The latest report from the Center for Disease Control, United States discovered cardiovascular diseases (including hypertension, stroke, coronary artery disease, cardiac failure) in 60.9% of patients with COVID-19 [32]. A UK study observed cardiac disease, chronic obstructive pulmonary disease, chronic kidney disease, obesity and liver disorders to be associated with a significant increase in mortality [33]. A recent report by the Ministry of Health and Family Welfare, India that analyzed the death of 15,962 patients with SARS-CoV-2 infection found the presence of one or more comorbidities in 57% of patients [34]. Unlike other studies, our Cox multinomial analysis did not provide evidence for an association between specific comorbidity and mortality.

Vital parameters play an important role in initial assessment and triaging of patients with pneumonia. Respiratory rate being one of the components of many severity scoring systems like CURB65 (Confusion, Urea, Respiratory rate, Blood pressure, Age > 65 years) score, APACHE II (Acute Physiology And Chronic Health Evaluation-II) score shows its importance. We found increased respiratory rate (> 23/min) to be an independent risk factor for mortality similar to a large American study [35]. A Chinese study on 344 critically ill patients also found higher respiratory rate was associated with poor outcome indicating more attention to be paid to vital signs [21].

Due to COVID-19 pandemic, there are accelerated publications without long-term follow-up of patients with mortality data [36]. There is sparse information on mortality rates post-discharge in severe COVID-19 pneumonia in the Indian population. We observed mortality rate of 56.60% (n = 560) in patients with severe COVID-19 pneumonia at 30 days which is lower than that from studies done in Pakistan (n-204, 77%) [37], the United States (n-373, 75.6%) [38] and China (n-344, 88.3%) [21]. However, studies carried out by Graselli *et al.* in Italy (n-1,581, 26%) [39] and Gupta *et al.* in the United States (n-2,215, 35.4%) [40] had lower ICU mortality than our study. A possible explanation for the disparity in mortality rates is that around 58% and 28% of the study cohort was still in ICU without an outcome projecting falsely low mortality in the studies done by Graselli and Gupta, respectively. In a study conducted by Zhou *et al.* (n-50) who



followed up all patients till the outcome, the mortality rate was 78% [41].

Strengths and limitations

One of the important strengths of our study is the presence of 30 days mortality data post-discharge which is lacking in many studies of patients with severe COVID-19 pneumonia. The evaluation of the timing of remdesivir administration after the symptom onset on mortality rates is an important finding as many studies which did not show any benefit of remdesivir had administered the drug late in the course of the disease. Limitations of our study include the usual limitations of a retrospective study, furthermore, information was collected from a single center.

Conclusion

We found age > 50 years, the duration of symptoms more than 4 days, $\text{SpO}_2/\text{FiO}_2 < 400$ on admission, serum ferritin > 450 $\mu\text{g/L}$ on admission, respiratory rate > 23/min on admission, the presence of comorbidities and non-usage of remdesivir and late initiation of remdesivir after the symptom onset to be independent predictors of mortality in patients with severe COVID-19 pneumonia.

Clinical implication/future directions

Mortality predictors found in the study could be identified early and treated to possibly reduce mortality in severe COVID-19 pneumonia patients. Mortality benefits of remdesivir with early initiation in the course of the disease need to be relooked with large randomized controlled trials.

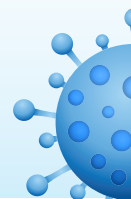
Conflict of interest

None declared.

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2. Digital interventions for COVID-19 Pandemic

SI No	Title	SDG IMPACT
13	Utility of Digital Technology in Tackling the COVID-19 Pandemic: A Current Review, PRASHANTH KULKARNI., SHRUTHI KODAD., MANJAPPA MAHADEVAPPA., SUSHANTH KULKARNI, Journal of Clinical and Diagnostic Research, 14, 1-3, 0973-709x	Goal 9: Industry innovation and infrastructure Goal 3: Good health and wellbeing
14	Tele dermatology practice in the COVID-19 pandemic, Dr Kanthraj G.R., Dr Jayadev B. Betkerur, International Journal of Health and Allied Sciences, 9, 3-10, 2278-4292	Goal 9: Industry innovation and infrastructure Goal 3: Good health and wellbeing



Utility of Digital Technology in Tackling the COVID-19 Pandemic: A Current Review

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ABSTRACT

The Coronavirus Disease (COVID-19) pandemic has rampaged across the globe, creating a major public health emergency and economic crisis. In this pandemic, digital technology tools, such as Artificial Intelligence (AI), big-data analytics, block chain technology, robotics, and drone technology are playing a vital role, and are increasingly being utilised by many countries for devising major public health strategies. This article discusses the utility of digital technology in combating coronavirus infection and also highlights the current limitations and future prospects of these tools.

Keywords: Artificial intelligence, Coronavirus, Robotics

INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, has emerged as one of the biggest health crisis of the 21st century, impacting lives, health care resources and economy across continents. A single centre study emerging from China revealed that the majority of COVID-19 patients were older, with a median age of 56 years. Approximately, 81% had mild pneumonia, 14% had severe infection, 5% were critical requiring mechanical ventilation, and the mortality was 4.3% [1]. The World Health Organisation (WHO) advocates early detection, containment, surveillance and preventive measures to stall the progress of the COVID-19 pandemic [2]. In this context, digital technology has emerged as a pivotal tool in tackling this pandemic. Indeed, in late December 2019, using AI, a Canadian health monitoring firm was one of the first to spot the rapid spurt of atypical pneumonia cases in Wuhan, China and alerted the world of an impending outbreak [3]. Many countries have harnessed the potential of digital technology for infection control and implementing public health and administrative measures to halt the spread of SARS-CoV-2. AI is a concept which incorporates human-like intelligence into a machine. It utilises deep and machine learning tools, and block chain technological algorithms to analyse data. This intelligence is synthesised by the machine to arrive at a decision-making process and take action like a human would do. Other advancements in AI applications like natural language processing, speech recognition, chatbots and facial recognition are increasingly being utilised to accomplish a vast array of tasks [4]. AI along with other digital tools like big-data analytics, robotics, and drone technology have revolutionised the major public health strategies in the context of the COVID-19 pandemic [5,6].

DIGITAL TOOLS FOR IMPLEMENTING PUBLIC-HEALTH MEASURES

Across the world, many governments enforced lockdown, curbed non-essential travel and advocated social distancing along with standard policies like infection control and public awareness to control the spread of COVID-19 infection. Digital technology tools have helped augment these efforts and aided in disease surveillance and containment. Human travel across continents has been one of the main factors responsible for the exponential spread of the virus. AI-enabled face-recognition cameras are being installed in public areas like hospitals, airports, and train stations to detect fever in individuals and track their movements [7]. AI is being leveraged to track and recognise individuals landing at airports from locations with a high volume of COVID-19 infection. These tools are also being used for contact tracing of COVID-19 patients, family

and friends, and thus supports the rapid containment of cases in specific localities.

The social media sources are analysed to study an individual's travel history, personal habits, visits to the hospital and the data obtained are utilised to predict risk profiles and devise policies to prevent the spread of the infection. Law enforcing agencies have increasingly deployed drones to implement lockdown measures. Drones are being used to monitor individuals violating the rules and to identify those not wearing facial masks, and for broadcasting awareness messages and disinfecting public spaces like roads, parks. These machines have been used in China to deliver essential items and medicines to those in quarantine and helped prevent virus exposure to transportation personnel [7]. Many state governments in India have developed a corona watch application for real-time monitoring and implementation of self-quarantining measures for individuals with suspected exposure to a COVID-19 patient [8].

The National Informatics Centre of the Government of India's Ministry of Electronics and Information Technology, has developed a bluetooth enabled smartphone application called "Aarogya Setu", which alerts an individual of the presence of a COVID-19 patient within a six feet radius. This app, using an encrypted social graph and data analytics, monitors an individual's travel history to a COVID-19 contaminated hotspot zone and thus helps in contact tracing. At present, this application is the world's most downloaded app with more than 90 million individuals in India using this application [9]. An Indian technology-driven company has developed a lockdown platform, which uses big data technology that provides an optimum plan for lockdowns, down to the village level that can be extrapolated to larger areas [10].

Robotic technology is being explored in this pandemic to aid sanitary workers and healthcare professionals to reduce their risk of exposure to the virus. They are being deployed to handle and dispose waste that are generated in hospitals. Robot-controlled, non-contact Ultraviolet (UV) surface disinfection is being used in high-touch areas in hospitals to prevent spread of the infection [11]. AI technology can be utilised to disseminate public-health education, and queries about COVID-19 infection can be effectively communicated. Virtual healthcare chatbots have been created in social media platforms to provide guidelines, advice on infection prevention and protective measures. These are used to recommend individuals with symptoms suggestive of the infection to seek doctor consultation and also provide information about self-isolation [7].

The Singapore government has partnered with Facebook-owned platform 'WhatsApp' to circulate correct and updated information about COVID-19 and to apprise citizens about the initiatives taken



by the government to address this pandemic [12]. In India, AI algorithms have been used to develop 'video-bots' in collaboration with hospitals. This platform will enable people to seek information on COVID-19 directly with a doctor through video interface [13].

DIGITAL TECHNOLOGY IN COVID-19 DIAGNOSIS AND RESEARCH

The burgeoning COVID-19 cases have overwhelmed and stretched healthcare resources worldwide. It is important that rapid diagnostic tests are available to identify the positive cases and immediate measures like isolation and quarantine can be employed to restrict the spread of the virus. A major hindrance to early diagnosis is an acute shortage of resources and the high volume of cases requiring more adept healthcare professionals. AI has helped to overcome these problems by improving the time taken to diagnose COVID-19 infection. AI-enabled medical analysis platform developed in China can detect coronavirus-infection associated with pneumonia on Computed Tomography (CT) scans with high accuracy of 96%. This was facilitated by an open-source AI model that analysed CT images of COVID-19 pneumonia in less than 60 seconds and identified the lesion pattern in terms of volume, number and proportion [14]. This analysis of CT chest correlated and complemented with the Reverse-Transcription Polymerase Chain Reaction (RT-PCR) COVID-19 diagnostic tests and was demonstrated in a study done in China [15].

The University of Tor Vergata in Rome, Italy, has conducted a pilot run for a patented AI-based tool developed by three biotechnology students from Mumbai, India, which was designed to test COVID-19 through voice-based diagnosis using a smartphone application. This testing platform has already been successfully tested in 300 COVID-19 patients with 98% accuracy [16]. AI-based triage systems in the hospitals for COVID-19 cases can be implemented and this could alleviate the clinical burden of health care professionals [17]. A Bengaluru based robotics start-up company is providing city hospitals with screening and diagnostic robots. The screening robot in a contactless manner initially helps with data collection such as the name of the patient, symptoms exhibited of coronavirus infection and later checks the temperature. The symptomatic patients will then be directed towards the diagnostics robot, which enables a video conversation with a doctor sitting in a remote location, and who in turn directs them to appropriate areas in the hospital for further management [18].

In contrast to SARS-CoV-1, the genome sequence of SARS-CoV-2 was deciphered within a month, using AI technology [19]. With international collaborative efforts, scientists have successfully identified an underlying genomic signature for 29 different DNA sequences of SARS-CoV-2, providing an important tool for vaccine and drug development. The researchers utilised AI and machine learning tools to achieve 100% accurate classification of the viral sequences [20]. Many biotech companies worldwide, both in the private and government enterprises are using AI tools to expedite drug discovery against the coronavirus [21]. Scientists have identified several promising molecules that inhibit SARS-CoV-2 protease, thus stalling viral replication. AI has helped to considerably shorten the initial drug design process from several months to only a few days now [22].

CURRENT LIMITATIONS OF DIGITAL TECHNOLOGY AND FUTURE PROSPECTS

Digital technologies like AI have made a promising start in aiding the fight against COVID-19. The use of these tools is constrained by enormous data that has to be adequately harnessed by a proper mechanism of human-AI interaction. Lack of rapidly available authentic data is hampering the full utilisation of technology in the present pandemic. Also, there are ethical and data privacy issues that need to be adequately addressed before implementation of these tools for public health measures [23].

Digital technology tools are expensive to implement and require skilled manpower which might not be adequately accomplished in this current pandemic [24]. Digital technologies have a great potential to fight future outbreaks if current enormous data on the pandemic is gathered and utilised to train and be better prepared for future calamities.

CONCLUSION(S)

Many countries are overwhelmed by the rapid and relentless spread of coronavirus infection across the globe. Technology has come to the aid of policymakers and health care systems to combat the COVID-19 pandemic. Digital tools have shown enormous potential in this outbreak, but have inherent limitations that need to be addressed adequately. Nonetheless, AI and other tools can help to keep track of the data generated from patterns of the cases in this crisis, and this data can be analysed to predict future outbreaks and aid in mounting an effective response against future pandemics.

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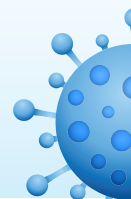
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Tele dermatology practice in the COVID-19 pandemic

Garehatty Rudrappa Kanthraj, Jayadev B Betkerur

Abstract:

Pandemics like influenza and plague have posed a great threat to humanity in the past. Recent outbreak of COVID-19, a viral pandemic, has motivated the global community for social distancing and enforcement of lockdown. Tele dermatology practice (TP) is an effective, safe, and fast medium to reach one who is difficult to reach. It is a medium for a dermatologist to cater the needy patients. Store-and-forward (SAF) tele dermatology mobile apps (e.g., WhatsApp) perform to capture, transfer, and store the clinical images. This overview provides an insight to TP. In an Indian scenario, SAF TP meets the technical requirement, economical, and easy to practice. Spotters, pediatric, geriatric, and chronic cases are managed with TP. The Indian Association of Dermatologists, Venereologists, and Leprologists in view of COVID-19 situation encourages its members to perform TP and provide care. The members may practice TP after observing all conditions as in telemedicine guidelines prepared by the National Medical Council with due caution.

Keywords:

COVID-19, messenger apps, online discussion forum, tele dermatology practice

History of Telemedicine

In 1906, Wilhelm Einthoven discovered telecardiogram^[1] and was successful in the transmission of electrocardiogram using a telephone network. The Nebraska Project,^[2]

USA, in 1959, used videoconference for psychiatry patients which was conducted between two hospitals within a distance of 150 km. Between 1960 and 1970, research to monitor astronaut's heart rate, blood pressure, and electrocardiogram was conducted.^[3] The term tele dermatology was introduced by Perednia and Brown.^[4] Tele dermatology in a nursing home setting was first demonstrated by Zelickson and Homan.^[5]

Tele dermatology practice (TP) is performed everywhere including as far as South Pole,^[6] as remote as Faroe Islands,^[7] rural India,^[8] USA,^[9] Africa,^[10] and in austere environments.^[11] Tele dermatology is a branch of dermatology involving

application of electronics, communications, and information technology to transmit the information between the patient and dermatologist and vice versa for research and practice to cater dermatology care.^[4,12]

Similar to radiology, dermatology is a visual specialty; availability of clinical and histopathological images for diagnosis makes it an ideal choice for TP.

A TP consultation is provided without exposing staff to viruses/infections in the times of contagious disease outbreaks like COVID. TP can prevent the transmission of infectious diseases, reducing the risks to both health-care workers and patients. Unnecessary and avoidable exposure of the people involved in delivery of health care can be avoided using TP. COVID-19, a viral pandemic, is a well-suited scenario, in which dermatologists can evaluate and manage patients.

Aim

The aim of TP is to reach the one who is difficult to reach. For dermatology care

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in remote geographic regions or needy population in situations like serious pandemics like COVID-19 where the population is under lockdown, early care is provided and difficult to manage cases that are not neglected.

Scope and Purpose/Indications

TP reduces multiple visits for follow-up care and benefits elderly, especially those coming from far-off places. It saves cost and time. A TP applies to diagnosis, treatment, and follow-up of skin disorders and education. Teledermatology was found to be cost-effective and reliable in reducing in-person visits, saves time, and allows for the faster delivery of care. TP provides triage and reduces waiting time. The various indications^[13-26] are summarized in Table 1.

Teledermatology for Geriatric Care

Store-and-forward teledermatology can improve diagnostic and therapeutic care for skin disease in the elderly who lack easy and/or direct access to dermatologists.^[27]

Teledermatology for Paediatric Care

Accurate triage and diagnosis of childhood dermatology cases decrease travel and outpatient clinic visits and provide an avenue for ongoing support and education for primary care physicians.

Teledermatology for Emergency Conditions^[29-31]

The Skin Emergency Telemedicine Service has proved to be a successful, sustainable, and valuable addition to the specialist dermatology services provided across Queensland, Australia.^[29] The use of teledermatology within the context of emergency-based care has gained a high degree of patient's acceptance and confidence.^[30] New-generation mobile devices reduce

Table 1: Summarizes the various indications for teledermatology practice

Diagnosis - Cases that present with characteristic morphology with typical distribution pattern
Follow-up care - Chronic cases that persists for a longer period and are characterized by remissions and exacerbations such as leg ulcer, ^[13-14] psoriasis, ^[15-17] leprosy, ^[18] and acne vulgaris ^[19-20]
Investigation procedure - Patch test in allergic contact dermatitis ^[21,22]
Skin cancer triage ^[23-25]
Dermatosurgery/esthetic care - Triage and counseling ^[26]
Second opinion for difficult to manage cases
Education - train residents and update knowledge for dermatologists

the cost of videoconferencing, increase the adaptability of teledermatology, and decrease general practitioner time.^[31]

Teledermatology and Diagnostic Agreement

Systematic reviews by Levin and Warshaw^[32] showed that there is a good diagnostic agreement when comparing a teledermatology diagnosis and in-person clinical diagnosis or histopathology with traditional face-to-face consultations. The diagnosis concordance between dermatologists and teledermatologists increased from 92% to 98% (95% confidence interval [CI]: 87%–100%) when overlaps between differential diagnoses were considered as partial agreements. The diagnostic accuracy of store-and-forward (SAF) TP was good and comparable to videoconference TP. Health-care providers need to plan for appropriate utility of SAF-TP either alone or in combination with videoconference TP to implement and deliver teledermatology care in India.^[33] Messenger apps (e.g. WhatsApp) are a medium for TP.

Teledermatology and Patient Satisfaction

One of the main areas of patient dissatisfaction for both live video and SAF teledermatology revolved around the lack of follow-up.^[34] Therefore, the referring physician plays a pivotal role in conveying the dermatologist's recommendations to the patient, which can have a major impact on patient satisfaction in the field.^[35] Patient satisfaction will play an integral role in the further growth, development, and implementation of teledermatology. Direct consult may increase patient satisfaction.

Teledermatology and Cost--Effectiveness

Teledermatology is cost-effective in terms of significantly decreasing the need for in-person visits.^[36] Real-time interactive teledermatology has been found to be time-consuming than store-and-forward dermatology.^[37] Video call is mostly used to counsel the patient.

The Organization of Teledermatology Practice

The organization of TP for a self-practicing dermatologist is illustrated in Figure 1. It comprises a basic model SAF teledermatology where a dermatologist interacts with the patients directly for regular cases (spotters) along with online discussion forum to obtain a second opinion on management of difficult-to-manage cases.^[12,38]



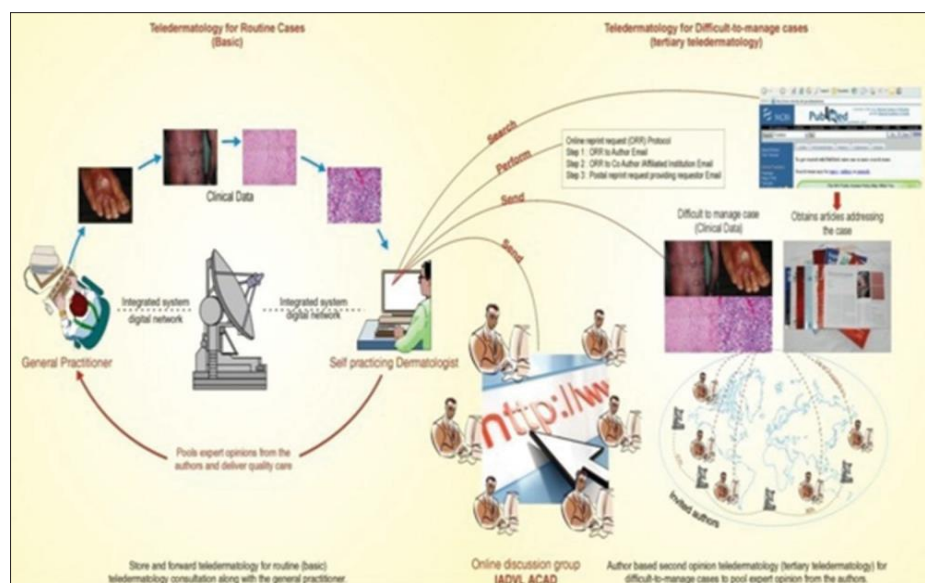


Figure 1: Illustration of the organization and process involved in teledermatology practice for a dermatologist to manage regular case (to use store and forward teledermatology practice) as well as difficult-to-manage cases (to use online discussion forum) and deliver care (modified with permission from Kanthraj GR. J Eur Acad Dermatol Venereol 2010;24:961-6. and Kanthraj GR. Indian J Dermatol Venereol Leprol 2011;77:276-87)

Prerequisites for Teledermatology Practice

1. A dermatologist should obtain a proper history
2. Patient should be able to provide electronic images of the skin disorder. Landow^[36] summarizes the requirements for a successful TP as: (1) image quality; (2) preselection of patients (tumoral conditions are the simplest; nevi evaluation should not exceed 1–2 lesions at most; multiple nevi patients should be excluded; and hair conditions are difficult to photograph and diagnose);^[39] and (3) a dermoscopic image is a requirement for pigmented and tumoral lesions; and good internet connectivity is a necessity.

Store-and-Forward Teledermatology

Static images of clinical and histopathological data are accessed anytime and anywhere. They are transferred from a general practitioner to a specialist to deliver the management. Dermatology cases that can be diagnosed by face-to-face examinations (spotters) have a good diagnostic accuracy by SAF TP. A diagnosis agreement of 89%^[40] has been documented. SAF TP is cheap and easy to set up and practice. It is the most common teledermatology tool as most of the cases are dealt and often regarded as a basic model for a TP.^[12]

Videoconference

It is a live or interactive teledermatology. General practitioner, patient, and specialist interact with one another using live/motion images. Various feasibility studies^[41,42] have confirmed good diagnostic accuracy

when videoconference is compared to face-to-face consultation.

Hybrid Teledermatology

This is a combination of both videoconference and SAF TP to overcome the shortcomings faced when either of them is used individually.^[43]

Store-and-Forward Teledermatology versus Videoconference

Good patient and physician satisfaction along with good diagnostic accuracy is achieved in all. The simultaneous presence of a health-care professional is required in videoconference and hybrid teledermatology and his or her presence may not be required in SAF TP. SAF TP is the most cost-effective and convenient compared to videoconference. The time taken for consultation is least for SAF TP and more in videoconference and hybrid teledermatology. Motion images are used in videoconference, still images are used in SAF TP, and both the types of images are used in hybrid teledermatology. A hybrid system with audio is no better than SAF TP alone.^[44] However, in the current context of mobile messenger apps -whatsapp consultation for example, still images and videos can be stored and forwarded. It has emerged as a widely used medium for TP.

Mobile Teledermatology

The term mobile teledermatology represents the transmission of images via mobile phones^[45,46] as well as through personal digital assistants.^[47] Motion



and still images are transferred. Advanced net-work technology along with the mobile messenger apps has revolutionized TP. Android technology and apps find an application medium to capture, transfer, and store the images.^[48,49]

Teledermatopathology

Transmission of histopathological images of the skin using information technology for expert opinion is called teledermatopathology.^[50] Teledermatopathology is achieved by (i) video-image (dynamic) analysis; (ii) SAF (static); and (iii) web-based virtual slide system.^[51] A virtual slide system is a recently developed technology where a robotic microscope is used; any field of the specimen is selected for better digitalization at any required magnification at the discretion of the dermatopathologist.

Teledermoscopy^[25,52-55]

Pigmented skin lesions and melanoma are analyzed based on the dermoscopic criteria^[52] that depend on characteristic changes in the epidermis and dermis. Dermoscopy images^[25] are transmitted for expert opinion using routine TP tools like SAF TP or tertiary TP for the second opinion. If these images are transferred using mobile technology, it is called mobile teledermoscopy. Pigmentary skin lesions are screened using mobile teledermoscopy.^[53]

Online Discussion Forums^[56-60]

Difficult to manage cases is a challenge to the health-care system. An online discussion forum is formed with a group of dermatologists who share constructive

suggestions^[56-58] for a submitted case. Feasibility studies have confirmed 81% concordance with face-to-face consultation.^[56] Members of academic societies such as the Indian Association of Dermatologists, Venereologists, and Leprologists (IADVL) have formed an online discussion forum at ACAD_IADVL@googlegroups.com (an e-mail group) and participate in regular academic discussions. Telederm.org,^[56] Rxderm,^[57] Virtual Grand Rounds in Dermatology,^[58] and Black Skin Dermatology Online^[60] are the examples of online discussion forums. Experts may be unavailable for an instant case or dermatologists and allied research workers who might have carried out research involving an online discussion forum may not have registered at the site and at times consensus may not be reached for a case without these experts are the limitations of online discussion forum.

The various teledermatology tools and health-care professionals involved to provide dermatology care are summarized^[61] in Figure 2.

Limitations

Poor net connectivity, poor image quality, and lack of referral pro forma data can limit TP. All cases may not be feasible with an objective of diagnosis in TP. The cases that are not diagnosed by spot examination are summarized in Table 2.

The requirements for real-time videoconferencing (synchronous encounters) and SAF teledermatology have been specified by the American Telemedicine Association.^[62] Monitors for viewing images shall have a minimum of 1024 × 768 pixel resolution, minimum contrast ratio of 500:1, minimum luminance of 250 cd/m², and minimum dot pitch of 0.19.^[62]

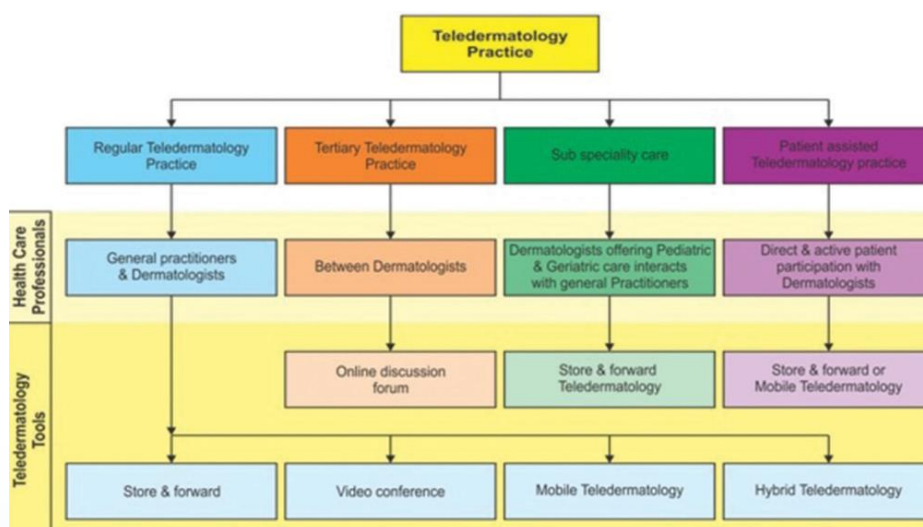


Figure 2: Summarizes the various teledermatology tools used for patient care (reproduced with permission from Kanthraj GR. Indian J Dermatol Venereol Leprol 2015;81:136-43)

Table 2: Summarizes the various clinical situations a dermatologist may choose not to offer tele dermatology practice for diagnosis purpose

Atypical/unusual presentation
Nonspecific presentation
Varied morphology
Requires palpation ex., Skin tumors
Multi-organ involvement for example, Steven-Johnson syndrome/toxic epidermo necrolysis
Rare diseases - syndromes/genodermatoses (apart from skin examination palpation for multisystem involvement may be needed)
Diseases that require criteria to diagnose, for example, atopic dermatitis, systemic lupus erythematosus, and Behcet's disease
Symptomatic presentation, for example, generalized itching and burning excessive sweating/hyperhidrosis (without any obvious lesions to capture the image and requires evaluation of the symptom/s by investigations)
Represent a clinical entity due to various causes, for example, erythroderma, palmoplantar keratoderma, urticaria and leg ulcer
In these situations, initial face-to-face examination needs to be performed followed by tele dermatology practice and deliver follow-up care

In India, till now, there was no legislation or guidelines on the practice of telemedicine through video-, phone-, and internet-based platforms (web/chat/apps etc.). Recently, the board of governors (BoGs) of the Medical Council of India (MCI) along with NITI Aayog have prepared the guidelines for telemedical practice.^[63] The detailed guidelines about the role of patient, health-care provider, and technology platform are highlighted.^[63] Each patient will be identified by a unique and universal patient identifier so that one central patient information record can be assimilated, comprehensive medical databases can be built, or if the patient wants, he/she can move across multiple providers without losing data. The same principles apply irrespective of the mode (video, audio, and text) used for a telemedicine consultation.^[63]

Guidelines for technology platforms enabling telemedicine prepared by the board of governors of medical council of India along with NITI Aayog^[63]

This specifically covers those technology platforms which work across a network of Registered Medical Practitioners (RMPs) and enable patients to consult with RMPs through the platform.

1. Technology platforms (mobile apps, websites, etc.) providing telemedicine services to consumers shall be obligated to ensure that the consumers are consulting with RMP duly registered with National Medical Councils (NMCs) or respective state medical council and comply with relevant provisions
2. Technology platforms shall conduct their due diligence before listing any RMP on its online portal. Platform must provide the name, qualification,

registration number, and contact details of every RMP listed on the platform

3. In the event some noncompliance is noted, the technology platform shall be required to report the same to BoGs, in supersession to the MCI who may take appropriate action
4. Technology platforms based on artificial intelligence/machine learning are not allowed to counsel the patients or prescribe any medicines to a patient. Only a RMP is entitled to counsel or prescribe and has to directly communicate with the patient in this regard. While new technologies such as artificial intelligence, Internet of things, and advanced data science-based decision support systems could assist and support a RMP on patient evaluation, diagnosis, or management, the final prescription or counseling has to be directly delivered by the RMP
5. Technology platform must ensure that there is a proper mechanism in place to address any queries or grievances that the end-customer may have
6. In case any specific technology platform is found in violation, BoG, MCI, may designate the technology platform as blacklisted, and no RMP may then use that platform to provide telemedicine.

Tele dermatology and Law

There is no definite legislation addressing the TP. One cannot take shelter on the pretext of tele dermatology consultation. A medicolegal principle of traditional consultation applies to TP.^[64] All prescriptions need to be signed duly by a RMP as per the Drugs and Cosmetic Rules 1945. The physician is responsible for the issues related to security, privacy, and confidentiality of patient data. The American Telemedicine Association Guidelines^[62] recommend that each health-care provider and patient should have a unique identifier and the images are stored confidentially in secured data base. Encryption for storage of patient data and for transmitting medical information should be inbuilt.

Use a disclaimer^[65] which may read as "the medical opinion is only based on records available without direct contact with the patient and hence, this advice is only to guide the referring doctor and cannot equate face-to-face consultation."

Medical ethics, Data Privacy, and Confidentiality^[63]

Principles of medical ethics including professional norms for protecting patient privacy and confidentiality as per the Indian Medical Council (IMC) Act shall be binding and must be upheld and practiced. RMP would be required to fully abide by the IMC



(Professional conduct, Etiquette, and Ethics) Regulations, 2002, and with the relevant provisions of the IT Act, data protection and privacy laws or any applicable rules notified from time to time for protecting patient privacy and confidentiality and regarding the handling and transfer of such personal information regarding the patient.^[66] This shall be binding and must be upheld and practiced.

RMP will not be held responsible for breach of confidentiality if there is a reasonable evidence to believe that patient's privacy and confidentiality has been compromised by a technology breach or by a person other than RMP. The RMPs should ensure that reasonable degree of care is undertaken during hiring such services.

Teledermatology and Education^[39,67-69]

TP plays a vital role in education. Resident training, exchange of knowledge and opinion between different dermatologists, and learning of dermatological diseases from different parts of the world are the roles of tele-education.^[67]

WhatsApp groups make it possible for dermatologists^[67] and other specialties to discuss various dermatological diseases and their appropriate management. It is one of the easiest media to exchange knowledge and experience on a one-on-one basis. It is considered to be one of the safest instant messaging media because of encryption technology.^[67] Dermatology residents feel more confident at handling various disorders with additional TD learning.^[68] TD can reduce the residents' empathetic nature toward patients and reduce the patient-physician relationship and loss of integral approach rather than focusing on single lesions.^[68,69]

Teledermatology and Reimbursement

Reimbursement policies for teledermatology services are rather new and vary significantly from place to place. The Netherlands offers full reimbursement for services and has completely integrated teledermatology into its health-care system.^[70] However, in the United States, reimbursement remains a major challenge in telemedicine and continues to evolve in recent years. Currently, all states and the District of Columbia have defined telemedicine law, regulations and Medicaid policies. In USA reimbursement varies from state to state.^[71] Reimbursement for live video teledermatology far exceeds the reimbursement for SAF teledermatology. Many states restrict reimbursement coverage to live video teledermatology only and exclude SAF teledermatology.^[71]

In the Indian context as per the recent NMC guideline,^[63] telemedicine consultations should be treated the same way as in-person consultations from a fee perspective: RMP may charge an appropriate fee for the telemedicine consultation provided.^[63] An RMP should also give a receipt/invoice for the fee charged for providing telemedicine-based consultation.

A Protocol for Teledermatology Practice

According to a survey completed by Armstrong *et al.*,^[72] most teledermatology programs have shifted from live interaction video to the SAF modality due to its technological flexibility and lower cost of service delivery. A dermatologist should screen the received clinical image from a general practitioner or self-acquired patient images^[73,74] (selfies) and define the objective/purpose of dermatology care [Figure 3]. If the case suits for diagnostic purpose, a treatment is offered. A clinician should be aware of the dermatological conditions where not to offer consultation for diagnostic purpose [Table 2]. In these cases, a dermatologist can perform face-to-face examination, investigate, analyze the case, offer treatment and provide follow-up care by TP [Figure 3].

Conclusion

In an Indian scenario, mobile teledermatology using messenger apps, for example, WhatsApp, can be used with good diagnostic accuracy and patient satisfaction. Mobile messenger apps provide a dermatologist to capture and transfer the clinical images either in still (SAF) and motion (video) or both. Recently, the BoGs (MCI) have proposed guidelines for telemedical practice. The IADVL in view of COVID-19 situation

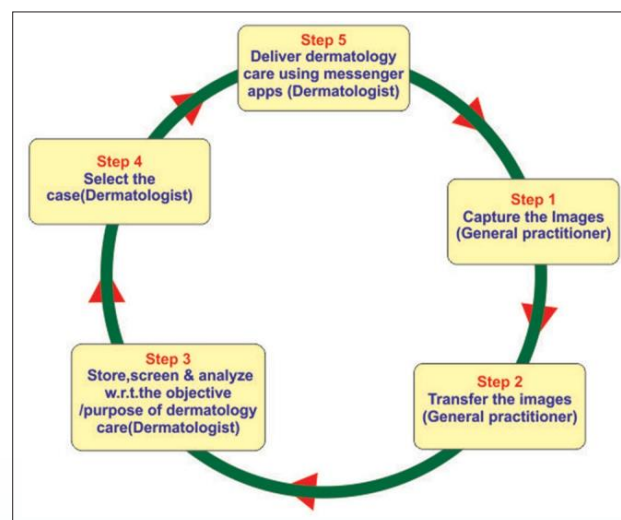


Figure 3: Illustrates the protocol for teledermatology practice

encourages its members to perform TP and provide care. The members may practice teledermatology after observing all conditions as in telemedicine guidelines prepared by NMC with due caution.

Financial support and sponsorship

Nil.

Conflicts of interest

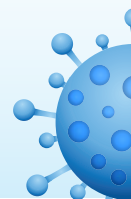
There are no conflicts of interest.

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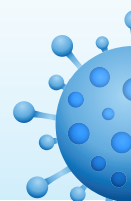


3. Learning never stops amidst Pandemic: Educational Research

Sl No	Title	SDG IMPACT
15	Psychiatry postgraduate examinations for the year 2020 in the middle of COVID19 Crisis: Suggestions from Indian teachers of psychiatry, Kishor m, Shah h, Chandran s, Mysore va, Kumar A, Menon V, Indian Journal of Psychiatry, 0019-5545	Goal 4: Quality education
16	Impact of COVID-19 Pandemic on Medical Education, Dr Praveen Kulkarni., Dr Basavana Gowdappa H., Higher Education Going Online: The Challenges in India, 89-98	Goal 4: Quality education
17	Technology Enhanced Neuroanatomy Learning during Covid-19 Pandemic - A Questionnaire Based Study from a Teaching Hospital in Mysore, Karnataka, India, Dr Vidya C.S., Dr Deepa Bhat., Dr Ravishankar M.V., Journal of Evolution of Medical and Dental Sciences, 10, 1130-1134, 2278-4748	Goal 4: Quality education
18	COVID-19 pandemic highlights the need to reconsider psychiatry training of Indian medical graduate, Manik C Bhise., Suhas Chandran., Shubhangi S Dere., Anil Kakunje., Dr Kishor M., Vikas Menon., H R Vinay., Mohan Isaac., Ajay Kumar., Naresh Nebhinani., Ravi Gupta., G Bharathi., M V Ashok., Anil Nischal, International Journal of Health and Allied Sciences, 9, 104-106, 2278-4292	Goal 4: Quality education
19	Psychiatry postgraduate examinations for 2020 in the middle of COVID19 crisis: Suggestions from Indian teachers of psychiatry, Henal Shah., Suhas Chandran., O P Singh., Dr Kishor M., Ashok V Mysore., Ajay Kumar., Vikas Menon., H R Vinay., Mohan Isaac, Indian Journal of Psychiatry, 62, 431-434, 0019-5545	Goal 4: Quality education



20	Academic Crisis During COVID 19: Online Classes, a Panacea for Imminent Doctors, Dr Sandeep S., Dr Shilpa C., Debayan Dey., S Kavya, Indian Journal of Otolaryngology and Head and Neck Surgery, 1-5, 0019-5421	Goal 4: Quality education
21	Does the Corpse teach the living? - Anatomy in the era of COVID -19, Dr Pushpa N.B., Kumar Satish Ravi, National Journal of Clinical Anatomy, 9, 79-81, 2277-4025	Goal 4: Quality education
22	Impact of COVID-19 Pandemic on Cardiology Resident Training and Education, Prashanth Kulkarni., Dr. Manjappa Mahadevappa, New Emirates Medical Journal, 2, 6-7	Goal 4: Quality education
23	Learning with Lockdown: Utility of WhatsApp Status Based MCQ Discussion on COVID- 19 among Medical students and Teaching Faculty, Sunil Kumar D, Journal of Education and Health Promotion	Goal 4: Quality education Goal 9: Industry innovation and infrastructure
24	Qualitative enquiry on the perceptions related to MCQ based discussion through WhatsApp status among medical students and teaching faculty during COVID-19 lockdown, Sunil Kumar Doddaih, Praveen Kulkarni, Aparna Mohandas, Narayana Murthy M.R, International Journal of Community Medicine and Public Health, 8, 675-685	Goal 4: Quality education Goal 9: Industry innovation and infrastructure
25	What to Teach and How to Teach Medical Students in the Middle of COVID-19? Guidance for Teachers in Psychiatry, M. Kishor, M. Indian Journal of Psychological Medicine Volume XX Issue X XXXX-XXXX 2021	Goal 4: Quality education
26	Ajay Kumar, Suhas Chandran, Kishor M. Use of electronic logbook in psychiatry training and its relevance during COVID-19 pandemic in India. Asian Journal of Psychiatry 64 (2021) 102763	Goal 4: Quality education Goal 3: Good health and wellbeing



VIEWPOINT

Psychiatry postgraduate examinations for 2020 in the middle of COVID19 crisis: Suggestions from Indian teachers of psychiatry

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ABSTRACT

The COVID19 pandemic is an unprecedented disaster. In India, the spread of COVID19 infection and the subsequent lockdown coincided with a crucial period of the annual examination in almost all educational institutions. The pandemic has created hurdles in the conduct of examination due to many reasons, some of which are spread of infection and associated safety issues, lack of public transport for patients as well as the postgraduates in outstation and examiners, and lack of workforce due to round-the-clock service for rendering health services leading to difficulty in arranging logistics at the examination center. Currently, there are no guidelines or policies on how examinations need to be carried out during such a pandemic. Hence, there is an urgent need to look at solutions within the profession for the completion of examination. Teachers of psychiatry play an important role in the national mental health services. Their expertise can be valuable for finding solutions that work. This article has compiled suggestions from Indian teachers of psychiatry.

Key words: Psychiatry, COVID19, Postgraduate examination

BACKGROUND

The COVID19 pandemic is an unprecedented disaster that has affected millions of people across the globe.^[1] In India, the spread of COVID19 infection and the subsequent lockdown


coincided with a crucial period of the annual examination in almost all educational institutions right from preschool to higher education. Health-care professionals are frontline workers in this crisis, and their presence is needed in large numbers for providing essential services, whose demand has increased drastically. Mental health services are an integral part of public health services, more so in disaster.^[2] However, in India, the numbers of mental health professionals are grossly inadequate for the population that needs these services.^[3]

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Annually, around 800 psychiatry residents from more than 200 medical institutions take up the final examinations in India.^[4] The successful ones start their practice as professionals to render mental health services. However, this year, the COVID19 pandemic has created hurdles for examination.

BARRIERS FOR POSTGRADUATE EXAMINATIONS AT THE TIME OF COVID19

The pandemic has created hurdles in the conduct of examination due to many reasons, some of which are spread of infection and associated safety issues, lack of public transport for patients as well as the postgraduates in outstation and examiners, and lack of workforce due to round-the-clock service for rendering health services leading to difficulty in arranging logistics at the examination center. The practical examination becomes more difficult as the process involves proximity with the patients and health-care professionals in the teaching hospitals, all of which can lead to high risk for infection. Some of the teaching hospitals have also been converted to designated COVID19 hospitals.

Currently, there are no guidelines or policies on how examinations need to be carried out during such a pandemic. However, there are equally compelling reasons for all stakeholders to complete the examination, and a further delay can adversely affect the students, faculty, and institutions in varied ways. Furthermore, the World Health Organization has warned that the pandemic and issues such as reinfection will prevent normalcy for many more months, ushering an unpredictable time frame to plan the ideal period for examination. Hence, there is an urgent need to look at solutions within the profession for the completion of examination.

POSSIBLE SOLUTIONS FROM INDIAN TEACHERS OF PSYCHIATRY

Teachers of psychiatry play an important role in the national mental health services.^[5] Their expertise can be valuable for finding solutions that work. The Indian Psychiatric Society (IPS) faculty training task force in association with the psychiatric postgraduate education subcommittee organized a focused webinar in early May 2020. The program invited all the Indian psychiatry postgraduate examiners and psychiatry faculty involved in the conduct of examinations to provide suggestions on how to carry out the examination. More than 200 faculty representing 65 educational institutions provided suggestions. These suggestions have been compiled here and presented for the dissemination of valuable input, particularly for this unprecedented postgraduate examination year 2020 in India.

Many have acknowledged that given the current crisis, there cannot be any single method or process, which is good for

all institutions. Hence, it is important to choose or decide a postgraduate examination process that is best suited for respective institutions. The following suggestions given here should be viewed in this context.

Many have urged that the psychiatry faculty, the heads of departments, and the potential examiners should proactively communicate or discuss the concerns and plans about this year's examination process with the respective examination authorities or registrars in their institution or university. This is because institutions or universities are currently responsive to such discussion and are accommodating various possible courses of action. It is important to voice out and facilitate discussions at all levels.

Many have suggested that the safety of examiners or facilitators, postgraduate residents taking examinations this year, as well as patients are all equally important. Hence, planning ahead and following all the prescribed safety measures is going to be crucial.

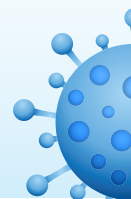
Suggestions highlighted that the examination process is also about the responsibility of examiners and that of institution toward society in certifying a budding professional for certain standards in service to public health. Hence, examination standards cannot be much compromised.

The theory examination was considered by many as a relatively feasible process compared to issues involved with practical examination. However, where possible, online theory examination with multiple choice questions or clinical application question can be used to evaluate a student who, in turn, answers from any place which can be monitored and considered as safe. Some institutions or universities, in recent years, have stepped up digital evaluation of answer scripts which are scanned and uploaded for examiners to evaluate in a safe environment. These methods can be considered by other institutions across India.

Practical examinations can be held as before, if the department or institution can manage the necessary resources and implement safety measures, for example, in green zone areas or as notified by the government.

If the department is planning to change the pattern of the practical examination after consultation with institution or university, it is important to notify the examination going postgraduate immediately and give minimum of 2 weeks' notice for the candidate, before examination or as per the policy of that institution. It is indeed important to orient postgraduates or train them in the new pattern of examination accepted by the institution or university.

There are ways to carry out practical examination by involving patients as examination cases. This includes patient



examination by maintaining social distance or live video streaming or playing recorded patient examination videos etc. It is important to explore all the methods examination and have them weighed against these three factors: reliability, validity, and resources. Checking these factors and discussing the possible issues in every department will assist in realistic and working solutions for the respective institution and those that can be implemented in all examination centers within the institution or university.

Wherever technology is involved in finding solutions, particularly video streaming or use of the Internet, many had apprehension about network issues that should be evaluated and ascertained at each geographical area.

It may become important for each institution or university to develop and archive e-resources such as video recording of simulated case vignette for examination. IPS can also develop and have a repository of such e-resources.

Similarly, one can conduct practical examinations by involving “nonpatients” such as simulated patients (considered as safe for health concerns) as “examination cases.” These simulated patients can be other postgraduates or interns or nurses or actors, who are trained and verified, so that they can act as real cases to facilitate examination. This method can be used for all examination cases such as long case or short case or neurology case.

The other ways to conduct practical examinations include the use of “written case scripts” or “audio recordings” or if institutions have designed mannequin (dummy/articulated doll) as examination cases. Designed mannequin can mimic a desired clinical condition. It is suggested considering these options for feasibility at the respective institution. Suggestions have also been received on the combination of the above methods and/or Objective Structured Clinical Examination (OSCE) or Tele OSCE to conduct examinations. If examiners and postgraduates are new to these concepts, it is important to discuss with the respective medical education unit in the institution or learning from experts or through video tutorials on the website. Training examiners will be the responsibility of the institution or university which chooses to go with such modifications.

About the requirement of external examiners where safe transport and infection are indeed a matter of concern, many have opined that having only regional examiners or available examiners in the respective city or examiners in neighboring cities, including former examiners, can be considered for conducting the examination. It is important to discuss with the respective institutional authorities about external examiners. All examiners should be oriented about the examination pattern well in advance.

There have also been suggestions to involve or encourage all postgraduates taking up the examination to contribute in patient care in all their capacity, particularly if there is a long delay in return to normalcy. It was suggested to look at ways and means to empower postgraduates in all aspects to utilize their acquired skill and knowledge in psychiatry services during pandemic. Some have suggested that if the postgraduates have been assessed periodically in a systematic manner that has been documented, the institutions can take a call on utilizing the documents to consider completion.

Along with the above suggestions, there was a consensus from all that, as a department or as an examiner or expert or institutional representative, this is an opportunity for the entire psychiatry collective to collaborate with decision-making authorities or policy-making bodies at all levels. It is necessary to proactively lobby for a safe and actionable plan for conducting examinations and associated issues.

CONCLUSION AND THE WAY FORWARD

It is important to be open to the ideas and suggestions, especially those which are based on available technology. Such methods can become a norm or an alternate method for conducting examination in the future, for example, to video stream the examination from one place to other or directly to the external examiner.

During the times of a pandemic of this magnitude, it is expected that each one, with their experiential wisdom and goodwill, shall do their best in relation to all issues arising out of COVID19 including that of the postgraduate examinations.

Disclaimer: It is important to note that these are suggestions from individuals and not to be considered as the official stand of IPS or any other organization or group or institution. These cannot be considered as guidelines. It is primarily intended for sharing imminent concerns regarding postgraduate examinations in psychiatry and looking at possible solutions. On 15 June 2020, the MCI released advisory to incorporate some suggestions mentioned as alternative in skill evaluation such as simulations, case scenarios etc as one-time exception in view of COVID19.

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Conflicts of interest

There are no conflicts of interest.



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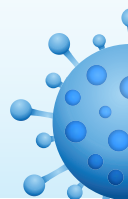
Impact of COVID-19 Pandemic on Medical Education

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Background The COVID-19 pandemic is a most crucial global health calamity of the century and the greatest challenge that the humankind faced since the 2nd World War.¹ The pandemic has posed serious challenges to almost all the sectors, including education. There is a fall in global trade and economy; industries have turned up semi-functional, infrastructure sector is functioning under limitations, health care industry is overburdened beyond its capacity. Impact of current pandemic on education sector is unprecedented and far reaching.² Medical Education which essentially takes care of producing human resource for health workforce has experienced major setback following this public health emergency of international significance. Medical Education in India As on today there are 542 medical colleges in India with 80,555 undergraduates,³ 75236 postgraduate and 7748 super-specialty admission provisions annually.⁴ Students enter medical schools after their pre university or 12th standard education through NEET & common entrance tests and pursue their under graduation for five and a half years. During this period, they are destined to learn the art and science of medicine through pre-clinical, paraclinical and clinical subjects through a regulation driven curricular spiral. Attention is paid to bring out a job ready primary care physician who can independently function as a health care provider in resource limited settings.⁵ The student who qualifies for post-graduation through NEET, selects the specialty of his/her choice/chance and develops Higher Education Going Online 90 specialized knowledge and skills in that subject over a period of three years. The major focus of post graduation is to bring out a specialist health care professional who has been certified for specific entrustable professional activities pertaining to the subject. Super-specialty programs bring out a super specialist in one particular area of Medicine through focused training and skill development for the period of three years.⁶ Impact of COVID-19 on Medical Education in India As COVID-19 is a novel infectious disease with lack of specific treatment options and preventive vaccination, social distancing, wearing mask with proper hand sanitization are adapted as major strategies to break the transmission of this dreaded infection. In order to materialize this strategy, nationwide lockdown was imposed in the last week of March 2020.⁷ This resulted in closure of all educational activities, including medical colleges and universities across the country. Most of the undergraduate students opted to go back to their native places and post graduate students were inevitably involved and forced to work in the management of COVID cases, flu clinics and take care of regular non COVID patients. In the initial days of Pandemic, the undergraduate medical education was severely hampered compared to post graduate programmes. Though the theory classes were conducted on virtual mode, the practical sessions, dissection sessions, clinical postings, field visits, and demonstrations were not feasible. The formative and summative assessment of the students has been heavily compromised.⁸ There was a major break in the connectivity between medical school campuses and students, leading to an intolerable vacuum in the system, sense of uncertainty, decay in confidence levels and unexplained fear among students. On the other hand there were other factors like apprehension about the spread of the disease, severity of illness, risk of mortality, rapidly disseminating misinformation (infodemic), unprepared health care delivery system, fastest changing treatment guidelines, government rules and regulations on quarantine and isolation have further kept students, faculty and parents in utmost psychological pressure.⁹ Medical Council of India has rolled out new competency based medical education curriculum from the year 2019. This curriculum has several Impact of COVID-19 Pandemic on Medical Education 91 new initiatives like Attitudinal Ethics and Communication (AETCOM) Modules, serial formative assessments, early clinical exposure, self-directed learning sessions, certifiable skills assessment etc. The current batch (2019) of first year MBBS students are expected to complete all these tasks before taking the final university examinations.⁵ As most of these initiatives are attitude and skill based, necessitating active involvement and interaction of the students and teachers were left partially covered by most of the medical colleges due to pandemic. One of the major domains of medical education is clinical/bedside teaching. Students interact with the patients in the hospital wards, understand their ailments, undertake basic clinical examination, observe clinical signs, interpret the laboratory



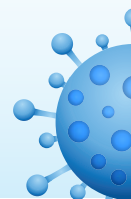
investigations, make provisional diagnosis, discuss with their findings with the teacher on bedside and deepen their knowledge and skills. The teachers on the other hand, demonstrate the clinical signs, show the minor procedures and elaborately discuss the clinical findings with the students.¹⁰ The physical presence of students in clinical subjects are very important and helps the students to learn finer details of medical science which is remarkably affected due to current pandemic. Community based education through family visits, community surveys, community diagnosis, environmental assessment; educational visits to peripheral health centers, field based short term research projects help the students to understand socio-cultural norms of the community. These activities facilitate the students to understand the causative factors for the diseases in community settings, provide opportunity to explore the health needs and demands of the people.¹¹ The students are again missing their learning in these human laboratories because of the pandemic situation. Assessment is the tail that wags the curriculum dog.¹² One of the major domains of medical education which has been worst affected due to current pandemic is assessment of the students. Medical students are assessed for their theoretical knowledge through written tests, application of knowledge and skills through practical exercises and adaptation of learnt knowledge and skills in real life situation through clinical case presentations. Though the assessment of knowledge domain can be undertaken through written tests and assignments, the assessment of skill based competency like Higher Education Going Online 92 clinical examination and communication skills are almost sacrificed due to lockdown.⁸ The students are also deprived of real time constructive feedback on their knowledge and performance by their facilitators. These factors may have long term impact on developing essential clinical competency among medical students. Unlike other technical courses, the medical education mandates final university examinations of both undergraduate and post graduate programmes in real life situation. Hence the scope for final theory or practical examination on online mode in MBBS/MD/MS/Super specialty programmes is hampered and unsatisfactory. Most of the universities across the country have to postponed the examinations due to lockdown and corona-phobia. Accessibility of students to the parent institutions was a major challenge to undertake examinations due to restriction of mobility. There were difficulties in convincing examiners from the neighboring states and the other colleges in the same states to visit the institutions and conduct practical examinations. Finally Board of Governors in Suppression of MCI had to make some amendments in the conduct of postgraduate examinations which were supposed to be completed by May 2020 by making some relaxation in the provision of appointment of external examiners, so that examinations can be completed by June 2020 during this pandemic period. The MCI also gave approval to get external examiners from outside the state to be on virtual mode.¹³ Silver Lining in the System- Activation of Online Learning Platforms E- learning/online learning method has emerged out as a silver lining in the collapsing medical education system. Deemed to be universities and private medical colleges were the first ones to explore these platforms to establish the connectivity between their campuses and students. There was a very positive response for this strategy from teachers, students, parents and management as this is a sole way to keep up the learning during pandemic times.¹⁴ Traditionally medical teachers are not very well accustomed to this virtual or online way of teaching process due to technophobia. The common reason for this could be the wider perception that medicine is taught more effectively on bedside than bench side (with computers). Lack of techsavvy attitude, strict regulatory guidelines on teaching-learning, inherent Impact of COVID-19 Pandemic on Medical Education 93 inertia to change, non availability of online learning platforms and related infrastructure, lack of training on use of virtual platforms are some of the other reasons worth to quote.¹⁵ The COVID-19 pandemic invariably forced the medical teachers to break all these barriers and adapt to online teaching-learning process in a tremendously fast manner. Few virtual learning apps like ZOOM, Go to webinar, Google Meet, google classroom, Cisco Webex, Microsoft team, Impartus have suddenly found their space in medical education system. Few universities developed and utilized their own virtual learning platforms to educate their students. There was a sudden shift in the teaching learning methodologies from classical chalk and talk to virtual classes. The students, parents and a portion of teaching fraternity found it really exciting in the midst of stagnant days of lockdown.¹⁶ Before rolling out these online classes, few institutions and universities conducted training sessions to their faculty members and students on the mode of using these platforms. Series of webinars were conducted to train the faculty on creating the lesson plan for online classes, monitoring the student's attendance during sessions, scheduling of classes in these platforms,



interacting with the students through virtual platforms etc. These activities to some extent helped to boost the confidence among teachers and made them ready to adapt to the new paradigm of medical education.¹⁴ Next came the phase of innovation in online teaching- learning methods. Few of the enthusiastic teachers from the fraternity developed innovations in online teaching like live surgical demonstrations, virtual small group teachings, flipped classrooms, student webinars, online case presentation and discussions, Whatsapp based discussions, computer assisted simulations, simple virtual reality, podcasts, facebook live sessions, online quiz competitions, case based discussions etc.¹⁶ These strategies helped to break the monotony of didactic online classes and helped the students to get actively involved in virtual classes. Online assessment mechanisms are one of the major adaptations by medical schools. Multiple choice questions, written assignments, theory examinations under virtual supervision, online viva voce, E spotters have been adapted with varying level of success across medical students to keep Higher Education Going Online ⁹⁴ the assessment activities intact.⁸ Pre and Paraclinical departments have also made attempts to conduct online practical examination through simulated case based exercises, case vignettes, short video clippings of clinical cases etc. Challenges Associated Learning Through Virtual Platforms Though virtual mode of learning acted as a savior for keeping the process of medical education intact during lockdown times, it has opened new set of challenges among teachers, students and the administrators of the institutes. As mentioned earlier, training the faculty members on this new mode of education was a major bottleneck in implementation. Teachers with little or no experience with online teaching methods, using of virtual learning apps, managing technical difficulties had to face serious drawbacks in initial days of implementation. As the time passed majority of them developed these competencies and performed the tasks without much hurdles.¹⁵ Adjusting to new norms of teaching learning process was another common problem among teachers. Teachers had to deliver lectures without maintaining eye to eye contact with the students, manage the activities of students during sessions, keep up the interest level of students during classes, explain the complicated concepts through power point presentation slides (without blackboards) and manage the student's attendance following sessions through chat boxes etc. This multi-tasking nature of work at a short span of time was difficult to understand and cope up among faculty members. Internet and connectivity related issues were the major distractors in the entire process. Teachers staying in the remote areas with limited internet access faced a lot of problems in handing online classes. Inability to take scheduled classes due to lower internet bandwidth created panic among teachers and confusion among student communities. The students staying in remote areas also had to face similar situation as they had fear of losing the course content as well as attendance for online classes.¹⁷ Managing the activities of students during the sessions was another problem. Some students create unnecessary distractions through regular unmuting of microphones, playing of songs/voices in the middle of ongoing sessions; Impact of COVID-19 Pandemic on Medical Education ⁹⁵ putting unusual messages in the chat boxes were common complaints. Common question is the extent to which students attentively listens to the teacher during the entire period of class. Ultimately the teachers had to explore the provisions for maintaining such activities in the apps and send warning messages to the students on this disciplinary action for this behavior. This kind of diplomatic handling of students and teachers was an uphill challenge for the institutes.¹⁸ Dealing with double burden of clinical care and online classes was another common challenge for the clinical faculty members. Hospitals being flooded with COVID and Non COVID cases which require utmost care and monitoring posed less time for the faculty to prepare for online teaching sessions.¹⁹ Though student's express satisfaction on virtual mode of education, there were few concerns from their side too. Lack of interactive learning, practical exposure, invisible body language, skill-based training, distraction by friends and family members during sessions, technical issues, variable competency of teachers to handle online sessions, were the common challenges.¹⁸ Managements of the institutions also faced the challenges with reference to developing IT infrastructure in the campus, faculty training for online teaching, coping with financial burden induced by COVID-19 in terms of lower patient inflow to hospitals, monitoring the online classes being conducted by teachers, collecting regular feedback from both faculty and students, keeping up the pace of academic activities without compromising the quality of patient care at hospitals were few to name. Conclusion COVID-19 pandemic has created major disturbance in the medical education sector. Undergraduate medical education is more seriously disrupted compared to post graduate and super specialty programs. Curriculum implementation,



teaching-learning activities, assessment, feedback, evaluation of the student's performance is heavily compromised. Traditional classroom and bedside teaching has largely got shifted to virtual mode of content delivery. Though the knowledge domain of education is kept intact, attitudinal and skill domains are sacrificed to a Higher Education Going Online 96 larger extent. Exclusive online learning may not be a satisfactory way of instructions in a country like India with larger diversity and geographical disparity. We need to work on the strategies of blended/ hybrid learning to impart knowledge, attitude and skills based training to the medical students in pandemic times. Future Thoughts 1. There is need of research and refinement on effective virtual teachinglearning process 2. There is need to upgrade the infrastructure and create efficient human resource to handle and adopt to the new norm 3. Clinical and practical training may need to be through hybrid mode of both virtual case scenario and blend of physical case demonstration or practical demonstration for small group of students 4. There is need for creating an acceptable competency-based training with both vertical and horizontal integration across the subjects. References 1. Chakraborty I, Maity P. COVID-19 outbreak: Migration, effects on society, global environment and prevention. *Sci Total Environ.* 2020;728:138882. doi:10.1016/j.scitotenv.2020.138882. 2. Roger Y. Wong. Medical education during COVID-19: Lessons from a pandemic. *BCMJ-Special Feature, COVID-19*;62(5):170-1 3. Medical Council of India. List of Medical Colleges teaching MBBS in India. URL available from <https://www.mciindia.org/CMS/information-desk/for-students-to-study-in-india/list-of-collegeteaching-mbbs>. Downloaded on 02.09.2020. 17:50 Hrs IST 4. Medical Council of India. Dashboard of Medical Faculty and PG students in India. URL available from, <https://www.mciindia.org/CMS/information-desk/faculty-medical-students-information>. downloaded on 02.09.2020, 18.00Hrs IST 5. BOARD OF GOVERNORS IN SUPER-SESSION OF MEDICAL COUNCIL OF INDIA AMENDMENT NOTIFICATION. Regulations on Graduate Medical Education (Amendment), 2019. URL available from, Impact of COVID-19 Pandemic on Medical Education 97 <https://mciindia.org/ActivitiWebClient/open/getDocument?path=/Documents/Public/Portal/Gazette/GME-06.11.2019.pdf>. downloaded on 02.09.2020, 18.10 Hrs, IST. 6. MEDICAL COUNCIL OF INDIA POSTGRADUATE MEDICAL EDUCATION REGULATIONS, 2000. URL available from <https://www.mciindia.org/documents/rulesAndRegulations/PostgraduateMedical-Education-Regulations-2000.pdf>. downloaded on 02.09.2020, 18.25Hrs IST 7. Kulkarni P, Prabhu S, Dumar SD, Ramraj B. COVID-19-Infodemic overtaking Pandemic? Time to disseminate facts over fear. *Indian J Comm Health.* 2020;32 (2-Special Issue):264-268. 8. Pattanshetti VM, Pattanshetti SV. The impact of COVID-19 on medical education in India. *J SciSoc*2020;47:1-2. 9. Chandratre S. Medical Students and COVID-19: Challenges and Supportive Strategies. *Journal of Medical Education and Curricular Development* 2020;7: 1–2 10. Carlos WG, Kritek PA, Clay AS, Luks AM, Thomson CC. Teaching at the Bedside Maximal Impact in Minimal Time. *AnnalsATS* Volume 2016;13(4):545-8 11. Kelly L, Walters L, Rosenthal D. Community-based medical education: Is success a result of meaningful personal learning experiences?. *Educ Health* 2014;27:47-50 12. Singh T. Basics of assessment. In: Singh T, Anshu, editors. *Principles of Assessment in Medical Education*. New Delhi: Jaypee Publishers; 2012. pp. 1–13. [Google Scholar] 13. Available from: [https://mciindia.org/MCIRest/open/getDocument?path=/Documents/Public/Portal/LatestNews/Advisory-relaxation-PG-22.05.2020%20\(1\).pdf](https://mciindia.org/MCIRest/open/getDocument?path=/Documents/Public/Portal/LatestNews/Advisory-relaxation-PG-22.05.2020%20(1).pdf). [Last accessed on 2020 Jun 01] 14. Preeti Sandhu and Maisie de Wolf (2020) The impact of COVID-19 on the undergraduate medical curriculum, *Medical Education Online*, 25:1, 1764740, DOI: 10.1080/10872981.2020.1764740. 15. SaiyadS, Virk A, Mahajan R, Singh T. Online teaching in medical training: establishing good online teaching practices from cumulative experience. *Int J App Basic Med Res* 2020;10:149-55 Higher Education Going Online 98 16. Goh PS, Sandars J. A Vision of the use of Technology in Medical Education after the COVID-19 Pandemic. *MedEdPublish*; 2020:9 17. Rajab M H, Gazal A M, Alkattan K. Challenges to Online Medical Education During the COVID-19 Pandemic. *Cureus*.2020 12(7): e8966. DOI 10.7759/cureus.8966 18. Rose S. Medical Student Education in the Time of COVID-19. *JAMA.* 2020;323(21):2131–2132. doi:10.1001/jama.2020.5227. 19. Gill D, Whitehead C, Wondimagegn D. Challenges to medical education at a time of physical distancing. www.thelancet.com Vol 396 July 11, 2020



Technology Enhanced Neuroanatomy Learning during Covid-19 Pandemic - A Questionnaire Based Study from a Teaching Hospital in Mysore, Karnataka, India

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ABSTRACT

BACKGROUND

The present Covid-19 situation has created an era of learning through the electronic devices, where YouTube channel is playing an important role. Neuroanatomy is a complex subject requiring three-dimensional orientation of the structures. Practical teaching by using the cadaveric specimens is a usual practice, but in the current situation the virtual platform is an indispensable and sustainable option for both teaching and learning activities. In the present study the utility of YouTube and digital content on neuroanatomy was assessed among I MBBS students using self-administered questionnaire during Covid -19 pandemic.

METHODS

The questionnaire based cross sectional study of prosected neuroanatomy specimens in the department of Anatomy were utilized to create digital content modules. According to the topics, PDF content was generated, and it was shared before the commencement of virtual class. Later YouTube link was shared with our I MBBS students through social media platforms like WhatsApp and Facebook regularly. At the end of completion of whole teaching schedule, a questionnaire was circulated to obtain the feedback on this teaching method. Finally, the responses were collected and interpreted.

RESULTS

In the present survey, 257 participants (176 females and 81 males) from 10 medical colleges responded to all 12 items of the questionnaire. We observed that 36 % of them graded excellent for content, 25 % for audio quality, 21 % for video quality, 29 % for specimens used, 25 % for labelling of specimens in YouTube videos. Out of 257 responses 35 % of them were graded excellent for pdf content, 30 % for pictorial representation of brain specimens, 30 % for labelling and 24 % for length. For overall rating for teaching learning method 35 % of them graded 8, 17 % graded 9 and 7 % of them have graded 10.

CONCLUSIONS

This mode of learning can be used for the purpose of distal education as per the convenience of the students, who are presently staying away from the campus. Our students have taken the benefit of teaching where the PDF and YouTube contents were appreciated by large number of students.

KEY WORDS

Neuroanatomy, YouTube, Digital Content, Technology, Learning Resources

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BACKGROUND

The Covid-19 pandemic has led to closure of educational institutions causing remarkable impact on education. Lockdown has compelled the teachers to instruct through online platform. It has disrupted the academic activities among all professions. Though digital platforms are used for learning, many of them are facing a great challenge to adjust to a sudden change.¹ Medical education is not an exception to face this challenge. Most of the medical schools have quickly adapted to the online classes by shifting to virtual modes. Various online platforms like ZOOM, web ex, Google classroom, Impart us etc. are utilised by different institutions. Neuro anatomy is a subdivision of anatomy which deals with detailed study of structure of nervous system. Application of neuro anatomy knowledge to clinical practice is perceived to be very significant. But complexity of the subject content, and its 3D orientation makes them difficult to learn, assimilate and recapitulate. It requires a great motivation to keep them interested to learn this area of anatomy.²

The intricate structures, with its 3-dimensional relationships, and challenge in clinical integration are cited among the potential causes for difficulty in learning. In the absence of direct contact teaching with faculty, undergraduate neuro anatomy education is vulnerable in the time of the Covid-19 lockdown.³ The use of social networks in medical education can remodel and enhance anatomy teaching and learning; one such network is the video-sharing site YouTube. They support independent learning and integration in a problem-based curriculum.⁴ There are various ways that online learning can be structured and implemented. Reinforcement of regular online teaching with any additional methods would supplement the asynchronous learning. The present situation has created an era of learning through the electronic devices where the YouTube channel has become a significant vehicle.

Currently the concept of teaching and learning methods have gone beyond the boards and books, because present day is revolutionized by the technology which can be accessed by each and every student. Electronic or E-learning means learning through internet or intranet connectivity through the electronic gazettes which is one of the important and widely used method of learning in many national and international universities, colleges, institutions, tutorials, learning web portals, etc. around the world. Hence YouTube videos of the relevant structures with additional learning resources were supplemented to routine zoom class teaching of undergraduate neuro anatomy.

The present study aims to assess the utility of YouTube and digital content on Neuroanatomy modules among I MBBS students using self-administered questionnaire during Covid - 19 pandemic.

METHODS

Ethical clearance was obtained from institute ethical committee. Questionnaire based cross sectional study was done between May 2020 and July 2020 during Covid pandemic, period. Routine online classes for I MBBS students were conducted in Department of Anatomy, JSS Medical

College, and Mysore. The neuro anatomy classes were conducted under 10 modules, covering all the parts of neuro anatomy as per the syllabus.

The projected specimens available at dissection theatre were demonstrated through video recording, which is synchronizing with the theoretical explanations. The recorded video was peer reviewed by subject experts, later it was edited and quality of audio and video were checked before uploading on the YouTube channel. Supplementary PDF study material and YouTube link of dissection videos were shared among students belongs to other colleges as well through the WhatsApp and Facebook groups. After a gap of 15 days of online teaching schedule, a 12-item expert validated questionnaire was utilised to obtain feedback on this teaching method. The responses were subjected to statistical analysis, and the results were interpreted.

All the 12 items were assessed (Table 1) and 1st the responses were subjected to statistical analysis, and the results were interpreted.

Sl. No.	Items	Grade
1	Overall score for YouTube videos	
	a. Content	
	b. Audio quality	1 - 4
	c. Video quality	1. Below average, 2. Average 3. Good 4. Excellent
	d. Specimens used	
	e. Labelling	
2	f. Length / duration	
	Overall score for PDF study material	
	a. Content	1. Below average, 2. Average 3. Good 4. Excellent
	b. Pictorial representation	
3	c. Labelling	
	d. Length / duration	
4	I would prefer a. YouTube videos b. PDF c. YouTube + PDF	a / b / c
5	Would you prefer to use videos and PDF?	
	a. Pre class	a / b
6	b. Post class	
	Can this YouTube / PDF content be utilised for learning clinical or applied anatomy	Yes / No
7	Were the handwritten diagrams in PDF reproducible?	Yes / No
8	Will the videos / PDF help in quick revision for assessment	Yes / No
9	Do you feel that YouTube videos assist to connect and relate anatomy learning than power point presentation alone	Yes / No
10	How often do you watch YouTube videos?	Answer
11	a. Everyday b. Every week c. Never	
	Overall rating for this teaching and learning mode	1 - 10 1 - least, 10 - maximum
12	Any suggestions for further improvement	Answer
13	Do you prefer to have more videos in future in other topics in anatomy	Yes / No

Table 1. Questionnaire on Digital Content and YouTube Videos of Brain Specimens

Statistical Analysis

All the responses were subjected to statistical analysis, and the results were interpreted. Frequency of responses were expressed in percentage.

RESULTS

In the present survey 257 participants (176 females and 81 males) from 10 Medical Colleges responded to all 12 items of the questionnaire. We observed that 36 % of them graded excellent for content, 25 % for audio quality, 21 % for video

quality, 29 % for specimens used and 25 % for labelling of specimens in YouTube videos as shown in Figure 1.

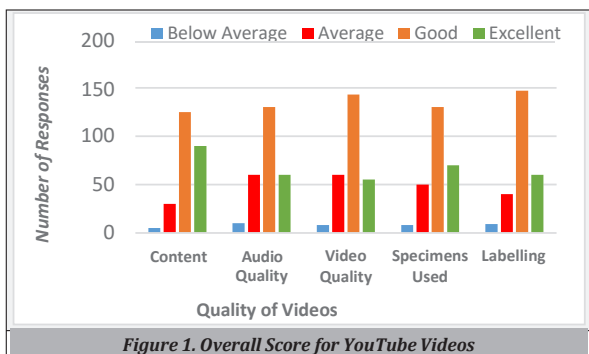


Figure 1. Overall Score for YouTube Videos

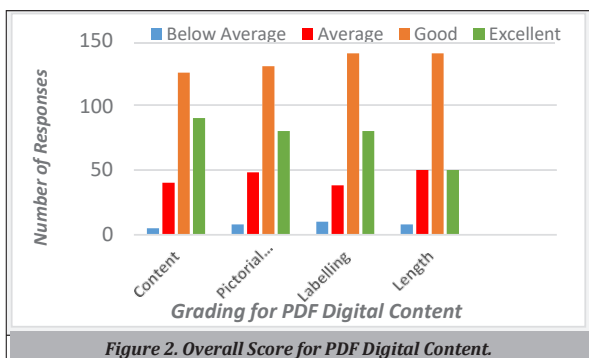


Figure 2. Overall Score for PDF Digital Content.

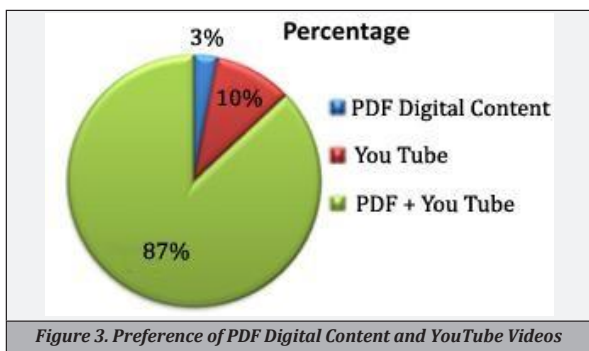


Figure 3. Preference of PDF Digital Content and YouTube Videos

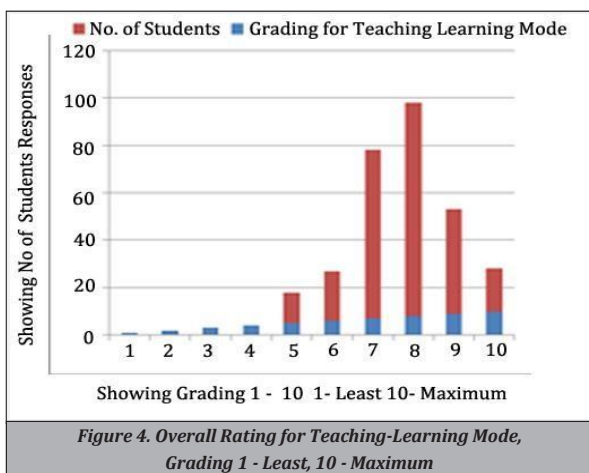


Figure 4. Overall Rating for Teaching-Learning Mode, Grading 1 - Least, 10 - Maximum

Out of 257 responses 35 % of them graded excellent for pdf content, 30 % for pictorial representation of brain specimens,

30 % for labelling and 24 % for length (Figure 2). 223 participants preferred both pdf and YouTube videos for self-directed learning (Figure 3). 72 % of students preferred Neuroanatomy videos and PDF access before the class and 28 % of students preferred in post class. 84 % of students responded positively that YouTube, and PDF content could be utilized for learning clinical or applied anatomy. 67 % of students responded that handwritten diagrams in PDF content were reproducible. 92 % of students responded that videos and PDF will help in quick revision for assessment and helps to score better marks. 76 % students opined that YouTube videos could assist to relate anatomy learning than power point presentation alone. 82 % of students preferred to have videos in other topics in Anatomy.

In overall rating for teaching learning method, 35 % of them graded 8, 17 % graded 9 and 7 % of them have graded 10 (Figure 4). Most of the students suggested that practical exposure was necessary as only videos alone would not be fully sufficient for learning. But this resource or supplementary material was a good asset for students that can be utilised for learning.

DISCUSSION

YouTube platform is one of the largest video sharing and learning virtual platform that not only caters to entertainment but also for an efficient delivery of teaching and learning across disciplines. It is one of the accessible and convenient alternate sources of learning to explore the concepts especially during the current critical pandemic lockdown situation, the students could access the learning material from the home at their convenience. Dr. Najeeb's virtual online YouTube lectures stand as a best illustration which is widely accepted by number of students around the world. Today teaching is supplemented with the power point presentations (PPT), animations, videos, smart board usage, etc. Its utility has enhanced the subject understanding by influencing more clarity on the concepts. Advent in the field of information science and technology has enabled us to extend the education through outreach programmes globally. It has influenced every field including medical education. We the medical teachers need to transform from the conventional and traditional teaching methods to virtual platforms, where the actual human involvement was playing an important role, but it was associated with the requirement of lot of manpower to cater to its need. Electronic mode of teaching can be delivered as a live transmission or it can be recorded well in advance; it can be released on the net for its access all around the world. Use of live video lectures and demos along with pre and post lecture assignments made a great impact on student learning and evaluation. The live online teaching is having an opportunity to dialogue with the students which mutually influence the interest in teaching and learning. Online teaching may require a pre and post session activities; it is having an advantage of monitoring at the end.

Study conducted by Ayman, a questionnaire survey on perception of YouTube videos in learning anatomy on Jordanian Medical Students was conducted. They reported that 79.1 % of the students used YouTube for learning gross anatomy, dissection videos were the most frequently viewed

anatomy related content. YouTube offered them as a most convenient, cost-effective, and anatomical supplementary tool supporting their subject understanding.⁵ A comparative study by Rocio including the 3rd year volunteer medical students who were learning radiology practical lessons through 3D virtual classroom v / s real world classroom, were assessed for their pre and post training knowledge in the taught subject. They reported similarity in acquisition in their interpretive skill on the radiology findings. The virtual classrooms facilitated an added advantage of free participation among the students without the fear of identity disclosure.⁶ In the present survey virtual learning of neuroanatomy module through YouTube and PDF together was appreciated by 87 % of students, but only 10 % of them appreciated YouTube videos alone. A study conducted in King Abdul-Aziz University, Saudi Arabia, in a circumstance where there was not enough number of teaching faculties were available for the conventional teaching, where virtual classroom was an inevitable option. A comparative study which was conducted to assess the outcome of live conventional face-to-face classroom teaching v / s E-learning classroom teaching. In both these modules, face-to-face and virtual classes were conducted by the same instructor to compare the outcome between these two groups and reported that not much difference in response among the learners from either of these two groups.⁷ Though the final year medical students have expressed their positive opinion about the virtual learning platforms, but it has failed to compensate their practical skill component, which can create an obvious deficit in fulfilling their clinical competency.⁸ Though E learning is not able to see its complete replacement to didactic conventional lectures, but in the present inevitable situation creating a barrier for students to attend their regular institutionalized academic activities where E-platform seems to be an indispensable option. In the present study overall acceptance of Neuroanatomy virtual teaching and learning module under "Likert's scaling has indicated an excellent score grade. In the present critical pandemic situation, virtual platform can foster an attitude of self-directed learning among the fraternity of medical students particularly during their preclinical learning activities.⁹

No platform can fulfil the complete academic requirement at any point of time. Despite having number of advantages and some limitations, the live online teaching is having an opportunity to have a dialogue with the students, which mutually influence the interest in teaching and learning between the teacher and student.¹⁰ Online teaching may require pre and post session activities to monitor the outcome at the end. The other advantages of E-learning are, its ease to access to an unconditional learning, it is a cost-effective educational resource, it can target specific and needful audiences, it offers a combination of acquiring the education along with work during their course, which is a common practice in western countries, and it mainly provides barrier less educational approach worldwide. Some of its limitations are including, difficulty to understand the student involvement under online learning due to lack of personal contact between the teacher and students.¹¹ The learning through the electronic media requires a basic expertise to handle the devices. The smart phones or android phones, advancement in optic fiber technology has revolutionized the accessibility of internet services to wider extent. They have a great potential

in mediating the learning especially in the field of medical education, where its application can access the required information on the spot; its justified usage has influenced the teaching and learning activities despite some technical drawbacks. Present Covid-19 pandemic situation, where web-based learning has created huge market for the industry stakeholders for providing proper learning resources, materials, contents, etc. which can be accessed tirelessly through different apps.

However, from the teaching and learning point of view, there are number of constraints to give a complete and satisfactory practical hand on exposure to the students of medical fraternity which still remains as a challenge in the present situation.

CONCLUSIONS

The present pandemic situation has given rise to a need for an alternate tool for asynchronous learning through media like YouTube. Despite a number of drawbacks, E-learning has emerged as a best alternate tool. Supplementing learning resources through the digital content would exponentially enhance the student learning. Our education system needs to imbibe technology to cope up with the changing needs of global educational standards, where one can access learning materials from the nook and corner of the world. YouTube is a powerful tool in this regard, in the current situation.

Limitations

Technical constraints and technical snag can disturb the learning sessions. Above all, the most difficult task to conduct the practical classes, especially in the field of medicine is that the students may fail to realize the importance of human touch, pain, and psychology of the patient.

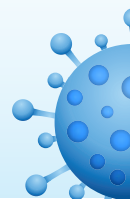
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Commentary

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COVID-19 pandemic highlights the need to reconsider psychiatry training of Indian medical graduate

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Abstract:

In the middle of COVID-19 crisis in India and the psychological impact on millions of peoples, is it time to reconsider psychiatry training for Indian medical graduate under the new competency-based curriculum? India has one of the highest numbers of medical colleges in the world and also has over a million doctors, including MBBS graduates working at the primary health-care centers who are important pillars for health-care delivery. In a major drawback that also plagued the earlier curriculum, the new competency-based curriculum has not incorporated a single mandatory skill in psychiatry which a medical trainee has to demonstrate to become doctor. Mental health and the COVID-19 pandemic are interlinked in a complex manner. Hence, millions are likely to have mental health consequences. With no skill required in psychiatry as a must for a medical trainee to become an MBBS doctor, the mental health services during or aftermath of a disaster are severely compromised and need urgent reconsideration under the new curriculum.

Keywords:

Competency-based medical curriculum, COVID-19, Indian medical education, mental health in disaster, undergraduate psychiatry training

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India has one of the highest numbers of medical colleges in the world; there are

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more than 500 medical colleges with an annual intake of over 70,000 medical students.^[1] India also has over a million doctors, including MBBS graduates working at the primary health-care centers who are important pillars for health-care delivery in India. The Medical Council of India has introduced a new medical curriculum for Indian medical graduates, which was implemented in 2019.^[2] In a major drawback that also plagued the earlier curriculum, the new competency-based curriculum has not incorporated a single mandatory skill in psychiatry which a medical trainee has to demonstrate to become a doctor.^[3] This has been criticized by experts based on the health-care needs of India.^[4] The increasing mental health burden has serious implications for India; the estimated economic loss due to mental

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health conditions, in the year 2012–2030, is 1.03 trillion US dollars.^[5] Clearly, not needing to learn a single mandatory skill in psychiatry to be able to practice as a doctor is a paradox for a country like India with over 1350 million people, having a high burden of mental health conditions and one of the highest suicide reports in the world.^[6] The Global Burden of Disease Study mentions that in India, one in seven has a mental health disorder that needs treatment, while only 5% of those suffering from even common psychiatry disorders receive appropriate treatment, indicating a massive treatment gap of 95%.^[7] In addition to these challenges, the ongoing major global health and humanitarian disaster, the novel coronavirus (COVID-19) pandemic has unleashed an unprecedented health-care crisis.^[8] The need for psychological services for millions of people including those who are being treated for infection in isolation or at quarantine center and their families is an important area that has to be addressed.^[9] Mental health and the COVID-19 pandemic are interlinked in a complex manner; millions are likely to have mental health consequences due to many reasons such as job loss, unemployment, financial constraints, and an uncertainty even after the pandemic is contained.^[10] There have been efforts for urgent multidisciplinary research on mental health issues during the COVID-19 crisis that can affect millions of people with the onset or recurrence of anxiety, depression, substance use, suicide, and self-harm.^[11] There seem to be many challenges in strengthening disaster mental health services at all levels of disaster management and in all stages of disaster response. Meeting these challenges would ensure that psychosocial support following disaster, would be a norm and not an exception in the affected country. Mental disorders are stigmatizing and walled off from the public health mainstream. Mental health needs to be accepted as an integral to almost every aspect of health and development. The greatest obstacle to promoting mental health in developing countries is that it remains largely ignored by health policies.^[12] This is particularly true for India, with no skill required in psychiatry as a must for a medical trainee to become an MBBS doctor; the mental health services are severely compromised. It is not difficult to estimate the deficiencies in services, even for minimal psychological services; the Indian doctor may not do justice for the people affected during disaster or the aftermath. There is an urgent need for competent MBBS doctors who have learned the required psychiatry skills in all domains, not just in cognitive domain, and are able to demonstrate affective and psychomotor skill to help the affected people. This is crucial, more so in a disaster because India has one of the lowest number of psychiatrists in the world with 0.4/100,000 population.^[13] The Indian medical curriculum should have provided adequate mandatory psychiatry skills for licensing and certification in the

new competency-based curriculum that incorporates learning in disaster management. Unfortunately, in the competency-based MBBS curriculum, disaster as a topic is covered only in six sessions in the entire medical curriculum:^[2] four competencies in community medicine (CM13.1 to CM13.4) that have vertical integration with general medicine and general surgery, one in forensic medicine (FM2.33) and one in psychiatry (PS 19.6). Almost all are core competencies in the knowledge (K) domain except forensic, which is in attitude and communication (A and C), all are in the “know-how” (KH) level of learning; the method of learning is through “Lecture and Small Group discussion,” and the assessment suggested for all is by written examination or viva voce, and none of these six competencies are required to certify a Indian medical graduate for becoming a doctor in India!!

Hence, in this unprecedented COVID-19 pandemic crisis engulfing India and its consequence on millions of people vulnerable for developing psychiatric conditions, it is right time to reconsider psychiatry training for Indian medical graduates under the new competency-based curriculum.

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Conflicts of interest

There are no conflicts of interest.

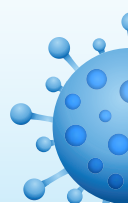
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VIEWPOINT

Psychiatry postgraduate examinations for 2020 in the middle of COVID19 crisis: Suggestions from Indian teachers of psychiatry

Kishor M, Henal Shah¹, Suhas Chandran², Ashok V. Mysore², Ajay Kumar³, Vikas Menon⁴, H. R. Vinay⁵, Mohan Isaac⁶, O. P Singh⁷

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ABSTRACT

The COVID19 pandemic is an unprecedented disaster. In India, the spread of COVID19 infection and the subsequent lockdown coincided with a crucial period of the annual examination in almost all educational institutions. The pandemic has created hurdles in the conduct of examination due to many reasons, some of which are spread of infection and associated safety issues, lack of public transport for patients as well as the postgraduates in outstation and examiners, and lack of workforce due to round-the-clock service for rendering health services leading to difficulty in arranging logistics at the examination center. Currently, there are no guidelines or policies on how examinations need to be carried out during such a pandemic. Hence, there is an urgent need to look at solutions within the profession for the completion of examination. Teachers of psychiatry play an important role in the national mental health services. Their expertise can be valuable for finding solutions that work. This article has compiled suggestions from Indian teachers of psychiatry.

Key words: Psychiatry, COVID19, Postgraduate examination

BACKGROUND


The COVID19 pandemic is an unprecedented disaster that has affected millions of people across the globe.^[1] In India, the spread of COVID19 infection and the subsequent lockdown

coincided with a crucial period of the annual examination in almost all educational institutions right from preschool to higher education. Health-care professionals are frontline workers in this crisis, and their presence is needed in large numbers for providing essential services, whose demand has increased drastically. Mental health services are an integral part of public health services, more so in disaster.^[2] However, in India, the numbers of mental health professionals are grossly inadequate for the population that needs these services.^[3]

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Annually, around 800 psychiatry residents from more than 200 medical institutions take up the final examinations in India.^[4] The successful ones start their practice as professionals to render mental health services. However, this year, the COVID19 pandemic has created hurdles for examination.

BARRIERS FOR POSTGRADUATE EXAMINATIONS AT THE TIME OF COVID19

The pandemic has created hurdles in the conduct of examination due to many reasons, some of which are spread of infection and associated safety issues, lack of public transport for patients as well as the postgraduates in outstation and examiners, and lack of workforce due to round-the-clock service for rendering health services leading to difficulty in arranging logistics at the examination center. The practical examination becomes more difficult as the process involves proximity with the patients and health-care professionals in the teaching hospitals, all of which can lead to high risk for infection. Some of the teaching hospitals have also been converted to designated COVID19 hospitals.

Currently, there are no guidelines or policies on how examinations need to be carried out during such a pandemic. However, there are equally compelling reasons for all stakeholders to complete the examination, and a further delay can adversely affect the students, faculty, and institutions in varied ways. Furthermore, the World Health Organization has warned that the pandemic and issues such as reinfection will prevent normalcy for many more months, ushering an unpredictable time frame to plan the ideal period for examination. Hence, there is an urgent need to look at solutions within the profession for the completion of examination.

POSSIBLE SOLUTIONS FROM INDIAN TEACHERS OF PSYCHIATRY

Teachers of psychiatry play an important role in the national mental health services.^[5] Their expertise can be valuable for finding solutions that work. The Indian Psychiatric Society (IPS) faculty training task force in association with the psychiatric postgraduate education subcommittee organized a focused webinar in early May 2020. The program invited all the Indian psychiatry postgraduate examiners and psychiatry faculty involved in the conduct of examinations to provide suggestions on how to carry out the examination. More than 200 faculty representing 65 educational institutions provided suggestions. These suggestions have been compiled here and presented for the dissemination of valuable input, particularly for this unprecedented postgraduate examination year 2020 in India.

Many have acknowledged that given the current crisis, there cannot be any single method or process, which is good for

all institutions. Hence, it is important to choose or decide a postgraduate examination process that is best suited for respective institutions. The following suggestions given here should be viewed in this context.

Many have urged that the psychiatry faculty, the heads of departments, and the potential examiners should proactively communicate or discuss the concerns and plans about this year's examination process with the respective examination authorities or registrars in their institution or university. This is because institutions or universities are currently responsive to such discussion and are accommodating various possible courses of action. It is important to voice out and facilitate discussions at all levels.

Many have suggested that the safety of examiners or facilitators, postgraduate residents taking examinations this year, as well as patients are all equally important. Hence, planning ahead and following all the prescribed safety measures is going to be crucial.

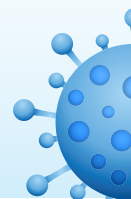
Suggestions highlighted that the examination process is also about the responsibility of examiners and that of institution toward society in certifying a budding professional for certain standards in service to public health. Hence, examination standards cannot be much compromised.

The theory examination was considered by many as a relatively feasible process compared to issues involved with practical examination. However, where possible, online theory examination with multiple choice questions or clinical application question can be used to evaluate a student who, in turn, answers from any place which can be monitored and considered as safe. Some institutions or universities, in recent years, have stepped up digital evaluation of answer scripts which are scanned and uploaded for examiners to evaluate in a safe environment. These methods can be considered by other institutions across India.

Practical examinations can be held as before, if the department or institution can manage the necessary resources and implement safety measures, for example, in green zone areas or as notified by the government.

If the department is planning to change the pattern of the practical examination after consultation with institution or university, it is important to notify the examination going postgraduate immediately and give minimum of 2 weeks' notice for the candidate, before examination or as per the policy of that institution. It is indeed important to orient postgraduates or train them in the new pattern of examination accepted by the institution or university.

There are ways to carry out practical examination by involving patients as examination cases. This includes patient



examination by maintaining social distance or live video streaming or playing recorded patient examination videos etc. It is important to explore all the methods examination and have them weighed against these three factors: reliability, validity, and resources. Checking these factors and discussing the possible issues in every department will assist in realistic and working solutions for the respective institution and those that can be implemented in all examination centers within the institution or university.

Wherever technology is involved in finding solutions, particularly video streaming or use of the Internet, many had apprehension about network issues that should be evaluated and ascertained at each geographical area.

It may become important for each institution or university to develop and archive e-resources such as video recording of simulated case vignette for examination. IPS can also develop and have a repository of such e-resources.

Similarly, one can conduct practical examinations by involving “nonpatients” such as simulated patients (considered as safe for health concerns) as “examination cases.” These simulated patients can be other postgraduates or interns or nurses or actors, who are trained and verified, so that they can act as real cases to facilitate examination. This method can be used for all examination cases such as long case or short case or neurology case.

The other ways to conduct practical examinations include the use of “written case scripts” or “audio recordings” or if institutions have designed mannequin (dummy/articulated doll) as examination cases. Designed mannequin can mimic a desired clinical condition. It is suggested considering these options for feasibility at the respective institution. Suggestions have also been received on the combination of the above methods and/or Objective Structured Clinical Examination (OSCE) or Tele OSCE to conduct examinations. If examiners and postgraduates are new to these concepts, it is important to discuss with the respective medical education unit in the institution or learning from experts or through video tutorials on the website. Training examiners will be the responsibility of the institution or university which chooses to go with such modifications.

About the requirement of external examiners where safe transport and infection are indeed a matter of concern, many have opined that having only regional examiners or available examiners in the respective city or examiners in neighboring cities, including former examiners, can be considered for conducting the examination. It is important to discuss with the respective institutional authorities about external examiners. All examiners should be oriented about the examination pattern well in advance.

There have also been suggestions to involve or encourage all postgraduates taking up the examination to contribute in patient care in all their capacity, particularly if there is a long delay in return to normalcy. It was suggested to look at ways and means to empower postgraduates in all aspects to utilize their acquired skill and knowledge in psychiatry services during pandemic. Some have suggested that if the postgraduates have been assessed periodically in a systematic manner that has been documented, the institutions can take a call on utilizing the documents to consider completion.

Along with the above suggestions, there was a consensus from all that, as a department or as an examiner or expert or institutional representative, this is an opportunity for the entire psychiatry collective to collaborate with decision-making authorities or policy-making bodies at all levels. It is necessary to proactively lobby for a safe and actionable plan for conducting examinations and associated issues.

CONCLUSION AND THE WAY FORWARD

It is important to be open to the ideas and suggestions, especially those which are based on available technology. Such methods can become a norm or an alternate method for conducting examination in the future, for example, to video stream the examination from one place to other or directly to the external examiner.

During the times of a pandemic of this magnitude, it is expected that each one, with their experiential wisdom and goodwill, shall do their best in relation to all issues arising out of COVID19 including that of the postgraduate examinations.

Disclaimer: It is important to note that these are suggestions from individuals and not to be considered as the official stand of IPS or any other organization or group or institution. These cannot be considered as guidelines. It is primarily intended for sharing imminent concerns regarding postgraduate examinations in psychiatry and looking at possible solutions. On 15 June 2020, the MCI released advisory to incorporate some suggestions mentioned as alternative in skill evaluation such as simulations, case scenarios etc as one-time exception in view of COVID19.

Acknowledgments

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Conflicts of interest

There are no conflicts of interest.



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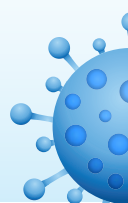
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Academic Crisis During COVID 19: Online Classes, a Panacea for Imminent Doctors

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Abstract

Introduction COVID 19 made a serious impact on many aspects of everyday life. The world saw a paradigm shift in the education system favouring online learning during the constraints of pandemic.

Methodology To assess the attitude of the students towards online learning in subject of ENT, we conducted an observational study among 170 third year MBBS undergraduate students of our institute attending online classes through the student portal of our university website.

Results Our survey revealed students favoured online learning to sustain their academic interest and development during this pandemic. Yet, they perceived many challenges during online learning like lack of face-to-face interactions, lack of socialization, distraction by social media, technology related issues etc. Students also opted for a combined approach of learning in the post pandemic period.

Conclusion This article reflects the challenges faced during online learning and added the innovative methods that can be included to overcome the obstacles of online learning. During this period of COVID, one must embrace the alternative to classroom learning to keep up with one's academic development and can consider an integrated approach of learning after the pandemic.

Keywords Covid-19 · Online learning · Classroom learning · Academic crisis

Introduction

COVID 19 made a serious impact on many aspects of everyday life. World Health Organisation (WHO) announced COVID19 as a global public health emergency of international concern on 30th January 2020 [1] and declared it a pandemic on 11th March 2020 [2]. The education system is one of the most impacted aspects of routine learning and daily life. The world saw a paradigm shift in the education system favouring online learning during the constraints of pandemic. Yet, the effects and efficacy of online education and the capacity to successfully teach digitally is questionable. This sudden and rapid transformation from an environment of conventional learning to virtual learning has made a great impact on the attitude of the students towards learning [3].

In our institute, regular undergraduate online classes are being conducted through student portal of our university website. This enables students to access the digital contents and the recorded lectures even after the class. To assess the attitude of the students towards online learning in subject of ENT, we conducted a short survey among third year MBBS undergraduate students of our institute attending ENT classes. This will also help us to assess the feasibility and mould our approach towards online classes.

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s12070-020-02224-x>) contains supplementary material, which is available to authorized users.

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Methodology

Study Design

An observational, descriptive study based on designed questionnaire was conducted through google forms which was circulated among the third MBBS undergraduate students of our institute. Online classes are being conducted.

Study Population

A total of 170 third MBBS undergraduate students participated in the study.

Study Conduct

The designed questionnaire consisted of set of questions to know the attitude of undergraduate students regarding online vs classroom learning and to know what are the reasons for their likes and dislikes about online and classroom learning.

Initial questions included socio demographic data and the Gadget being used for online classes. Part A of the questionnaire was based on the opinion of students towards classroom and online classes. Part B consisted of statements for which their opinion was obtained by Yes/ No/ May be responses and end questions on what kind of approach they would prefer during the pandemic either online or classroom and after this pandemic with the options of Online classes, Classroom classes and a combined approach were given.

Results

Our study included 170 students of which 78 were males and 92 were females within the age group of 20–24 years. The average attendance for online class was found to be 96%.

52% of the students opted for using mobile, 36% laptops and 12% of them used tablets as devices for online classes (Fig. 1).

Part A of the questionnaire (Table 1) suggested a comparable result in terms of content covered in both online (37%) and classroom learning (41%). 58% of the students felt understanding concepts is better in classroom learning while 52% students felt retention of the topic was better through classroom learning.

Majority of the students (59%) felt that they had better access to online study materials. Students favoured classroom learning in terms of student teacher interaction (54%), punctuality & discipline (77%), acquiring practical

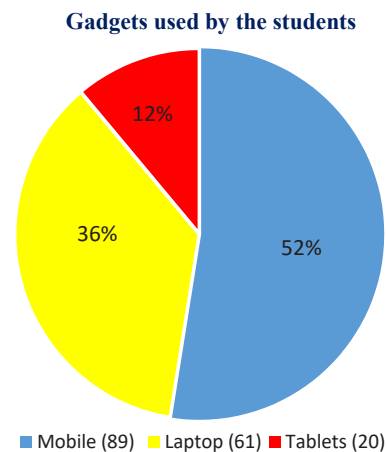


Fig. 1 Distribution of Gadgets used by the students

skills (90%). Students predominantly favoured online classes for doubt clarification (57%). Apprehension of exams were nearly equal in both.

Part B (Table 2) revealed students preferred online classes in terms of ease of participation, attending classes (91%) and time investment (67%). Students felt that the outdoor activities, group projects and development of communication skills were better in classroom learning (82%). 78% of the students sensed that poor internet connections, social isolation and eye strain as the commonest problems faced during online learning.

When asked a specified question regarding preference of classes during the pandemic, majority of the students preferred online classes (89%) to sustain their academic interest and development during this pandemic (Fig. 2).

For the opinion of preferred approach of learning after COVID 19 pandemic, 31% of students opted for the option of only classroom learning, 16% opted for only online learning where as 53% of the students opted for combined approach of classes (Fig. 3).

Discussion

Since the serious outbreak of this global pandemic Covid-19 [1], majority of the countries practiced lockdown. Currently there are in excess of 26 million cases of Covid-19. Social distancing and restrictive movement policies are being implemented to curb this rising curve of cases [4]. It also has markedly deranged conventional education practices as most of the schools and colleges are being temporarily shut down. This present situation has made us implement an alternative and innovative approach in sustaining academics of medical undergraduates through online classes.

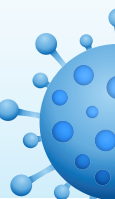


Table 1 Part A of the questionnaire

S.no	Question	Online learning (%)	Classroom learning (%)	Both (%)
1	Understanding concepts of ENT is easier in	41	53	6
2	Coverage of content of particular topic is more in	37	41	22
3	Retention rate of content of the topic is better in	42	48	10
4	We can get access to good amount of study material in	59	27	14
5	Interaction among student and teacher is better in	41	54	5
6	Punctuality and self-discipline are acquired better in	16	77	7
7	Acquiring practical knowledge of ENT is more effective in	6	90	4
8	Clarification of doubts is easier in	55	33	12
9	Appearing for internal assessments is easier in	41	43	16

Table 2 Part B of the questionnaire

S.no	Statement	Yes (%)	No (%)	May be (%)
1	Ease of participation and attending classes during lockdown is better online	91	7	2
2	Online learning requires less of a time investment	67	18	14
3	Multiple choice questions incorporation during online learning adds up to the interest among students	74	14	12
4	Classroom learning prevents social isolation of the individual	72	16	12
5	Poor internet connections during the class causes loss of interest in online learning	78	13	9
6	Online learning causes decreased out-door activity, group projects, communication skills	82	11	7
7	Increased screen time during online learning can cause eye related problems	75	5	20

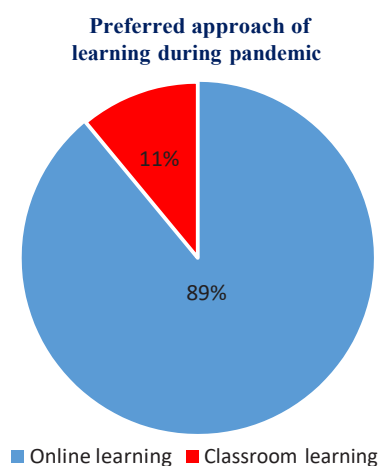


Fig. 2 Preferred approach of learning during pandemic

Due to the constraints of classroom learning in this indeterminate time course of pandemic, online learning has come to the forefront to partly resolve perplexity. Online classes are being conducted through the student portal since the outbreak of pandemic. The average attendance for the online classes was found to be 96% over a period of 5 months. Most of our students possess a mobile phone,

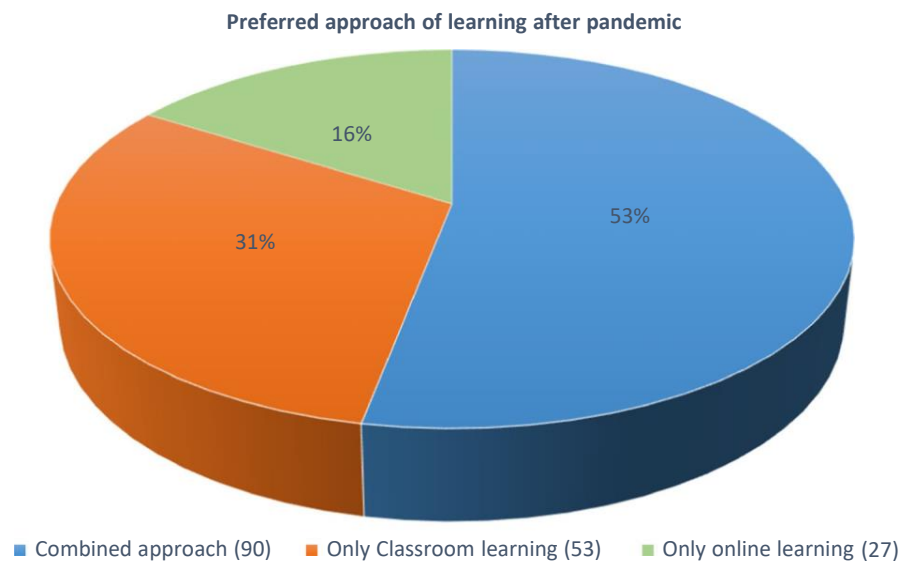
making it the most accessible and feasible platform to attend online classes (52%). 36% and 12% students preferred using laptops and tablets respectively as they might feel more distracted while using mobile phones. Students themselves gave the feedback that accessing online classes on mobile was sometimes distracting them. They feel the urge to access social media, check messages, answer calls while using mobile phones which leads to loss of interest and attentiveness during the class.

Conventional learning has face to face interactions, motivates one to learn, better interactions among student and teacher and most important a feel of togetherness in learning and sharing opinions. [5] Some of these aspects lack in online learning. Our survey suggested that although both methods of teaching covered almost equal content of a particular topic yet the students preferred classroom learning for understanding and retention of a topic. The students also preferred classroom learning as practical knowledge, punctuality and self-discipline is better acquired through a reciprocal interaction among teachers and student in a classroom.

Online learning creates a good platform for acquiring newer methods of learning with less apprehension among students in clearing their doubts, ease of participation, good coverage and understanding of the topic by usage of 3D



Fig. 3 Preferred approach of learning after pandemic



animations, less time investment and easy availability of the resources to review the topics through the online portal. [6, 7] Our survey revealed a similar preference among the students. They also relished the concept of multiple choice questions incorporation during the class as it added up to their interest and attentiveness during the class. Flexibility and lowering the cost of transportation and accommodation with access from any part of the world are engrossing aspects of online learning. [7]

Long duration of online classes can cause eye related problems, distraction by social media. [3] Decreased outdoor activity, group projects, communication skills causes social isolation in an individual. [5] Our students also reported that 79% of them lost interest during online classes due to issues with the internet connection when the class went on for more than an hour. Sedentary life with decreased outdoor activity and project works was a major disadvantage of online classes as pointed out by 80% of our students. 75% of the students complained eye related issues like eye strain, epiphora and headache while attending long online sessions.

Technology related challenge and clinical skill training are the two paramount constraining factors. [7, 8] Other crucial constraining factors include student interest captivation and emotional wellbeing. These could be overcome by using simulation based training apps, establishing a fast and reliable internet connection, prior training of teachers in using this technology, flexibility in time and a shorter duration of classes. Incorporating virtual whiteboards, videos on clinical examination, 3D images, surgical videos if applicable, weekly one to one student teacher counselling sessions, regular feedback from the students may help in overcoming the obstacles and escalating favourability of online classes.

In view of present scenario our students preferred online classes during pandemic which is similar to other studies. [3, 6, 9] Majority of our students preferred for a combined approach of teaching after the pandemic for their better academic development. This finding is similar to the study done by Rajab et al. [10].

Conclusion

One of the participants of our survey rightly said ‘There is a difference to play football on ground and in mobile’ but in this apprehensive socially distanced period of COVID, one must embrace the alternative to classroom learning to keep up with one’s academic development. Though the replication of classroom learning is not completely attainable through online learning, yet it is a convenient method with ease of participation, sustaining the academics and maintaining the student teacher interaction amidst pandemic. A combined approach can be considered post pandemic for a finer learning with more innovative methods.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval Appropriate ethical clearance has been obtained from the institute. Informed Consent Informed consent was obtained from all individual participants included in this study.

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Does the Corpse teach the living? - Anatomy in the era of COVID -19

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INTRODUCTION

The COVID-19 pandemic is the biggest global health crisis of this era and the greatest challenge mankind have faced since the Second World War. Coronavirus appeared in Asia but since its occurrence it has touched all the continents except Antarctica. This pandemic is not only a health crisis but an unprecedented socio-economic predicament as well. Indian Government is taking all possible measures and steps to face this unprecedented global challenge of COVID-19.

COVID-19 is an infectious ailment caused by Novel Coronavirus. Since its recent discovery, the pathogen was named because of its distinct spiky appearance. Word "COVID-19" is derived from the CO of Corona, VI of Virus, and D stands for the disease. The novel coronavirus also called severe acute respiratory syndrome (SARS) coronavirus 2 is an RNA virus, spherical bearing club shaped surface projection giving it a spiky appearance. The viral disease was first reported in Wuhan City of China in December 2019 and within a short period, it disseminated worldwide affecting millions of people owing to its high transmission rate.^[1]

The chief mode of transmission of this virus is through droplets (talking, sneezing, or coughing). With an average incubation period of 2–14 days, these viruses can cause a spectrum of flu-like symptoms and critically in a few cases death. The virus remains infectious on various nonliving things ranging from hours to several days. Although the mortality rate of COVID-19 is low, both the nonavailability of a specific regimen of treatment and vaccine has made the disease more ominous.^[2,3] On March 11, 2020, the World Health Organization announced COVID-19 as pandemic which barrelled through more than 114 countries within a short period of 3 months.^[4] Currently, the deadly disease has resulted in 32,508,287 cases, killing 9,89,246 people around the globe.^[5]

Pandemics are not new, the world has witnessed many such conditions starting from black death (Plague), Columbian exchange, Great plague of London, Cholera Pandemics to recent Flu pandemics.^[6] There is a vast literature on the great pandemics but very sparse information available regarding the management of corpses during these catastrophes. In olden days, where there was a lack of both man power and a proper protocol for handling the dead. The cadavers were left in the street piling up as there was a dearth of embalmers and Coffins too, eventually leading to rotting.^[7]

HISTORY

The flu pandemics which mostly spread by respiratory route can cause disastrous effects. Although the chances of spread of novel coronavirus from a dead body are very negligible, utmost care has to be taken by the health-care workers, burial ground staff and family members as the body fluids of the corpse may prove to be a source of infection.^[8] Nowadays, with in advert use of social media which can both inform and misinform the public by giving different dimensions to burning issues corpus management during the pandemic has become a social issue too.^[9,10]

GUIDELINES ON CORPSE HANDLING

In view of the declared pandemic on March 15, 2020, the Government of India has issued guidelines on the management of the dead body due to COVID-19. The main infection control practices include maintaining proper hand hygiene, use of personal protective equipment, safe handling of sharp objects, instruments, and disinfection of environmental surfaces which comes in contact with the corpse therefore, the health care workers and staff who are involved in the isolation area, mortuary, transportation, and burial ground should be trained meticulously in the above said infection prevention control measures. Further, staff should be trained and proficient to perform the last rites, not only in a dignified manner but also with adequate mandatory social distancing norms. In this regard, the relatives may be allowed to do the religious rituals according to their customs, which does not require touching of the cadaver such as bathing and kissing. Again, here the relatives should be urged to maintain strict social distancing norms and also to wear PPE kit as suggested by the authorities.

As of now embalming of cadavers due to COVID-19 is not allowed owing to the potential risk of virus transmission through body fluids. However, the autopsy of such cadavers can be done by adept staff who are well versed with infection control measures. In all these cases, a suitable disinfectant, preferably 1% hypochlorite is used to disinfect the surfaces and instruments.^[8]

COVID 19 - AND ANATOMICAL SCIENCES EDUCATION

Medical education has suffered a mammoth impact because of the COVID-19 pandemic, starting from procuring cadaver for dissection to cancellation of classes and clinical postings



to medical students.^[11] Medical institutions are temporarily closed no didactic lectures, small group teaching, and clinical postings. The reduced exposure among specific specialities will result in detrimental effects on competencies and skills.^[12] This break in the fast-paced medical curriculum will have magnanimous impact and future repercussions not only on the budding doctors by posing limitations to hands-on learning but also to the society as a whole.^[13]

During previous pandemic SARS, few medical colleges in China, Canada had withdrawn formal teaching and in one medical college online teaching was adopted. During this pandemic to follow social distancing norms to avoid medical students in becoming potential vectors for viral transmission, and to flatten the curve of the pandemic, most of the medical institutions have switched on to recorded lectures or online teaching using various platforms to complete the curriculum, which has become quite popular in various other countries. These impressive accomplishments emphasize that even in times of adversity, curriculum can be completed within the stipulated time frame.^[12]

Anatomy and cadavers are two inseparable terms. Dissection being an integral part of anatomy,^[14] COVID-19 has adversely affected cadaver procurement for teaching purposes as embalming is not allowed during this pandemic. In the light of guidelines issued by the Government of India not to perform embalming of the cadavers of COVID-19 patients.

Many medical institutions are dependent on body donation programs and procurement of unclaimed cadavers for dissection purpose. As a result of COVID-19, body donation and organ donation has come to a standstill in most of the medical colleges. Although there are reasonable guidelines for organ donation, due to their nonspecific nature and lack of adaptability the process has suffered a huge setback.^[15] This can add to the existing shortage of cadavers for dissection and learning purpose^[16] this can imperatively result in switching from traditional methods to virtual dissection, which is being followed by a handful of medical colleges in India.^[11] With the newly introduced curriculum based medical education, learning anatomy dissection virtually is unrealistic as the tactile element and real-world complexities of the body cannot yet be simulated satisfactorily.^[17] Dissection hall is a place where the students conceive the minds of the future surgeon. While virtual dissection overcomes the problems associated with wet laboratories such as scarcity of cadavers, cost of management, formalin allergy,^[14,18] the debate continues between real and virtual classes. Although medical education and indeed medicine as a profession was never designed to be fully online, necessity has compelled the medical educators to adopt virtual teaching, where team-based learning, interaction, the act of dissection and physical examination skills is effectively learnt.^[19]

CLOSING REMARKS

Indeed, it is very tough to come to an inference due to uncertain unique challenges and the knowledge gap that exists

concerning novel coronavirus. There has to be a feisty quest for the development of safe and effective methods of embalming of COVID-19 cadavers ensuring standard precautions. Embalming of cadaver is essential to withstand the body donation programs for dissection to overcome the cadaver predicament. The paucity of cadavers is bound to ensue in days to come. In majority of the medical institutions, Anatomical Sciences is studied by the dissection of the corpse. The dissected corpse being the most accepted means of teaching-learning modalities of Anatomy. This may severely affect the teaching and learning of Anatomy as corpse dissection may not be feasible in days to come. A road map has to be configured in view of CBME else virtual dissection with other added methods of blended learning becomes inevitable.

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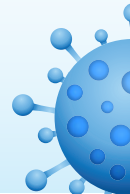
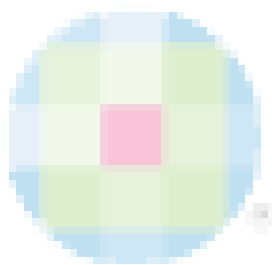


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LETTER

Impact of COVID-19 Pandemic on Cardiology Resident Training and Education

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Abstract:

The novel coronavirus (COVID-19) pandemic has created an unprecedented global health emergency. This crisis has impacted educational activities worldwide, including India. It is imperative to understand the challenges faced by institutions in imparting resident training when dealing with patients during this pandemic. This correspondence briefly discusses the effect on the cardiology residency program and research activities. It also highlights the measures to impart education safely amid a current pandemic.

Keywords: COVID-19, Pandemic, Coronavirus, Cardiology, Acute coronary syndrome, Education.

DEAR EDITOR,

The World Health Organization (WHO), on March 11, 2020, declared the rapidly spreading Covid-19 (SARS-CoV-2) infections a global pandemic [1]. In response to this crisis, many governments across the world implemented a tough nationwide lockdown to stem the spread of infection. Since then, restrictions are in place for non-essential travel, advocating social distancing and cancellations of large gatherings in the community. To optimise the resources and prevent virus exposure to healthcare workers and the patients, many hospitals have cancelled the elective procedures. They have restructured the system to provide emergency care and telehealth enabled outpatient services. Most institutions are experiencing a significant reduction in acute cardiac patient admissions and procedures, as well as a decrease in research and educational activity, adversely impacting resident training.

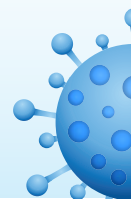
Conventional training in cardiology residency program encompasses rotational postings in outpatient clinics, non-invasive and invasive cardiac laboratory, and through elective and emergency in-patient admissions for investigations and interventional procedures. The cardiac catheterisation laboratory activities have transformed to provide predominantly emergency intervention procedures such as primary angioplasty in acute coronary syndrome patients. As the cardiovascular non-emergency surgeries have ceased, most residents are worried they would be deprived of hands-on experience in invasive procedures affecting their skills. Because of the pandemic, the Indian National Board of Examinations (NBE), the apex regulator of the hospital-based

residency training, has extended the tenure of final year students in all specialties by a period of at least six weeks [2]. This has further increased the anxiety of the trainees about the possible delay in the exit examinations.

During this crisis, in many of the cardiac centres across the world, including India, rotating teams with reduced resident staffing have been formed to ensure continuity in essential services. Some of these trainees would be caring for patients with Covid-19 during assigned deployment in areas of need like the intensive care unit (ICU). Like their counterparts in other countries, there are several reports of Indian health care personnel getting exposed to the COVID-19 infection in the hospital, sometimes fatally [3]. Acute shortage of personal protective equipment (PPE) has compounded the difficulties faced by the caregivers [4]. To reduce the risk of exposure to residents, the programs have rapidly transformed into virtual video conference sessions and webinars, compensating for the in-person teaching activities, rounds, and conferences. In most institutions, the research activities have completely ceased, disrupting the timely completion of the dissertation of the students.

CONCLUSION

It is a daunting task to impart the residency program at the time of a crisis. Training programs must adapt quickly to the challenges of a pandemic and continue to impart education safely and at the same time providing patient care. Once this pandemic abates, the educators should carefully analyse this calamity, and devise innovative policies to ensure unhindered training of the fellows.



CONSENT FOR PUBLICATION

All authors have participated in the work and have reviewed and agree with the content of the article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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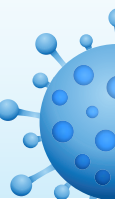
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Learning with lockdown: Utility of whatsapp status-based multiple-choice question discussion on COVID-19 among medical students and teaching faculty

Sunil Kumar Doddaiiah, Praveen Kulkarni, Aparna Mohandas, M. R. Narayana Murthy

Abstract:

BACKGROUND: Following the COVID-19 pandemic, the Government of India announced lockdown from March 25, 2020, which included measures such as social distancing, canceling mass gatherings, and closure of schools and colleges. Since the present generation of students spends a lot of time on social media, especially WhatsApp, the utility of the same to discuss the various public health domains of COVID-19 through multiple-choice questions (MCQs) was explored.

MATERIALS AND METHODS: This longitudinal study was conducted among 154 participants (undergraduates, interns, postgraduates, and teaching faculty) for 3 months. MCQs on COVID-19 were disseminated through WhatsApp status of the investigator, and feedback regarding the same was taken at the end of 3 months. The activity log was maintained, and the information was downloaded as a comma-separated value (CSV) file and exported to MS Excel. Descriptive statistics were applied. The location of the participants was entered into the Microsoft Excel sheet and converted into CSV file. The Geographical data were analyzed in the Quantum Geographical information System (QGIS).

RESULTS: Among the 154 study participants, 48% were undergraduates, 10.4% were interns, 30.6% were postgraduates, and 11% were teaching faculty. Eighty-nine percent of the participants felt that WhatsApp can be used as a platform for discussing MCQs. 89%, 93%, and 89.6% of the participants felt that the exercise improved their analytical skills, helped in self-directed learning, and improved collaborative learning, respectively.

CONCLUSIONS: Majority of the participants responded that WhatsApp can be used as a platform to discuss MCQs and that the exercise helped in collaborative and self-directed learning.

Keywords:

COVID-19, multiple-choice question, self-directed learning, WhatsApp

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Introduction

In December 2019, a series of pneumonia cases of unknown etiology began to emerge in Wuhan, Hubei province of China, and the World Health Organization was notified on January 3, 2020.^[1] India reported its first case on January 30, a medical student who had returned from Wuhan after the

epidemic started.^[2] The new disease was named COVID-19 on February 11, 2020.^[3]

Lockdown is a measure of restricting personal movement so as to break the chain of transmission. It ensures social distancing and, along with other measures such as isolation and quarantine, hand hygiene, and canceling mass gatherings,

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keeps the spread of COVID-19 at check. Further, it prevents increased caseload on health infrastructure and buys time for researchers to develop drugs and vaccines.^[4]

The Government of India announced lockdown from March 25, 2020, which included measures such as canceling public transport, restricting personal movement, social distancing, strict curfew, canceling mass gatherings, and closure of offices, schools, and universities including professional colleges.^[4] Many companies have switched to “work from home” system for their employees, and schools and colleges have shifted to online classes during the lockdown.^[5] India has 542 registered colleges teaching MBBS, which makes it the country with the highest number of medical colleges.^[6] Hence, in the period of lockdown, it is important to ensure the continuity of medical education. E-learning (technology and electronic device based) has been a part of medical education, however, its full spectrum needs to be explored and utilized in this period.^[7]

Smartphones have become an indispensable part of our life, so has mobile learning (M-learning) in medical education. Medical students and faculty can access applications such as Medscape, peer-reviewed journals, and social media networks such as YouTube, Facebook, and WhatsApp, which aids and supplements their learning.^[8] WhatsApp, launched in 2009, is one of the most widely used instant messaging applications with over 1 billion active users per month worldwide.^[9] It is a free messenger application which is available across platforms such as android and iPhone. It allows instant messaging, group chats, and to share and download multimedia messages. WhatsApp is a learner-friendly application which helps students and teachers to create, communicate, and share information in real-time.^[10,11]

While it is necessary to keep the learning process ongoing, it is also important that the students and staff be kept informed on the updates on COVID-19 while trying to keep it interesting. Hence, in this study, we try to assess the utility of WhatsApp status-based multiple-choice question (MCQ) discussion on COVID-19 among medical students and teaching faculty and to assess their perceptions on the same.

Objectives

1. To assess the utility of WhatsApp status-based MCQ discussion on COVID-19 among the medical students and teaching faculty
2. To assess their perception on learning through MCQ-based discussion through WhatsApp status
3. Geospatial distribution of participants.

2

Materials and Methods

Subjects

The present longitudinal study was conducted among medical students, interns, postgraduates, and teaching faculty for a period of 3 months after obtaining clearance from the institutional ethics committee.

Designing of multiple-choice questions

Keeping in mind the principles of epidemiology, management, prevention, and control of nCOVID-19, the MCQs were framed by the experts who have formally received training in designing and implementing MCQs through medical education unit. Each MCQ was prepared with a stem and four responses, out of which one was the right answer and three were distractors. A mix of questions at different cognitive levels of Bloom's taxonomy was framed to enhance the learning and understanding of the participant. Recall-based, case scenario-related, calculation-based, picture-based questions were framed. Each MCQ framed by the faculty was validated by the other faculty member before releasing for the students to respond.

Dissemination of multiple-choice questions through WhatsApp status

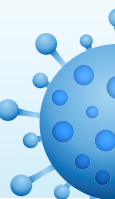
MCQs framed through the above mentioned technique were disseminated to the study participants through WhatsApp status of principal investigator. One MCQ per day strategy was used for the ease of responding and sustaining the motivation level of students. Students had sufficient time to understand the question and refer to the relevant resources before responding to the question. The participants were invited to discuss any doubt, query, or clarifications in the process of solving the MCQ with the faculty. The correct answer to the MCQ was displayed on the same WhatsApp status wall 24 h after the release of question. The activity log of the status with number of participants attempting the activity was maintained.

Feedback

After 3 months of this sustained educational experience, feedback was obtained from the participants using a pretested semi-structured questionnaire through online Google survey proforma. The items in the questionnaire were prepared based on the literature search and cognitive interview with experts and students. The hence prepared draft questionnaire was face and content validated by the experts. A pilot study was conducted among postgraduate students to assess the correctness and comprehension of items in the questionnaire.

Items in the feedback questionnaire

Feedback questionnaire had items to capture information on the designing of MCQs, difficulty level, whether



they helped the students in preparing for competitive examinations, provoking the thought process, ability to comprehend with items, whether the exercise facilitated self-directed learning, encouraged motivation to learn, and collaborative learning.

Collection of information

The link of questionnaire was shared on the same WhatsApp status wall where the MCQs were posted and the response from the participants was collected. The survey was kept active for 1 week from the starting date to provide enough time for the participants to complete the task.

Geospatial analysis

The location of the participants who took part in the online "COVID-19: Novel Coronavirus MCQS" WhatsApp status discussion has been entered into the Microsoft Excel sheet and converted into a comma-separated value (CSV) file which is a delimited text file that uses a comma to separate values. The geographical data were analyzed in the Quantum geographical information system (QGIS), a free and open-source geographic information system version QGIS 3.12.3 "Bucuresti" which was released on May 15, 2020. It is an open-source software available under the terms of the GNU General Public License.

Statistical analysis

The information was downloaded in the form of a CSV file and then transferred to MS Excel 2010 for analysis. Descriptive statistical measures such as percentage, mean, standard deviation, median, and interquartile range (IQR) were applied. Data were presented as table/graphs as relevant.

Results

A total of 154 participants took part in the study. The average age of the participants was 25.3 ± 7 years. The participants had been using WhatsApp for an average of 5.4 ± 2 years. The median time of usage of WhatsApp by the participants was 1.5 h (IQR of 1–3 h) per day, and the median number of times the participants checked the WhatsApp status was 5 (IQR of 3–8) per day. Forty-four percent of the participants were males and 56% were females.

Among the 154 study participants responding to the feedback survey, 48% were undergraduates, 10.4% were interns, 30.6% were postgraduates, and 11% were teaching faculty. 55.8% and 38.3% of the participants suggested WhatsApp group and WhatsApp status as the preferred platforms to discuss MCQs, respectively. 63.7% of the participants were from Karnataka, and the other participants hailed from

Kerala (9.2%), Uttar Pradesh (6.5%), Tamil Nadu (5.8%), New Delhi (5.8%), and other states [Table 1].

Figure 1 represents the geospatial distribution of participants in the study. The feedback obtained from the participants at the end of 3 months of MCQ discussion is represented in Table 2. The participants rated the exercise on a scale of 1–10 (1 being the lowest and 10 being the highest); 97.4% and 2.6% of the participants gave a score of >5 and ≤ 5 , respectively.

On analysis of feedback obtained on Likert scale, 89% of the participants felt that WhatsApp can be used as a platform for discussing MCQs. 78.6% felt that the MCQs helped in preparing for competitive examinations, and 82.5% said it enhanced their confidence to face such examinations. 89%, 93%, and 89.6% of the participants felt that the exercise improved their analytical skills, helped in self-directed learning, and improved collaborative learning, respectively. Eighty-nine percent of the participants said that the moderator would attend to their queries as and when approached, and 95% said that the moderator was open to remarks/comments/suggestions. 96.7% suggested that similar activities should be continued [Figure 2].

Table 1: Distribution of participants based on the demographic details and the platform suggested for discussing multiple-choice questions (n=154)

Variable	n (%)
Gender	
Male	68 (44)
Female	86 (56)
Designation	
Undergraduate	74 (48)
Intern	16 (10.4)
Postgraduate	47 (30.6)
Teaching faculty	17 (11)
State-wise distribution of participant	
Karnataka	98 (63.7)
Kerala	14 (9.2)
Tamil Nadu	9 (5.8)
Andhra Pradesh	1 (0.6)
Uttar Pradesh	10 (6.5)
New Delhi	9 (5.8)
Gujarat	1 (0.6)
Rajasthan	3 (2)
Haryana	5 (3.2)
Jharkhand	1 (0.6)
Telangana	2 (1.4)
West Bengal	1 (0.6)
Suggested platform for discussing MCQs	
WhatsApp status	59 (38.3%)
WhatsApp group	86 (55.8)
Telegram	6 (3.9%)
Webex	3 (2)

MCQ=Multiple-choice questions



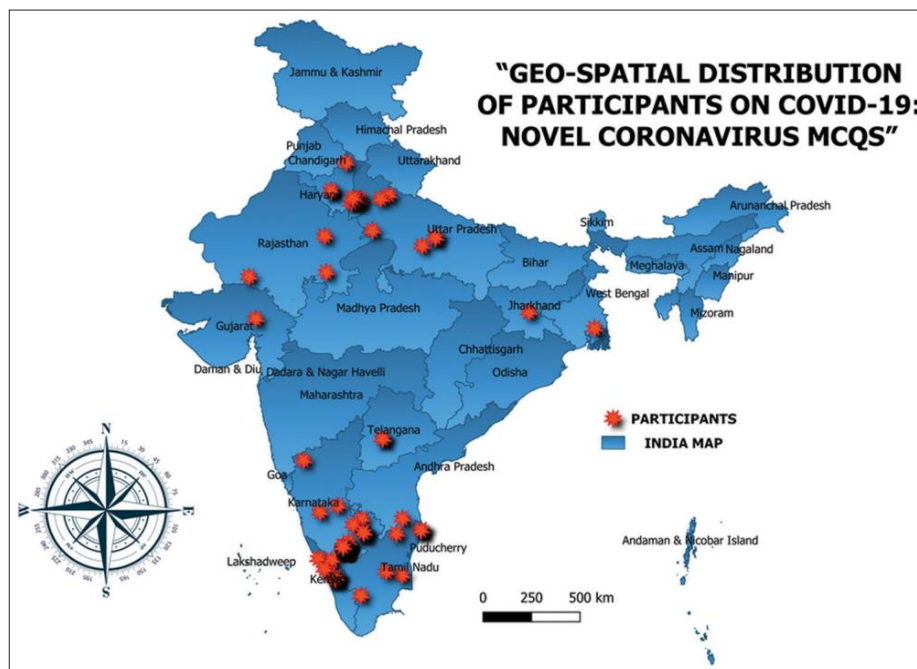


Figure 1: Geo-spatial distribution of participants; $n = 154$

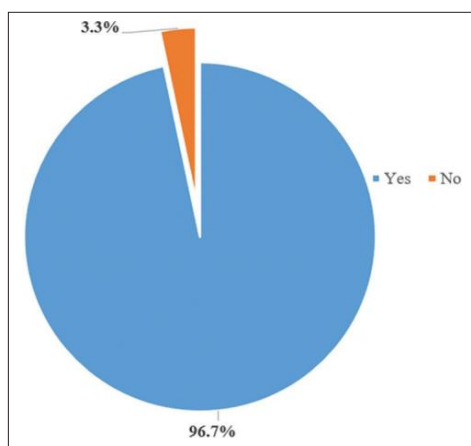


Figure 2: Feedback of participants if they suggest similar activities in the future; $n = 154$

Discussion

Traditional learning was more teacher-centric and preferred “face-to-face” interaction, however, changing times have seen a shift to student-centric and technology-based learning.^[12]

The present generation of students spends a major portion of time on social media. Roy and Ray, in a study conducted among 1st-year medical students, reported that 55% of the students spend more than 1 h on WhatsApp, which were similar to the results obtained in the present study. WhatsApp is a widely used instant

messaging application and is extremely user friendly and hence can be used easily by teaching faculty and students.^[12] In the studies conducted by Roy and Ray, 97% of the students responded that they “liked the use of WhatsApp in supplementing classroom teaching,” and Glad Mohesh and Meerasa in their study among 1st-year students to discuss viva voce questions in physiology reported that 100% students liked M learning, which were similar to the findings in our study.^[12,13]

In the constructivist theory of learning, teachers act as facilitators while students are encouraged to take charge of their learning by bringing in their experiences and knowledge and reflecting on them. The medical council of India, in the competency-based curriculum, also stresses the need for students to constantly acquire skills and the need to promote “self-directed learning.”^[12] In the present study, 93% of the study participants responded that the activity helped in self-directed learning. Similar were the findings of Gon and Rawekar in a study among 2nd-year students, where 70% of the students said that WhatsApp-based pathology discussions promoted self-directed learning.^[10] According to Latif *et al.*, learning through WhatsApp promotes an environment of interactive learning and keeps teachers and students motivated to learn and refer to other resources.^[14] Eighty-eight percent of the participants in the present study felt that the WhatsApp-based learning made them visit other resources which also increased their motivation to learn. Similar findings were reported by Zulfikar *et al.* in a study conducted among students

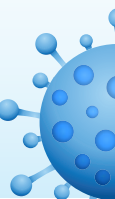


Table 2: Feedback given by the participants (n=154)

Item	Strongly agree (%)	Agree (%)	Neutral (%)	Disagree (%)	Strongly disagree (%)
WhatsApp can be used as a platform to study MCQs	66 (42.8)	71 (46.3)	15 (9.7)	1 (0.6)	1 (0.6)
WhatsApp status of MCQs enhanced my preparation for entrance examinations	39 (25.3)	82 (53.3)	31 (20.1)	2 (1.3)	0
MCQs improved my analytical skills	52 (33.8)	85 (55.2)	17 (11)	0	0
They helped me in self-directed learning	53 (34.5)	90 (58.4)	10 (6.5)	1 (0.6)	0
They helped me to enhance my ability to retrieve and utilize the information	55 (35.8)	86 (55.8)	12 (7.8)	1 (0.6)	0
It increased my motivation to learn	57 (37)	80 (51.9)	14 (9.1)	3 (2)	0
It encouraged collaborative learning and participation	55 (35.7)	83 (53.9)	14 (9.1)	2 (1.3)	0
I got an update about the disease in a structured manner	65 (42.2)	74 (48.1)	15 (9.7)	0	0
The knowledge gained through this approach has enhanced my confidence to face entrance examinations	44 (28.5)	83 (54)	24 (15.5)	3 (2)	0
These questions made me visit resources other than textbooks to gain additional information	38 (24.7)	98 (63.6)	16 (10.4)	2 (1.3)	0
I used to curiously wait for what questions will be posted for the day	43 (27.9)	81 (52.6)	24 (15.6)	6 (3.9)	0
Moderator could solve the doubts as and when I approach	54 (35)	83 (54)	16 (10.4)	1 (0.6)	0
The answers to the questions were logical	52 (33.8)	95 (61.6)	3 (2)	1 (0.6)	3 (2)

MCQ=Multiple-choice questions

attending final-year surgery rotation in Pakistan, where majority of them agreed that WhatsApp-based case discussion was a motivation for learning and Oyewole *et al.*, where 83% of the participants preparing for a licensing examination agreed that WhatsApp-based discussion increased their motivation to learn.^[15,16] Roy and Ray reported that 82% of the students felt that WhatsApp-based learning “provoked them to search other resources” which indirectly promoted self-directed learning.^[12]

89.5% of the participants in the present study felt that the activity encouraged collaborative learning and participation. Oyewole *et al.* also reported similar findings in their study, where 80% of the participants said that WhatsApp-based discussions helped in collaborative learning.^[16] The present study findings suggest that majority of the participants (89%) felt that it is possible to clear the doubts as and when they approach the instructor. Similar findings were observed by Gon and Rawekar who reported that 73% of students said that doubts could be cleared immediately in WhatsApp-based learning.^[10] 96.7% of the participants in the present study suggested that similar activities should be continued which were similar to the findings of Indu *et al.* among 3rd-year BDS students, where 94% of the study participants expressed the need of social media-based learning to continue along with conventional methods.^[17]

Limitation

The study being WhatsApp status based was open to attempt by the participants on a voluntary basis. Hence, we could not reach all the students and faculty from the institution. Furthermore, the queries were clarified

between the moderator and the enquirer, and it was a limitation of this method that we could not conduct group discussions on these queries.

Conclusions

The findings of the present study indicate that the sustained involvement of the medical student through WhatsApp-based MCQ discussion could enhance the collaborative and self-directed learning attributes. These discussions motivate students to gather the information, retrieve it, and utilize for their future benefits like preparing for competitive examinations. We recommend multidisciplinary approach of conducting such intervention through various departments in medical college for the career guidance and advancements of medical students.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

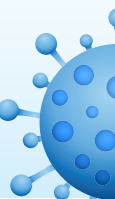
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Original Research Article

Qualitative enquiry on the perceptions related to MCQ based discussion through WhatsApp status among medical students and teaching faculty during COVID-19 lockdown

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ABSTRACT

Background: Ever since the government of India announced countrywide lockdown, medical institutions across the country has shifted to virtual learning. Being in an era of smartphone users, the utility of a popular social media platform like WhatsApp in efficient learning needs to be explored. The aim of the study was to determine the perceptions related to multiple choice question (MCQ) discussion through WhatsApp status among medical students and teaching faculty.

Methods: This longitudinal study was conducted among 154 participants (medical students and faculty) for three months. MCQs on COVID-19 were disseminated through WhatsApp status of the investigator and feedback regarding the same was taken at the end of three months. The qualitative data collected as descriptions were compiled and analyzed as per classical content analysis. Specific codes were assigned to responses and were put under different categories with similar characteristics.

Results: A total of 154 participants took part in the study. Participants felt that the approach to convert a popular social media like WhatsApp to a learning platform was innovative. According to them, the activity motivated them to learn more and kept them updated on COVID-19. A major advantage of WhatsApp based learning, being that it can be used anytime and anywhere, which is relevant in the lockdown period.

Conclusions: In this study, participants found learning via WhatsApp to be interesting and motivating. Learning through this platform helped the participants to keep themselves engaged in the academics in spite of lockdown and also provided opportunity to clarify their doubts.

Keywords: COVID-19, MCQ, Medical education, WhatsApp

INTRODUCTION

The novel corona virus disease forced China and many other countries across the world to impose a lockdown.¹ Two months after the disease was notified, on March 11, 2020, COVID-19 was declared as a pandemic by the World health organization. By then there were 1, 18,000 cases across 114 countries and 4291 people had succumbed to death.²

India reported its first case on 30th January, 2020, a medical student who returned from Wuhan after the epidemic started.³ Cases soon began to rise reaching a total of 563 and the Government of India announced countywide lockdown with effect from 25th March, 2020.⁴ Measures included cancelling public transport, restriction of movement, strict curfew, social distancing, cancelling mass gathering and closing down of offices, schools and colleges, including medical colleges.¹ This

was challenging as far as medical education is concerned as, for one, India has the largest number of registered medical colleges and it's important to maintain continuity of medical education and secondly, acquisition of clinical skills is imperative which is hard to meet through virtual mode.^{5,6}

Medical council of India (MCI) has long stressed that medical education is a continuous process and students' need to constantly acquire new skills and acknowledges the importance of e-learning to achieve the competencies. Ever since, institutions across the country have supplemented regular teaching methods with e-learning with more weightage to cloud based learning.⁷ However, being in an era of smartphone users, wherein the younger generation tends to spend a longer time on social media, the utility of social media in effective learning needs to be looked into.⁸

WhatsApp messenger is equally popular among all generations as it is a free application and extremely user friendly. It is available across android and iPhone platforms, and makes it easy to share text, documents, images, audio and videos in real time. WhatsApp provides an interactive platform for teachers and students to share information and discuss it further.^{8,9} Considering all these, the aim of the study was to determine the perceptions of students and teaching faculty regarding a WhatsApp based multiple choice question (MCQ) discussion on COVID-19.

METHODS

The present longitudinal study was conducted for the period of three months from March 2020 to June 2020, after obtaining approval from the Institutional Ethics Committee.

Study population and method of data collection

Study was conducted among medical students, interns, Post Graduates and teaching faculty who voluntarily attempted the multiple-choice questions (MCQ) posted on the WhatsApp status of the principal investigator. Convenient sampling was used. Responses from 154 medical students, interns, Post Graduates and teaching faculty who participated daily during this period were included and those responses received from subjects other than these were excluded.

MCQs were framed by the experts who have formally received training in designing and implementing MCQs through the medical education Unit. MCQs were based on epidemiology, management, prevention and control of COVID-19. Each MCQ was prepared with a stem and four responses, out of which one was the right answer and three were distractors. Recall based, case scenario related, calculation based, picture based questions were framed. Each MCQ framed by the faculty was validated by the

other faculty member before releasing for the participants to respond.

One MCQ per day was disseminated to the study participants through WhatsApp status of principal investigator so that participants' had sufficient time to understand the question and refer to relevant resources. The participants were invited to discuss any doubt, query, or clarifications in the process of solving the MCQ with the faculty. The correct answer to the MCQ was displayed on the same WhatsApp status wall 24 hours after the release of question. Activity log of the status with number of participants attempting the activity was maintained.

After three months, feedback was obtained from the participants using an open ended questionnaire including items on what went well during these sessions, what are the areas of improvements and suggestions to make this mode of learning more effective. The questionnaire was sent through an online google survey form, the link of which was shared on the same WhatsApp status wall where the MCQs were posted. The survey was kept active for one week from the starting date to provide enough time for the participants to respond.

Data analysis

The information was downloaded in the form of .csv (comma separated value) file and then transferred to MS excel-2010 for analysis. Descriptive statistics like percentages and mean were used. The qualitative data collected as descriptions were compiled and analyzed as per classical content analysis. Specific codes were assigned to responses and were put under different categories with similar characteristics. Verbatim of the participants involved in the study were also depicted. The entire analysis was done manually by two investigators trained in qualitative data analysis and consensus was arrived for depicting final results.

RESULTS

General characteristics of participants

A total of 154 participants took part in the study. Majority of the participants were using WhatsApp over last five years and they used to spend almost 1.5 to 2 hours daily with this app. Among the 154 study participants responding to the feedback survey, 44% of the participants were males and 56% were females. 48% were under graduates, 10.4% were interns, 30.6% were post graduates and 11% were teaching faculty.

Qualitative results

Suggestions for improvement

Discussion of the MCQs: The question was displayed on the status and 24 hours later the answer to the question



was displayed on the same status. Participants were free to clarify any query with the investigator. One of the main themes which arouse in the feedback was regarding the need to discuss the answers further.

“10-15 minutes of video conferencing per week can be done” (participant 1).

“Answers require explanation for why they are right or wrong” (participant 2).

“Group discussion and video conferencing can be done” (participant 3).

Participants also suggested that creating a WhatsApp group will be helpful. For one, this will help to retain the question and answer for further reference and for another it can be used as a platform to discuss the topic further.

“A WhatsApp group can be made where questions and answers (with brief context) should be put up to glance upon later on also” (participant 1).

“Create a group and post questions so that the questions & answers will be with the students & more discussion will happen” (participant 2).

Number of questions: One MCQ per day strategy was used in the intervention so that participants would not be overburdened and had sufficient time to refer to other resources. Participants suggested that the number of questions can be increased, as they felt they had more time in the lockdown period.

“Can increase the number of questions since it’s anyways a lockdown period and there is enough time to brush up our knowledge” (participant 1)

“5 questions per day quiz like, made with help of Google docs” (participant 2)

Resources: Few of the undergraduates expressed that they were unfamiliar with the terms used in the questions and hence suggested that the resources to be referred to, needs to be provided.

“A list of suggested resources could be provided with each MCQ answer” (participant 1)

“Since some of the target group are in third year, I wasn’t able to understand some of the terms used in the questions and didn’t understand which chapter to refer to for more knowledge on the topic. Maybe after the answer to a question is revealed, some additional information about that topic can be provided so that reading up about it in the textbook becomes easier” (participant 2).

Sharing of MCQs with answers: Participants suggested that all the MCQs with answers if made available will help for future references.

“It would have been having been good if we get printed copies of such questions.” (Participant 1)

“Kindly make all the questions available at one platform, it would be of great help in future referencing” (Participant 2).

Platform: We used WhatsApp status based exercise, some participants suggested WhatsApp groups as an alternative as the status disappears in a day and through groups it is possible to retain the questions and answers as well as it provides a platform for discussion.

“Another platform, because there are too many status from other people” (Participant 1)

“Group can be created instead of asking questions as status, may not open status all the time, if questions are asked in group students can access to any question at any time they are free, that’ll help us” (Participant 2)

“I prefer WhatsApp group over WhatsApp status for MCQ, because through group we can have better discussions.” (Participant 3)

“Maybe we can have a WhatsApp along with the status, so that the questions and answers can be there together as a collection of questions in a particular group. Since WhatsApp status disappear after 24 hours, so one can’t go through the questions again or revise them for exams until a screenshot is taken.” (Participant 4).

Variety of questions: Participants suggested that to make the exercise more interesting, variety of questions can be incorporated.

“Better variety of questions could be approached” (Participant 1)

“Image based or graph analysis type questions to be included” (Participant 2)

“More questions but in the form of connections, riddles, pictures to make it more interesting” (Participant 3)

Another suggestion given was that similar activities can be continued with other topics.

“continue theme based each month after corona stops and compile as MCQ resource” (participant 1) “cover more topics and subtopics” (participant 2)

Inter-departmental activity: It was suggested that activity can be extended, so as to include more departments in a group, to make discussion more comprehensive.

“Can be done by other departments. Or maybe like a college group with such discussions.” (Participant 1)

What was best about the intervention?



Good utilization of time in Lockdown:

The majority of the participants felt that the intervention was an effective way of utilizing time in lockdown period.

“To utilise the lockdown time by learning and practising something new. Make use of this time in a productive way.” (Participant 1)

“Also, a good exercise to brain storm when getting bored or otherwise.” (Participant 2)

“Best way to gain knowledge in a lockdown period.” (Participant 3)

Updates on COVID-19: Participants felt that the intervention was useful in keeping them updated on epidemiology and guidelines related to COVID-19.

“Being aware and updated of the current pandemic.” (Participant 1) “getting to know more about the disease and recent guidelines.” (Participant 2)

“It helped me to get a better idea about the virus and COVID-19.” (Participant 3)

A participant responded that the exercise motivated them to refer more resources.

“Have basic and sound knowledge about pandemic and this exercise is motivating us to read more”. (Participant 1)

Knowledge: Participants were of the opinion that the exercise helped them in gaining knowledge and it was assessed as well, on a daily basis.

“Daily assessment of knowledge.” (Participant 1)

“Gaining knowledge when we're away from college.” (Participant 2)

A participant felt that the exercise helped with the problem solving capacity.

“Knowledge base, thinking capacity and to solve question.” (Participant 1)

Another participant said that since they already spend a good deal of time on WhatsApp and the activity was through the same, they were benefitted.

“Due to lockdown we spend more time on this app. So it was good to spend some time gaining knowledge through the app.” (Participant 1)

About the initiative: Participants felt that the approach to convert a popular social media like WhatsApp to a

learning platform was innovative. It supplemented the regular learning in an interesting way.

“A very good initiative.” (Participant 1)

“Innovative and Informative” (participant 2)

“It became a good platform for learning and sharing new information.” (Participant 3)

“The effort from moderator's side is appreciable. Sir answered all the doubts immediately.” (Participant 4)

“Good initiative and one of the best intervention taken to help med students ... Most of the students Take social media as a distraction but helping them to do both, take a break and gaining knowledge meanwhile.” (Participant 5)

Learning: Majority of the participants felt that the approach to learning in this activity was interesting, which motivated them to learn more.

“Active participation with learning.” (Participant 1)

“Different and interesting way of learning.” (Participant 2). “Easy way to learn a concept.” (Participant 3) “Motivates to learn more” (Participant 4)

Advantages: The participants felt that the intervention had many advantages. The main being the convenience, since it was through a platform which they used daily.

“Convenient” (Participant 1)

“Easier access and concise information” (Participant 2)

“Easy way to gain knowledge and improve confidence” (Participant 3)

“Interactive method of studying” (Participant 4)

“Through these MCQs we could learn and revise the concepts of epidemiology” (Participant 5)

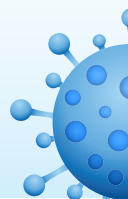
“Helped in reasoning and analysing” (Participant 6)

About the process: Participants felt that this activity motivated them to learn more and enhanced their knowledge.

“Encouragement to study more about the disease and community medicine.” (Participant 1)

“Questions were logical helping me enhance my knowledge.” (Participant 2)

“Meticulous work by the framer is commendable.” (Participant 3)



Learning various concepts in community medicine:

Participants felt that this was a great way of learning various concepts of Community Medicine.

“It piqued your interest as it applied whatever we have learnt in community medicine to our current state of the world” (Participant 1)

“It was a very good method to learn community medicine. Since it used the current world crisis, it made the entire subject more interesting.” (Participant 2)

“Horizontal and Vertical integration of PSM” (Participant 3)

Helpful for entrance exams: A major theme which came up was that, it helped them focus on preparing for competitive examinations.

“It reminded me to start preparing for PG entrance” (Participant 1)

“We became more confident solving MCQs day by day” (Participant 2)

“It will be helpful for NEET PG entrance exam” (Participant 3)

The responses of the participants with categories are represented in Table 1, 2.

Table 1: Participant's responses with categories for suggestions on improving the method for effective learning.

Categories	Responses of the participants#
1 Discussion	10 to 15 minutes of video conferencing per week can be done.
	answers require explanation for why they are right or wrong
	Group discussion and video conferencing can be done
	Create a group and post questions so that the questions & answers will be with the students & more discussion will happen
	Takes too long for the answers. Answers should have been posted along with the question in the next status
2 Number of questions	Can increase the number of questions since its anyways a lockdown period and there is enough time to brush up our knowledge
	5 questions per day quiz like, made with help of Google docs
3 Resources	A list of suggested resources could be provided with each MCQ answer
	Since some of the target group are in third year, I wasn't able to understand some of the terms used in the questions and didn't understand which chapter to refer to for more knowledge on the topic. Maybe after the answer to a question is revealed, some additional information about that topic can be provided so that reading up about it in the textbook becomes easier
4 Preserve	It would have been good if we get printed copies of such questions.
	Kindly make all the questions available at one platform, it would be of great help in future referencing.
5 Platform	Another platform, because there are too many status from other people
	Group can be created instead of asking questions as status, may not open status all the time, if questions are asked in group students can access to any question at any time they are free, that'll help us
	Since WhatsApp status disappear after 24 hours, so one can't go through the questions again or revise them for exams until a screenshot is taken.
	Maybe a google docs can be used to have MCQ session each and maybe it would be useful if all the subjects follow the same pattern. It's a great initiative by our faculties.
6 Questions	Cover more topics and subtopics
	Can be more case based.
	Continue theme based each month after corona stops and compile as MCQ resource
	Cover all kinds of community medicine questions
	Image based or graph analysis type questions to be included
7 Inter-departmental activity	More questions but in the form of connections, riddles, pictures to make it more interesting”
	Can be done by other departments. Or maybe like a college group with such discussions.

Responses with similar context has been merged

Continued.



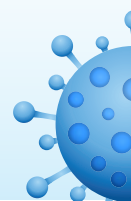
Table 2: Participant's responses with categories on what was best about the intervention.

Categories		Responses of the participants#
1	Lockdown	To utilise the lockdown time by learning and practising something new. Make use of this time in a productive way.
		Best way to gain knowledge in a lockdown period
2	About disease	Being aware and updated of the current pandemic.
		Getting to know more about the disease and recent guidelines
		Have basic and sound knowledge about pandemic and this exercise is motivating us to read more
3	Knowledge	Due to lockdown we spend more time on this app. So it was good to spend some time gaining knowledge through the app.
		Daily Assessment of knowledge
		Gaining knowledge when we're away from college
		Knowledge base, Thinking capacity and to solve question
4	About the initiative	Informative
		Innovative
		It became a best platform for learning and sharing new information
		It is an extra effort from the teachers for us which helps us to evaluate our knowledge based on our theory learning
		sir answered all the doubts on the spot
		Good initiative and one of the best intervention taken to help med students ... Most of the students Take social media as a distraction but helping them to do both, take a break and gaining knowledge meanwhile.. Hope everyone will make the best out of it
5	Learning	Active participation with learning
		Different and interesting way of learning
		Easy way to learn a concept
6	Advantages	Convenient
		Easy and cover broader aspect of topic
		Helped in reasoning and analysing
		Interactive method of studying
		Kept engaged during real time situations
		Makes us curious
		Motivates us to learn more
		Novelty
		Through these MCQs we could learn and revise the concepts of Epidemiology.
7	Process	Was able to brush up Community Medicine once again
		Encouragement to study more about the disease and community Medicine
		Questions were logical helping me enhance my knowledge.
8	Learning of Community Medicine	Meticulous work by the framer is commendable
		It piqued your interest as it applied whatever we have learnt in community medicine to our current state of the world.
		It was a very good method to learn community medicine. Since it used the current world crisis, it made the entire subject more interesting.
9	Helpful for entrance exam	It will be helpful for NEET PG entrance exam
		It reminded me to start preparing for my PG
		We become more confident solving the MCQs day by day

DISCUSSION

WhatsApp is a widely used social media platform by teachers and students, hence the need to explore more on its utility in learning, especially in this lockdown period was essential. In this study we tried to assess the perceptions of students and faculty regarding WhatsApp based MCQ discussion on COVID-19. The MCQs were displayed on the investigators' status and 24 hours later

the answer was displayed. Participants felt the need for discussing answers further, either through video conferencing or a WhatsApp group. They felt that WhatsApp group discussion would promote better interaction and that discussions can be used for future reference. Roy et al, in his study reports that the major advantage with WhatsApp based learning being "the resources remaining forever".¹⁰



A major drawback of WhatsApp status being that it disappears in 24 hours, participants felt that they might miss it when there are too many statuses from other contacts. Hence, they suggested an alternate of WhatsApp group for the exercise. The messages posted in them can be read anytime according to their convenience and that they can involve in further discussion about the topics.

The use of WhatsApp for learning was well appreciated by the participants who felt that similar activities can be extended to other topics, involving the faculties from various departments. This will help in an integrated learning environment. Mohesh et al in a study among first year medical students reported that the majority of the students suggested the use of WhatsApp based learning in all the subjects and that a WhatsApp group can be used to supplement classroom teaching to raise queries and discuss the subject further.¹¹

COVID-19 pandemic has also seen an avalanche of information. Some of which were inaccurate, causing confusion and anxiety among the people.¹² In this study, the MCQs were prepared by experts, relating to epidemiological aspects, guidelines and management of COVID-19, which helped the participants in keeping updated on COVID-19 in the best way.

The participants used WhatsApp on an average of 1.5 to 2 hours per day. They felt that this time of WhatsApp use was put to good use to gain knowledge and this was assessed on a daily basis as well. According to the participants, this approach to utilize a commonly used media like WhatsApp, where they already spend a large amount of time to a learning platform was quite innovative. This made learning more interesting, motivating them to refer other resources and promoting active, self-directed learning. Literature suggests that WhatsApp based learning is a good way to promote self-directed learning. Nanda et al reported that due to the interest that the students develop through WhatsApp based learning, it significantly improved their knowledge level and writing skills.¹³ Zulfikar et al also reported that students felt WhatsApp based discussion was a motivation for learning.¹⁴ Compared to the conventional methods, a major advantage of using a WhatsApp like platform is that students can discuss and clarify their doubts almost immediately. Besides this, participants felt that this method was convenient, as they could use it anytime, anywhere, similar to the findings of Guo et al.¹⁵ Participants responded that the intervention, enhanced reasoning and problem solving skills and they felt confident in answering MCQs which would help them in preparing for competitive exams. Grover et al reported that after a WhatsApp based intervention students felt they could perform better in MCQ exams.¹⁶

CONCLUSION

In this study, participants found learning via WhatsApp to be interesting and motivating. The learning through this

platform helped the participants to keep themselves engaged in the academics in spite of lockdown and also provided opportunity to clarify their doubts regarding the subject. Majority of the participants recommended to continue this intervention in interdisciplinary manner by including more number of faculty members.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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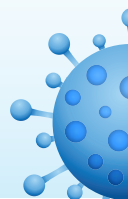
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What to Teach and How to Teach Medical Students in the Middle of COVID-19? Guidance for Teachers in Psychiatry

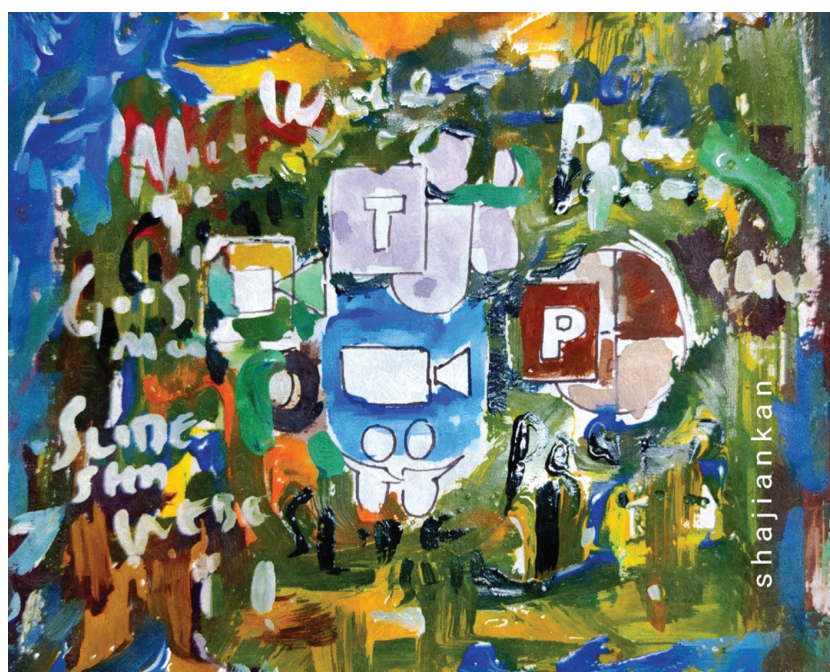
M. Kishor¹ 

The second wave of the COVID-19 pandemic has already hit India, disrupting the medical teaching-learning in most parts of the country. Until the last week of May 2021, nearly 3.5 million people had died worldwide because of COVID-19, and India had the highest number of active cases with over 300,000 new cases every day. The COVID-19 outbreak is an unprecedented humanitarian crisis that India had to face in recent times.¹ Education of medical students, who, in turn, are key human resources during times of a pandemic, is severely affected in this time. Most medical educational institutions have not been fully functioning since the lockdown of March 2020. While most have moved to the online platform, with the second wave, it is time for teachers, students, and medical education institutions to reflect and look at the continuity of education in the current scenario.

Teachers of psychiatry play an important role in national public health services.² They must learn to balance the standard of psychiatry education

with other duties related to COVID-19 care. The new medical education curriculum implemented in 2019 has raised the need for faculty training.³ The

pandemic module for Indian medical graduates released has major lacunae, with exclusion of mental health, and was duly criticized.⁴ The new module



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has incorporated necessary changes. More importantly, an increased need for mental health services during the pandemic has indeed highlighted the necessity for psychiatry training of Indian medical graduates, which the psychiatry teachers should emphasize at all times.⁵

Enthusiastic psychiatry teachers find joy in teaching irrespective of the hurdles they face. Learning new methods of online teaching is one of them. For responsible students, there is a real need to learn. In India, in the first wave of COVID-19, there have been media reports about students who committed suicide because of unaffordability to access digital teaching-learning programs.⁶

There is a great need for the teaching-learning process to make up for the lost time. Also the teachers have to bear in mind that COVID-19 pandemic has been unpredictable with multiple waves across the world, including India. Psychiatry teaching-learning in Indian undergraduate medical education is a time-dependent process of listening, assimilation, practice, and application of knowledge; in the process forty hours have been allotted for theory and four weeks to clinical posting. The pandemic has taken away the valuable time allocated for the subjects. There is a need for psychiatry teachers to urgently reflect upon how each phase of psychiatry education can be completed in the middle of the COVID-19 pandemic.

Information technology is booming, and virtual communication has accelerated during the pandemic. It has heralded a new era of teaching, including psychiatry teaching-learning; teaching programs can now be attended from anywhere and anytime. For students, this can be truly called “Selfie” time, an age for self-learning of all subjects, including psychiatry. Although there are concerns related to the technology issues such as network problems and the issue of internet addiction, the young medical students of India are tech-savvy, and online learning thus is expected to be a positive development. Psychiatry teachers may have to speed up and learn adapting to technology-enabled online teaching methods.

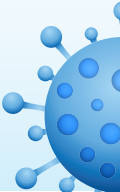
The teaching in medical schools that was formal, with actual classes in the

physical presence of students, may not be possible during the COVID-19 pandemic. The informal pattern of an online class that is streamed live and/or stored at web portals or mobile application shall be the new norm or alternative for some time. Mobile-application-based learning has not been evaluated, but it does give flexibility to students, and in self-learning mode, they can decide when to learn and what to learn. It is important to consider how psychiatry education can continue. The pandemic is a time when the entire psychiatry curriculum of each phase of MBBS or each section can be effectively carried out by dividing it into components that are predominantly the knowledge or cognitive domain, affective domain or communication skills, and the psychomotor domain. Psychiatry teachers and undergraduate students can together decide which aspect of the topic falls into which section. It is important to customize the selection of psychiatry topics based on the necessity and priority in the current pandemic: For example, the teaching of depression, anxiety disorders, suicide prevention, alcohol dependence syndrome, and sleep disorders may be considered more relevant in the context of COVID-19. Prioritizing the topics to be covered will ease the process of designing the teaching plan in the available time frame. If the topic for psychiatry teaching selected is alcohol-dependence syndrome, the knowledge or cognitive domain will include prevalence, etiology, clinical criteria for diagnosis, etc. The affective component can be “How to elicit alcohol dependence syndrome as per WHO-ICD (World Health Organization International Classification of Diseases)?” The psychomotor domain shall involve steps in the examination of the patient (or virtual/simulation) such as observation, palpation, percussion, and auscultation in relation to signs of alcohol withdrawal, alcoholic liver disease, and cerebellar dysfunction. Psychiatry teachers can carefully design specific-learning objectives for each session. With active feedback, the teachers and students can make the teaching-learning interesting and interactive.

Learning in the knowledge or cognitive domain is considered easy for students, as they can read and learn by themselves. To read, comprehend, and

recall the information is the focus of the cognitive process. Information is available from recommended medical textbooks or online sources that psychiatry teachers can list out. The psychiatry teacher has a minimal role in cognitive learning, and that can be reserved for providing guidance and clarity when the students need it and for highlighting the key aspects or relevant additions. Psychiatry teachers can facilitate peer-to-peer interaction for learning and self-evaluation, such as mock examination. In a pandemic, contact classes can be avoided, and only limited online theory classes can be held. Thus, they should be more interactive and provide a recap of clinically relevant aspects. Teachers can bring in predetermined methods of rewards that can be incorporated in the total marks during the assessment, if any.

Psychiatry teachers can spend more time in the affective and psychomotor domains. A psychiatry teacher conducts a demonstration first on developing rapport and elicits alcohol dependence, for example. The teacher later facilitates the learning through role-play carried out by the students, through the online platform. Role-play with normal people (non-COVID), with safety methods, can also be incorporated. The process can be streamed live or recorded video clips can be made available. While learning an affective or psychomotor component, the students should repeatedly perform it to master the skill. They can perform the method with the help of family members or friends (with their consent). Once the students start appreciating the process in any skill domain, the other steps in learning are much easier. With the least exposure to infection, modified clinical sessions can also be carried out in small groups. The skill acquisition can be monitored online by the teacher evaluating each student individually or through peer-to-peer evaluation. Wherever or whenever patients are available in a safe environment for examination (e.g., patients with alcohol-dependence syndrome or depression), teachers can use the “Fish Bowl” teaching methodology. The basic idea is that the psychiatry teacher conducts a coaching session with an individual student and the other



students observe and learn vicariously. Problem-based learning, flip classroom, and other teaching-learning methods can be incorporated as feasible.

Psychiatry teachers may have to break the old methods and discover newer ways that may be needed during a pandemic. Assessments, if any, need to be carefully planned and pilot tested, and novel ideas of assessment can be incorporated. Digital student assessments such as those using Google Forms or Microsoft Teams can be utilized.

In institutions where the pandemic has adversely affected the teachers or where resources are constrained, professional organizations such as the Indian Psychiatric Society can provide free access to teaching-learning on online platforms.

In this time of a pandemic, there is an urgent need for psychiatry teachers to innovate efforts for continuity of psychiatry teaching-learning in medical institutions so that upcoming doctors are reasonably competent in psychiatry

and ready to serve the society with the required psychiatric knowledge and skills.

Enthusiastic psychiatry teachers and medical students can join hands to ensure the continuity of people-centric learning. Learning should never stop; however, “how” we learn needs to change.

Declaration of Conflicting Interests

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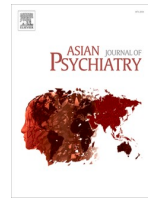
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Letter to the Editor

Use of electronic logbook in psychiatry training and its relevance during COVID-19 pandemic in India



ARTICLE INFO

Keywords

eLogbook
Electronic logbook
psychiatry training

Sir,

Accurate evaluations and assessments are of prime importance for maintaining the standard of medical training. Traditionally, the battery of assessment tools used as summative and formative assessment's purpose (Schuwirth and Van der Vleuten, 2011). But, having an assessment tool of precision is a challenge yet to meet in medical training, especially in psychiatry (Bhugra and Malik, 2011). The need for an alternative or a robust assessment system strongly felt during the ongoing stringent condition of the COVID-19 pandemic, where some traditional assessment methods are rendered impractical or unsafe. The specific requirements of the COVID-19 pandemic in the background of growing demand for psychiatrists and the opening of a row of newer medical institutions concern the level of psychiatry training (Philip et al., 2021; Richards and DeBonis, 2020). Here we intend to discuss and highlight the utility of an electronic logbook for post-graduate psychiatry training, which perhaps can answer some of our quests.

A logbook is a "verified record of the learner's progression documenting the acquisition of the requisite knowledge, skills, attitude and competencies" (Medical council of India, 2020). It is considered a continuous formative assessment and recommended to use even as an electronic form for post-graduate psychiatry training (Medical council of India, 2020). Though the concept of an electronic logbook is not new, its utility in psychiatry training is yet to explore in India. An e-logbook has several advantages over a traditional paper-pen logbook due to the ease of recording, storage, and data analysis (Sehmbi and Shah, 2013). We conceptualize two model electronic logbooks for psychiatry training that can utilize as per the requirement and available resources in the institution or department.

1. Offline or asynchronous type electronic logbook

An offline or asynchronous electronic logbook does not require an internet connection; data entered and stored manually in a computer using database management software, spreadsheet or Microsoft excel, or Statistical Package for Social Sciences (SPSS®), depending on the available resources.

This model advantage of better data control and security, no third party access, require minimal or no internet connectivity and does not

warrant much technical competency (Fig. 1). The disadvantages are the risk of data loss; data needs to be backup manually by using an internal or external Hard disk drive (HDD).

2. Online or synchronous type electronic logbook

An online e-logbook uses a database program or Personal Digital Assistants (PDA) with a device connected to the internet, unlike an offline logbook. The cost involves may vary from freely available eLogbook software to expensive database programs used at the departmental or university level. The safety can compromise due to third-party access and data theft; usually, good security features are needed, such as a unique user name and password for admission, a one-time password (OTP) and an updated anti-virus subscription. It has technical advantages to access by multiple devices and connected to the internet anywhere anytime, and data usually auto-backup (Fig. 2). Online e-logbook enables learners to see their performance, peer assessment and supervisors feedback in real-time (Sehmbi and Shah, 2013). This model has a better acceptance, significant degree of transparency and flexibility to upgrade with advancing technology (Iqbal et al., 2015).

The eLogbook can potentially use with e-learning tools, e-calendar and auto-reminder, to provide an edge for better organization and time management of the student. The academic roster can sync with the e-calendar, and the student gets the alert and reminders for an upcoming educational event on their smartphone. An eLogbook with such sophistication is not just an eLogbook but a robust training tool and a new horizon for futuristic psychiatry training (Fig. 2). The relevance of the electronic logbook further appreciated in context to the COVID-19 pandemic or any natural disaster wherein examination cannot be carried out in the physical presence of the examiner. Sharing an electronic logbook provide a comprehensive longitudinal report of student performance is much more sophisticated, helping proper decision making by the examiner along with other summative assessments.

Declaration of Competing Interest

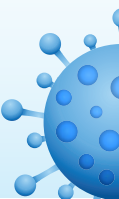
The authors report no declarations of interest.

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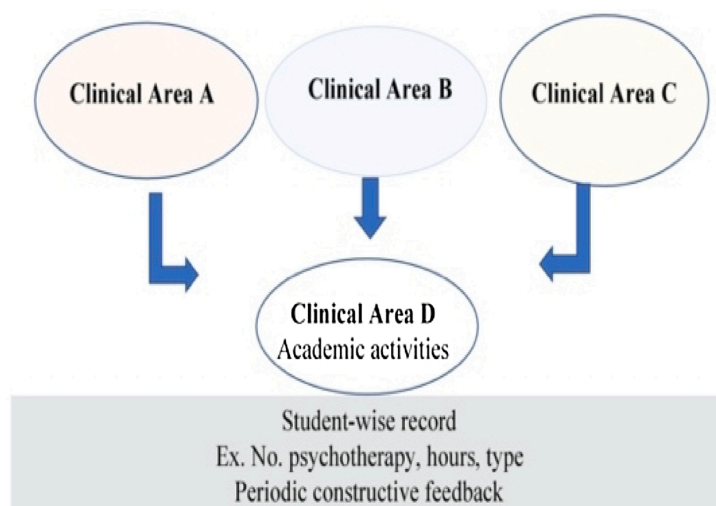


Fig. 1. Students posted in a clinical area (ex. Clinical Area A) make required entries in a computer placed in that area. The data from various areas compiled to assess the performance of the student.

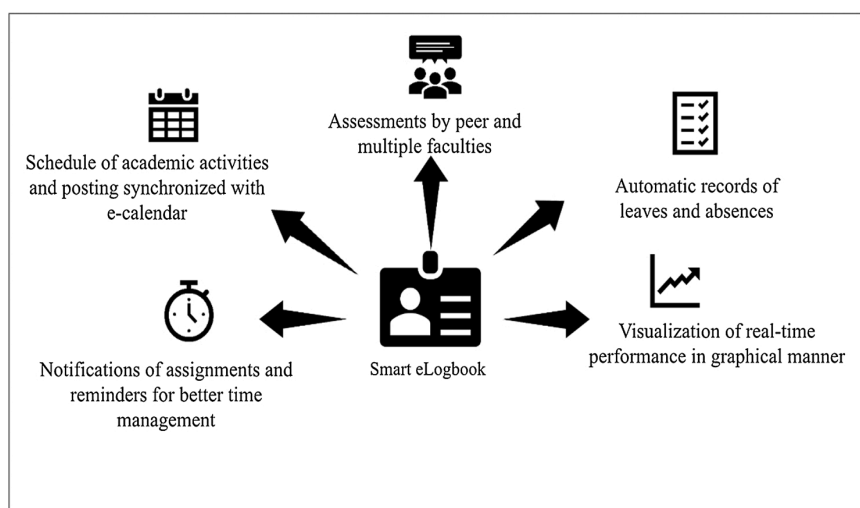


Fig. 2. eLogbook with an extension of auto-reminder, e-calendar, accessibility to see peer performance, supervisor feedback, and the student's real-time performance.

Acknowledgement

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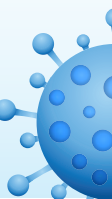
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4. Impact of Pandemic on Health care delivery Sector

SI No	Title	SDG IMPACT
27	Novel Coronavirus – 19 pandemic impact on private health-care services with special focus on factors determining its utilization: Indian scenario, Sathish Raju Nilakantam., Dr Kishor M., Dr (Col).Dayananda M., Amogha Shree, International Journal of Health and Allied Sciences , 9, 77-80, 2278-4292	Goal 3: Good health and wellbeing Goal 9: Industry innovation and infrastructure
28	Role of medical institution amidst the crisis: Sustaining the academic milieu and contributing to components of COVID-19 pandemic response, Dr Anil S Bilimale., Dr BasavanaGowdappa H., Dr Suma M.N., Dr Narayana Murthy M.R., Dr Praveen Kulkarni, International Journal of Health and Allied Sciences, 9, 114-116, 2278-4292	Goal 3: Good health and wellbeing Goal 9: Industry innovation and infrastructure



Perspective

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Novel Coronavirus – 19 Pandemic Impact On Private Health-Care Services with Special Focus on Factors Determining Its Utilization: Indian Scenario

Sathish Raju Nilakantam, M Kishor¹, M Dayananda, Amogha Shree²

Abstract:

The novel coronavirus disease (COVID-19) outbreak, caused by severe acute respiratory syndrome coronavirus 2, has rapidly escalated into a global pandemic which leads to declaration of national health emergency in several countries and is having a profound impact on private health-care systems globally including India in unprecedented manner. However, the impacts are very serious, especially on global economics and health care due to COVID-19 pandemic. During this pandemic, private hospitals and clinics are experiencing a reduction of in patient footfalls due to nationwide lockdown and several other factors as well which are leading to inadequate utilization of health-care services by the patients and decrease in medical services volumes which resulted in acute economic crisis. In this article, various factors that caused a significant reduction in utilization rates of private health-care systems such as hospitals and clinics were outlined and discussed.

Keywords:

COVID-19, novel coronavirus, pandemic, private health-care systems

Introduction

The World Health Organization declared COVID-19 infection as a global pandemic which is presently engulfing 213 countries affecting over 2 million people and 157,970 deaths as of April 20, 2020.^[1] It is expected that the number will grow in the next few weeks. India is also suffering with over 17,000 cases and nearly 550 deaths as of April 20, 2020.^[2] Being one of the developing countries, India is suffering with humanitarian crisis with severe restriction on people's movement like complete lockdown that predominantly affected millions of migrant workers and daily wage workers.^[3]

This worldwide COVID-19 infection has also affected the day-to-day life of the

people, their businesses, and problem in getting their essentials and even the health-care sector largely. COVID-19 has affected the entire departments in the hospital where they are unable to concentrate on their regular patients.

The central and the state governments across the nation enlisted almost all district government hospitals for the identification and management of COVID-19 in the initial phase. The private health-care systems consist of 58% of the hospitals in the country, 29% of beds in hospitals, and 81% of doctors, which account for 82% of outpatient visits, 58% of inpatient expenditure, and 40% of births in institutions.^[4] Hence, it is important to understand the determinants of hospital service utilization during COVID-19 specifically for the private hospitals not only because they are major contributors to

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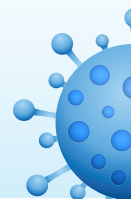
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Nilakantam, *et al.*: Novel Coronavirus – 19 Pandemic Impact On Private Health- Care Services with Special Focus on Factors Determining Its Utilization: Indian Scenario

the health-care delivery system in India but also due to a fact that some private hospitals continued to serve in the middle of COVID-19 crisis for non-COVID-19 patients.

Few private hospitals were also shut down during the pandemic times, due to the high rate of infections in those hospitals. The probable reason could be due to the early phases of pandemic, where hospitals were not prepared to identify and manage effectively and also due to lack of experience of hospital staffs in dealing with such a novel agent and with such a degree of infectivity. According to the National Family Health Survey-3, the private medical sector remains the primary source of health care for 70% of households in urban areas and 63% of households in rural areas.

The health-care sector is at the epicenter of this unprecedented global pandemic challenge, and the private health sector has risen to the occasion, by offering to the government all the support it needs, be it testing support, preparing isolation beds for the treatment of COVID-19-positive patients, or deploying equipment and staff in identified nodal hospitals.

As the lockdown began, the government at all levels repeatedly highlighted the fact that health-care services come under essential services and hence shall be exempted. However, there was a complete collapse of the public transport system which acts as one of the important means for patients to reach the hospital. In this period, the utilization of private hospital services was evaluated. The tertiary care teaching hospital in Mysuru, which is 1800 bedded, attached to medical college received 42,096 outpatients in March 2020 and 28,221 outpatients in April 2020 against 54,976 outpatients in March 2019 and 53,271 outpatients in April 2019 in the same period of the last year and these accounts to almost 60% drop in the footfalls of patients to the hospital, which directly or indirectly impacted the utilization hospital and health-care services.

Although it is easily assumed that lockdown, lack of public transport, fear of contracting COVID-19 infection might have played a role in underutilization of hospital services, it is important to explore the perspectives of patients who are the end users of services. The Government of India has, on March 21, 2020, released guidelines for the hospitals to prepare for the coronavirus outbreak. Among other things, hospitals are required to reserve beds, create isolation wards, and mobilize additional workforce and train staff, in addition to arranging for adequate high-oxygen masks and ventilators. This resulted in sharp drop in footfalls of private hospital services such as utilization of outpatient departments (OPDs), diagnostic testing, prioritizing only urgent and emergency cases which resulted in canceling

of many medical appointments, and cancellation or postponement of elective surgeries until there is clarity on infection prevalence in the region and means to control it. In the tertiary care teaching hospital in Mysuru, a survey of 60 patients who utilized services during the lockdown and 60 patients who did not utilize despite the scheduled appointments revealed many factors that help us to understand the factors contributing to significant reductions of health-care utilization in ongoing COVID19 crisis. At the time of writing this article,, the information obtained from the survey has not been analyzed, but few important factors have been outlined here to discuss their impact on private hospitals and health-care systems.

The Following are The Factors that Affected the Utilization Rates of Private Health Care Services

Nationwide lockdown

Since March 24, 2020, India has been under a nationwide lockdown, now extended by the Central Government till May 17, 2020, to curb the spread of the coronavirus. This lockdown has been causing huge disruption, and distress, to the lives around the world and also achieved modest reductions in overall hospital admissions and substantial reductions in the use of daily OPDs and elective services.

Lack of public transport

As a part of nationwide lockdown, the closure of public transportation has exacerbated challenges for patients in accessing health-care services, especially those living in rural areas and economically underserved

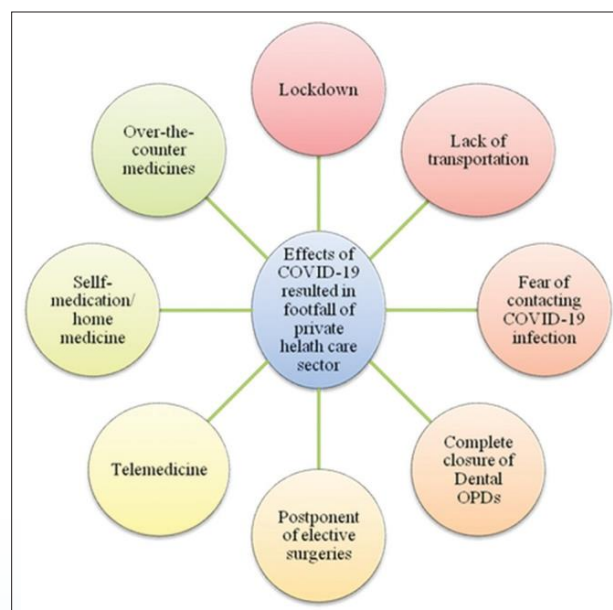


Figure 1: Reasons for decline in footfall of patients in private health-care facilities



Nilakantam, *et al.*: Novel Coronavirus – 19 Pandemic Impact On Private Health- Care Services with Special Focus on Factors Determining Its Utilization: Indian Scenario

settings, as rural populations are more likely to have to travel long distances to access health-care services, particularly subspecialist services. In urban areas, public transit is also generally an option for patients to get to medical appointments. Rural communities often have more elderly residents who have chronic conditions requiring multiple visits to outpatient health-care facilities. This becomes challenging without availability of transportation whether it is public or private.

Postponement of elective surgical/diagnostic procedures

Measures like restrictions on the non-urgent use of hospitals were imposed, which impacted the private hospitals performance on surgical services. [5] These restrictions resulted in shrinkage in the rate of admissions for elective procedures; however, subject to the restrictions, majority private hospitals continued to allow few essential elective admissions. Because, higher priority should be given to the patients, who are clinically unstable or if the intervention is predicted to end in substantial overall survival gain or improvement of quality of life. Postponement of elective surgeries and procedures could have an adverse impact on the quality of life while the patients wait for the right time to get the treatment they need. Surgeries have been reduced by approximately 50% nationwide.

Telemedicine

As patients under lockdown and health workers at the risk of infection, health-care system is adopting virtualized treatment approaches that reduced the physical meeting between patients and health providers. Digital health technologies are being adopted at a huge rate now without any technological barriers in the adoption of virtual health care.^[6] As a result of this, most of the outpatient visits have been shifted from hospitals toward telehealth visits.

Fear of contact

Patients' fear of seeking hospital-based care may have been an important determinant of hospital services utilization during the SARS COVID-19 outbreak. Although it was concluded at an early stage that the infection spreads by droplets and it was not immediately recognized that the virus was so tenacious that it could survive outside the body on surfaces for long periods. The estimates of the time that the virus could survive on various surfaces grew longer and longer – from hours to days throughout the outbreak – as an understanding of the virus increased. The fears of SARS COVID-19 significantly influenced people's health-care-seeking behavior and that this fear seriously compromised their access to quality care. It is not just a problem of common people, even nearly 70% of the medical students were reluctant to attend clinics from fear of getting infected

or passing on to others during the outbreak^[7] because of initial lack of awareness of the mode of spread of the virus.

Closure of private clinics

Many of the private medical practitioners across various cities, especially on the fringes, have stopped opening their clinics during the lockdown fearing close contact with coronavirus-infected patients. With no option left, many patients despite having minor illness are forced to rush to crowded hospitals, defeating the purpose of social distancing.

Homemade medicines/self-medications

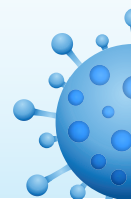
Many patients have started self-medication, risking health. Since the commencement of lockdown, there is a lot of usage and preparation of homemade medicines by patients. Many families have fallen back to traditional ayurvedic and herbal medicines that can be easily prepared at home. This practice of using homemade medicines has also picked up in villages and towns as they do not have transportation facilities to reach the hospitals and clinics. This concept has gained more importance when the AYUSH ministry brought measures for enhancing the body's natural defense system (immunity) which also included homemade remedies for illnesses such as dry cough and sore throat.^[8]

Over-the-counter medicines

Due to this lockdown because of the COVID-19 pandemic, people who are suffering from non-COVID illness are unable to reach the hospital on time which resulted in further deterioration of their health condition. Only those with the knowledge and smartphone could access virtual treatment, whereas the poorer are still devoid of these facilities which made them take the over-the-counter medications including many with little evidence to support their safe use.^[9] Thus, both virtual treatment and over-the-counter medicines indirectly resulted in less utilization of hospital services.

Expected Changes in Post Covid 19 phase

Once the lockdown is lifted, people may rush to hospitals with new diseases or with the complications of existing disease. As the lockdown was for a very long period (already completed 28 days of lockdown as on April 20, 2020), we can expect the surge in new cases related to mental health among who suffered from COVID-19 and their immediate family due to nonacceptance of them and among daily wage workers and migrant laborers due to economic instability and suicidal tendency among alcoholics, etc. Another challenge is an epidemiological shift toward noncommunicable diseases where



Nilakantam, *et al.*: Novel Coronavirus – 19 Pandemic Impact On Private Health- Care Services with Special Focus on Factors Determining Its Utilization: Indian Scenario

lack of physical activity plays an important role. Furthermore, elective surgical procedures, checkups, and other treatments that have been postponed will likely now be jammed into the second half of this year in order to comply with insurance plans. Patients of chronic disease, being wary of going out, or facing difficulties in movement due to lockdown restrictions might miss on treatment, ending up with long-term sequelae. These can eventually increase the possibility of complications and worsening of the disease, raising the overall burden of diseases of the country to a certain extent. Hence, private health sectors should also be ready to tackle the other side of the footfall. It is also expected that patient visits to psychiatry will be increased not only due to fear of isolation and stigma attached to those who are being quarantined and isolated but also because of psychosocial and socioeconomic impacts. The health-care community will begin to prepare for life after COVID-19, and the gradual re-opening of hospitals and practices of health-care providers will turn their attention to addressing their equipment purchases that were delayed or deprioritized. In addition, new equipment needs will emerge in order to protect patients such as testing devices, telemedicine, and safe waiting areas for patients.

Health care will continue to take center stage as we continue to battle this pandemic and the anticipated return of viruses. There will be more robust discussions of universal health care and basic universal income. Regardless of the outcome of these debates and the passage of various new policies, the strengthening of our health-care system and the preparation for future pandemic risks will be widely supported by our politicians and our citizens. There will be mounting pressure to ensure each state, and its health-care providers to have adequate access to necessary equipments and supplies, as well as tighter control of the supply chain by the government.

Conclusion

During COVID-19 pandemic, health-care utilization and medical services decreased significantly which

resulted in significant loss of revenue and increased use of resources. The immediate shutdown of elective surgeries, dramatic decreases in patient volumes, and the measures taken to prepare for a potential surge in hospitalizations have created immediate and long-term financial impacts on the system. The private hospitals and laboratories, which were already facing multiple challenges, will witness an acute crisis due to COVID-19 and the subsequent lockdown, which has resulted in occupancy levels to fall to a mere 40% by late March and April vis-a-vis pre-COVID occupancy levels of 65%–70%. This is expected to reduce even further. Hence, to conclude, SARS COVID-19 pandemic brought about not only relatively discernable economic losses but also observable damage to health-care organizations, and this has resulted in a lower health-care utilization rate.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Role of medical institution amidst the crisis: Sustaining the academic milieu and contributing to components of COVID-19 pandemic response

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Abstract:

In early March 2020, the whole world was startled due to the COVID-19 pandemic. Amidst the crisis, a private medical college relentlessly worked toward sustaining the academic momentum and contributing to the mitigation of COVID-19. The areas of involvement were as broad as it had its roots. Educating the larger public through schools, colleges, and primary health-care centers was initiated. The hospital was operationally segregated into COVID and non-COVID zones. The screening centers and isolation wards were made operational. The health-care personnel were trained and motivated. The outreach and public health activities were in tandem with district health priorities, namely mass screening, health system strengthening at district COVID hospital, answering public queries, panel discussions, webinars, and TV shows. Apart from these activities, teaching and learning went on, as usual, using online platforms. Research, innovations, and publications were accomplished without interruption.

Keywords:

Academic sustainability, COVID response, hospital preparedness, outreach activities

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On January 30, 2020, the World Health Organization (WHO) reiterated all the member countries to take immediate actions and scale up their response to detect and contain the virus transmission to save people's lives.^[1] The WHO declared the novel coronavirus disease (COVID-19) outbreak as a Public Health Emergency of International Concern and directed to treat this as a global pandemic by March 11, 2020. Further, India reported its first confirmed case of COVID-19 on January 30, 2020. A medical student returning from the Wuhan University of China to Kerala state was tested positive. Subsequently, two more cases were reported in early February from the same state.^[2] This tally increased substantially in subsequent months to a

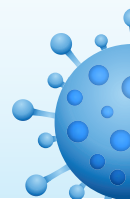
total of 77,729 confirmed cases and 2535 deaths as of May 13, 2020.^[3] The first case in Karnataka was reported in March, and over 2 months, the numbers have climbed to 951 cases with 32 deaths till May 13th, 2020. Mysuru, a district situated in the southern part of Karnataka, known for its heritage and culture reported its first case on March 21, 2020. After a sluggish start, the number of cases in the district increased quickly to reach the tally of 89 by mid of April with no deaths so far.^[4]

Mitigation of COVID-19 demands intersectoral, interdisciplinary, and multipronged approach. Medical colleges of both government and private sectors play a vital role in this process. JSS Medical College, a premier health-care and research

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institution affiliated to JSS Academy of Higher Education (JSSAHER), shouldered this responsibility with the district health administration and efficiently delivered the tasks assigned to it. In this commentary, we will be discussing the role played by JSS Medical College in mitigation of pandemic at district level through its systems approach without compromising its academic milieu.

In February, well before the first case was reported in the state of Karnataka, the institution took the initiative to educate the public and school children on prevention and control of COVID-19. The medical college was offered representation in District Task Force on COVID-19 to provide technical guidance and support in combating the pandemic.

As a part of preparedness toward handling the crisis, situation analysis of the hospital was conducted to understand the strengths, weaknesses, opportunities, and threats by involving all the clinical, nonclinical departments and the paramedical staff. The Department of Community Medicine and Public Health undertook this activity using standard checklists from the Centre for Disease Control and the Ministry of Health and Family Welfare. Subsequently, a panel discussion was conducted by involving the experts from the field of microbiology, community medicine, general medicine, pulmonology, and hospital administration to cement the approach. On March 24, a FLU clinic was established in JSS Hospital. Patients were screened at the hospital entrance using a standard checklist and thermal scanner, adequate physical distancing was created in waiting area, triaging was done to differentiate and isolate the suspected cases of COVID-19, and critically ill patients were shifted through dedicated lifts to identified intensive care units. The departments which contributed significantly toward these endeavors are emergency medicine, general medicine, pediatrics, microbiology, intensivists, and ENT.

The nationwide lockdown was implemented from March 24, 2020. As an emergent response, a COVID-19 screening center was established at JSS Hospital. A dedicated multispecialty team was setup. A nodal officer was identified to act as a liaison between hospital and district health authorities. The Hospital Infection Control Committee started training the medical, nursing, and Group D staff regularly on COVID-19. Stockpiling and auditing of disinfection and infection prevention materials were undertaken periodically. The biomedical waste management team was trained, and aggregated wastes were disposed of according to the standard safety protocols.

The onslaught of fresh cases in Mysuru leads to a revision of layout and protocols to expand

the facilities including separate screening area, isolation ward, triage, lift, and ICU. Duty rosters for postgraduates (PGs) and consultants were revised and updated. The training under the iGoT platform, as per MoHFW instruction, was provided to all faculties, PGs, and interns.

A series of public health and outreach activities were undertaken across the district before and during the lockdown:

- Nanjangud Cluster Containment – Nanjangud, a town in Mysuru district, turned out to be a hotspot of COVID transmission. PGs from the Department of ENT supported in the screening of contacts by collecting the throat swab for testing
- The Department of Community Medicine and School of Public Health undertook the following initiatives.
 - a. District COVID hospital – Faculty members and PGs worked as a part of screening team at designated COVID hospital, provided inputs toward preparation, training, developing protocols, communication materials, human resources, and consumable estimation, quality improvement, and auditing activities
 - b. District health administration – Contact tracing through telephonic conversation with the confirmed cases of COVID-19 (primary and secondary contact) and entering data into the software, designing a questionnaire, and regularly discussing the different models of COVID response from various countries
 - c. Corona helpline at District Control Room – PG students addressed the queries of the public concerning testing, public gathering, do's, and don'ts during and before lockdown
 - d. Faculty members were involved in training NSS volunteers, community social radio, urban local bodies, taluka level officers throughout the state in collaboration with UNICEF, State Institute for Urban Development, Administrative Training Institute, and National Institute of Rural Development and Panchayati Raj.

Dissemination of technical information

Illustrious speakers and technical experts took the lead to address the concerns of people and medical fraternity through various webinars, editorials, panel discussions, and technical reports. The messages spread by these experts reached masses through renowned news channels such as NDTV, News One, and various online platforms.

Academic initiatives

Adhering to the motto of learning never stops at JSSAHER, online academic sessions were initiated for



both undergraduate and PG students. Faculties were adequately trained on conducting online classes, and students were also sensitized on the same. Meanwhile, online assessments and modifications in the examination patterns were brainstormed and necessary materials were produced.

Research activities

To efficiently utilize the lockdown period, faculty members undertook short-term research projects through online surveys, submitted research protocols for funding agencies, and prepared and submitted their research work as scientific publications to various journals. There were few innovative ideas which were executed. The Institutional Ethics Committee conducted an online meeting to clear the research protocols submitted to them.

Leadership

In this situation of crisis, the leadership of JSSAHER adapted and updated itself to hold the grip on the situation through expert consultations. Meanwhile, second-level leaders were kept in the loop and ensured everyone is safe and at the same time prepared to respond. Mental health counseling and seminars were arranged to prepare faculty to deal with stress. Transparency was maintained at all levels. This exemplary leadership helped the faculty to work with a high level of spirit in the difficult days.

Conclusion

COVID-19 created an avenue to show the ability of a private institute for playing a major role in providing helping hand in such challenging situation and a huge public health crisis through a thorough plan of resources and aid in the betterment of society along with sustaining its academic and research milieu in momentum.

“Amidst the crisis, finding a way to be productive and useful was the motto of our institution.”

Financial support and sponsorship

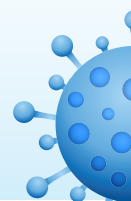
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Conflicts of interest

There are no conflicts of interest.

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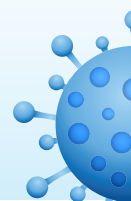


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30	A case of mixed anxiety depression in the COVID-19 Lockdown, Dr KishorM, Dr Hrishikesh, Digital Journal of Clinical Medicine, 22582-3868	Goal 3: Good health and wellbeing
31	Psychosocial effect of covid 19 lockdown – suicidal cutthroat injury a case report, Dr.Sandeep S Dr.ShilpaCDr.NitishAgrawal, International Journal of Otorhinolaryngology and Head and neck surgery	Goal 3: Good health and wellbeing
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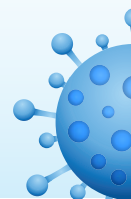
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A Case Of Alcohol Induced Psychotic Disorder with Depression presenting during COVID19 lockdown- Published in Digital Journal of Clinical Medicine (ISSN:2582-3868) www.djcm.jssuni.edu.in

July 2020

 Kishor Manohar Rao · Sopan Sardesai

Overview

Stats

Comments

Citations

References

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Abstract

A 35 year old male agriculturist residing in rural area, married and has family with two children, living in a extended nuclear family presented to the emergency in the night with complaints of shaking of hands and body, and hearing voices since 1 day, fatigue since 4 days consumption of alcohol since 8 days, sadness for the last 10-12 weeks. The patient and the spouse reported that he has incurred a loss of approximately Rs 100,000 (INR) as he was not able to sell his harvest due to the COVID19 lockdown which had increased his prior financial burden. The patient already had a loan of Rs 4,00,000 (INR). The patient reported that he will have to take loan again to buy seeds and materials for the new harvest. He reported feeling helpless and worried with loss of interest in various day to day activities. He also reported that he takes alcohol periodically once in 2-3 months but drinks for a few days continuously, from morning till night and then remains abstinent for many weeks. He was abstinent during the entire lockdown but on the day of resumption of alcohol sale on 4th May 2020, patient started alcohol and drank in a binge pattern (560 ml -720 ml, from morning till night) neglecting all other activities. He was able to buy alcohol on credit and binge. The patient reported that he got into a verbal altercation with his relative on a trivial issue which made him consume alcohol citing sadness and frustration as the reason. A day before admission he started to hear many voices of people related to the altercation even though there was no one around him. The patient had two previous episodes of binge drinking in the past few years which were also accompanied by similar depressive episodes. He also had history of one suicide attempt two months back during one of his binge drinking episodes. He did not have any history suggestive of mania or hypomania. The patient had a family history of alcohol dependence syndrome in his father and his elder brother. The elder brother had committed suicide.



A Case of Mixed Anxiety Depression in the COVID-19 Lockdown- Published in Digital Journal of Clinical Medicine (ISSN:2582-3868) www.djcm.jssuni.edu.in

May 2020

 Kishor Manohar Rao ·  Hrishikesh Solunke

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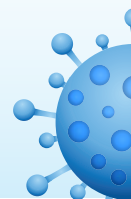
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Abstract

A 43 year old male patient from rural area, educated up to Pre-university, electronic technician by profession, married and living with his wife and two children, reported to the psychiatry outpatient department complaints of tiredness for 3-4 weeks, feeling worried, fearful about having a corona infection even without any contact or symptoms. The patient expressed that he would feel like sanitizing his hands often since the news of corona virus emerged. He also reported that watching the news would increase thoughts with sweating, shiver and racing heartbeat. These episodes would last for five to ten minutes and would occur once or twice a day. The patient had visited a local ayurvedic practitioner twice to get investigated and treated as acidity for these complaints but symptoms did not reduce. The patient complained of feeling sad, off and on due to this, along with a decreased interest, loss of libido and could not carry day to day activities. He also complained of disturbed sleep, with a delay in initiation of sleep by more than an hour and decreased appetite. There was no significant past history, and no history of psychiatric illness in the family.



Case Report

Psychosocial effect of COVID-19 lockdown suicidal cut throat injury: a case report

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ABSTRACT

The novel coronavirus pandemic of 2020 presents vast challenges to the population particularly to vulnerable ones such as those with addictive disorders amid lockdown with no access to alcohol and difficult to reach overburdened healthcare. We present such a case of a 45 years old alcohol dependent in withdrawal with self-inflicted cut throat injury.

Keywords: COVID-19, Delirium tremens, Laryngotracheal trauma

INTRODUCTION

The COVID-19 pandemic and measures required to address it are taking a toll on those with addictive disorders. Various factors such as poverty, physical and mental health vulnerabilities and disruption of services due to restrictions placed on alcohol sales are having major psychological impacts leading to social isolation, increased domestic tensions and serious symptoms of alcohol withdrawal among the dependant population. These include seizures, delirium tremens, hallucinosis and self-harm.¹ Here we describe one such case of delirium tremens with self-inflicted laryngeal trauma.

CASE REPORT

A 45 years old male, known case of alcohol dependence since, 8 years and history of no consumption for the past 6 days amid COVID-19 lockdown was brought to the emergency department of our hospital with history of self-inflicted neck trauma using a sharp weapon. The patient was unconscious on arrival with a fall in oxygen saturation, pulse rate of 110bpm and blood pressure

recording of 110/90 mmHg. Peripheries were warm and bilateral air entry was reduced on chest auscultation. There was a cut laceration in the anterior aspect of neck of 8 cm × 4 cm exposing the laryngeal cartilages. Epiglottis was partially cut causing the floppy segment to obstruct the airway and air leak was also present (Figure 1). Urgent airway management in the form of orotracheal intubation under vision using video-laryngoscopy was done and patient was put on 100% supplementary oxygen support. Pressure dressing to control bleeding was put. Intravenous lines secured and fluids were started. Head end elevation done and patient was prepared for neck exploration and repair. Neck exploration was done under local anaesthesia, large mucosal laceration with exposed thyroid cartilage was noted consistent with Schaefer type III laryngeal injury. No thyroid cartilage fracture was present and anatomy was maintained. Displaced segment of epiglottis blocking the airway was repositioned and sutured to the surrounding soft tissue (Figure 2). No major blood vessels were injured. A Tracheostomy was done at the level of 2nd to 3rd tracheal ring. Continuity of laryngeal framework was checked with intra-op direct laryngoscopy using Kleinsasser operating laryngoscope.



Neck was closed in layers using vicryl suture material. Post operatively patient was kept under ICU care and adjunctive therapy started with intravenous antibiotics, piperacillin and tazobactam 4.5 gm BD and metrogyl 500 mg TID. IV steroids and anti-reflux medications were also started. Inj. thiamine was started owing to history of dependence. Head end elevation was done and neck extension was avoided. Chest X-ray was essentially normal with no evidence of pneumothorax/pneumomediastinum. Patient regained consciousness but was restless and irritable. Psychiatry opinion was taken and a diagnosis of delirium tremens was established. Patient was started on risperidone and oxazepam. Nasogastric tube was inserted post operatively and patient was kept Nil orally for 2 days following surgery and feeds were gradually started. Patient improved eventually and repeat laryngoscopy done on 10th day was normal.

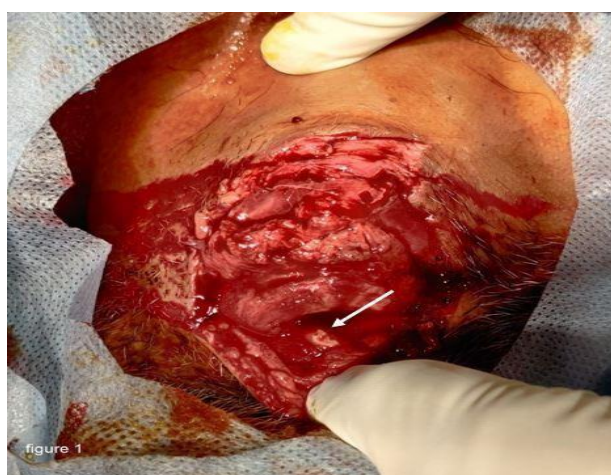


Figure 1: Intra-operative image showing the wound with mucosal laceration, exposed cartilage and cut and displaced part of the epiglottis (white arrow).

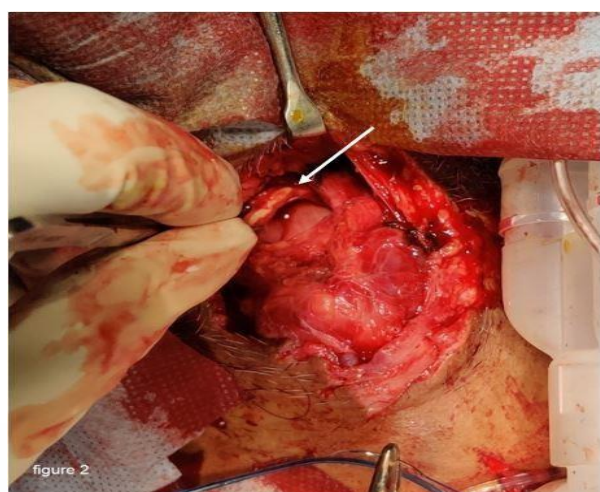


Figure 2: Intra-operative image showing repositioned epiglottis (white arrow) and tracheostomy tube in situ.

DISCUSSION

Laryngotracheal trauma accounts for less than 1% of all cases seen at major trauma centres.² Various modes of laryngeal injuries include blunt trauma, penetrating trauma (gunshot and stab) and blast injuries. Our patient had a suicidal penetrating trauma with a knife. Various classifications have been put forth to classify neck injuries. One such classification was given by Roon and Christensen who divided the neck into three zones localising the site of trauma.³ These were zone I: sternal notch to cricoid cartilage, zone II: cricoid cartilage to angle of mandible and zone III: mandible to base of skull.

Schaefer proposed to classify the patients into four groups on clinical, endoscopic and radiographic bases.² Group I patients have minor endo-laryngeal hematomas/tears, without fractures. Group II have oedema, lacerations and disruption of the laryngeal mucosa without exposure of the cartilage, nondisplaced fractures. Group III have severe oedema and mucosal disruption, displaced fractures, cord immobility and airway compromise. Group IV have two or more fractures or anterior commissure trauma and Group V have complete laryngotracheal separation. Our patient according to above mentioned classification was in zone II and Schaefer type III due to mucosal disruption, exposed cartilage and displaced epiglottis with airway compromise (Figure 1). Most common presenting symptoms seen in conscious patients are midline neck pain, hemoptysis, odynophagia, dyspnoea.⁴ Our patient however was in an unconscious state with falling saturation on arrival. Management is mainly conservative with injuries that are Schaefer grade II or less with serial flexible fiberoptic laryngoscopy (group I), direct laryngoscopy and esophagoscopy (group II) to carefully evaluate the airway.^{2,4,5} CECT is almost a rule to completely evaluate the patient however it could not be done in our patient pertaining to airway compromise. For higher-grade injury (III, IV and V) early surgical intervention is the key to success but first step in management of neck trauma is to secure an adequate airway. Airway management with laryngotracheal injury is controversial. Some prefer orotracheal intubation provided it is performed by a well-trained physician, under direct visualization.⁶ This was done for our patient by an emergency physician under direct vision using a video laryngoscope. On the contrary, some authors also advocate immediate tracheostomy as the preferred airway, believing that intubation may worsen mucosal and cartilage injuries.^{2,7} Tracheostomy was performed along with neck repair under LA for our patient. Epiglottis was reduced to its normal position and sutured with surrounding soft tissues (Figure 2). Patient was kept under ICU care for 4 days with a total hospital stay of 15 days which is similar to a study by Jalisi et al where mean duration was 12.3 days.⁴ Adjunctive measures were started such as antibiotics and steroids, exact role for which is unclear and anti-reflux medications to limit potential for laryngeal inflammation.⁸ Complete



psychiatric evaluation was done and delirium tremens was established. Oral oxazepam, a benzodiazepine and risperidone, an atypical antipsychotic were started both of which have proven effects in alcohol withdrawal symptoms.⁹ COVID-19 lockdown has had profound effects on the epidemiology of addictive disorders and treatment gap as non-emergency services have been shut down with almost twice the number of usual cases presenting to emergency department.¹ Most of these patients are now unemployed, malnourished commonly presenting with alcohol withdrawal seizures, delirium tremens and withdrawal hallucinosis and not in a state to provide travel or contact history. Given this, it is unlikely that such patients can adhere to social distancing and cough etiquettes and thus are at a higher risk of contracting COVID-19. They are also likely to have severe form of illness due to immunosuppressed state and other comorbidities. Learning from this case we must move towards finding a solution for this neglected issue through a multidisciplinary approach.

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Review article

'The dual pandemic' of suicide and COVID-19: A biopsychosocial narrative of risks and prevention

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ABSTRACT

The Coronavirus disease 2019 (COVID-19) has emerged as a new global health threat. By increasing the risk of isolation, fear, stigma, abuse and economic fallout, COVID-19 has led to increase in risk of psychiatric disorders, chronic trauma and stress, which eventually increase suicidality and suicidal behavior. There is limited data on association of pandemics and suicides. Cases of suicides have been rising since COVID-19 first emerged in China. The association between suicides and pandemics can possibly be explained through various models like Durkheim's theory, Joiner's interpersonal theory, social stress theory, biological theories, etc. The frontline workers, elderly, migrants, homeless, socio-economically impoverished classes as well as those with pre-existing mental disorders, substance abuse and family history of suicides are at higher risk. Suicides are preventable and need early detection, awareness and socio-culturally tailored interventions. This narrative review draws global perspectives on the association of suicidality and pandemics, the theories and risk factors related to same based on the available evidence. It also hypothesizes neuroimmunity and immune based risk factors as possible links between the psychosocial vulnerabilities and suicide during outbreaks like COVID-19. Proposed strategies of suicide-prevention, as an integral part of public health response to the pandemic are subsequently discussed.

1. Introduction

The last few months have marked an unprecedented impact on the global landscape, courtesy the Coronavirus disease 2019 (COVID-19) pandemic. Originating at Wuhan, China towards the end of last year, the infection took less than two months to evolve into a public health threat, with all nations facing unique challenges (Singhal, 2020). The effect is much beyond just medical concerns. Such large-scale outbreaks might bring about immense psychosocial and economic implications, that long outlast the infection itself. Travel has been restricted, international and national borders have been sealed, economies slashed, and jobs lost, billions isolated at their own homes in order to contain the spread of infection. Social interaction and structured schedules, the two main pillars of human civilization have been distorted leading to major psychological effects. In the absence of an effective biological cure or vaccine against the virus, social distancing and hygiene remain the main strategies to counteract it. This has made various countries enforce lockdown, thus disrupting social structures. The increased incidence of psychosocial problems, exacerbation of pre-existing psychiatric

disorders and fear of infection, uncertainty, isolation, unemployment, stress and mass panic have all contributed to one of the most concerning cause of mortality: suicides (World Health Organization, 2020). The risk factors of suicidality converge along with the impact of the pandemic, to create a dual vulnerability. Suicide prevention as an integral part of mental health interventions has been prioritized by the United Nations (U.N.). Pandemics like COVID-19 will not inevitably lead to increase in suicides, but the myriad of socio-economic and psychological factors might lead to a sustained and chronic increase in risk. As the ripple effect of suicide might be related to the increasing spread of COVID-19 and subsequent effect on human lives, this article reviews the rising problem statement, highlights the possible contributing factors and discusses the strategies for suicide prevention during the present pandemic crisis.

2. COVID-19 and suicide: the problem statement

COVID-19, caused by the novel coronavirus SARS-CoV-2, has affected more than 49 million globally and 12,40,000 have succumbed to the infection (Worldometer, as on November 7th, 2020). The case

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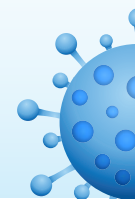
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fatality rate is however much lower than its earlier congeners (Severe Acute Respiratory Syndrome, SARS and Middle East Respiratory Syndrome MERS). What makes the infection so contagious and thus so unpredictable is the high human-human transmission and the prolonged viability on various inanimate surfaces (Singhal, 2020). This contributes to the panic and uncertainty related to the virus. Studies in China show the significant impact of the outbreak on mental health, with increase in health anxiety, acute stress reactions, adjustment disorders, depression, panic attacks and insomnia. Cases of severe mental disorders, obsessive compulsive disorder and anxiety disorders are suffering from relapses and increased hospitalization rates (Yao et al., 2020). Both these groups have a high suicide risk. The contributing factors are discussed later. Pandemics and suicides have some association though systematic literature is limited. Most studies have discussed suicidal risk following acute traumatic events like natural calamities. The pandemic being a chronic phenomenon with uncertain and sustained biopsychosocial effects for months to come is different from them, and thus that research cannot be translated to relevance for the current crisis (Devitt, 2020). Suicide rates had increased during the classic 'pestilences' of the bubonic plague

(Benedictow and Benedictow, 2004). During the Spanish Flu of 1918-19, the United States reported increased deaths due to suicide (Wasserman, 1992). Fatality due to suicides increased in the elderly, women and lower socio-economic class during the SARS outbreak in China (Cheung et al., 2008). The Ebola infection increased self-harm and suicidality in Africa (Bitanhirwe, 2016). Fear, financial crisis and stigma were attributed as the main factors. Vulnerable groups like the frontline workers, elderly, homeless, migrants and daily wage workers have their own unique challenges and thus are at increased risk. A review by Torales et al. (2020) reported increased self-harm thoughts in the medical staff attending to COVID-19 centers. Similar reports have been found in people who have tested COVID-19 positive (Reger et al., 2020). Though the death rate is low, the fear of the outcome and stigma attached to it, often make people distressed, thus leading to impulsive decisions. A recent systematic review studying the impact of COVID-19 on psychosocial wellbeing in the South-Asian countries highlighted the increased sleep disturbances, generalized anxiety, substance use, depression and self-harm behavior among the frontline physicians (Banerjee et al., 2020). In the same paper, the Indian Psychiatric Society (IPS) has mentioned in its advocacy statement about the need for multi-disciplinary action to preserve mental health during the ongoing crisis; suicide prevention, management and research being an integral and important component of the same. It is also important to understand that the pandemic has affected various nations, ethnicities and groups disproportionately and hence the risk and research related to suicides need to be sensitive to these socio-cultural differences (O'Connor et al., 2020). Suicide and suicidal behavior have been conceptualized through various theories. Table 1 summarizes certain such propositions which might explain the propensity for suicidality during pandemics such as COVID-19. The authors would like to highlight that these theories are not listed as causative implications but as constructs which help to theorize the possible increased risk for suicides during large-scale infectious disease outbreaks.

In a given year, roughly 12 per 1,00,000 people die by suicide. For every death due to suicide, there are 15-20 reported suicide attempts. Suicide remains among the top ten causes of death globally (Ferrari et al., 2010). Rates are usually higher in men, in those with psychiatric disorders and past attempts, substance abuse and in developing countries (Vigo et al., 2016). The global burden is increasing, and the World Health Organization (WHO) has called upon for a global action to prevent suicides (Fleischmann and De Leo, 2014). On this background, the COVID-19 crisis is surely a 'double-hit' increasing the susceptibility. The pandemic is still spreading its global clutches and systematic studies of suicides are yet to come. However, suicidal deaths have been reported from China, India, Bangladesh, Italy and United States (Mamun and Griffiths, 2020; Thakur and Jain, 2020). Montemurro (2020) reports an increased suicidality to be common offshoot in both the general

Table 1

Possible propositions of increased suicidal risk during pandemics based on the theories of suicide.

Theory	Proposition	Factors in Pandemics
Durkheim Egoistic - Anomic	2- Insufficient integration within a specific group 2- Lack of social regulation, unexpected amount of stress and frustration	2- Social distancing, quarantine, confinement 2- Extreme financial loss due to unemployment, situational change, loss of loved ones, disruption of societal and living structure by the pandemic and lockdown
- Fatalistic	2- Extreme social regulations and expectations	2- The new social norms of distancing, restricted travel and lockdown, lack of social rituals, using suicide as 'means of escape' from the threatening pandemic situation
2- Altruistic (Taylor, 1982)	2- High and enmeshed social involvement	2- Self-sacrifice (due to infection/fear of infection) for the benefit of loved ones, families, etc.
Joiner's Interpersonal theory (Joiner et al., 2009)	Experience of simultaneous thwarted belongingness (lack of reciprocation) and perceived burdensomeness. Acquired capability	Hopelessness about future Change in social reciprocation Existential issues (more in elderly)
Social stress theory (Rubenstein, 1986)	Perceived deficiency in social integration	Loneliness Individualism, perceived competition for survival
Klonsky and May (2015) 'Three-step theory'	Ideation (hopelessness and mental 'pain') to action (situational factors leading to suicidal behavior)	Distress and panic due to the infection to lockdown, unemployment and uncertainty (situational factors)
Biological theories (Decatanzaro, 1980)	Social exclusion triggers HPA axis and inflammation	Inflammation has mutual relationships with COVID-19 pathogenesis, mental disorders and immunity

population and medical staff. Yao et al (2020) while reporting a cluster of 50 COVID-19 inpatients in a psychiatric hospital mentioned mental health disorders and infection as 'dual-vulnerability' to suicides. The attributing factors are stated to be increased stigma, lack of medical protective equipment and inadequate access to health care. The medical staff were interviewed in the Second Xiangya Hospital, one of the main COVID-19 centers of Wuhan and self-harm thoughts were related to loneliness, guilt, isolation, burnout and lack of sleep (Chen et al., 2020). Nation-wide surveys have detected high prevalence of depression and anxiety in China and Italy related to COVID-19 which can serve as independent risk factors for suicide (Barari et al., 2020; Qiu et al., 2020). However, the exact number of suicidal deaths are largely unknown. Anecdotal news reports from certain countries have also reported decrease in suicides during the lockdown period. Such data is yet to be scientifically corroborated (Deutsche Welle, 2020; The Guardian, 2020). Under-reporting and medico-legal issues play a role in these cases. The suicide rates in the South-East Asian countries are already high and increasing currently due to fear, misdiagnosis, social perceptions, misinformation and xenophobia (Montemurro, 2020). Added to that is the burden of homelessness and migration, which share neglect and social apathy. Multiple theoretical models have associated increase in suicides with predicted rise in unemployment and financial crisis (Kawohi and Nordt, 2020; Moser et al., 2020). These authors have mentioned a 1% global increase in suicides and used prison incarceration as a proxy measure for the effects of social distancing during the pandemic. Google Trends search patterns have also been used to estimate suicide risk (Knipe et al., 2020), though such methods have been



earlier criticized due to the inherent instability and inconsistencies (Tran et al., 2017). The International COVID-19 Suicide Prevention Research Collaboration (ICSPRC) has called for a global representation for risk-assessment, preventive and management responses for suicide. The collaborative network emphasizes on ethical yet systematic research during the early phases of the pandemic, highlighting the need of sharing high-quality suicide research data, designing appropriate assessment tools and platforms, and harmonizing data collection approaches from various settings (International Association for Suicide Prevention, 2020). Niederkrötenhaler et al. (2020) in their recent paper "Suicide Research, Prevention, and COVID-19" stressed on an international response towards suicide prevention and collaborative research during the ongoing pandemic. They mentioned about the urgent need for unbiased and authenticated data from multiple sources to estimate population-based risks and possible pathways of suicide-prevention strategies.

3. Suicide in pandemics

The possible contributing risk factors for suicide during pandemics are summarized in Table 2. Some of these have been already studied, while the others need to be explored with the progression of COVID-19.

Table 2
Proposed risk factors and contributors for suicide during pandemics.

Risk factors for suicide	Contributors
Loneliness, isolation and boredom	Social (along with physical) distancing Travel restriction Lack of access to technology Quarantine and confinement
Fear and uncertainty	Unknown nature of the infection/lack of biological cure Misinformation / 'information pollution' Irresponsible media reporting Competition for health care
Marginalization	Social stigma Prejudice Blame and xenophobia Communal sentiments
Psychological disorders	Health anxiety Depression Grief/bereavement Acute stress, paranoia Post-traumatic stress disorder Substance abuse
Relapse of psychiatric disorders	Limited access to healthcare Lack of medications and supervision (non-compliance) Lack of awareness Stress diathesis directly related to the pandemic
Economic fallout	Recession/financial crisis Employment and salary loss Collapse of small-scale industries Guilt Daily-wage workers Uncertainty of future
Domestic abuse and Intimate partner violence	Increased contact time between partners (entrapment with abusive partners) Substance abuse Sexism and prejudice against the opposite gender Responsibility for children
Increased access	Pesticides, medicines and firearms Lack of administrative vigilance
Special vulnerabilities	Adolescent, Elderly (more prone to isolation, loneliness, depression and increased baseline suicidal risk) Frontline health workers (health workers, police, essential service providers, volunteers, delivery personnel, etc.) Migrants and homeless Poverty and lower socio-economic status

4. Populations at increased risk

4.1. Frontline workers

A significant amount of research has been ongoing in the mental health care of frontline health workers. They are being the backbone of a country's battle against COVID-19 are equally susceptible to its physical and psychosocial risks. Apart from staying in constant fear about the threat of infection, they are guilty about transmitting it to their loved ones. The increased work pressure, witnessing the morbidity, chronic stress and need for self-isolation can contribute to depression, absenteeism, burnout, frustration and eventually suicidality. Studies of psychological wellbeing among medical staff have showed increased hopelessness, decreased self-esteem, guilt and self-blame, and insomnia, all of which can be risk factors for suicide (Chen et al., 2020). Lack of adequate personal protective equipment, lack of flexibility in shifts due to decreased health care resources and inadequate insurance facilities can be additional burden in developing countries (Heymann and Shindo, 2020). Moreover, stigma and discrimination have been prevalent against frontline workers with threats of eviction from their residences, difficulties in cremation and shrinkage of social circle, as they are at increased risk of exposure (Logie and Turan, 2020). This further leads to isolation and social disconnectedness.

4.2. Elderly

Age and ageism are also special concerns at times of COVID-19. Apart from being the single most important risk factor for severity and mortality in the infection, age also predisposes an individual to the psychosocial adversities. Quarantine and isolation can cause profound loneliness, depression and suicidality in the elderly (Armitage and Nellums, 2020). Frailty, cognitive and sensory impairment further contribute to the risk while neglect, abuse, overcrowding and noncompliance to precautionary measures are added troubles in those institutionalized. Autonomy, self-dignity and mobility, the important indicators of their wellbeing can be compromised during such pandemics, when they are not involved in the decision making (Banerjee, 2020). Many of them are stranded alone, with inadequacies of domestic help and basic living amenities due to the lockdown, which makes them

isolated and increases self-neglect. Suicidality is often under-reported and more in the seniors and late-life depression can be polymorphic, which leads to higher number of suicidal deaths in older adults (Lindesay, 1991). Existential issues might arise, when 'suicide' is considered to shorten the misconstrued fear of infection and over-estimated threat of mortality during the pandemic.

4.3. Homeless and migrants

The world shelters around 1.5 billion homeless, most of them being in the South Asian and African countries (Ortiz-Ospina and Roser, 2017). Besides having physical risks of infection, the principles of 'social distancing' are but ironical in their overcrowded and impoverished shelters. Administrative unaccountability and societal apathy lead to poor testing rates and improper awareness in them. Mental disorders and substance abuse are common accompaniments, which together with the perceived vulnerability of the infection increases the risk of suicides. Post lockdown, especially in countries like India, thousands of migrants have been stranded on the streets and stations with no food or money for survival. They often welcome death, suffering from hunger and unable to survive far from homes, when living conditions are a greater threat than the virus itself (Banerjee and Bhattacharya, 2020).

4.4. Victims of abuse and violence

Entrapment of various families during the COVID-19 induced lockdown has led to unprecedented circumstances, when couples cohabit



together for extended periods like never before. In families with pre-existing marital discord, interpersonal violence and substance abuse, the problems have exacerbated leading to marked increase in domestic abuse and intimate partner violence during the present times. The United Kingdom Domestic Abuse helpline has been registering an increase in number of complaints, some of whom have expressed death-wishes (World Health Organization, 2020). The national helplines that we are operating in a tertiary mental health care institute in India, receive consistent calls of domestic violence associated with suicidality as an easy escape. Normalization by families, sexism, objectification of women and aggression are known to increase during disasters. Under-reporting, fear of legal hassles, acceptance and underlying untreated depression can lead to suicides, which otherwise could have been prevented.

4.5. Stigmatized groups

Though data is sparse for adolescents, sexual and racial minorities, theoretical risk of depression and suicidality are high among them. Social disconnectedness, unhealthy use of technology, substance abuse and isolation can be high in adolescents as interaction and peer-support form important aspects of their identity. Virtual connections can never be a total replacement of human-human interactions and psychological distress post lockdown has been shown to be complex and chronic for young children and adolescents. Racial and sexual 'othering' are common in pandemics and have been sporadically reported during COVID-19. From terming the disease as 'Kung-flu' to discriminating against people of mongoloid origin, reports of suicide have been increasing in response to prejudice and xenophobia, with relation to the infection (Coates, 2020). Lack of abused substance, withdrawal symptoms and difficulties in health-care access have shown to increase the suicidal risk in addiction disorders.

4.6. Financial crisis

Lastly, COVID-19 has led to restrictive implementations that had significant impact on the global economy. The unemployment rate has risen sharply, and 2.5 million people have lost their jobs in the United States alone (Buera et al., 2020). The most developed economies have been struck hard, which can lead to a fair assumption as how other countries might fare. This effect is rippling and can have long-term consequences. Many small-scale industries especially those involved in travel, tourism, entertainment, etc. have closed down in the lockdown period, with uncertainty shadowing their futures. In a study on effect of unemployment on suicide based on global data of 63 countries, suicide risk was elevated by 20-30 percent during the 2000-2011 period. The peak was during the 2008 'Great Recession'. Data from this period showed that increase in suicides preceded the actual unemployment rate (Nordt et al., 2015). Considering that the International Labor Organization (ILO) predicted a loss of around 25 million jobs due to the COVID-19 pandemic period alone, the aftermath can have prolonged challenges (International Labour Organization, 2020). Based on a model proposed by Kawohl and Nordt (2020) to describe non-linear connection between unemployment and suicide, the worldwide unemployment rate might lead to an increase of suicides by around 6000-9570 per year. The downsized economy coupled with vulnerabilities in society, can lead to a surge in suicidal mortality for many more months to come. The preparedness of health-care facilities at all levels might be vital in its understanding and prevention.

5. Immunity, suicide and COVID19: a linking pathway?

The pneumonia caused by COVID-19 has already been well-known all over the world. The direct neuropsychiatric effects of the virus have been discussed in a recent systematic review (Rogers, 2020). The increased penetration of blood-brain barrier, delirium and acute

behavioral effects have been reported in the acute stage. Whereas the authors caution about the possibility of depression, anxiety, fatigue, post-traumatic stress and adjustment disorders in the long run, each of which can contribute to the suicidal risk. Besides, the clinical assessment of COVID-19 infections have indicated mild to severe cytokine storms in symptomatic patients and this has accounted for the death in many such patients. Consequently the focus had also been on the treatment of cytokine storm for treating severe cases. It was found that Interleukin-6 (IL-6) plays a significant role in cytokine release syndrome (CRS) and hypothesized that if the signal transduction pathway of IL-6 is blocked, it helps to develop a new method for the treatment of severe cases. Research has been looking at Tocilizumab, potential blocker of IL-6R, that might effectively block IL-6 signal transduction pathway and potentially help patients to treat with severe manifestations of COVID-19. Further it was reported that IL-6 levels were elevated in the cerebrospinal fluid of suicide attempters and related to symptom severity. This adds a possible new dimension in explaining suicidal symptoms in COVID 19 infected patients associated with IL-6 effects (Zhang et al., 2020). Hence with all the psychosocial and biological risk factors, stress and immune-mediated diathesis for COVID-19 can be hypothesized as a possible linking pathway for increase in suicidality during this pandemic (Fig. 1). Research correlating severity, neuroimmunity blood markers and suicidal risk will help understand the pathogenic effects of COVID-19 and associated comorbidity like suicidal behavior (Lindqvist et al., 2009).

There have been established relations between the immune system and suicides (Pandey et al., 2019). One such example is the abnormal change in Toll-like receptors (TLRs) having a significant role in the neuropathogenesis of depression and suicide. The TLRs interact with the pathogen-associated molecular patterns (PAMP), damage-associated molecular patterns (DAMP) and induce cytokines through the activation nuclear factor kappa beta (NF- κ B). Earlier studies showed that the protein and mRNA expression of TLR3 and TLR4 in the prefrontal cortex (PFC) of depressed suicidal (DS) subjects were increased when compared to normal control (NC) subjects. These findings provided a valuable insight that very specific TLRs were altered in DS, some of which might be targeted for suicidal treatment in translational psychiatry (Pandey et al., 2019). TLRs have already been studied in the pathogenesis of COVID-19 and extra-pulmonary manifestations, which might again provide a possible biological link for suicide risk.

The frequently asked question is how does SARS-CoV-2 alter the immune system? It is already known that CD4⁺ and CD8⁺ have significant antiviral properties. The CD4⁺ T cells favor the elevation of viral-specific antibodies through T cell-dependent B cells activation. But CD8⁺ T cells being cytotoxic kill virus infected cells. Actually, CD8⁺ T cells significantly increase in the pulmonary interstitium in SARS-CoV-2 infection killing coronaviruses in infected cells. Further, the cytokines like IL-17 are involved in the recruitment of monocytes and neutrophils to the infection site. Studies have clearly shown that T cell response relevance to S, M and N proteins is assumed to be persistent and this pathway may be a target for vaccines for SARS-CoV-2, which is currently under research. Also, it was found that the ACE2 protein fused with human immuno-globulin G Fc domain (ACE2-Fc) of SARS-CoV-2 patients may have involved in the traditional neutralizing antibody. Hence there is a need to focus on clinical trials to understand the benefits and side effects of ACE2-Fc treatment. These studies are crucial to understand the complex immune responses to COVID-19 and its effects on the central nervous system. The alterations of psychoneuroimmunity seen in brain and other organs tend to cause multiple other effects of COVID-19 which leads to the unanswered questions on immunity, brain and mental health issues in relevance to this infection (Vellingiri et al., 2020). These might directly or indirectly increase suicide risk, as inflammation and immunity dysregulation have been linked both to the neuropathogenesis of depression and suicides.



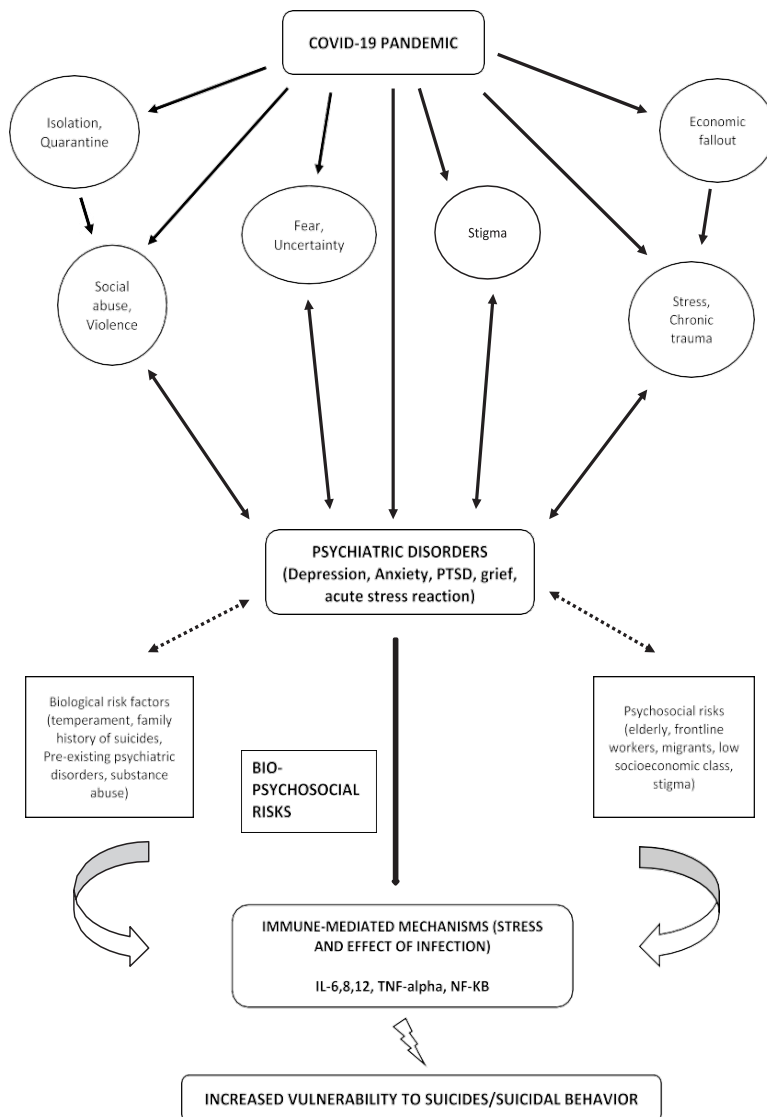


Fig. 1. Coronavirus disease 2019 (COVID-19) has led to various unique challenges (isolation, loneliness, stigma, fear, uncertainty, economic fallout, etc.), which together with biological risk factors (temperament, family history of suicide, pre-existing mental disorders and substance abuse) and psychosocial vulnerabilities (elderly, migration, homeless, low socioeconomic classes) increase the risk of primary psychiatric symptoms. This in turn combined with the interaction between stress and immunity related to infection can serve as a possible link (increase in inflammatory mediators like IL-6,8,12, Tumor Necrosis Factor-alpha, Toll-like Receptors, NF-KB, etc.) to increase suicidality and suicidal behavior.

6. Suicide prevention during COVID-19: special considerations

The basic premise of any management strategy is that suicide is preventable. A qualitative study of psychological autopsies based on interviews conducted with relatives of 66 suicide victims showed that more than half of them had availed some sort of professional help within past one month of the attempt (Owens et al., 2005). Those who did not were either 'help-resisters' or the families were not aware of the suicidal signs, that they acknowledged later on retrospect. The various guidelines like WHO, Centre for Disease Control and Prevention (CDC), The U. S. National Strategy for Suicide prevention, etc. mention certain generic principles. They include strengthening economic supports, enabling access and delivery of suicide care, creating protective environments, promoting connectedness, training public with coping and problem-solving skills, early identification of risk, gatekeeper training at community level and futuristic harm-prevention (Bernert et al., 2014). Besides, prompt treatment of psychiatric disorders, increasing mental health promotion and awareness as well as reducing social risks like poverty are other broader strategies for suicide prevention. While all of these measures are equally important and applicable even to the pandemic situation, certain specific risks during COVID-19 crisis might need special measures at different levels. Few such possible ways are

proposed in Table 3. In the absence of specific evidence on suicide risks during pandemic, these strategies are merely conceptualizations that can be used in interventions and research. Besides, administrative changes in the pandemic acts of countries might need to include suicide prevention programs, crisis management and mental health integration in public health infrastructure.

People in suicidal crisis, require enhanced attention and surveillance. Stigma, fear of being discriminated, legal hassles and avoidance of 'health-care setups' due to pandemic fear can be potent barriers to health care access. Early identification of the at-risk population, especially those who are quarantined, are suffering from mental disorders, are working on the frontline, are affected with COVID-19 or relatives of the affected, might be helpful. Online mental health services in China used risk detection, community training and weekly sessions to deal with suicidal individuals in isolation (Liu et al., 2020). Community-based programs in Iran, France and the United Kingdom have included training health-care providers dealing with COVID-19 cases in suicide prevention (Fiorillo and Gorwood, 2020; Zandifar and Badrfam, 2020). Banerjee and Nair (2020) have proposed a community-based toolkit for the current pandemic, modeled on the Zika outbreak, to detect mental health issues at grass-root levels and train multi-purpose health workers and ASHA workers in suicide risk

Table 3
Proposed suicide prevention strategies during pandemics.

Problem situation	Interventions
Mental disorders	Tele-psychiatry & tele-psychotherapy Active digital follow-up Online medication refill Ensure availability of psychotropics at district levels
Psychological distress due to pandemics	Psychoeducation of caregivers Encourage professional help Staying away from the social media Online counseling
Suicidal crisis (acute)	Clear assessment and intervention guidelines Online-based crisis interventions Digital resources for coping Flexible crisis helplines (24/7) Volunteer workforce for outreach Training of the local authorities for emergency response
Substance abuse	Safe drinking and monitoring messages
Domestic abuse	Integrate mental health helplines with women, child and elder services Hassle-free reporting Ensuring safe shelter
Isolation and quarantine	Digital connectedness Community support Ensure living amenities Weekly sessions for mental health support
Misinformation	Mental health education through social media: IEC activities Community awareness programs (street plays, infographics on print/digital media) Government messages and policies Tele-training of primary health care providers to debunk fake news Media-health sector collaboration Advocating authentic information sources (WHO, CDC)
Economic crisis	Financial packages by Government Ensure food, housing, and emergency funds for the unemployed and homeless Ensure safety, awareness and transportation to homes for migrants Long term labor sustenance policies
Vulnerable population	For frontline workers (mental health care sessions, peer support, flexible shifts, ensure safety in isolation, adequate rest, debriefing, medical protective equipment) For the elderly and those stranded alone (delivery of food, water, medicines and other essentials)

IEC Information, Education and Communication, WHO World Health Organization, CDC Center for Disease Prevention and Control

detection. Few ways that suicide prevention can be improvised on during pandemics are as follows:

- 1 Increase in mental health helplines, liaising with the COVID-19 information services and integration with the health centers/ambulance facilities for crisis interventions.
- 2 Tele-consultation (digital/call) for those facing psychological distress, active follow-up of registered patients from the various hospitals. Tele-conferences between primary and tertiary care centers for appropriate for mental health services. Digital privacy need to be ensured.
- 3 Gatekeeper training for community and primary care centers (Red flag warnings: excessive fear due to the pandemic [catastrophic thinking], death wishes, expressions of hopelessness, helplessness, panic attacks, grief, difficulty in coping for families of those affected, history of suicide, substance abuse, low social support, staying alone, low self-worth). Behavioral and verbal cue-based assessment of risk are useful.
- 4 Use of media for Information-Education-Communication (IEC) related to suicide prevention: making evidence-based online

sources and socio-culturally appropriate infographics in multiple languages.

- 5 Training the lay counselors in brief and solution focused interventions for crisis management. Digital training resources can be used.
- 6 Public health responses and detection of abuse and domestic violence: early sensitization and rapid response by the police/local authorities. Safe drinking messages can be propagated.
- 7 Sale restrictions on pesticides, medications and firearms, especially during the lockdown.
- 8 Community support for those living alone, in isolation, for the elderly, bereaved individuals. The lockdown can aid foster bonds and relationships.
- 9 Ensuring essential services (food, water, medication) delivery is hassle-free for the elderly, disabled and those quarantined.
- 10 Media and health services collaboration to debunk misinformation and bridge the knowledge-attitude-practice (KAP) gap related to COVID-19 and suicide. Suicide is a sensitive topic and the its portrayal in popular media can potentially influence reactions to it. Responsible reporting of suicide is necessary for mitigating stigma, falsification and prejudice towards this important aspect of mental health. Public health agencies like the WHO has clear guidelines for suicide-reporting by the media, especially in sensitive situations (WHO, 2017). Few facets of the same are highlighted in Table 4. These are however more commonly overlooked than implemented.

7. Conclusion: the way forward

Suicide itself is considered to be a pandemic. A large-scale outbreak like COVID-19 can easily overwhelm the available public health resources, needing more workforce on the ground. This review glances at various possible hypotheses linking pandemics, suicides and suicidal behavior and propositions to mitigate the risk, based on the limited evidence available. These conceptualizations are definitely not 'causal and definitive' and can be critiqued and debated. However, they might form the basis of epidemiological and interventional research for the

Table 4
Responsible reporting of suicides by media.

Preferred ways of reporting	Practices to be avoided
<ul style="list-style-type: none"> • Accuracy of information • Authentic sources of help-seeking • Facts & risks of suicide • Suicide-prevention methods • Vulnerable groups at risks for suicide • Expert opinions for qualified professionals / first person accounts of coping • Sensitive and humane interviewing of the bereaved • Peer debriefing and support among the media personnel to deal with trauma • Factual reporting of the suicide event 	<ul style="list-style-type: none"> • Personal assumptions, biases, 'tales' of suicide • Conspiracy theories • Detailed and repetitive reporting • Sensationalizing, fantasizing or normalizing suicides • Reporting self-harm as 'heroic' or 'constructive' • Generation of fear, stress and panic • Extensive debate and discussion with multiple professionals about the same incident: which generates confusion • Avoid using 'catchy' or sympathetic headlines/phrases • Coercive questioning of the bereaved on camera • Avoid visual content (photographs, videos, social media links, etc.) whenever possible • Excessive emphasis of personal life, contextual information
(especially celebrity suicide)	<ul style="list-style-type: none"> • Judgmental comments • Explicit details of methods used

Modified from World Health Organization (2017). Preventing suicide: A resource for media professionals, update.



current and futuristic crises. Both for the frontline workers and the general public, these are unprecedented times that no amount of preparedness can account for. As mentioned before, suicide prevention by early detection of risks is the main strategy. This is a collective responsibility irrespective of socio-economic status, occupation or class. It is but natural to be stressed during a pandemic, however the differentiation between the 'acceptable limits' of panic and 'over the edge' psychiatric symptoms that need professional help is vital. All sectors of society need awareness of the same. Suicide prevention responses need to be comprehensive and they need to be backed up by increased surveillance of COVID-19 specific risk factors (Gunnell et al., 2020). Data and systematic research on self-harm behaviors and suicidality can inform further protocols and policies.

As the epidemic is still in its early stages, both cross-sectional and longitudinal community-based studies might help estimate the population level risk, that can help preparedness for such futuristic crises. Rapid dissemination of data and adequate surveillance of national mortality, surveys and published literature will help researchers and policy makers alike. The suggested areas of exploration are the mental health consequences, economic offshoots, mortality burden and grief, the healthcare crisis response as well as workplace and educational effects of the pandemic (International Association for Suicide Prevention, 2020). As mentioned before, the ICSPRC is collaborating with the International Association for Suicide Prevention (IASP) and WHO to formulate a strategic and evidence-based intervention protocol for reducing suicidal deaths during COVID-19. The effectiveness and implementation of these strategies will depend on filling the gaps in understanding of suicides and suicidal behavior during this outbreak (Niederkrötenhaler et al., 2020). Lived experiences of the vulnerable population, mental health care providers and the patients affected with COVID-19 in the months that follow will help in risk estimation and resource allocation. At each level, these approaches need adequate funding and appropriate coordination. Every nation's public health infrastructure, socio-cultural milieu and demographic parameters are unique to deal with the suicide risk. However, it is expected that global collaboration through public health agencies like the WHO or CDC can shape further insights into suicide prevention during such pandemics (Thakur and Jain, 2020). Technology can be harnessed in these times of 'social distancing' for staying connected and also providing adequate mental healthcare. Resource-poor settings need more intense surveillance and care. Stigma and misinformation are important contributors to mental distress and need to be mitigated (World Health Organization, 2020). The world stands at a difficult juncture. Mental health implications of this ongoing pandemic might peak much beyond the infection, and suicide might add to the fatality burden. However, the resilience of humankind throughout history during any disaster has been remarkable. Positivism and hope, two salient markers of coping often arise out of collectivism, optimism and mutual support. Global strategies, collaborative research and collective responsibility might hopefully enhance the efforts against the 'dual pandemic' of COVID-19 and suicide.

CRedit authorship contribution statement

Debanjan Banerjee: Conceptualization, Visualization, Validation, Writing - original draft, Writing - review & editing. **Jagannatha Rao Kosagisharaf:** Conceptualization, Validation, Writing - original draft, Writing - review & editing. **T.S. Sathyanarayana Rao:** Conceptualization, Validation, Writing - review & editing.

Declaration of Competing Interest

None.

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Nil.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.psychres.2020.113577](https://doi.org/10.1016/j.psychres.2020.113577).

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“#Intimacy” at Times of COVID-19: The Renewed Impetus Behind Cybersex

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Sex is something you do. Sexuality is something you are.

—Anna Freud¹

In the words of the renowned psychoanalyst and the youngest child of Sigmund Freud, sexuality forms a vital aspect of one's "self" and social identity. Healthy manifestations of sexuality, safe sexual practices, and enjoying reproductive/sexual rights help in coping and psychological resilience. One of the best times to put it into perspective is the last year of the unprecedented Coronavirus disease 2019 (COVID-19) pandemic havoc, which is still plaguing the world. With the geopolitical, socioeconomic, and ecological landscapes undergoing rapid transformations due to the global pandemic, lives and living have been affected equally. It is understandable that on the background of a highly contagious infection that mandates face masks and social distancing, it is natural that the fear of infection, stress, reduced interactions, personal circumstances (like frontline work), travel restrictions, and financial setbacks have all contributed to deprivation of affective touch and physical intimacy.² Global misinformation and uncertainty during the ongoing pandemic have further affected sexuality and sexual relationships, which form an important aspect of psychosocial well-being.² Adopting the transition to "new normal" like other aspects of life, sexual practices too have increasingly borrowed the virtual platform. Cybersex, digital intimacy, use of pornography, and so on, have gained a renewed impetus during the COVID-19 pandemic, which may have continued implications in the post-pandemic aftermath as well.

virtual sex, sexting, and so on, which have been in vogue since the 1990s.⁴ In the absence of clear operational definitions, Smith mentions,⁵ "an internet-based affair or digital sexual practice involves chat sessions and sexually stimulating conversations or cybersex, which may include (among other things), filming mutual masturbation with a web camera.... With the internet, we are moving away from just physical ideas about infidelity and acknowledging emotional infidelity." Like any other relationship, this also has an emotional and a sexual (virtual) component. Though cybersex involves sexual practices exclusively involving the Internet/cyberspace, for the subsequent discussion certain aspects of digital sex (online sexting, nudes, etc) and pornography will also be included.

Traditionally, it has been difficult to systematically collect data related to cybersex, due to its personal and secretive nature. Research from Sweden and Australia report that 10% to 30% of younger participants engaged in intimate online relationships and online affairs.⁴ More than one-third of people preferred cybersex compared to abstinence or masturbation alone in long-distance relationships. Expression of virtual sexuality grants anonymity enabling one to explore and experiment various sexual identities and fantasies, without being impaired by environmental and situational constraints. These fantasies may be concealed in real life due to various beliefs and social stigma, which are brought to light within cyberspace that offers limitless possibilities to change identities (such as gender, race, or even different species). Jiang⁶ highlights that an "important element of

Dimensions of Cybersex

The widespread availability of the Internet and broadened arena of cyberspace has provided the scope for digital intimacy. Though there is considerable heterogeneity in the definitions of "cybersex" and individual variability, it has been consistently defined as an interactive activity.³ Digitally mediated sexual interactions through the use of technology can be in the form of cybersex, electronic sex, chat/cam sex,

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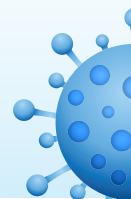
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cybersex eroticism” is that people can try various vicarious sexual experiences, that they may not have tried in their real life. This element of “surprise” on the other end adds to the excitement and risk-taking in certain participants. In short, cybersex allows a “private, safe, and anonymous” environment to explore sexuality.

Digitalization of Intimacy During the Pandemic

Compared to the traditional sexual practices in some societies, making love and expressing desire digitally can be considered unconventional and revolutionary in certain cultures. Expression of sexuality has been historically linked with infectious disease outbreaks, from the time of the Spanish Flu to modern day acquired immunodeficiency syndrome (AIDS).⁷ Manifestation of “free love” was restricted by AIDS, while “digitalization of love” is being propagated by COVID-19. What constitutes normal sexuality is a highly debatable construct! Considering that sexual practices are heavily influenced by traditions, myths, beliefs, social stereotypes, cultural connotations, and ethnic variations, its polymorphic nature and adaptation to “novel” circumstances are expected. Expressing love via the virtual platforms has even been termed as “sexual renaissance of the Gen Z” at times of the pandemic.⁸ The quarantine, lockdown, and travel restrictions have further bolstered sexual experimentation, be it sharing nudes, thirst traps of Instagram, mutual masturbation and recording the same (Zoom, Skype, Google Meet, etc), sexting, digitally sharing pornography, and so on. As opposed to the popular conception that a video-screen barrier is always isolating, research in psychosexual health needs to understand if contactless sex can be safely “actualized” through technology to eliminate the void of social distancing. There remains, however, a plethora of social, legal, ethical, and moral dilemmas that need further debate and discourse.

It has been seen that deprivation of sexual pleasure is associated with infection-related anxiety, grief, loneliness, substance abuse, domestic violence, loneliness, and poor coping in stressful situations, though a causal attribution could not be established.^{7,9} Lehmiller et al¹⁰ highlighted “redefining” of recreational sex during the COVID-19 pandemic. The authors reported an online survey of 1,559 adults among which more than 50% revealed a decline in their relationship intimacy while 20% expanded their sexual interest by trying new fantasies, modes of foreplay, sexual positions, sexting, and digital sex. Those who attempted these novel additions were thrice more likely to have improvements in their sex lives. Further, in a large study involving 3,593 participants from 57 countries, perceived partner responsiveness even virtually helped improve poor relationship quality associated with the pandemic-related stressors over a period of 3 months.¹¹ To glance at a cross-cultural perspective, a cross-sectional online study involving

3 South-Asian countries (India, Bangladesh, and Nepal) showed that 45% of the participants felt that their sexuality (types and frequency of sexual practices) was affected by COVID-19 while more than half of them reported having positive changes in emotional bonding during the lockdown as a consequence of “innovative sexuality,” even when the partners were away.¹² Though preliminary evidence points toward the fact that contactless manifestations of sexuality, not a substitute of physical intimacy, can be one of the better options during a long-distance relationship compared to complete abstinence.

We need to consider here that cybersex is not just about partnered sexuality. Besides, more telephonic and online sexual interactions between couples, even solo sex has been benefited by digital platforms. Masturbation, an ever debated and stigmatized topic, has been “celebrated” by social media platforms in a new vigor. Prescriptive as well as descriptive narratives of masturbatory practices have been reported during the pandemic.¹³ Die Bild¹⁴ mentions the compensatory ability of masturbation using digital erotica in the absence of partnered sex and recommends it to help stress and anxiety, though evidence for the positive outcomes of masturbation is superficial.¹⁵ The New York City Health Department¹⁶ even mentions it as a guideline, “You are your safest sex partner. Masturbation will not spread COVID-19, especially if you wash your hands (and sex toys) with soap and water for at least 20s before and after sex.” Banerjee and Rao⁷ provide a more detailed advocacy review on the safe sexual recommendations during the pandemic. Parallel to self-stimulatory practices, the use of pornography has literally exploded during the outbreak and especially the global lockdown. In order to cater to and capitalize on this soaring demand, one of the leading providers of online pornography Pornhub.com granted free premium access globally till April 23, 2020.¹⁷ In a verbal pact of free registration and premium pornography access on Pornhub in return of adequate social distancing, this platform changed its name to “StayHomeHub” on a lighter note. In fact, an entirely new genre of pornography termed as “Coronavirus porn” emerged during the pandemic, which centered around the outbreak-stricken areas with protagonists in the video wearing masks, medical protective devices, gloves, and so on.¹⁷ Themes of pornographic videos often reflect the ongoing global events, and in that sense this “Coronavirus porn” does not really appear as a bizarre form of fetishism. Lehmiller et al¹⁰ has linked these apparently strange fantasies with eroticization of the threat as a coping mechanism, fear defense, curiosity about the “bizarre” to combat uncertainty, desire to cross-geopolitical borders to fight social distancing, and instill hopes of recovery. Both media statistics and that from Pornhub.com reflected enhanced interest in this form of pornographic content since March 2020.¹⁷ Further research is warranted to understand the usage patterns and likely social effects of Coronavirus porn consumption. The pandemic has led to significant bottle-necking of prostitution and “body-related services” due to the risks of physical proximity



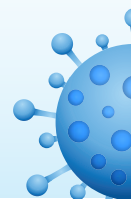
and infection, that has led to marked rise in poverty, social inequality, and homelessness.¹³ Furthermore, the “anti-prostitution” movements have gained boost during this pandemic, so much so that the SARS-CoV-2 virus has been termed the “Abolitionist virus” as it prevents people from spending time for sex.¹⁸ Public health groups and various nongovernmental organizations have actively vouched for the human rights of commercial sex workers (CSW) and their rehabilitation during the ongoing crisis, which has led to emergency funds, promoting psychosexual healthcare, and shifting of some CSW to the digital platform, further boosting pornography and facilitating cybersex.¹⁹ Over time, as the pandemic has spread its clutches, most porn studios have closed down too leading to widespread unemployment in the porn industry and erotic material being changed to phone sex, online sex, and solo sex recordings.¹⁰ Paraphilias have also been on the rise.

Cons in the Path

Understandably, cybersex and digital intimacy have various dimensions. It encourages casual sexual encounters and exploration without risking unplanned pregnancies and abortions. In fact, research during the pandemic showed that virtual sexuality has helped to counteract the coronavirus baby-boom (due to relationship sex) to some extent. There is evidence from the U.S. and China to show that a significant number of people had reduced sexual partners and sexual frequency in order to reduce the risks of infections during COVID-19.^{20,21} In such circumstances, sexual relationships over virtual media help to reduce frustration, loneliness, and stress, while at the same time nourishing emotional bonding in distanced relationships. Online sex, once considered to be tabooed and deviant form of sexuality, has now been recommended as a preventive measure in public health. To quote the International Society for the Study of Women’s Sexual Health (ISSWSH), “The new ‘really safe’ sex in many cases may require ‘e-sex’.”²² As mentioned before, cybersex also contains an appreciable amount of uncertainty and surprise, which adds to the eroticism. It allows anonymity and free experimentation of sexual fantasies. Queer sex parties, online fetish concerts, and LGBTQ+ related PRIDE festivals have been organized over social media.² However, it has aptly been considered as a “double-edged sword.”⁷ Besides the cultural barriers in acceptance, technological mindedness and technical feasibility, as well as network access issues in rural areas, sex within cyberspace can never really replace social or affiliative touch. A virtual void cannot, perhaps, completely compensate for a tight hug, a warm embrace, an assuring cuddle, or a passionate kiss. The intention, rather, is not to compensate but to complement partnered sexual interactions at times of such crisis or when the couples are distanced due to various reasons. The most important concern, however, is that cybersex needs a certain degree of skills and knowledge to be

able to express sexual fantasies and desires through the audio-visual, text, and pictorial media. Also, the mutual visibility can be compromised by the logistic issues. Accessibility, anonymity, and affordability are often the factors regulating cybersex.²³ The digital screen time has had an unprecedented rise during the pandemic. Unchecked, this can affect the students and younger population who are bound to spend most of their times in cyberspace. This can have the unintended effects of technology use, exposure to illegal aspects of digital sex (based on legal systems in various nations), pornography addiction, risks of online extortion, cyber-fraud, cyber-bullying, and cyber-security threats. Furthermore, it runs the risks of online stalking, revenge pornography, online sexual harassment, online grooming, online dating scams, and so on.^{7,24,25} Also, people who have a pre-existing history of unhealthy technology use can potentially have exacerbation of their problems during a continued practice of cybersex. What constitutes excessive or problematic cybersex is again a debatable area that has no clear consensus. Sharing features with addiction medicine, symptoms like excessive time consumption, loss of control, and significant adverse consequences of use have been related to cybersexual disorders.²⁶ Though various users have reported sexual arousal, emotional satisfaction, stress reduction, and expression of hidden sexual fantasies as reasons for indulging in digital sex,²⁷ studies have reported associations of cybersex with loss of interest in partnered sex, sexual dysfunctions, depression, anxiety, and high-risk sexual behaviors.²⁶ A detailed review of conceptualization, assessment, and treatment of problematic cybersex is provided by Wéry and Billieux.²⁸ Lived perceptions of cybervictims, technical coping strategies, cyberspace regulatory policies, and targeting at-risk groups like adolescents and students help in prevention of cybersexual crimes.²⁹

There is no easy solution! Like any other form of sexuality, sex education forms the anchor stone in healthy exploration of sexual fantasies, validation of mutual emotions and respect, as well as open communication and bonding.³⁰ Informed consent of partners is of utmost importance, especially when it comes to recording online sexual interactions. Similarly, the use of pornography and online sexual practices needs to be regulated and researched to understand the differential effects and public reactions during the pandemic crisis. Besides cross-cultural and cross-country, research should focus on cultural effects on virtual sexuality and effects of cybersex on psychosexual health. Longitudinal mixed-method studies and exploring lived experiences related to partnered and solo sex are essential to formulate policies and guidelines that can be rooted within the participant perceptions. The pandemic may also provide us the chance of using online platforms for destigmatizing sexuality, busting the social myths related to sex, enable healthy discussion concerning psychosexual health, and facilitating sexual rights of the gender minorities. Long-distance relationships have the potential for a renewed importance, better bonding, and sustenance using virtual



media. Cybersex is a growing practice and has various tenets to its implementation. Whether this will lead to enduring change remains unknown. Nevertheless, the COVID-19 pandemic offers us a full advantage of the connectivity established by technology to extend the boundaries of love and sex, now and for the future.

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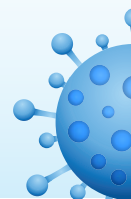
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Research Article

Psychological Impact of COVID-19 Lockdown among Healthy Individuals in India: A Self-Assessed Cross-Sectional Study

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ABSTRACT

Background: The pandemic coronavirus disease-19 (COVID-19) is spreading rapidly in India and worldwide. As a preventive measure, the Indian government put in place the nationwide lockdown which may be impacting the psychological distress among healthy individuals.

Aims: To assess the psychological impact of COVID-19 lockdown among healthy individuals in India.

Method: A self-assessed cross-sectional web-based survey was conducted between 1st April and 14th April 2020. Centre for Epidemiological Study for Depression questionnaire was administered for assessing the depressive symptoms among general public during the COVID-19 lockdown. Using the google forms the questionnaire was circulated among the public through social media. Descriptive analysis was performed to represent the study characteristic, Chi-square test for assessing the associations of depressive symptoms among the study variables, and the logistic regression analysis for identifying the factors influencing the depressive symptoms.

Results: A total of 1176 participants with a mean (SD) age of 27.59 (8.72) years were responded to the questionnaire. The prevalence depressive symptoms were higher among males (54%) compared to females (36%). It was identified that the participants with educational background of pre-university education/diploma (58.22%) and middle school (71.42%), and occupation as semiskilled (60%) and unskilled workers (70%), social history of consumption alcohol (56.52%) and smoking (75%), and belong to joint family (53.10%) were the predictors for depressive symptoms. Subgroup analysis identified that these factors influence depressive symptoms especially among male population.

Conclusion: It is an alarming situation that the depressive symptoms found in approximately 45% of healthy individuals during the COVID-19 lockdown. Educational interventions by the government and non-government organizations are very much required to combat the progression of depressive symptoms into disorder.

Keywords: COVID-19, India, healthy individuals, Depressive symptoms.

INTRODUCTION

In the history of mankind, there has been marked psychological impact on healthy individuals during each pandemic of infectious diseases such as Plagues, Spanish flu, Asian flu, severe acute

respiratory syndrome (SARS) (Huremovic et al., 2019). A similar frightening public health emergency was emerged in China at the end of 2019 and continued on a global scale with the spread of one of the Coronavirus strains called

novel Coronavirus (SARS-CoV-2) and the disease formally called as Coronavirus disease (COVID-19) Quarantine has proved to be an effective way in controlling the spread of infections for instance, in recent pandemics such as Ebola and SARS, many countries of West Africa, China and Canada has imposed lockdowns thus reducing the spread of infections (Brooks et al., 2020). However, it was found that the long-term psychiatric conditions such as post-traumatic stress disorder (25.6%) and depression (15.6%) among the SARS infected patients after 30 months of post SARS pandemic (Mak et al., 2010). In a study conducted in Africa, it was identified that the depressive symptoms, anxiety, Post Traumatic Stress Disorder (PTSD) were more common in household individual during EBOLA outbreak (Keita et al., 2017).

India being the second most populous countries in the world (DESA et al., 2019) has 1,01,261 confirmed cases as of 19th May, 2020 (JHUM et al., 2020). Despite many educational programs by the governments on awareness of COVID-19. In India, there were around 300 non-coronavirus deaths (Suicides) reported from March 19th to May 2nd 2020. Majority (80) of them died due to fear of being tested positive to corona virus and loneliness followed by migrants dying in accidents (51) on their way back home and financial distress (36) (Economic times 2020). This was due to changes in mental state of people due to the current pandemic, lockdown social isolation, loss of livelihood and fear of infection. To the best of our knowledge, there are no research findings on psychological aspects of healthy individuals of India during this prolonged COVID-19 lockdown period. Hence, we aimed to assess the psychological impact of COVID-19 lockdown among healthy individuals in India.

METHODOLOGY

A self-assessed cross-sectional web-based survey was conducted (after one week of first phase intensive lockdown in India) between 1st April 2020 and 14th April 2020. The questionnaire was adopted based on Center for Epidemiologic Studies Depression Scale (CES-D) [English Version]. The CES-D scale is a 20-point self-administered questionnaire; which assess the symptoms of depression over a period of one week in individuals. This questionnaire has four factors Depressive effect (blues, depression, failure, fearful, lonely, crying, sad), Positive effect (good, hopeful, happy, enjoyed life), Somatic and retarded (bothered, appetite, mind, effort, sleep, less talk,

get going) and Interpersonal (unfriendly, disliked) (Radloff et al., 1977).

The responses of each question consisted 4 options. The response 'rarely or none of the time (less than one day)' was given score "0", some or a 'little of the time (1-2 days)' was given score "1", 'occasionally or a moderate amount of time (3-4 days)' was given score "2" and 'most or all the time (5-7 days)' was given score "3". The minimum and maximum score the individual who answers CES-D is '0' and '60' respectively. The cut off score varies based on the gender. Individuals who scored more than or equal to 17 and 23 in males and females respectively are considered as presence of depressive symptoms. (Keita et al., 2017)

The healthy individuals who are self-isolated during the COVID-19 lockdown phase were the study population. The web-based questionnaire was distributed to the public of India through Google forms via emails and social media like WhatsApp, Facebook and Instagram, irrespective of their educational, economic and occupational status. Also, we also asked individuals to share the web-based survey link between their family members, friends and colleagues.

Mean with standard deviation for continuous variables and number with percentage for categorical variables were applied. Chi-square test was used to find the association between demographic details of people and their depressive symptoms, and the factors influencing depressive symptoms were identified by using odds ratio with 95% CI. The results were considered statistically significant with $p < 0.05$. All statistical analyses were performed using Statistical Package for Social Sciences (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY, USA: IBM Corp).

ETHICS

Institutional Human Ethics Committee of JSS college of Pharmacy Mysuru, gave exemption to conduct this study since this study has no minimal risk research.

RESULTS

A total of 588 healthy individuals completed the survey. The mean (SD) age of the participants is 27.59 (8.72) years and ranging from 18-70 years. Nearly half of the participants were post graduates ($n=289$, 49.14%) and 40.64% of participants were professionals by occupation ($n=239$). Majority of the study population were from urban ($n=402$, 68.36%) and upper middle socioeconomic status



(n=300, 51.02%). Majority (82.99%) of participants do not have any social history of consumption of alcohol and smoking. Three fourth (n=443, 75.34%) of the study participants belong to nuclear family. More details of demographic characteristics of the study participants with gender wise distribution were presented in table 1. Age, occupation, socio economic status, social history and type of family are significantly different between male and female participants.

It was found that, three fourth of the female participant (75.33%) had poor appetite rarely or none of the time. Comparatively most or all the time male participants (9.24%) felt depressed than female participants (8.44%). Majority (44.59%) of the female had felt hopeful about the future most or all the time compared to male participant (39.38%). Most of male participant (46.23%) enjoyed the life during lockdown compared to female participants (40.54%). The male and female participants response for each questionnaire is presented in the table 2.

In the depressive effect factor, it was found that, majority of the participants felt depressive effect rarely or none of the time. However, approximately 15% and 13% of total participants felt lonely and failure respectively most or all the time (5-7 days). In the positive effect category, majority of the study participants (43.36%) enjoyed life most or all of the time followed by hopeful (42%) and happy (39.96%). In the somatic and retarded category, approximately three fourth (73.63%) of participants stated of decreased appetite followed by disturbed mind (56.12%) and bothered (55.78%) symptoms rarely or none of the time. Approximately equal percentage of participants felt unfriendly (58.67%) and disliked (58.84%) rarely or none of the time (Table 3).

Out of 588 participants, 265 (45.06%) respondents presented with the depressive symptoms and 323 (54.93%) were without depressive symptoms. More than half of the male participants (54.05%) had depressive symptoms while the percentage of female participants with depressive symptoms was only 35.95%. Logistic regression analysis identified that the male gender [OR 2.10 (95% CI 1.51-2.92); $P < 0.001$], educational status of PUC / diploma [OR 2.24 (95% CI 1.35-3.71); $P = 0.002$] and primary school [OR 15.98 (95% CI 2.02-126.55); $P = 0.001$], occupation as skilled/semiskilled worker [OR 2.16 (95% CI 1.19-3.92); $P = 0.011$], social history of alcohol consumption [OR 1.84 (95% CI 1.0-3.39); $P = 0.047$], smoking [OR 4.25 (95% CI 1.14-15.88); $P = 0.020$] and both alcohol

consumption and smoking [OR 2.83 (95% CI 1.45-5.51); $P = 0.002$], and joint family [OR 1.54 (95% CI 1.05-2.24); $P = 0.025$] are the predictors for depressive symptoms among study participants (Table 4).

By conducting the subgroup analysis, we tried to identify the predictors for depressive symptoms among males and females separately. Education level of graduate [OR 2.47 (95% CI 1.37-4.44); $P = 0.002$] and PUC/diploma [OR 2.55 (1.30-4.99); $P = 0.006$], occupation as clerk/shop/farmer/self-employed [OR 2.39 (95% CI 1.05-5.45); $P = 0.035$] and skilled/semiskilled worker [OR 2.69 (95% CI 1.23-5.87); $P = 0.011$], income of 11,708-19,515 INR [OR 3.91 (95% CI 1.51-10.15); $P = 0.004$] and 19,516-29,199 INR [OR 4.56 (95% CI 1.18-17.55); $P = 0.019$], socioeconomic status such as upper middle [OR 1.94 (95% CI 1.07-3.52); $P = 0.028$] and lower middle [OR 2.76 (95% CI 1.25-6.08); $P = 0.011$], social history of both alcohol and smoking [OR 2.17 (95% CI 1.04-4.52); $P = 0.036$] and joint family [OR 1.70 (95% CI 1.02-2.84); $P = 0.041$] were the predictors for depressive symptoms among male participants. In contrast, only the primary school educational background [OR 13.59 (95% CI 1.63-113.47); $P = 0.004$] was found to be the predictor for depressive symptoms among female participants.

DISCUSSION

To the best of our knowledge, this is the first Indian data on psychological impact of COVID-19 lockdown among healthy individuals. This cross-sectional study had the participants from all age groups, various educational background, occupation and socioeconomic status. In our study, it was observed that 45% of participants experienced depressive symptoms. Our results were approximately two folds higher when compared to study conducted (22.4%) during COVID-19 pandemic (Zhang et al., 2020). Previous studies concluded that females have more depressive symptoms than males (Qiu et al., 2020) but interestingly in our study, a greater number of male participants experienced depressive symptoms than females during the COVID-19 lockdown. However, we cannot conclusively say that males are more prone to have depressive symptoms than females. In Indian scenario, majority of the breadwinner of the family are males. This study revealed that most of the male participants with skilled/semiskilled and Clerk/shop/farmer/self-employed by occupation showed depressive symptoms. A similar result was also found in the study conducted which concluded



that the skilled workers had experienced severe depressive symptoms (Qiu et al., 2020). In our study, students of PUC/intermediate/diploma were having depressive symptoms comparatively higher than other participants with various educational level. This result supports with a study in which, 22% students had depressive symptoms due to negative impact on academic progress. Therefore, it is suggested that the institution and authorities should start implementing online portals for assigning the academic and physical activities which might help students to keep themselves busy and further helps in reduction of depressive symptoms (Qiu et al., 2020). Majority of the depressive symptoms was experienced in participants with monthly income of 11,708-19,515 and 19,516-29,199 INR. It is observed in our study that the depressive symptoms were seen in participants who belong to upper middle socioeconomic class. However, to our knowledge there are no studies conducted to identify the relationship between SES and Depression in pandemic situations. This study found that participants who consume alcohol and nicotine have developed depressive symptoms. The prevalence of alcohol consumption in India (2019) is 30.9% (Wangdi et al., 2020). Unavailability of alcohol owing to the national shutdown has taken life's in south Indian states Kerala, Karnataka and Telangana, says the decan herald (Deccan herald 2020). In our study half of the participants who belong to joint family are found to have depressive symptoms

Due to increasing in the outbreak of COVID19, as a part of public response, the WHO department of Mental health and Substance use, recommends public to stay connected and maintain social network, paying attention to feelings during times of stress, perform regular exercise, maintain good health on view of protection and prevention of psychological consequences (World health organization 2020). Apart from these practices, The Indian Psychiatry Society and Indian Academy of Health Psychology has started up with state wise online mental health services for supporting the people who are in need of psychiatric consultation during the COVID-19 pandemic and a toll-free number has been provided by the National Institute of Mental Health and Neuro Science (NIMHANS) (Hiremath et al., 2020).

LIMITATION

The CES-D scale was used as screening method and not as diagnostic device. The CES-D score obtained narrate the psychological state of the

individual during the week before the questionnaire administered. Hence, we were unable to follow up the participant presented with depressive symptoms and we did not collect the details of other comorbid conditions of participants therefor results of this study can be generalized.

CONCLUSION

COVID-19 lockdown had a major impact on psychological symptoms among the healthy individuals. Our study found male participants are more prone to have depressive symptoms with predictors were educational status of PUC / diploma and primary school, occupation as skilled/semiskilled workers, social history of alcohol consumption & smoking and joint family.

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No financial support was received for this research.

PRESENTATION AT A MEETING

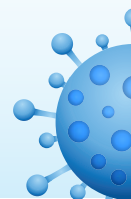
This research is presented at the virtual ISPOR Europe 2020 conference.

CONFLICTING INTEREST

None of the authors have any conflicts of interest that are directly relevant to the content of this article.

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Table 1: Demographic details of study population

Category		Male N=592 (%)	Female N=584 (%)	Total N=1176 (%)	Chi ² P-Value
Age	18-30 Years	302 (51.01)	378 (64.72)	680 (57.82)	0.001
	31-59 Years	286 (48.31)	204 (34.93)	490 (41.66)	
	>60 Years	4 (0.67)	2 (0.34)	6 (0.51)	
Education	Post Graduate	282 (47.63)	296 (50.68)	578 (49.14)	0.154
	Graduate	114 (24.32)	166 (28.42)	306 (26.36)	
	PUC/diploma	100 (16.89)	58 (9.93)	158 (13.43)	
	High School	48 (8.10)	46 (7.87)	84 (7.99)	
	Middle school	10 (1.68)	4 (0.68)	14 (1.19)	
	Primary school	6 (1.01)	12 (2.05)	18 (1.53)	
	illiterate	2 (0.33)	2 (0.34)	4 (0.34)	
Occupation	Professional	278 (46.95)	200 (34.24)	478 (40.64)	



	Semi	26 (4.39)	20 (3.42)	46 (3.91)	<0.001
	Clerk/shop/farm/self employed	62 (10.47)	26 (4.45)	88 (7.48)	
	Skilled/semiskilled	74 (12.50)	36 (6.16)	110 (9.35)	
	unskilled	18 (3.04)	2 (0.34)	20 (1.70)	
	Unemployed/student	134 (22.63)	300 (51.36)	434 (36.9)	
Income	≤3,907	152 (25.67)	158 (27.05)	310 (26.36)	0.134
	3,908-11,707	36 (6.08)	56 (9.58)	92 (7.82)	
	11,708-19,515	62 (10.47)	50 (8.56)	112 (9.52)	
	19,516-29,199	28 (4.72)	28 (4.79)	56 (4.76)	
	29,200 -39,032	46 (7.77)	70 (11.98)	116 (9.86)	
	39,033-78,062	102 (17.22)	64 (10.95)	166 (14.11)	
	≥78,063	166 (28.04)	158 (27.05)	324 (27.55)	
Socio Economic Status	Upper (I)	126 (21.28)	70 (11.98)	196 (16.66)	0.001
	Upper Middle (II)	314 (53.04)	286 (48.97)	600 (51.02)	
	Lower Middle (III)	90 (15.2)	114 (19.52)	204 (17.34)	
	Upper Lower (IV)	62 (10.47)	110 (18.83)	172 (14.62)	
	Lower (V)	0 (0.00)	4 (0.68)	4 (0.34)	
Residency	Rural	174 (29.39)	198 (33.9)	372 (31.63)	0.239
	Urban	418 (70.60)	386 (66.09)	804 (68.36)	
Social History	Alcohol	78 (13.17)	14 (2.39)	92 (7.82)	<0.001
	Smoking	22 (3.72)	2 (0.34)	24 (2.04)	
	Both	76 (12.83)	8 (1.36)	84 (7.14)	
	None	416 (70.27)	560 (95.89)	976 (82.99)	
Type of Family	Nuclear Family	418 (70.60)	468 (80.13)	886 (75.34)	0.007
	Joint Family	174 (29.39)	116 (19.86)	290 (24.65)	

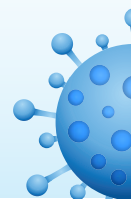
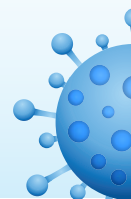


Table 2: Responses on symptoms of depression among male (N=592) and female (N=684) participants

		Rarely or none of the time (<1 day)		Some or a little of the time (1-2 days)		Occasionally or a moderate amount of time (3-4 days)		Most or all of the time (5-7 days)	
		Male	Female	Male	Female	Male	Female	Male	Female
1	I was bothered by things that usually don't bother me.	338 (57.09)	318 (54.45)	88 (14.86)	168 (28.76)	55 (9.29)	110 (18.83)	48 (8.1)	28 (4.79)
2	I did not feel like eating; my appetite was poor.	420 (70.94)	446 (76.36)	74 (12.5)	86 (14.72)	27 (4.56)	54 (9.24)	36 (6.08)	30 (5.13)
3	I felt that I could not shake off the blues even with help from my family or friends.	370 (62.5)	418 (71.57)	108 (18.24)	98 (16.78)	32 (5.4)	64 (10.95)	42 (7.09)	34 (5.82)
4	I felt I was just as good as other people	196 (33.1)	176 (30.13)	102 (17.22)	86 (14.72)	35 (5.91)	70 (11.98)	216 (36.48)	234 (40.1)
5	I had trouble keeping my mind on what I was doing.	330 (55.74)	330 (56.5)	130 (21.95)	154 (26.36)	31 (5.23)	62 (10.61)	62 (10.47)	42 (7.19)
6	I felt depressed.	344 (58.1)	326 (55.82)	118 (19.93)	158 (27.05)	34 (5.74)	68 (11.64)	54 (9.12)	50 (8.56)
7	I felt that everything I did was an effort.	244 (41.21)	212 (36.3)	82 (13.85)	136 (23.28)	58 (9.79)	116 (19.86)	142 (23.98)	120 (20.54)
8	I felt hopeful about the future.	124 (20.94)	110 (18.83)	134 (22.63)	112 (19.17)	48 (8.1)	96 (16.43)	230 (38.85)	264 (45.2)
9	I thought my life had been a failure.	330 (55.74)	350 (59.93)	96 (16.21)	102 (17.46)	40 (6.75)	80 (13.69)	78 (13.17)	80 (13.69)
10	I felt fearful	340 (57.43)	280 (47.94)	114 (19.25)	192 (32.87)	36 (6.08)	72 (12.32)	58 (9.79)	52 (8.9)
11	My sleep was restless.	278 (46.95)	272 (46.57)	128 (21.62)	150 (25.68)	48 (8.1)	96 (16.43)	82 (13.85)	94 (16.09)



12	I was happy.	138 (23.31)	78 (13.35)	114 (19.25)	108 (18.49)	53 (8.95)	106 (18.15)	226 (38.17)	244 (41.78)
13	I talked less than usual	268 (45.27)	314 (53.76)	136 (22.97)	136 (23.28)	52 (8.78)	104 (17.8)	76 (12.83)	62 (10.61)
14	I felt lonely.	290 (48.98)	300 (51.36)	120 (20.27)	162 (27.73)	41 (6.92)	82 (14.04)	92 (15.54)	80 (13.69)
15	People were unfriendly.	362 (61.14)	328 (56.16)	92 (15.54)	136 (23.28)	30 (5.06)	60 (10.27)	70 (11.82)	54 (9.24)
16	I enjoyed life.	118 (19.93)	78 (13.35)	94 (15.87)	106 (18.15)	51 (8.61)	102 (17.46)	270 (45.6)	240 (41.09)
17	I had crying spells.	408 (68.91)	300 (51.36)	82 (13.85)	148 (25.34)	24 (4.05)	48 (8.21)	46 (7.77)	62 (10.61)
18	I felt sad.	324 (54.72)	244 (41.78)	128 (21.62)	186 (31.84)	33 (5.57)	66 (11.3)	66 (11.14)	60 (10.27)
19	I felt that people dislike me.	346 (58.44)	346 (59.24)	90 (15.2)	94 (16.09)	39 (6.58)	78 (13.35)	70 (11.82)	70 (11.98)
20	I could not get "going."	328 (55.4)	318 (54.45)	102 (17.22)	144 (24.65)	37 (6.25)	74 (12.67)	80 (13.51)	52 (8.9)



12	I was happy.	138 (23.31)	78 (13.35)	114 (19.25)	108 (18.49)	53 (8.95)	106 (18.15)	226 (38.17)	244 (41.78)
13	I talked less than usual	268 (45.27)	314 (53.76)	136 (22.97)	136 (23.28)	52 (8.78)	104 (17.8)	76 (12.83)	62 (10.61)
14	I felt lonely.	290 (48.98)	300 (51.36)	120 (20.27)	162 (27.73)	41 (6.92)	82 (14.04)	92 (15.54)	80 (13.69)
15	People were unfriendly.	362 (61.14)	328 (56.16)	92 (15.54)	136 (23.28)	30 (5.06)	60 (10.27)	70 (11.82)	54 (9.24)
16	I enjoyed life.	118 (19.93)	78 (13.35)	94 (15.87)	106 (18.15)	51 (8.61)	102 (17.46)	270 (45.6)	240 (41.09)
17	I had crying spells.	408 (68.91)	300 (51.36)	82 (13.85)	148 (25.34)	24 (4.05)	48 (8.21)	46 (7.77)	62 (10.61)
18	I felt sad.	324 (54.72)	244 (41.78)	128 (21.62)	186 (31.84)	33 (5.57)	66 (11.3)	66 (11.14)	60 (10.27)
19	I felt that people dislike me.	346 (58.44)	346 (59.24)	90 (15.2)	94 (16.09)	39 (6.58)	78 (13.35)	70 (11.82)	70 (11.98)
20	I could not get "going."	328 (55.4)	318 (54.45)	102 (17.22)	144 (24.65)	37 (6.25)	74 (12.67)	80 (13.51)	52 (8.9)



Table 3: Responses of participants on CES-D factor model

Factors	Questions	Rarely or none of the time (<1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	Most or all of the time (5-7 days)
Depressive effect	Blues	788 (67.00)	206 (17.51)	106 (9.01)	76 (6.46)
	Depression	670 (56.97)	276 (23.46)	126 (10.71)	104 (8.84)
	Failure	680 (57.82)	198 (16.83)	140 (11.9)	158 (13.43)
	Fearful	620 (52.72)	306 (26.02)	140 (11.9)	110 (9.35)
	Lonely	590 (50.17)	282 (23.97)	132 (11.22)	172 (14.62)
	Crying	708 (60.20)	230 (19.55)	130 (11.05)	108 (9.18)
	Sad	568 (48.29)	314 (26.70)	168 (14.28)	126 (10.71)
Positive effect	Good	372 (31.63)	188 (15.98)	166 (14.11)	450 (38.26)
	Hopeful	234 (19.89)	246 (20.91)	202 (17.17)	494 (42)
	Happy	216 (18.36)	222 (18.87)	268 (22.78)	470 (39.96)
	Enjoyed life	196 (16.66)	200 (17.00)	270 (22.95)	510 (43.36)
Somatic & Retarded	Bothered	656 (55.78)	256 (21.76)	188 (15.98)	76 (6.46)
	Appetite	866 (73.63)	160 (13.6)	84 (7.14)	66 (5.61)
	Mind	660 (56.12)	284 (24.14)	128 (10.88)	104 (8.84)
	Effort	456 (38.77)	218 (18.53)	240 (20.4)	262 (22.27)
	Sleep	550 (46.76)	278 (23.63)	172 (14.62)	176 (14.96)
	Less talk	582 (49.48)	272 (23.12)	184 (15.64)	138 (11.73)
	Get going	646 (54.93)	246 (20.91)	152 (12.92)	132 (11.22)
Interpersonal	Unfriendly	690 (58.67)	228 (19.38)	134 (11.39)	124 (10.54)
	Disliked	692 (58.84)	184 (15.64)	160 (13.6)	140 (11.9)

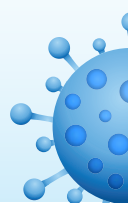


Table 4: Demographic factors responsible for the characteristic symptoms of depression among study participants

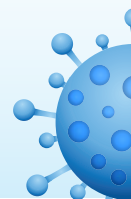
Category		Total no. of study participants N=1176	No. of participants with characteristic symptoms of depression N=530 (45.06%)	No. of participants with no characteristic symptoms of depression N=646 (54.93%)	OR (95% CI); P-Value
Age	18-30 Years	680 (57.82)	308 (58.11)	372 (57.58)	Reference
	31-59 Years	490 (41.66)	216 (40.75)	274 (42.41)	0.95 (0.68-1.33); 0.771
	>60 Years	6 (0.51)	6 (1.13)	0 (0)	4.83 (0.53-43.62); 0.183
Gender	Female	584 (49.65)	210 (39.62)	374 (57.89)	Reference
	Male	592 (50.34)	320 (60.37)	272 (42.1)	2.10 (1.51-2.92); <0.001
Education	Professional	578 (49.14)	222 (41.88)	356 (55.1)	Reference
	Graduate	306 (26.36)	148 (27.92)	162 (25.07)	1.47 (0.99-2.17); 0.057
	PUC/diploma	158 (13.43)	92 (17.35)	66 (10.21)	2.24 (1.35-3.71); 0.002
	High School	84 (7.99)	40 (7.54)	54 (8.35)	1.19 (0.64-2.22); 0.589
	Middle school	14 (1.19)	10 (1.88)	4 (0.61)	4.01 (0.77-21.02); 0.115
	Primary school	18 (1.53)	18 (3.39)	0 (0)	15.98 (2.02-126.55); 0.001
	illiterate	4 (0.34)	0 (0)	4 (0.61)	0.53 (0.56-5.19); 1.000
Occupation	Professional	478 (40.64)	196 (36.98)	282 (43.65)	Reference
	Semi	46 (3.91)	18 (3.39)	28 (4.33)	0.93 (0.39-2.22); 0.861
	Clerk/shop/farm/self employed	88 (7.48)	48 (9.05)	40 (6.19)	1.73 (0.90-3.30); 0.096
	Skilled/semiskilled	110 (9.35)	66 (12.45)	44 (6.81)	2.16 (1.19-3.92); 0.011
	unskilled	20 (1.70)	14 (2.64)	6 (0.92)	3.36 (0.85-13.30); 0.101
	Unemployed/student	434 (36.9)	188 (35.47)	246 (38.08)	1.10 (0.76-1.60); 0.617
Income	≥78,063	310 (26.36)	136 (25.66)	188 (29.1)	Reference
	39,033-78,062	92 (7.82)	78 (14.71)	88 (13.62)	1.23 (0.72-2.09); 0.497
	29,200 -39,032	112 (9.52)	50 (9.43)	66 (10.21)	1.05 (0.57-1.92); 0.881



	19,516-29,199	56 (4.76)	34 (6.41)	22 (3.4)	2.14 (0.94-4.85); 0.066
	11,708-19,515	116 (9.86)	62 (11.69)	50 (7.73)	1.71 (0.93-3.16); 0.083
	3,908-11,707	166 (14.11)	38 (7.16)	54 (8.35)	0.97 (0.50-1.89); 0.935
	≤3,907	324 (27.55)	132 (24.9)	178 (27.55)	1.03 (0.66-1.60); 0.913
SES	Upper (I)	196 (16.66)	74 (13.96)	122 (18.88)	Reference
	Upper Middle (II)	600 (51.02)	270 (50.94)	330 (51.08)	1.40 (0.85-2.15); 0.209
	Lower Middle (III)	204 (17.34)	100 (18.86)	104 (16.09)	1.59 (0.90-2.79); 0.108
	Upper Lower (IV)	172 (14.62)	82 (15.47)	90 (13.93)	1.50 (0.83-2.71); 0.174
	Lower (V)	4 (0.34)	4 (0.75)	0 (0)	4.90 (0.49-48.77); 0.298
Residency	Rural	372 (31.63)	162 (30.56)	210 (32.5)	Reference
	Urban	804 (68.36)	368 (69.43)	436 (67.49)	1.09 (0.77-1.55); 0.614
Social History	None	976 (82.99)	404 (76.22)	572 (88.54)	Reference
	Alcohol	24 (2.04)	52 (9.81)	40 (6.19)	1.84 (1.0-3.39); 0.047
	Smoking	84 (7.14)	18 (3.39)	6 (0.92)	4.25 (1.14-15.88); 0.020
	Both	92 (7.82)	56 (10.56)	28 (4.33)	2.83 (1.45-5.51); 0.002
Type of Family	Nuclear Family	886 (75.34)	376 (70.94)	510 (78.94)	Reference
	Joint Family	290 (24.65)	154 (29.05)	136 (21.05)	1.54 (1.05-2.24); 0.025

Table 5: Demographic factors responsible for the characteristic symptoms of depression among male and female participants

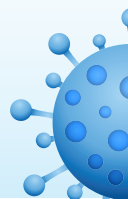
Category		Total no. of study participants N=1176	Male N=592			Female N=584		
			Characteristic symptoms of depression N=320 (54%)	No characteristic symptoms of depression N=272 (45.9%)	OR (95% CI); P-Value	Characteristic symptoms of depression N=210 (35.9%)	No characteristic symptoms of depression N=374 (64%)	OR (95% CI); P-Value
Age	18-30 Years	680 (57.82)	172 (56.95)	302 (43.04)	Reference	136 (35.97)	242 (64.02)	Reference



	31-59 Years	490 (41.66)	144 (50.34)	142 (49.65)	0.77 (0.48-1.21); 0.256	72 (35.29)	132 (64.70)	0.97 (0.59-1.61); 0.907
	>60 Years	6 (0.51)	4 (100.00)	0 (0.00)	2.28 (0.23-22.38); 0.636	2 (100)	0 (0.00)	3.54 (0.32-39.71); 0.555
Education	Professional	578 (49.14)	122 (43.26)	160 (56.73)	Reference	100 (33.78)	196 (66.21)	Reference
	Graduate	306 (26.36)	94 (65.27)	50 (34.72)	2.47 (1.37-4.44); 0.002	54 (32.53)	56 (67.46)	0.95 (0.53-1.67); 0.846
	PUC/diploma	158 (13.43)	66 (66.00)	34 (34.00)	2.55 (1.30-4.99); 0.006	36 (44.82)	32 (55.17)	1.59 (0.71-3.57); 0.256
	High School	84 (7.99)	36 (54.16)	22 (45.83)	1.55 (0.65-3.70); 0.321	14 (30.43)	32 (69.56)	0.86 (0.33-2.22); 0.751
	Middle school	14 (1.19)	6 (60.00)	4 (40.00)	1.97 (0.32-12.14); 0.654	4 (100.00)	0 (0.00)	5.82 (0.59-57.41); 0.124
	Primary school	18 (1.53)	6 (100.00)	0	5.23 (0.57-47.93); 0.172	12 (100.00)	0 (0.00)	13.59 (1.63- 113.47); 0.004
	Illiterate	4 (0.34)	0	2 (100.00)	0.65 (0.06-7.37); 1.000	0	2 (100.00)	0.97 (0.09-10.96); 1.000
Occupation	Professional	478 (40.64)	130 (46.76)	148 (53.23)	Reference	66 (33.00)	134 (67.00)	Reference
	Semi	46 (3.91)	16 (61.53)	20 (38.46)	1.82 (0.57-5.85); 0.308	2 (10.00)	18 (90.00)	0.23 (0.03-1.86); 0.170
	Clerk/shop/farm/ self employed	88 (7.48)	42 (67.74)	20 (32.25)	2.39 (1.05-5.45); 0.035	6 (23.07)	20 (76.92)	0.61 (0.16-2.36); 0.546
	Skilled/semiskilled	110 (9.35)	52 (70.27)	22 (29.72)	2.69 (1.23-5.87); 0.011	14 (38.88)	22 (61.11)	1.29 (0.46-3.64); 0.627
	unskilled	20 (1.70)	14 (77.77)	4 (22.22)	3.99 (0.80-19.86); 0.091	0	2 (100)	1.02 (0.09-11.61); 1.000
	Unemployed/ student	434 (36.9)	66 (49.25)	68 (50.74)	1.11 (0.62-1.98); 0.737	122 (40.66)	178 (59.33)	1.39 (0.82-2.36); 0.220
Income	≥78,063	310 (26.36)	74 (44.57)	92 (55.42)	Reference	62 (39.24)	96 (60.75)	Reference
	39,033-78,062	92 (7.82)	58 (56.86)	44 (43.13)	1.64 (0.81-3.31); 0.167	20 (31.25)	44 (68.75)	0.70 (0.29-1.69); 0.429
	29,200 -39,032	112 (9.52)	24 (52.17)	22 (47.82)	1.36 (0.54-3.42); 0.518	36 (37.14)	44 (62.85)	0.92 (0.40-2.08); 0.832



	19,516-29,199	56 (4.76)	22 (78.57)	6 (21.42)	4.56 (1.18-17.55); 0.019	12 (42.85)	16 (57.14)	1.16 (0.37-3.67); 0.799
	11,708-19,515	116 (9.86)	48 (77.41)	14 (22.58)	3.91 (1.51-10.15); 0.004	14 (28.00)	36 (72.00)	0.60 (0.23-1.61); 0.309
	3,908-11,707	166 (14.11)	18 (50.00)	18 (50.00)	1.24 (0.45-3.45); 0.675	20 (35.71)	36 (64.28)	0.86 (0.35-2.11); 0.742
	≤3,907	324 (27.55)	76 (50.00)	76 (50.00)	1.24 (0.67-2.32); 0.494	56 (35.44)	102 (64.55)	0.85 (0.45-1.62); 0.622
SES	Upper (I)	196 (16.66)	50 (39.68)	76 (60.31)	Reference	24 (34.28)	46 (65.71)	Reference
	Upper Middle (II)	600 (51.02)	176 (56.05)	138 (43.94)	1.94 (1.07-3.52); 0.028	94 (32.86)	192 (67.13)	0.94 (0.43-2.05); 0.873
	Lower Middle (III)	204 (17.34)	58 (64.44)	32 (35.55)	2.76 (1.25-6.08); 0.011	42 (36.84)	72 (63.15)	1.19 (0.46-2.70); 0.804
	Upper Lower (IV)	172 (14.62)	36 (58.06)	36 (41.93)	2.11 (0.88-5.04); 0.093	46 (41.81)	64 (58.18)	1.38 (0.57-3.32); 0.475
	Lower (V)	4 (0.34)	0 (0.00)	0 (0.00)	NA	4 (100)	0 (0.00)	5.54 (0.52-58.76); 0.281
Residency	Rural	372 (31.63)	82 (47.12)	92 (52.87)	Reference	80 (40.4)	118 (59.59)	Reference
	Urban	804 (68.36)	238 (56.93)	180 (43.06)	1.48 (0.90-2.45); 0.123	130 (33.67)	256 (66.32)	0.75 (0.45-1.24); 0.257
Social History	None	976 (82.99)	208 (50)	208 (50)	Reference	196 (35.00)	364 (65)	Reference
	Alcohol	24 (2.04)	44 (56.41)	34 (43.58)	1.29 (0.65-2.58); 0.462	8 (57.14)	6 (42.85)	2.48 (0.54-11.29); 0.251
	Smoking	84 (7.14)	16 (72.72)	6 (27.27)	2.67 (0.69-10.33); 0.142	1 (100.00)	0 (0.00)	3.70 (0.33-41.28); 0.287
	Both	92 (7.82)	52 (68.42)	24 (31.57)	2.17 (1.04-4.52); 0.036	4 (50.00)	4 (50.00)	1.86 (0.26-13.39); 0.615
Type of Family	Nuclear Family	886 (75.34)	210 (50.23)	208 (49.76)	Reference	166 (35.47)	302 (64.52)	Reference
	Joint Family	290 (24.65)	110 (63.21)	64 (36.78)	1.70 (1.02-2.84); 0.041	44 (37.93)	72 (62.06)	1.11 (0.61-2.01); 0.727



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Structured action plan for mental and behavioral preparedness against virus COVID19 outbreak in India (SAMBAV Bharath): Proposal for augmenting mental health services

M Kishor, Deeksha Ekanand¹

Abstract:

The World Health Organization (WHO) has designated the novel coronavirus outbreak (COVID19) as a pandemic. It is estimated that 125 million to 250 million people in India will be affected and 70% of humanity is likely to be infected within 1 year. The psychological impact can be from stress or economic-socio-occupational disruption, and people may suffer from fear of infection, anger, anxiety, depression, suicidal ideation, increased substance use, or relapse of psychiatric disorders. This can be of great concern for India, which already has high mental health morbidity but the lowest number of mental health experts, according to the WHO. Hence, it is imperative to consider the empowerment of available human resources. Here, we propose a structured action plan for mental and behavioral preparedness against virus COVID 19 disaster currently but virtually for any disaster in the country (SAMBAV Bharath). It designed to enable people by providing online training for individuals as mental health facilitators, who can assist the needy during and aftermath of the disaster.

Keywords:

COVID19, India, mental health, psychological impact of disaster

The World Health Organization (WHO) has designated a novel coronavirus outbreak (COVID19) as a pandemic.^[1] It is estimated that 125 million to 250 million people in India may get infected with Covid19, according to the center for disease dynamics, economics, and policy in collaboration with John Hopkins University, USA. Leading epidemiologist from Harvard, Marc Lipsitch has estimated that 70% of humanity will be infected within 1 year.

The psychological impact on millions of people, including those who are quarantined due to COVID19, can be devastating. The psychological impact can be from stress or economic-socio-occupational disruption and people may suffer from fear of infection,

anger, anxiety, depression, suicidal ideation, increased substance use, or relapse of psychiatric disorders. This can be of great concern for India, which already has high mental health morbidity, with 197.3 million people affected which includes 45.7 million due to depression and 44.9 million due to anxiety.^[2] In the month of March 2020, there have been media reports about suicide-related to the COVID19 scenario in India and case studies on self-harm reported.^[3] Moreover internationally, suicide among people in leadership such as that of German finance minister of state can be warning for the probable increase in suicide globally. It is in this background, there is an urgent need to consider a plan of action for mitigating the psychological impact of the

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COVID19 outbreak in the coming months and to enable the psychological recovery of people in India. It is a matter of concern that, India has the lowest number of mental health experts according to the WHO mental health atlas 2017, there are 0.3 psychiatrists per 100,000 populations.^[4] Hence, it is imperative to consider the empowerment of available human resources. Interestingly, India has the largest number of young people in the world, 600 million people under the age of 25 years. India also has one of the largest number of mobile phone users in the world, about 400 million. Youth in India, more so in health and allied sciences institutions can play an important role. Imparting training to students in health and allied sciences across the country can be one of the feasible ways to build a human resource that enables psychological support for millions of affected people in the COVID19 crisis and during the aftermath of COVID19, particularly in coming months. Hence, it is possible in India (literally means SAMBAV Bharath in Hindi) to build a human resource for mental health support. To the best of our knowledge at the time of writing this proposal, there are no certificate courses offered from recognized universities in India for facilitators of mental health in relation to the disaster. Here, we have proposed a model as a question (Q) and answer (A) format for ease of presenting.

Q1) What is SAMBAV Bharath?

A: It is an acronym for Structured Action plan for Mental and Behavioral preparedness Against Virus COVID 19 disaster (Virtually for any disaster) in the country (Bharath). However, the model is built on the premise that it should be useful for all disasters. It designed to enable people and capacity building of human resources for providing mental health services and addressing the psychological impact of the disaster. It proposes to provide online training for individuals as mental health facilitators during or the aftermath of the disaster.

Q2) Who can be trained?

A: Any adult aged 18 years and above, who knows English can be trained in the first phase. This can be easily made available in most of the regional languages. Initially, 10% of all health and allied sciences students in India can be trained at the earliest period to enable them as mental health facilitators.

Q3) What will be they trained in?

A: They will be trained as mental health facilitators through brief modules that enhances mental and behavioral abilities in addressing psychological distress and in assisting people during or the aftermath of the disaster.

Q4) Who will train them?

A: A team of psychiatrists, psychologists, and psychiatry social workers

Q5) How will the training occur?

A: Predominantly with Information and Communications Technology (ICT), including simulated or virtual reality-based, through online portals, or mobile applications. Moreover periodically, if needed contact classes can be offered after re-opening of institutions. Such training can be held in institutions of health and allied sciences such as medical, dental, nursing, physiotherapy, pharmacy, and others.

Q6) What will be the benefits for those who complete the training?

A: It shall provide an opportunity for serving the people in the national disaster. They can serve as mental health facilitators. They will be awarded certification at the successful completion of the course and the course can be considered for credit points in their semester and or other benefits that can be considered.

Q7) Which center can be the nodal center for providing online training in India?

A: Educational institutions such as JSS Academy of Higher Education and Research (Deemed to be University), which are already providing online courses, can be a nodal center and other centers can be considered as needed.

Q8) How will the SAMBAV Bharath mental health facilitator course-integrated or aligned with other agencies that are working for COVID19?

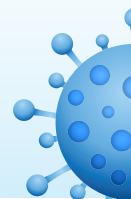
A: It can be integrated or aligned with resources or guidance from the WHO, National Institute of Mental Health and Neurosciences (NIMHANS) and National Disaster Management Authority (Govt of India)

Q9) How much time does it require for completing the SAMBAV Bharath certificate course as Mental Health Facilitator?

A: The course can have five modules, each delivered in two sessions of 60 min each. The total course can be carried out in twenty sessions and the total duration of 600 min (10 h).

The five modules can be

1. Understanding disaster and the psychological impact
2. Identifying and screening for the mental health conditions



3. Risk assessment and prevention
4. Approach and management of the mental health issues
5. Integration of services and facilitating care.

Q10) Can one component of the module be described?

A: The BATHE technique is a globally accepted psychotherapeutic procedure and serves useful for anxiety, depression, and situational stress disorders.^[5] The BATHE technique consists of four specific questions about the individual background, affect, troubles, and handling of the current situation, followed by an empathic response; the procedure takes approximately a few minutes according to studies. The trainee may use the BATHE technique to connect meaningfully with people, screen for mental health problems, and empower people to handle many aspects of their life in a more constructive way.

The BATHE Procedure: session begins with an assessment of "Background" of the person, the sociocultural factors, and recent adverse events (What is happening or what has happened?), which gives reasonable information about "the individual."

Then "Affect" associated with it are explored "How he/she feel about it? It is important to facilitate "Troublesome" feelings and "Their meaning of the situation".

Assess "Handling"-How are you handling that? Then, trainee assists an individual by suggesting methods of "Handling" through education and reassurances about common reactions to adversaries of life as perceived by the people

Empathetic listening to an individual's view, beliefs, and uncertainties, followed by appropriate empathy, "This must be very difficult for you." Empathetic education, problem-solving approaches, coping strategies, reassurances, and support to reduce worry, reduce the feeling of helplessness, and irrational fears.

Q11) What are the strengths and limitations of this proposal? Has this proposal been critically evaluated by the experts?

A: The proposal is about enabling people as facilitators of mental health, it is economically feasible and training can be provided by existing resources. Trained facilitators can bridge the gap in mental health services by identifying and referring more serious conditions to available mental health experts in India, such as psychiatrists, psychologists, and psychiatric social workers. It can also serve as a foundation course on which more customized

courses can be designed, such as enabling faculty in educational institutions to address psychological issues related to the disaster among students rejoining the institution after lockdown period.^[6,7] It can also be incorporated and customized for enabling team leaders in industries such as Information Technology to address mental health issues of team members, in the aftermath of the disaster.

The course content has to be critically evaluated but considering the time-constrained at the time of presenting this model, it has received comments from an external expert who has worked in India on mental health issues related to the disaster, Dr. Mohan Isaac, Clinical Professor of Psychiatry, University of Western Australia, Visiting Professor of Psychiatry, NIMHANS.

Acknowledgment

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Conflicts of interest

There are no conflicts of interest.

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"Watching the watchmen:" Mental health needs and solutions for the health-care workers during the coronavirus disease 2019 pandemic

Debanjan Banerjee, Hariprasad Ganapathy Vijayakumar, T S Sathyanarayana Rao¹

Abstract:

The coronavirus disease 2019 (COVID-19) has emerged as a global public health threat. As international borders are sealed, economies slashed, and billions quarantined at their homes to prevent the spread of infection, this pandemic has affected society at large, having a long-lasting psychological impact, more than ever. Certain vulnerable groups are more susceptible to this trauma. These include the health-care workers, one of the prominent frontline force against COVID-19. Their mental health needs are not only limited to work pressure, burnout, frustration, and guilt toward the family but also a constant fear of infection, health anxiety, paranoia, and depressive disorders. Complex posttraumatic stress and grief can be the added compounding factors leading to absenteeism and decreased efficiency. This commentary reviews the evidence for the various mental-health care needs of these frontline workers and highlights the possible solutions during such a biological disaster.

Keywords:

Coronavirus, coronavirus disease 2019, health care workers, mental health, pandemic

Introduction

"We were promised sufferings. They were part of the program. We were even told, "Blessed are they that mourn," and I accept it. I've got nothing that I hadn't bargained for. Of course, it is different when the thing happens to oneself, not to others, and in reality, not imagination."^[1] These lines of C. S. Lewis may have resonated with many health-care staffs, at least once in their lifetime in various dialects, as they toil through their day-to-day lives. Although the profession of health care is vested with the responsibility of reducing the distress and burden of others, the health-care staff are the ones who undergo tremendous distress due to their occupation. The World Health Organization theme for the World Mental Health Day "Mental Health in Work Place"

may apply to only a few occupations as much as it applies to the health care.^[2] It is an irony that nearly or sometimes more than half of the health-care workers across countries have been found to have symptoms of burnout and suffering from psychiatric morbidity.^[3] This woeful state of mental health in these professionals reflects their unmet mental health needs, which might not only be accentuated but also be made worse in a pandemic. Health-care workers are at increased risk of infection and various forms of psychological trauma during a pandemic, having to confront a variety of patients with a diverse set of physical and emotional issues. With more than three million cases and nearly two lakhs confirmed deaths across countries, the pandemic of coronavirus disease 2019 (COVID-19) is expected to impose an unprecedented burden on the mental health of the health care professionals.^[4] The ever-increasing

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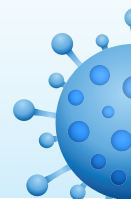
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number of cases, ever-changing protocols, and the ever-dwindling resources does not seem like a good prognosis to the community, which in turn might impact the health of everyone as stated in one of the studies as “no health without a healthy workforce.”^[5] As we are invested with this almost apocalyptic future ahead of us, everyone who ponders upon the solutions to change this even by a little bit would eventually end up in the conduit of existing mental health needs and gaps in their delivery, before elsewhere.

Mental Health among Doctors

Despite being so close to accessing the mental health facilities and having a relatively good social capital, health care staffs seem to be more likely to have symptoms of “burnout” and dissatisfied with their work-life balance than other workers. This observation might emerge as a surprise to the public, but not to those who have worked in the health care department, who will only acquiesce to this observation. Burnout and dissatisfaction have been so common in the profession that it has become more of a norm rather than an exception. “Burnout” is a syndrome characterized by emotional exhaustion, feelings of cynicism, and a low sense of personal accomplishment. This might not only have detrimental effects to the patients such as poor quality of care, increased medical errors, and lack of professionalism but also personal consequences to the staffs such as interpersonal relationship issues, an increase in substance use, and even suicidal ideations.^[6] Although this has been an area of research in the past few decades, the tenets of the stoic philosophy in medicine are so deep-rooted to uproot, as evident by doctors continuing to work hard, despite the stress and poor well-being, leading to this state of affairs many a times. The attitude toward distress as a sign of “professional-weakness,” has also been perpetuated by the stigmatization of mental distress and the glorification of self-sacrifice in the community, which also prevents these individuals from seeking help.^[7] This has been most often than not found to have detrimental effects on both the individual and the system. The individual factors which lead to “burnout” and psychiatric morbidity which have been identified are vulnerable physicians with traits of idealism, perfectionism, and a great sense of responsibility; prolonged patient contact; avoidance based coping strategies; presenteeism due to fear of career repercussions and letting down colleagues; and failure to prioritize one’s own health needs and recognize their vulnerability to illness. The systemic factors would include the imposition of heavy workload and long working hours trying to compensate the resources in hand and achieve a higher quality of care; rigid organizational structures; adoption of maladaptive patterns of teachers that are often reinforced; and highly regulatory systems of clinical governance leading to

reduced autonomy.^[8,9] While the medical profession seems to be demanding its subjects to be working longer in a scrupulous and austere way, it is the same demand that is inflicting suffering on its individuals. It is so much so to the point that it makes one think if the system cares enough about its workers as much as it does about its service, which brings us back to the stoic philosophy of medicine.

Several barriers are noticeable as one walks towards the path of solutions and interventions for this public health issue. Lack of time, confidentiality issues, stigma, costs, academic concerns, fear of being labeled weak, and shuffling work, and fear of an unwanted intervention are few barriers that have been identified in seeking help, among medical students and resident doctors.^[10] Another major challenge in individual-level interventions is the poor awareness of the staffs to the modalities of seeking help.^[11] Randomized controlled trials focused in stopping stigma by teaching doctors about distress have been successful in significantly reducing burnout and anxiety among doctors.^[7] Key components of positive mental health, such as general coping and personal growth autonomy, have also been noted to be particularly important in the workplace.^[12] While individual interventions such as improving individual resilience and teaching relaxation techniques have been found to reduce burnout, they were more effective in combination with organizational interventions, and the latter was found to have long-lasting positive effects. A systems-level approach of fostering a supportive organizational culture; eliminating harassment and perfectionist expectations; integrating doctors’ well-being to professionalism and patient care and recognizing the same as a missing quality indicator; and an internationally coordinated research effort has been strongly advocated to address this global public health issue.^[13]

Mental Health Needs of Health Care Staff in Coronavirus Disease 2019

Health-care facilities evolve from cisterns of stress and psychological trauma to reservoirs of the same amidst pandemics. The major challenge of the health-care system during a pandemic is that it cannot manage the pandemic without any collateral damage to itself. The health-care workers face a tremendous amount of stress through a high and persistent risk of exposure, prolonged case shifts, separation from family, experiencing workforce quarantine, moral injury, scarce supplies, the uncertainty of the event, a sudden surge in death count, death of colleagues, lack of reinforcements, and fatigue and burnout. The loneliness and increased burden of work may result in anger, which might lead to inter-personal issues with family members and sometimes assaults in the work setting, causing further distress.^[14] These



reservoirs of stress are fertile grounds for psychiatric disorders, the incidence of which might further impair the workforce over and above the impairment caused by the unattended distress and “burnout” in the community. Chronic levels of distress contribute to unhealthy coping methods, resulting in poor health and decreased efficiency.^[15] Those working in isolation caring for critically ill patients are particularly more vulnerable, with about 20% of them reporting posttraumatic symptoms during the SARS outbreak.^[16] A study among health-care workers in hospitals with fever clinics or wards for COVID-19 reported 50.4%, 44.6%, 34.0%, and 71.5% of symptoms of depression, anxiety, insomnia, and distress in the participants, respectively. Women, frontline workers, and nurses were found to be the most affected.^[17]

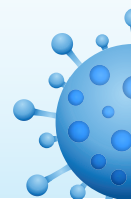
With an extra 1.7 million mental health workers needed in the low and middle income countries and about 40%–60% of patients with severe mental disorders not receiving adequate care even in routine circumstances, this parallel pandemic of psychological issues stands as a gargantuan threat to the whole of health care. Hence, organization of the resources will be the need of the hour. There are international guidelines to address the mental health and psychosocial support needs in humanitarian aid workers during emergency situations. However, they are not being successfully implemented.^[15] Even when institute specific plans are made and implemented, these have not been without any obstacles. An institute in China attending to the COVID-19 pandemic observed that the medical staffs were reluctant to participate in their interventions as they felt the interventions were not in concordance with their needs. They were worried about carrying the infection to their families more than them being infected. They perceived that they were not adequately trained in dealing with uncooperative patients and psychological issues expressed by the patients. They were feeling incapable when faced with critically ill patients. Furthermore, they were disappointed with the shortage of supplies of protective equipment and expressed that they needed more rest.^[18] In the preparation for a pandemic, a few viable interventions that might reduce the psychological burden significantly are clear guidelines and expectations, communication, concern for the well-being of service providers, logistical support, peer and spiritual support, and psychological support.^[16] The key actions advised by the inter-agency standing committee in emergency situations also almost resonates with these interventions, which includes a concrete plan to protect and promote staff well-being; prepare staff for their roles; facilitate a healthy working environment; address potential work-related stressors; ensure access to healthcare and psychosocial support; provide special support to staff who are traumatized; and make support available after the mission.^[19]

Fostering individual and organizational resilience have also been found to play an important role in preparing for the pandemic. Folkman and Greer’s framework for maintaining psychological well-being and psychological first aid have been considered to be apt in promoting individual resilience during pandemic situations. Organizational justice, which includes relational and decisional justice, is one of the factors attributed to the development of organizational resilience.^[20]

Conclusion

“Emergencies erode normally protective supports, increase the risk of diverse problems and tend to amplify pre-existing problems of social injustice and inequality.”^[21] Therefore, it is imperative to understand the preexisting supports, needs, and barriers in the mental health-care of the staffs, clearly. Prioritization, organization, and customization are the pillars that translate the scarce mental health services into a functional capacity, paving way for all these interventions. It is more effective to evaluate and improvise existing interventions rather than developing new ones. Recent researches have re-emphasized on the importance of organizational interventions as much as individual interventions, especially in a pandemic where a sustained response is necessary.^[9,13,14] Interventions made should emphasize working relationship and belongingness and arouse confidence among the staffs in the interventions.^[5] Opportunities for staff feedback and integration of individual perspectives with organizational structure should be made, to not only improve the efficacy of the interventions but also to stay relevant to the community.^[15] Avoidance is a core symptom of trauma and supervisors or peer supports should actively reach out, to protect the mental health of the workers.^[14] As mentioned before, they clearly have an increased prevalence of various issues like burnout, absenteeism, depression, health anxiety, and suicidality. Last but not the least, the well-being of the workforce should be of the utmost concern, for there is “no health without a healthy workforce.”^[13] COVID-19 has emerged as a global health threat. The health-care workers being on the frontline fighting the infection evidently has unique psychosocial vulnerabilities. The solutions include preparedness, awareness, and planning. As much it is important to plan meticulously, it is also vital not to plan in an undue manner, for the end of this crisis will not be the end of distress or suffering and the summons of the clinical workforce are perpetual and not transitory. To best put it in the old words of Keller, “Although the world is full of suffering, it is also full of the overcoming of it.”^[22]

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Conflicts of interest

There are no conflicts of interest.

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ACCELERATED RESEARCH

Psychological impact of COVID-19 lockdown: An online survey from India

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ABSTRACT

Background: The COVID-19 pandemic has led to a complete shut-down of the entire world and almost all the countries are presently in a “lockdown” mode. While the lockdown strategy is an essential step to curb the exponential rise of COVID-19 cases, the impact of the same on mental health is not well known.

Aim: This study aimed to evaluate the psychological impact of lockdown due to COVID-19 pandemic on the general public with an objective to assess the prevalence of depression, anxiety, perceived stress, well-being, and other psychological issues.

Materials and Methods: It was an online survey conducted under the aegis of the Indian Psychiatry Society. Using the Survey Monkey platform, a survey link was circulated using the Whatsapp. The survey questionnaire included perceived stress scale, Patient Health Questionnaire-9, Generalized Anxiety Disorder-7, Warwick-Edinburgh Mental Well-being Scale to assess perceived stress, anxiety, depression, and mental well-being, respectively. The survey link was circulated starting from April 6, 2020 and was closed on April 24, 2020.

Results: During the survey, a total of 1871 responses were collected, of which 1685 (90.05%) responses were analyzed. About two-fifth (38.2%) had anxiety and 10.5% of the participants had depression. Overall, 40.5% of the participants

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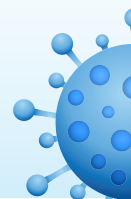
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had either anxiety or depression. Moderate level of stress was reported by about three-fourth (74.1%) of the participants and 71.7% reported poor well-being.

Conclusions: The present survey suggests that more than two-fifths of the people are experiencing common mental disorders, due to lockdown and the prevailing COVID-19 pandemic. This finding suggests that there is a need for expanding mental health services to everyone in the society during this pandemic situation.

Key words: Anxiety, COVID-19, Depression, Stress

INTRODUCTION

One of the extreme challenges for survival is facing a pandemic of an infectious disease of the COVID-19 type.^[1] The World Health Organization (WHO) declared COVID-19 as a pandemic on March 11, 2020 and as on March 24, 2020, more than 3.5 lakhs cases have been confirmed and more than 14,000 deaths have been reported, affecting 190 countries worldwide (WHO website dated March 24, 2020 at 21:00 pm Indian standard time)^[2] and these figures have exponentially increased to about 27.19 lakhs cases with about 1.9 lakhs deaths in 1 month time (WHO website date April 25, 2020 at 05:30 pm Indian standard time).^[3]

To tackle the rapid rise of cases in India and to curb the community spread, national level “lockdown” was declared starting from midnight of March 25, 2020 initially for 21 days, which was later extended up to May 3, 2020, with assurance that the basic needs of the general public will be taken care of.^[4]

“Lockdown” is an emergency protocol that prevents public from moving from one area to the other. Complete lockdown further means that persons should stay where they are currently and no entry/exit movements would be allowed further. It can be both a preventive and an emergency strategy in order to save the lives of the vulnerable or at-risk persons. In this scenario, all educational institutions, shopping arcades, factories, offices, local markets, transport vehicles, airports, railways, metros, and buses are completely shut down except hospitals, police stations, emergency services like fire station, petrol pumps, etc., and groceries. In recent times, lockdown had been very well documented during September 9/11 attacks in New York (3 day lockdown) and during riots in several countries. As social distancing is an important public health solution to tackle the spread of COVID-19, many affected countries such as China, Italy, the United States, France, and Malaysia have also enforced lockdowns of public spaces effectively.^[5,6]

While lockdown can be a significant and effective strategy of social distancing to tackle the increasing spread of the highly infectious COVID-19 virus, at the same time, it can have some degree of psychological impact on the

public. It is well known that quarantine/isolation for any cause and in the context of a pandemic (Severe Acute Respiratory distress Syndrome, 2003) has been associated with significant mental health problems ranging from anxiety, fear, depressive symptoms, sense of loneliness, sleep disturbances, anger, etc., in the immediate few days of isolation, and later with symptoms of posttraumatic stress disorder and depression after discharge from the hospital.^[7] However, the psychological impact of lockdown on the general public has not been studied yet. Man being a social animal, such restrictions on free movements can lead to anger, frustration, loneliness and depressive symptoms. There can be fear/apprehension among the public related to supply of basic amenities like groceries and milk supplies, medicines, care of previously sick persons in the family due to other medical causes, elderly persons staying alone, restriction of free movements, having a prevailing sense of being imprisoned in one's own house or “being in house arrest,” etc., Moreover, lockdown can lead to a “panic” mode of stockpiling of essential commodities without maintaining social distancing as advised by the government.^[8]

Lockdown can have different effects on different age groups. It may be difficult to engage the children at home throughout the day. This can be a source of stress to the parents. Similarly, due to the vulnerability of elderly for COVID-19 infections, others would avoid to meet the elderly, which can be a major source of distress, both for the elderly and their family members.

Unlike western countries, Indians are thought to be more social and have more social networks, engage in several religious festivals, and get-togethers across the year.^[9] This can be attributed to India's diverse culture and traditions.^[10] In this regard, a complete lockdown can have a downgrading effect on the psyche of the general public. It can also have a long lasting effect on the economy, farming and daily wage earners of the country. While it is an utmost necessary step to be taken at present to combat the COVID-19 infection, steps should be taken to mitigate the possible psychological impact of lockdown in the general public.

Moreover, recent reports suggest that the government's sudden enforcement of lockdown has created many hurdles to the economically disadvantaged populations



as evident from the mass exodus of migrant workers and concerns about starvation among people in slum areas.^[4] A recently published sentiment analysis of lockdown through twitter (analysis as evident from tweets extracted from 25th to 28th March 2020; $n = 24,000$ tweets) reported that the prominent sentiment was positive and trust on the government; further, many respondents reported sadness and worries about the problems of daily wage laborers during lockdown.^[11] However, no national-wide data on the psychological impact of lockdown in India are available. Therefore, the current study was planned with an aim to evaluate the psychological impact of lockdown on the general public with an objective to assess the fear, perceived stress, and psychological problems related to lockdown due to COVID-19 infection in India.

MATERIALS AND METHODS

It was an online survey conducted under the aegis of Research, Education and Training sub-Committee of Indian Psychiatric Society. Using the Survey Monkey platform, a survey link was circulated using the Whatsapp. The survey questionnaire was translated into 11 Indian languages (Hindi, Odia, Bengali, Marathi, Tamil, Telugu, Kannada, Malayalam, Punjabi, Gujarati, and Urdu) besides being used in English. The link was designed in such a way, that only 1 response can be generated using one device. The survey questionnaire consisted of the following instruments:

Demographics and personal characteristics

A basic information sheet which included information about the subject's age, gender, marital status, educational qualifications, and current work profile.

A questionnaire to evaluate the effect of lockdown on relationship with family members/neighbors/significant others and how lockdown had affected one's emotions, feelings, and behaviors in different aspects of life.

The Warwick-Edinburgh Mental Well-being Scale^[12]

It is 14-item scale covering both hedonic and eudaimonic aspects of mental health including positive affect (feelings of optimism, cheerfulness, and relaxation), satisfying interpersonal relationships and positive functioning (energy, clear thinking, self-acceptance, personal development, competence, and autonomy). It has good content validity and high test-retest reliability.^[12] The total score was determined by adding the score of all the 14 items. A higher score indicates greater positive well-being. A score of ≤ 40 has been reported to indicate high risk for depression.^[13,14]

Patient Health Questionnaire-9

The Patient Health Questionnaire (PHQ) is a self-administered version of the PRIME-MD diagnostic instrument for common

mental disorders.^[15] The PHQ-9 is the depression module, which scores each of the 9 Diagnostic and Statistical Manual-IV criteria as "0" (not at all) to "3" (nearly every day). This questionnaire is found to have excellent reliability and validity, and sensitivity and specificity of 88% for major depression.

Generalized Anxiety Disorder-7 Scale

It is a 7-item anxiety scale with good reliability as well as criterion, construct, factorial, and procedural validity. Cutoff points of 5, 10, and 15 are interpreted as representing mild, moderate, and severe levels of anxiety on the Generalized Anxiety Disorder (GAD)-7.^[16] Increasing scores on the scale are strongly associated with multiple domains of functional impairment. Although GAD and depression symptoms frequently co-occurred, factor analysis confirmed them as distinct dimensions. Moreover, GAD and depression symptoms have differing but independent effects on functional impairment and disability. There is good agreement between self-report and interviewer administered versions of the scale. This study employed self-reported version.

Perceived stress scale

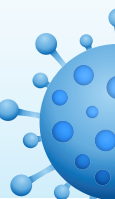
It is a 10-item scale widely used to assess the perception of stress. It is a measure of the degree to which situations in one's life are appraised as stressful. Items were designed to tap how unpredictable, uncontrollable, and overloaded respondents find their lives. The scale also includes a number of direct queries about current levels of experienced stress.^[17] The questions are of a general nature and hence are relatively free of content specific to any subpopulation group. The questions in the perceived stress scale (PSS) ask about feelings and thoughts during the last month. It has adequate psychometric properties.^[18] For this survey, we had reduced the time limit to 15 days.

The survey link was circulated in 12 Indian languages starting from April 6, 2020, i.e. after 10 days of declaration of lockdown, and the survey was closed on April 24, 2020. The link was circulated by the Exponential Non-Discriminative snowballing method, people receiving the message were requested to complete the survey and then forward the link to their close contacts in various Whatsapp group, Facebook, and Twitter platforms.

The study was approved by the Ethics Committee of the Indian Psychiatric Society, for the research purposes. Descriptive statistics were applied and the data collected was analyzed using SPSS 20.0 version. Pearson's co-relation co-efficient and Spearman's co-relation co-efficient were used to find the association between different variables.

RESULTS

During the survey, a total of 1871 responses were collected of which 1685 (90.05%) responses were analyzed (which were complete in all aspects, except for information on age available



for 1653 participants only). The median duration of completing the survey was 12th day of the lockdown period (mean: 12.84, standard deviation [SD]:2.04); Range: 11th day to 21st day).

The mean age of the participants (1653 responses) was 41.26 (SD: 13.67) years. About three-fifths of the participants (63.7%) were male, about three-fourth were married (72.6%), three-fifth had completed postgraduation (61.8%), majority were employed (self-employed/employed in government sector or private sector) (78.9%). With regard to profession, slightly less than half of the responders (47.1%) were health-care workers (HCWs). In terms of current level of working during lockdown, about one-fifth of responders (21.1%) were not going to work and rest were either working from home for few hours (17.7%) or for usual hours (8.5%) and some were going for work for few hours (16.6%) [Table 1].

Perceived stress, anxiety, depression, and mental well-being during lockdown

The mean PSS score for the study participants was 16.56 (SD - 5.60) and about 70% of the participants reported moderate level of stress and one-fourth reported mild stress after the onset of the lockdown period. The mean GAD-7 score was 4.14 (SD - 4.84) and about one-fourth participants (23.7%) fell into the category of moderate symptom severity. The mean PHQ-9 score of the participants was 3.63 (SD - 4.81) with majority of the participants reported "no or minimal depressive symptoms" but 18.5% reported mild depressive symptoms and a small proportion of the participants reported moderate (5.8%) and moderate-to-severe depression (3.0%). The mean Warwick-Edinburgh Mental Well-being Scale (WEMWBS) score for the study participants was 43.92 (SD - 8.79). When the cut off for high risk of depression (i.e., score ≤ 40) was applied, about 70% of the participants (71.7%) had score ≤ 40 , suggesting poor mental well-being [Table 2].

Comparison of anxiety, depression, stress, and well-being of health-care workers and non health-care workers

As about a half of the responders were HCWs (47.1%), we compared the data of the HCWs and those who were not HCWs. Compared to HCWs, non-HCWs had significantly higher mean PHQ-9 score, higher proportion of them had depression, if mild depression is taken into account, and lower proportion of them had poor mental well-being. Details are mentioned in Table 2.

Effect of lockdown on relationships

Nearly half of the responders reported marked improvement in their relationships with their spouse/partner (47.4%), children (44.2%), and with parents (47.3%) after the beginning of lockdown period. Further, about three-fifth of the participants reported marked improvement in their relationship with their neighbors (61.8%) and office colleagues (59.6%) during the lockdown period [Table 3].

Table 1: Sociodemographic profile (n=1685)

Variables	Frequency (%)/ mean (SD)
Age (n=1653)	41.26 (13.67); range: 14-87
Sex	
Male	1074 (63.7)
Female	611 (36.3)
Marital status	
Married	1223 (72.6)
Unmarried	401 (23.8)
Widowed	16 (0.9)
Divorced/separated	22 (1.3)
Others	11 (0.7)
Details not available	12 (0.7)
Educational qualification	
Less than matriculation	7 (0.4)
Matriculation	21 (1.2)
Intermediate/+2	57 (3.4)
Graduate	539 (32)
Postgraduate	1041 (61.8)
Diploma	20 (1.2)
Occupation	
Self-employed	410 (24.3)
Employed in government sector	413 (24.5)
Employed in private sector	511 (30.3)
Home maker	86 (5.1)
Unemployed	77 (4.6)
Retired	99 (5.9)
Student	83 (4.9)
Others	6 (0.4)
Profession	
Doctor	764 (45.3)
Nurse	30 (1.8)
Engineer	117 (6.9)
Lawyer	40 (2.4)
Bureaucrat	38 (2.3)
Businessman	103 (6.1)
Business management consultant	65 (3.9)
Home maker	87 (5.2)
Politician	4 (0.2)
IT professional	30 (1.8)
Student	10 (0.6)
Retired	5 (0.3)
Teaching	64 (3.8)
Others	328 (19.5)
Level of working	
Not going to work	490 (21.1)
Working from home for few hours	299 (17.7)
Working from home for usual hours	143 (8.5)
Working from home for more than usual hours	92 (5.5)
Going to work for few hours	279 (16.6)
Going to work as usual	160 (9.5)
Going to work and doing work, more than usual hours	67 (4.0)
Others	147 (8.7)
Details not available	8 (0.5)

SD – Standard deviation

Effect of lockdown on one's emotions, feelings and various aspects of life

The effect of lockdown on one's emotions, feelings, and various aspects of life was evaluated on likert scale with the following options "no change," "slightly increased," "markedly increased," "slightly decreased," "markedly decreased," and "can't



Table 2: Perceived stress, anxiety, depression, and mental well-being during lockdown and comparison of these variables between health care workers and nonhealth-care workers

Variables	Whole sample (n=1685) Mean (SD)/frequency (%)	Non-HCWs (n=891), n (%)	HCWs (n=794), n (%)	t-test/Mann-Whitney U-value/Chi-square test (P)
Mean PSS-10 score, range (median)	16.56 (5.60), 0-37 (17.0)	16.61 (5.40)	16.51 (5.81)	0.356 (0.722)
Severity of stress				
Low stress (0-13)	437 (25.9)	225 (25.3)	212 (26.7)	1.351 (0.509)
Moderate stress (14-26)	1181 (70.1)	634 (71.2)	547 (68.9)	
Severe stress (>27)	67 (4.0)	32 (3.6)	35 (4.4)	
Mean GAD-7 score, range (median)	4.41 (4.84), 0-21 (3.0)	4.61 (4.93)	4.19 (4.73)	U=334575.0 (0.052)
Severity of anxiety				
Normal (0-4)	1042 (61.8)	535 (60.0)	507 (63.9)	5.612 (0.132)
Mild (5-9)	400 (23.7)	216 (24.2)	184 (23.2)	
Moderate (10-14)	147 (8.7)	79 (8.9)	68 (8.6)	
Severe (≥15)	96 (5.7)	61 (6.8)	35 (4.4)	
Mean PHQ-9 score, range (median)	3.62 (4.81), 0-27 (2.0)	3.90 (4.93)	3.33 (4.66)	U=328912.5 (0.011)*
Severity of depression				
Minimal (1-4)	1197 (71.0)	613 (68.8)	584 (73.6)	10.275 (0.036)*
Mild (5-9)	311 (18.5)	173 (19.4)	138 (17.4)	
Moderate (10-14)	98 (5.8)	55 (6.2)	43 (5.4)	
Moderate severe (15-19)	50 (3.0)	36 (4.0)	14 (1.8)	
Severe (≥20)	29 (1.7)	14 (1.6)	15 (1.9)	
Mean mental well-being score, range (median)	43.9 (8.8), 14-56 (45.0)	43.42 (8.94)	44.48 (8.60)	-2.465 (0.014)*
Number of participants with WEMWBS score ≤40	1208 (71.7)	617 (69.2)	591 (74.4)	5.562 (0.018)*
Overall prevalence				
Percentage of responders reporting GAD score ≥5	643 (38.16)	356 (40.0)	287 (36.1)	2.581 (0.108)
Percentage of responders reporting PHQ-9 score ≥10	177 (10.5)	105 (11.8)	72 (9.1)	3.296 (0.069)
Percentage of responders reporting only GAD score ≥5 but PHQ-9 <10	506 (30.0)	275 (30.9)	231 (29.1)	0.627 (0.429)
Percentage of responders reporting PHQ-9 score >10 but GAD-7 <5	40 (2.4)	24 (2.7)	16 (2.0)	0.834 (0.361)
Percentage of responders reporting both GAD score ≥5 + PHQ-9 score >10	137 (8.1)	81 (9.1)	56 (7.1)	2.335 (0.127)

*p<0.05. SD – Standard deviation; HCWs – Health-care workers; PSS – Perceived stress scale; GAD – Generalized anxiety disorder; WEMWBS – Warwick-Edinburgh Mental Well-being Scale; PHQ – Patient health questionnaire

say” [Table 3]. In most of the areas, majority of the participants reported no change, yet about one-third of the study participants reported slight worsening (increase) of negative emotions such as sadness (30.7%), anxiety (36%), irritability (32.2%), frustration (32.3%), and fear and apprehension (33.8%). About one-fifth of the participants reported increase in feelings of loneliness (21.3%) and fear of death (20.8%). Another 10%–15% of participants reported marked worsening of these negative emotions. Slight increased in social connectedness was reported by 18.7% and marked increase in use of social media was reported by about one-third (35.1%) of the participants.

Regarding somatic symptoms, sleep, appetite and fatigue, there was slight worsening (increase) in these features in about one-fifths of responders [Table 4]. About one-third to about three-fifth of the participants reported slight or marked increase in activities such as exercise, faith in God, watching movies, internet gaming, playing indoor games, sexual activity, reading books, painting, cooking, and cleaning [Table 4]. There was marked reduction in shopping and spending in a significant proportion of the participants.

Stress due to COVID-19 infection

More than one-third of the participants (38.5%) had fear of getting infected with COVID-19 infection, always wore masks and protective equipment even in open spaces (37.9%),

invested majority of their time reading or watching COVID-related facts (38.5%), and had anxiety when dealing with febrile patients/family members (38.8%). One-fourth of the responders reported feelings of pessimism or hopelessness (23.3%), feeling detached from others (24.0%), feeling exhausted (24.3%) and had trouble falling asleep/frequent awakenings (27.7%). Further, about one-fifth of the responders reported having avoided COVID-19-related information (20.8%), had anxiety/palpitations (19.3%) and had deterioration in the work performance (19.3%). About 30% of the participants reported of feeling irritated and angry on self or others, and with the uncertainty about frequent modifications of infection control procedures (32.0%). About one-fourth of the participants also reported fear of going out of home, because of fear of infecting family members. Only 10% of the responders reported experiencing stigma and rejection in neighborhood because of working in the hospital/being kept in quarantined facility, and a similar proportion was reluctant to work or considered resignation after discharge [Table 5].

Relationship between anxiety, stress, sadness, mental well-being, and duration of lockdown period

Higher level of stress, depression, and anxiety correlated positively with each other and negatively with the well-being. It was further seen that there was significant

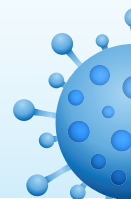


Table 3: Effect of lockdown on relationships

Variables	Frequency (%)				
	No change	Slightly improved	Marked improved	Slightly worsened	Markedly worsened
Relationship with family members	661 (39.2)	563 (33.4)	304 (18.0)	122 (7.2)	35 (2.1)
Relationship with your spouse/partner	277 (16.4)	476 (28.2)	799 (47.4)	121 (7.2)	12 (0.7)
Relationship with children	387 (23.0)	477 (28.3)	744 (44.2)	56 (3.3)	21 (1.2)
Relationship with parents	274 (16.3)	544 (32.3)	797 (47.3)	57 (3.4)	13 (0.8)
Relationship with your neighbors	123 (7.3)	424 (25.2)	1042 (61.8)	82 (4.9)	14 (0.8)
Relationship with your office colleagues	123 (7.3)	411 (24.4)	1004 (59.6)	127 (7.5)	20 (1.2)

Table 4: Effect of lockdown on one's emotions, feelings, and various aspects of life

	Frequency (%)					
	No change	Slightly increased	Markedly increased	Slightly decreased	Markedly decreased	Cannot say
Sadness	613 (36.4)	518 (30.7)	181 (10.7)	175 (10.4)	96 (5.7)	102 (6.1)
Anxiety	509 (30.2)	606 (36.0)	218 (12.9)	203 (12.0)	98 (5.8)	51 (3.0)
Irritability	595 (35.3)	545 (32.3)	213 (12.6)	184 (10.9)	97 (5.8)	51 (3.0)
Frustration	59 (35.2)	545 (32.3)	231 (13.7)	146 (8.7)	101 (6.0)	69 (4.1)
Loneliness	709 (42.1)	359 (21.3)	248 (14.7)	160 (9.5)	127 (7.5)	82 (4.9)
Social connectedness	579 (34.4)	315 (18.7)	167 (9.9)	295 (17.7)	268 (15.9)	61 (3.6)
Social isolation	527 (31.3)	378 (22.4)	385 (22.8)	176 (10.4)	139 (8.2)	80 (4.7)
Fear and apprehension	575 (34.1)	569 (33.8)	222 (13.2)	165 (9.8)	91 (5.4)	63 (3.7)
Fear of death	893 (53.0)	351 (20.8)	176 (10.4)	73 (4.3)	60 (3.6)	132 (7.8)
Sleep	652 (38.7)	367 (21.8)	225 (13.4)	285 (16.9)	104 (6.2)	52 (3.1)
Appetite	880 (47.5)	378 (22.4)	182 (10.8)	261 (15.5)	39 (2.3)	25 (1.5)
Pain	1103 (65.5)	190 (11.3)	158 (9.4)	97 (5.8)	37 (2.2)	100 (5.9)
Fatigue	836 (49.6)	372 (22.1)	162 (9.6)	157 (9.3)	98 (5.8)	60 (3.6)
Exercise	569 (33.8)	376 (22.3)	193 (11.5)	247 (14.7)	248 (14.7)	52 (3.1)
Substance use, including alcohol	1009 (59.9)	173 (10.3)	125 (7.4)	78 (4.6)	157 (9.3)	143 (8.5)
Use of social media	323 (19.2)	489 (29.0)	591 (35.1)	140 (8.3)	108 (6.4)	34 (2.0)
Faith in god	844 (50.1)	308 (18.3)	358 (21.2)	74 (4.4)	67 (4.0)	34 (2.0)
Watching movies	515 (30.6)	534 (31.7)	436 (25.9)	107 (6.4)	58 (3.4)	35 (2.1)
Internet gaming	913 (54.2)	311 (18.5)	269 (16.0)	57 (3.4)	50 (3.0)	85 (5.0)
Playing indoor games (without using the gadgets)	813 (48.2)	417 (24.7)	227 (13.5)	69 (4.1)	54 (3.2)	105 (6.2)
Sexual activity	945 (56.1)	241 (14.3)	165 (9.8)	109 (6.5)	112 (6.6)	113 (6.7)
Shopping	477 (28.3)	196 (11.6)	61 (3.6)	188 (11.2)	707 (42.0)	56 (3.3)
Spending	377 (22.4)	160 (9.5)	60 (3.6)	370 (22.0)	681 (40.4)	37 (2.2)
Reading books	599 (35.5)	529 (31.4)	264 (15.7)	133 (7.9)	114 (6.8)	46 (2.7)
Drawing/painting	1018 (60.4)	252 (15.0)	211 (12.5)	23 (1.4)	33 (2.0)	148 (8.8)
Cooking	596 (35.4)	461 (27.4)	449 (26.6)	72 (4.3)	42 (2.5)	65 (3.9)
Cleaning	380 (22.6)	603 (35.8)	505 (30.0)	118 (7.0)	52 (3.1)	27 (1.6)

positive correlation between the perceived stress and severity of depression with the duration of lockdown period [Table 6].

DISCUSSION

With no alternative ways to escape from the COVID pandemic, almost all the countries have adopted the lockdown strategy as a potentially effective strategy to fight against the COVID-19. India was also quite early in its response to impose lockdown, as early as, within 2 weeks of declaration of COVID-19 as a pandemic, i.e., March 25 (WHO declared COVID-19 to be pandemic on March 11, 2020). Even though this strategy is an important measure to tackle the exponential rise of COVID cases, it has widespread impact on the economy, psyche, and daily living of the public. In this regard, the current study was

planned to evaluate the psychological impact of lockdown on the general public with an objective to assess the fear, perceived stress, and psychological problems related to lockdown due to COVID-19 pandemic in India.

Some of the strengths of the survey were that it was translated into 11 Indian languages along with English. Further, the survey questionnaires also included the evaluation of impact of lockdown on relationship with significant others and how the lockdown affected one's emotions and feelings. Besides, the use of some self-designed questionnaire, the survey also included well-validated scales usually used for community surveys such as GAD-7, PHQ-9, PSS, and WEMWBS (for well-being).^[19-22]

The prevalence rates of depressive symptoms and anxiety symptoms based on cut off scores of PHQ-9 and GAD-7



Table 5: Stress due to coronavirus disease-19 infection

Variable	Frequency (%)		
	Yes	No	Not applicable
Feared getting infected more severely with corona virus	648 (38.5)	900 (53.4)	137 (8.1)
Feeling pessimism or hopelessness	393 (23.3)	1172 (69.6)	120 (7.1)
Absence of emotional response - feeling numb/no happiness or sadness	324 (19.2)	1162 (69.0)	199 (11.8)
Feeling exhausted	409 (24.3)	1119 (66.4)	157 (9.3)
Reduced awareness or being in a daze/feeling confused/unable to think clearly	311 (18.5)	1249 (74.1)	125 (7.4)
Feeling detached from others	404 (24.0)	1155 (68.5)	126 (7.5)
Always wore mask and protective equipment even in open spaces	639 (37.9)	940 (55.8)	106 (6.3)
Invest majority of free time reading or watching corona virus-related information	649 (38.5)	968 (57.4)	68 (4.0)
Anxiety when dealing with febrile patients/family members	653 (38.8)	781 (46.4)	251 (14.9)
Avoided corona virus related information	350 (20.8)	1186 (70.4)	149 (8.8)
Had anxiety/palpitations	325 (19.3)	1284 (76.2)	76 (4.5)
Felt irritated/angry on self or others	526 (31.2)	1087 (64.5)	72 (4.3)
Had trouble falling asleep/frequent awakening	467 (27.7)	1156 (68.6)	62 (3.7)
Uncertainty about frequent modification of infection control procedures	540 (32.0)	1001 (59.4)	144 (8.5)
Poor concentration and felt indecisive	409 (24.3)	1156 (68.6)	120 (7.1)
Afraid to go to home because of fear of infecting family	402 (23.9)	1013 (60.1)	270 (16.0)
Deteriorating work performance	325 (19.3)	1103 (65.5)	257 (15.3)
Reluctant to work or consider resignation after discharge	163 (9.7)	1109 (65.8)	413 (24.5)
Depressed mood - feeling low most part of the day	276 (16.4)	1238 (73.5)	171 (10.1)
Stigmatization and rejection in neighborhood because of hospital work/being kept in quarantined facility	173 (10.3)	1069 (63.4)	443 (26.3)

Table 6: The association between day of response of lockdown with reported perceived stress, sadness, anxiety, and mental well-being during lockdown

Variables	Total PSS score, <i>r</i> (<i>P</i>)	Total GAD score, <i>r</i> (<i>P</i>) [#]	Total PHQ-9 score, <i>r</i> (<i>P</i>) [#]	Total well-being score, <i>r</i> (<i>P</i>)
Total GAD score	0.528 [#] (<0.001)***			
Total PHQ-9 score	0.321 [#] (<0.001)***	0.448 [#] (<0.001)***		
Total well-being score	-0.469 (<0.001)***	-0.481 [#] (<0.001)***	-0.391 [#] (<0.001)***	
Days of response of lockdown	0.062 (0.011)*	0.031 (0.197)	0.053 (0.029)*	-0.006 (0.810)

*Spearman correlation coefficient. GAD – Generalized anxiety disorder; PSS – Perceived stress scale; PHQ – Patient health questionnaire

were 10.5% and 38.2%, respectively. A comparison of our findings with those of the National Mental Health Survey (NMHS)^[23] shows that psychiatric morbidity of common mental illnesses may be higher in our study (40.5%) than the estimated prevalence of 10% in the NMHS.^[24] It can be argued that the significantly higher prevalence of psychiatric morbidity in the present study compared to the NMHS may be due to the use of different sampling methods and use screening instruments (whereas NMHS employed Mini International Neuropsychiatric Interview), but the screening instruments have been found to have high sensitivity and specificity against the diagnosis made by mental health professionals.^[25,26] Thus, the difference in the prevalence rates cannot be completely attributed to the difference in the methodology. Hence, it is possible that lockdown period has led to a significant increase in the mental morbidity of mostly milder intensity in the general public. A web-based survey from China, which evaluated the psychological problems among the Chinese people (*n* = 1074) close to the COVID-19 epidemic peak and subsequent lockdown, reported anxiety (mild/moderate/severe as evident from Beck's Anxiety Inventory) in 29% of participants and depression (mild/moderate/severe as evident from Beck's Depression Inventory) in 37% of participants, and poor mental well-being in one-third of its participants.^[27] The prevalence

of anxiety found in the present study is comparable to the previous study from China, but the prevalence rate of depression is lower. The lower rate of depression in the present survey, compared to the study from China, could be due to the difference in the timing of the study, in terms of the number of COVID-19 cases in the country. The present survey was done at the beginning of the epidemic in the country, compared to the survey from China, which was done, close to the peak of epidemic. The association of higher prevalence of depression, close to the peak of the epidemic, can be understood by the fact that the COVID-19 was associated with higher mortality rate in China, compared to current statistics from India. In the present study too, the association of depression and longer duration of lockdown was seen, which could be an indicator of increase in prevalence of depression with an increase in the number of cases of COVID-19 infection. The prevalence of mild-to-moderate anxiety and depression, in 40.5% of the participants in the present survey indicate that the pandemic and the lockdown is having a big toll on the mental health of people in the country and suggest an urgent need to address the same. The Indian Psychiatric Society took a lead in this direction, in the early stages of the lockdown, by providing free mental health aid to the people desirous of seeking mental health care.



In the present survey, 47.1% of the participants were HCWs and when the prevalence of psychiatric morbidity was compared between the HCWs, when the mild depression (i.e., PHQ-9 score of 5-9) was also included as an indicator of depression. However, when the cut-off of ≥ 10 was used for depression, there was no significant difference between the 2 groups. and non-HCWs, it was seen that the prevalence of depression to be significantly higher among the non-HCWs. Existing literature on the mental health problems faced by the HCWs in China during the COVID-19 crisis suggests a significant proportion of HCWs (36.9%) suffered from subthreshold mental health disturbances (as assessed by PHQ-9, GAD-7, Insomnia Severity Index)^[28] and about 22.4%–50% of HCWs reported experiencing depression, anxiety, significant distress and insomnia.^[29] Our findings are comparable to these studies among HCWs, if mild anxiety and mild depression are taken into account.

In the present study, in general, majority of the participants reported positive impact of the lockdown on the relationship dimension in terms of relationship with parents, children, spouse, colleagues, and neighbors. The improved relationship could be attributed to the availability of more free time, less work pressure and possible fulfillment of long desired free time. Findings of the present study are supported by many available websites/blogs, which have reported positive aspects of lockdown such as improvement in air quality/healing of nature,^[30] making people realize value of re-connecting with families^[31] and improvement in love/dating and family relationships.^[32] However, the improved relationship dimensions could also be attributed to the fact that, when everyone is fighting a common enemy, the interpersonal relationship issues are forgotten, which is possibly reflected as improved relationships.^[33,34] Another explanation for the improved relationship could be a fear of death, which often makes people perceive themselves as weak, and hence, have less initiative to fight with others.^[35]

However, despite improvement in the interpersonal dimension, there was increase in the prevalence of negative emotions such as sadness, loneliness, anxiety, frustration, and fear and apprehension in about one-third to nearly half of the participants. These findings again support the possible increase in the prevalence of depression and anxiety, in the wake of the pandemic. When asked about the COVID-19 infection *per se*, about one-fourth to one-third of the participants reported presence of symptoms related to possible COVID-19 infection to be stressful. Some of the other reported areas for which a significant proportion of participants reported significant stress were fear of getting infected with COVID-19 infection, always wore masks and protective equipment even in open spaces, invested majority of their time reading or watching COVID related facts, had anxiety when dealing with febrile patients/family members, feelings of pessimism or hopelessness, feeling detached from others, feeling exhausted and had trouble falling

asleep/frequent awakenings, avoiding COVID-19-related information, having anxiety/palpitations, deterioration in the work performance and some experiencing stigma and rejection due to their profession related to HCWs or due to being under quarantine. All these findings reflect the fear of infection of contracting COVID-19. While fear of contracting COVID-19 can be considered as justified, considering the worldwide mortality and infection rates, but these could also be attributed to the issues such as media hype and prevailing myths related to COVID-19 infection.

This survey has certain limitations. Despite attempts to circulate widely in all possible social media platforms, wider participation was expected. Accordingly, it can be said that the response rate for the survey was low. About half of the participants were doctors, which suggest that the survey did not have the desired snowballing effect, as much as it was expected. A majority of the participants were postgraduates, which was possibly again influenced by the higher proportion of participants being doctors. The survey was limited to those, who had access to a smart phone device and it can be said that the study participants may not be representative of people from various strata of the country. However, considering the situation, this was the possible best methodology to reach to the people to understand the psychological impact. These limitations suggest that the findings may not be generalizable to every strata of the society.

CONCLUSIONS

To conclude, the present survey suggests that more than two-fifth of the people are experiencing anxiety and depression, due to lockdown and the prevailing COVID-19 pandemic. This finding suggests that there is a need of expanding the mental health services to everyone in the society during this pandemic situation.

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Conflicts of interest

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Special Article

Emotional Well-being, Mental Health Awareness, and Prevention of Suicide: Covid-19 Pandemic and Digital Psychiatry

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Abstract

Emotional well-being is a state of positive mental health where the individual is able to handle his emotions and all life activities. He understands his emotions, learns, and copes with all the negative situations, achieves, and finds a positive emotional state which finally leads to success. Covid-19 is a disease caused by newly discovered novel corona virus. The outbreak came to light in December 2019 with the emergence of unexplained fever and pneumonia. In the next few months, the disease spread to various countries worldwide and turned into a pandemic. Governments around the world took drastic measures to control the pandemic and safeguard the citizens. Strict isolation, quarantine, and lockdowns were introduced. People were confined to their home for multiple days which led to intense mental stress. Day-to-day activities were disturbed, and people also suffered huge-economic losses. With the reduction in interpersonal contact and social activities, various psychological problems have emerged and suicides are being reported. Health-care personnel went through great stress and sleepless nights in taking care of the Covid-19 patients. In times of these stressful situations, the mental health awareness can play a crucial role. Simple behavior changes and mindfulness can make significant changes toward positive mental health. The maintenance of proper mental hygiene and regular support from mental health-care workers played a significant role in this regard. However, routine personal health care became less accessible to the general public during the pandemic. This has paved the way for the development of digital psychiatry. Thus, we bring out this review to provide an overview of the emotional well-being, mental health awareness of people during lockdown, prevention of suicide, and emergence of digital psychiatry during Covid-19 pandemic.

Keywords: Covid-19, digital psychiatry, emotional, mental health, pandemic

INTRODUCTION

Emotional well-being plays a significant role in maintaining positive mental health. It controls the health-seeking behavior, improves decision-making skill, increases interpersonal communication, and helps recover from stressful situations or illness. Thus, they play a significant role in overall well-being of an individual. However, this psychological aspect called emotion is usually neglected. Covid-19 emerged in the Wuhan province of China in the end of 2019 and over a span of next 4 months, it has spread to majority of the countries around the world. Strict quarantine was implemented, and several countries went in to lockdown to control this unprecedented pandemic. The implementation of quarantine had life-saving benefits, but it also led to many adverse consequences. Social isolation produced incredible stress and led to the

emergence of new psychological challenges.^[1] The diseases such as anxiety, depression, posttraumatic stress, panic attack, obsessive compulsive disorder, and suicides emerged and led to an increase in the chronic cases. Thus, sudden change in the lifestyle of people due to economic constraints and social problems led to serious psychological issues. Health workers also work under immense stress during a pandemic. Thus, regular screening, counseling, and support from mental health

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workers can play an important role in their psychological well-being. Mental health awareness can play a significant role in improving emotional well-being of the people. It involves prevention, identification, treatment, and overall management of mental illness without any kind of judgment or shame. However, health-care system has become less accessible to public during social isolation. With transport services going into shutdown, traveling to tertiary facilities has become impossible to many. Prioritization by the government in concentrating all the health resources and workforce toward controlling Covid-19 has adversely affected the physical and mental health issues.^[2] Thus, in times, of this grave pandemic, digital mental health can improve service delivery. From providing emergency mental health services and treatment to performing suicide risk assessment and counseling its domains are multiple. With its various modes of functioning, telepsychiatry consultants can directly reach the clients at home and provide support.

EMOTIONAL WELL BEING DURING ISOLATION AND LOCKDOWN

Aristotle once said, “Man is a social animal.” He is supposed to live in groups as a family and as a large community. These groups and social living have a deep impact on his mental health and helped maintain psychological integrity. Group cohesiveness has important influence on his mind and behavior, and it makes him fully functional. When this component or part of his life is hampered, it invokes high levels of stress in him and these stressors play an important role in the onset of mental illness.^[3]

Social isolation is defined as inadequate quality and quantity of social relationship with other people in a group or in the community.^[3] It is said to cause a significant negative effect on mental well-being. Taylor *et al.* performed a study during the equine influenza outbreak in Australia^[4] in which the general population showed that extreme high level of nonspecific distress was found in 34% of the general population during the epidemic. Jeong *et al.* studied 1692 participants on the isolation during the middle east respiratory syndrome pandemic of 2015 among whom they found that anxiety and anger were the predominant psychological problems during the isolation.^[5] During the follow-up visit after 6 months of release, there was a significant drop in psychological symptoms. He demonstrated that fear of social isolation, lack of food supplies, reduced social networking activities, and financial losses continued to bother the participants even after the release.^[6]

Loneliness, on the other hand, is a subjective painful emotional state occurring due to reduced social interaction.^[3] It is also associated with poor interpersonal relationship. Quarantine has led to increased chances of loneliness in all groups of people.^[7] One of the initial responses of people to pandemic is that of fear and anxiety which leads to insomnia and panic. Fear of contamination and infection among people has led to the

demonstration of certain ritualistic behaviors. This has, in turn, led to the exaggeration of symptoms of obsessive compulsive disorder in patients, such as repeated hand washing, wearing masks, and use of sanitizers.^[8] Studies have also shown that there is a strong association between loneliness and depression. They have shown that loneliness is associated with depression in both men and women, but later they found that association is stronger for men.^[9] Stravynski and Boyer performed a survey in Quebec and found that there is a positive correlation between loneliness and suicidal ideation. A study also demonstrated that severe distress also increased the frequency of suicidal thoughts.^[10]

The present pandemic has invoked a lot of stress in the general population. A study by Zhang and Ma on the local residents in China showed that 52.1% of the participants felt horrified and apprehensive about the pandemic.^[11] They also showed that up to 77.9% of the study population reported that family support helped them cope well with the situation and thus 53.3% did not feel helpless during the pandemic.

Infodemics play a crucial role in exaggerating the anxiety during isolation and pandemics.^[12] Media frenzy topics such as pandemics go instantly viral and lead to information explosion. Huge amount of opinions and false information are fed into media which creates excessive confusion, uncertainty, and fear among generally public. People staying indoors for many days tend to use electronic devices for many hours in a day. With more and more days of staying indoors usage of electronic media has drastically increased which may lead to Internet addiction.^[12]

The Government in India has banned the sales of alcohol and tobacco products to strictly implement isolation.^[13] With reduced peer support and unavailability of substances, the rate of substance use has reduced. It provided a good opportunity for people who are willing to quit for stopping substance use. Lockdown has led to the rise of alcohol withdrawal state, seizures, and delirium which are difficult to handle in state of isolation.^[14] People on opioid replacement therapy had trouble accessing the health-care center to acquire the regular dose of drugs resulting in a high chance of relapse.^[13]

Factors that affect the mental state of people during pandemic lockdown are:

1. Rumors and false information
2. Lack of education resulting in fear of unknown, unfamiliar, and unexpected
3. Fear of infection
4. Sudden change in the routine activity
5. Restriction of movement with a fear of being trapped and helplessness
6. Reduced interpersonal or emotional support causing boredom, frustration, and loneliness
7. Separation from loved ones
8. Economic problems and shortage of household commodities and medicines
9. Safety of family, especially children and old age.



MENTAL WELL-BEING OF HEALTH-CARE WORKERS

Risk assessment and categorization are the important aspects of all health-care management including mental health services. Health-care workers form the group of population at the highest risk in a pandemic. They work under incredible stress with constant monitoring to avoid getting infected. Fear of getting infected, long periods of quarantine, days of separation from family and loved ones, fear of accidentally infecting their own family, and witnessing death of colleagues and several patients add to their misery.^[15] Worldwide, death of health-care workers has been rising since the beginning of Covid-19 pandemic. With increased exposure of health-care workers to Covid-19 stigma against them have increased. They are subjected to social isolation, and rejection due to their increased contact with Covid cases with the presumption that they may be infective. Violence against doctors also has been reported in certain countries which have added to their misery.

Several studies from the past pandemics show that they cause a significant effect on the mental health of health-care workers. Maunder *et al.* who studied the long-term mental health of health-care workers after severe acute respiratory syndrome (SARS) outbreak in 2003 found that they had significantly higher level of burn out, psychological distress, and posttraumatic distress.^[16] Another study by Chong *et al.*^[17] on health-care workers in Taiwan after SARS outbreak showed that there was increased psychiatric morbidity. Psychiatric morbidity was three times more (75.3%) than in the general population in Taiwan. Hence, the authors rightly termed the incident as a bio disaster.^[17]

Lai *et al.* performed a study on the mental health outcome of health-care workers during Covid-19 pandemic in China.^[18] They showed that there was a high incidence of mental health issues in health-care workers posted in fever clinics and Covid-19 wards. Among the 1257 participants they showed that 50.4% had depressive symptoms, 44.6% had anxiety, 71.5% distress, and 34% suffered from insomnia. Thus, overall around 70% of health-care workers reported psychological distress during the pandemic.

Zhang *et al.* performed another nationwide survey and showed that medical health workers had significantly high psychiatric morbidity.^[19] They showed that health workers had higher prevalence of insomnia, anxiety, depression, somatization, and obsessive compulsive symptoms. Being female, living in rural areas and being at the risk of contact with Covid-19 cases were the most important risk factors for the above mental illness.

Another study by Kang *et al.* on health-care workers during corona outbreak in China had similar results. They examined 994 people and showed that 22.4% suffered moderate psychological disturbances and 6.2% suffered severe psychological disturbances. Among the participants, 50.4% accessed mental health resources through media and significant 17.5% participated in counseling and psychotherapy.^[20]

Diseases such as Covid-19 which emerge without any warning lack clear guidelines for its treatment which can add to the increased stress among medical fraternity.^[21] These diseases make the medical fraternity take unexpected decisions during the treatment which can seriously hurt their moral values and ethics causing severe moral injury.^[22] Experiences from our past clearly show that pandemics cause lasting damage on the mental health of health-care workers.^[16]

Doctors and health-care workers have shown immense courage in handling the pandemic. In spite of acute shortage of personal-protective equipment and medical resources, they have managed to fight the pandemic effectively. The health-care workers due to their medical knowledge are better equipped mentally in handling the pandemic, but they are not invincible. Hence, all mental health workers need good psychological support programs for the intense job.^[23] Most important necessity for the health-care workers to function effectively is the maintenance of good personal health. Good nutrition, quality sleep, maintenance of proper hygiene, and good relaxation are absolutely necessary. Sharing thoughts and experiences with friends can have an important role in reducing stress. Talking to family and emotional support can help them work effectively.

Another important need of the day is to mentally prepare the staff for the management of disasters.^[22] They have to be educated and counseled regarding the decision-making techniques and handling grief. With continuous days of hard work, burnout among health-care professionals is expected. Good leadership and formation of support groups can help in this regard. If the symptoms turn to be pathological, then mental health professional are to be consulted. Continuous monitoring of health workers by mental health professional is very beneficial in this regard. Health-care professionals also need special recognition for their intense hard work. Benefits in the form incentives can act as rewards which will support and motivate them in their fight against disease.

VULNERABLE GROUP

Children and adolescents form a group of vulnerable population during a pandemic. Closure of schools, separation from friends, and loneliness can have a negative influence on mental wellbeing.^[24] School mental health programs and Anganwadi supplementary nutrition programs have been disrupted due to lockdown. Thus, people from low economic strata having difficulty to provide good care and nutrition to the kids make them more vulnerable to the infections.

The patients suffering from chronic mental illness have also felt the effect of Covid-19 pandemic. The process of social isolation and quarantine is known to cause multiple psychological issues in the vulnerable population.^[21] Due to the rule of social isolation and lock down, patients with chronic mental illness had to avoid their routine doctor consultations.^[25] This has also resulted in poor drug compliance and reemergence of certain psychiatric symptoms. More number of beds in



specialized hospitals have to be reserved to manage fever cases during the pandemics which has indirectly resulted in the reduced admission of psychiatric cases.^[25] The presence of psychiatric disability can result in poor self-care, reduced cognitive capacity, difficulty to maintain social distancing, and also failure to consult emergency services when needed. Poor insight also has resulted in late identification of new psychiatric symptoms and delayed consultations during emergencies.

Studies on schizophrenia have shown that fear of the new disease or higher level of predicted fear due to swine flu was associated with increased chance of willingness to adopt protective measures.^[26] This correlation was only effective as long as the patient was calm or less anxious. As the patient became anxious, the perceived threat from the disease dropped and chances of person taking protective measures against disease too dropped. Thus, patients affect plays an important role in how effective safety measures are taken.

PREVENTION OF SUICIDE

Social isolation reason is an important risk factor for suicidal death. It contributes to the high number of deaths in the age group of adolescents and young adults. With the emergence of Covid-19 pandemic and imposition of quarantine social activities of an individual is seriously curtailed resulting in isolation. Several studies have shown that subjective feeling of loneliness is a potential factor associated with suicidal thoughts.^[10] The factor called loneliness is also associated with various psychiatric conditions such as depression, substance abuse, and excessive stress which, in turn, contribute to suicide.

Loss of sense of purpose or sense of belongingness in life has acted as the important factors contributing to loneliness and in turn to suicide. Drastic measures taken by the governments in some countries during pandemic like not to resuscitate terminally ill case of cardiac or other illness which can cause high amount of anxiety among patients. These serious measures taken during the pandemics can easily effect the vulnerable population. Certain personality characteristics, guilt/fear of spreading the illness to family members, and past family history can act as significant contributors which can drive people to take serious decisions like suicide.

Suicide is a condition associated with various risk factors in young adults. Features such as aggression, impulsivity, and poor frustration tolerance can be the factors that increase the likelihood of suicide. Emotional state of a person plays an important role is staying calm. Emotional turmoil of young adolescents, anger, and irritability results in poor interpersonal relationships. The long periods of quarantine also contributes to higher incidents of child abuse, physical, and sexual abuse which, in turn, results in posttraumatic stress, panic, and depression. All the above factors in unison or in combination can drive a person to suicide.^[27]

Zamora-Kapoor *et al.*'s study on adolescents has shown that social connectedness has an important role in their

development.^[28] A sense of social isolation, disapproval, and exposure to the past incidents of suicides are the causative factors for suicidal behavior. Several studies around the world have shown that social isolation is significantly associated with suicide in adolescents. Chan *et al.* studied 2789 adolescents of 16–17 years' age group and showed that loneliness, anxiety, worry, and lack of friends significantly contributed to suicidal ideation in adolescents.^[29]

A less explored fact of this pandemic is the problem of weight gain and metabolic disorders. Due to multiple days of reduced physical activity, the chances of obesity increases. Body weight also plays an important role in maintaining over all mental well-being of an individual. Studies by Zeller *et al.* showed that adolescents who are obese have a high chance of having suicidal ideation.^[30] They also showed that adolescents who were accurate in their weight perception have significantly high chance of getting suicidal ideation.

Elderly age is another group of population at the high risk of suicide. Unique feature of elderly people is that they show less-warning signs and use highly lethal methods of death. Hence, the suicides in the elderly are often well planned and highly successful as they are more determined to end their life. Personality characteristic in the form of "narcissistic crisis" consisting of inflexibility and rigid thinking strongly contributed to suicides in the elderly.^[31] Due to advanced age-related physical debility, they often turn angry, irritable, and demanding.^[32] Various studies have demonstrated that a past history of suicide in the elderly is a significant risk factor for future attempt. Juurlink *et al.* demonstrated that multiple common physical and psychiatric conditions often contribute to suicidal behavior in the elderly.^[33] Their study has shown that there is a strong relationship between severe pain and suicidality in the elderly. Patients with severe physical pain and inadequate analgesia often try suicide as a method to escape from the intolerable suffering.

Social media can play a significant role in shaping the emotions of a person during pandemic. Recently, Goyal *et al.* from India reported a case of suicide due to the fear of contracting Covid-19 infection.^[34] The subject had witnessed few videos on the social media on the death of suspected Covid-19 cases. Later, when a local doctor diagnosed him to be infected with some unknown viral infection, he wrongly assumed it to be Covid-19. Due to the fear of infecting Covid-19 to his family members, he quarantined himself and later died due to hanging. This case clearly showed us how misinformation acquired from media can turn lethal during a pandemic.^[35]

Mental illnesses have been found to be inherently associated with the increased chances of death.^[36] Schizophrenia has been associated with a high risk of suicidal thoughts inherently and due to secondary depression. The hallucinations and delusions can push the patients to suicidal behavior in the times of intense stress.



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EMOTIONAL WELLBEING IN AN EPIDEMIC

Pandemics can cause serious mental health issues, but a planned systematic approach toward quarantine can help and ease it. In the times of pandemic and isolation, family forms the most important support group. Stravynski and Boyer showed that marriage acted as a significant protective factor in reducing loneliness.^[10] Avoiding boredom and isolation are also important in maintaining good mental health care. During these stressful times, all people besides you are your family. Maintaining loving and caring interpersonal relations play a significant role in preventing mental breakdown. It is hardly possible to feel lonely when you are preoccupied with useful activities. Hence, investing the stay during isolation on useful activities can greatly reduce boredom and stress.

Maintenance of proper mental hygiene is a key to success. Lack of adequate information and uncertainty increase the fear response. Hence, it is absolutely necessary to get adequate and reliable information on the current status of the disease. The reliable health-related websites often supported by the government are the best ones to consult. Eg: <https://www.mohfw.gov.in/> or <https://www.icmr.nic.in/> or <https://ncdc.gov.in/> is to be consulted in India for all the Covid-related authentic reports. As fake news reports create panic in public, government has to monitor the Covid-19 related reporting in media and also remove the fake news reports. Educational programs in the media by health-care workers have to be encouraged which can also help general public with managing the stress.

Skill-enhancement programs can be helpful in the personal development. In the present day, various online educational platforms offer short-term courses which can help in this regard. Performance of regular physical exercise, relaxation methods such as yoga and good sleep are essential to maintain positive health. Picking new hobbies and performing cognitive exercises increase help in this regard.

The prevention of suicides is also an important area to be looked for in pandemics. Introduction of toll-free help lines, continuous monitoring of at risk people, targeted delivery of mental health care services can be undertaken wherever feasible by recognizing the target population. Enhancement of resilience and coping factors are highly essential in managing stress. This can be enhanced with better understanding of personal self and psychoeducation. One of the predominant stresses for the general population during the pandemic is inadequate household commodities. The prevention of this helplessness is crucial in this regard. Anticipation of stressful circumstances and disaster preparedness help people prepare themselves for stressful situations. The government can help the people by providing economic support, subsidies, and insurances and also by instilling hope and positivity.

RISE OF DIGITAL PSYCHIATRY

Providing psychiatry services and training through digital media is an integral part of working solutions during the time

of pandemic crisis and aftermath. The Covid-19 pandemic which had spread like wildfire made cities go into lockdown. It has made hospitals and clinics inaccessible to public. With the public transportation facilities coming to closure, it has been a good time to explore newer methods for consulting doctors and maintain doctor-patient relationship.^[37] Hence, the time has come for the doctors to reach to their patients at home through digital medium.^[38] With the technological revolution in the field of telecommunication in India, the field of telepsychiatry has shown lot promise to the people.

The field of telepsychiatry has made a significant development in the last decade. Tele psychiatry is a branch of psychiatry that uses digital medium for consultation and treatment. Starting with digital data management system, it has extended itself to video conferencing and latest to the use of artificial intelligence in the treatment. Technological advances in the last few years have made the field of telepsychiatry more accessible and feasible in the rural and urban settings. In the past due to lack of direct human touch, physical signs, and emotional connection, it was less preferred by most psychiatrists. However, with the outbreak of Covid pandemic telepsychiatry has found to be highly effective in treating most of the psychiatric illness during emergencies. During the time of pandemics and other emergencies or disasters, the normal mental health services in the hospital may go disrupted.^[39] During those days, the system of telepsychiatry can help in the emergency management of cases and also provide psychological first aid to the patients.

Digital or telepsychiatry has been effective in treating various psychiatric emergencies. It has found to be useful in emergency consultations and disasters. Current Covid-19 outbreak and isolation has led to increased amount of stress, depression, and posttraumatic stress disorders (PTSDs) in the first responders and also the general public. This has made telepsychiatry highly crucial in the current setting. With more and more people suffering and constraint of mental health resources, the system has turned to be highly effective. Bolton *et al.* studied the effectiveness of telepsychology on PTSD.^[40] By evaluating total of 472 patients from 11 studies, they showed that video and Internet act as potentially effective modalities in short-term psychiatric care. They showed that telepsychiatry modality was highly comprehensible and gave a good outcome in PTSD patients. Only trouble faced by the patients performing videoconferencing was with performing cognitive restructuring exercises which could be better performed with mobile applications.

Telepsychiatry is highly effective in providing emergency psychiatric care to patients.^[39] By performing this effective process, it significantly reduces the crowding of emergency rooms. By providing immediate treatment to many psychiatry emergencies such as suicides, it can drastically reduce suicidal deaths. Studies have also shown that tele-mental health screening has dropped the stay in emergency department from 4.2 days to <1 day in more than 80% of patients. Telepsychiatry has also led to preservation of time, reduced use of psychiatric



intensive care unit ICU, reduced transfer to emergencies, and less overall psychiatric admissions by up to 50%.

Rees and MacLaine performed a systematic review on the videoconference delivered psychological treatment for anxiety disorders and showed that this mode of treatment is highly effective for the management of anxiety disorders.^[41] The study showed that greatest evidence of improvement was in the treatment of PTSD. Another review published by Hilty *et al.* showed that telepsychiatry is highly reliable and preferred by patients as well as doctors.^[42]

Although telepsychiatry is highly effective in the present age is not without limitations.^[43] Most important drawback is it lacks human touch. The energy and expressiveness in communication are reduced during the communication. It can be overcome to certain extent by being more loud and adaptive to the telepsychiatry sessions. The videoconferencing maybe at times delayed due to technological glitches which the patient has to be used to. Usually, introductory sessions and demonstrations are useful which help the patients to adapt to the newer methods of consultations. At times, certain physical cues and signs maybe missed during online consultations; hence, proper interview of the patient's relatives is highly important and beneficial. There are also reports saying that telepsychiatry is ineffective in the treatment of acute suicidal patients, acute intoxication, and borderline personality disorder cases.

Digital psychiatry also incorporates utilizing digital world for providing the awareness to public on the psychological aspects of pandemic and providing psychiatry training in the digital format for building human resources. Government bodies and medical educational institutions across India have enhanced digital psychiatry teaching learning. However, it is important to critically review digital psychiatry versus conventional psychiatry in the coming years.

CONCLUSION

Covid-19 has wreaked havoc affecting the health-care system and economy of various countries. With just few months of experience, various studies have clearly shown the negative psychological impact of Covid-19 on the population. Social isolation and quarantine have led to the emergence of multiple psychological disorders in the general population as well as health care workers. As day goes by the number of infected only increases and add on to the psychiatric morbidity. The long-term psychological outcome is still unknown. Thus, it is the responsibility of everyone to take proper mental health precautions and safety measures. Specific mental health intervention strategies are also to be introduced for general well-being of the society. In order to increase the accessibility of health-care facility during the isolation, the development of telepsychiatry consultation is the need of the hour.

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Conflicts of interest

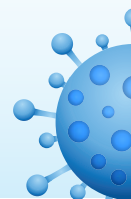
There are no conflicts of interest.

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ACCELERATED RESEARCH

Changes in sleep pattern and sleep quality during COVID-19 lockdown

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ABSTRACT

Introduction: To mitigate the spread of the pandemic coronavirus infection (COVID-19), governments across the world have adopted “lockdowns” which have confined many individuals to their homes. This disrupts normal life routines, elements of which are important circadian cues. The pandemic is also associated with new stressors, altered roles, and uncertainties about health and economic security, which are also likely to affect sleep. The current study is an online survey of sleep experience, routines, physical activity, and symptoms of anxiety and depression, to study the alterations associated with the lockdown.

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Materials and Methods: The survey was conducted in early May 2020 using a questionnaire circulated through social media platforms. Questions related to demographic characteristics, current and previous sleep schedules, routine, and working patterns. Insomnia (Insomnia Severity Index - 4), Stress (Perceived Stress Scale - 4), anxiety and depressive symptoms (Patient Health Questionnaire - 4) and physical activity (International Physical Activities Questionnaire) were assessed using standardized instruments.

Results: A total of 958 valid responses were received. Compared to the prelockdown period, there was a shift to a later bedtime and waking time, with a reduction in night-time sleep and an increase in day-time napping. These effects were visible across occupational groups, but mostly affected working individuals except health professionals. Sleep quality deteriorated across groups. Reductions in sleep duration were associated with depressive symptoms.

Conclusions: The COVID-19 lockdown is associated with changes in sleep schedule and in the quantity and quality of night-time sleep. Although these changes are associated with elevated rates of emotional symptoms, it is unclear from these cross-sectional results, whether sleep deterioration produces psychological distress, or vice versa.

Key words: Coronavirus, COVID-19, home-confinement, lockdown, pandemic, sleep

INTRODUCTION

The lockdown during the recent COVID-19 pandemic has resulted in a changed lifestyle for many of us.^[1] These changes were mostly restrictive in terms of social interaction, creativity, opportunities, and positive relationships.^[1] The restriction was also extended to physical activity, mobility, and availability of nutritional food.^[1,2] In effect, these have disrupted chronobiological rhythms as these are influenced by not only the light but also other zeitgebers such as meal, social interaction, and physical activity.^[1,3] Thus, a structured routine can help in improving sleep duration and quality through multiple intrinsic and extrinsic factors.

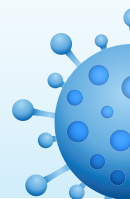
Most people are confined to their homes. This confinement is stressful in itself as individuals are sharing the limited space for a prolonged period with few close contacts. In addition, they experience a lack of novel stimuli, disruptions of routine activity, increased parenting responsibilities, especially for women, and altered productivity expectations for those engaged in professional duties from home.^[3] In addition to the ever-present fear of contracting COVID-19 as it spreads across the country, uncertainty about jobs, economic situation, and the health and safety of loved ones. The pandemic has also been described as an information epidemic, as most people have constant access to news about negative consequences, much of it through electronic media and consequent increase in "screen time." In short, lockdown resulted in home confinement during prevailing anxiety and reduction of positive stimuli.^[3] Stress, in general, but not always, has an inverse relationship with sleep. The effect of stress on sleep quality, timing, and duration is influenced by sleep reactivity.^[4] Persons with high reactivity develop insomnia during stressful situations while those without do not. Thus, home-confinement resulting from lock-down increases the chances of disturbed sleep and insomnia through stress.

Initiation and maintenance of sleep-wake cycle are explained by two-process models, whereby circadian factors and homeostatic factors interact constantly to induce and

maintain sleep.^[5] This model posits that owing to circadian factors, human have higher chances to fall asleep at night as we are designed to behave as a diurnal species by nature.^[5] Sleep pressure represents the homeostatic factor, which is proportional to the time awake. In other words, longer the time awake, higher the sleep pressure, and higher the chances of falling asleep.^[5] Being a diurnal species, human stay awake during the day and accumulate sleep pressure, which reaches maximum at night, where it interacts with circadian factors to induce sleep.^[5] Confinement to home can disrupt circadian rhythms as well as homeostatic process (reduced sleep pressure) due to opportunities for extending sleep in the morning and taking naps during the day.

The present COVID-19 epidemic is a rare situation where a sizable population is confined to the home and are not compelled to follow a structured routine. Earlier studies that have assessed the effect of confinement on sleep have been done in astronauts preparing for Mars mission, incarcerated women, and seafarers.^[6-8] However, the results of these studies cannot be extrapolated to home confinement during COVID-19 lockdown as the nature of confinement is different. First, data from the Mars mission simulation involved only six members of different nationalities, limited space for physical activity, active engagement in training, and prolonged confinement, i.e., 520 days.^[6] Although the study among incarcerated women had a larger sample size, it cannot be extended to the general population as stressors, and sleep environments were different from those in home confinement.^[7] The third study included seafarers who were on the ship and engaged in a normal routine. Besides that, the study population in these studies did not have responsibilities other than the profession related, had little opportunities for leisure activities and were not anticipating any threat to life. As discussed, these factors play a role in sleep quality and quantity.

Considering the paucity of literature, the present study was planned under the aegis of the Research, Education, and



Training sub-Committee of the Indian Psychiatric Society to assess the proportion of subjects with insomnia and poor sleep-quality during lockdown. In addition, we wanted to compare sleep patterns and changes in sleep duration after lockdown compared to the prelockdown period. Finally, we wanted to analyze the effect of occupation on insomnia, sleep quality, sleep duration, and sleep pattern after considering confounders that affect any of these sleep parameters.

MATERIALS AND METHODS

This online survey using the Survey Monkey platform among the general population was done after obtaining approval from the ethics committee of the institute of the first author and the Indian Psychiatric Society. The survey tool was made available in four languages, i.e., English, Hindi, Odiya, and Bengali, with translations being carried out by the authors who were fluent in the language, and consultant psychiatrists (Hindi- SKP, Bengali- AB). The survey went online on April 28, 2020, and the last response was collected on May 10, 2020. All participants above the age of 18 years, regardless of gender, were invited by sending them a link through E-mail or groups on social media (e.g., WhatsApp) and their consent was taken. The participants who completed the survey were asked to forward the survey further if they felt so, to have a snowballing effect.

However, participants who had memory troubles, those taking sleeping pills, pregnant women, and individuals who have self-identified as having COVID-19 infection were excluded from the study. A semi-structured performa was developed to gather information about sociodemographic data, work responsibilities, sleep patterns, screen time, other medical comorbidities, and medication intake.

Sociodemographic data included age, gender, residence, occupation, educational qualifications, years of education, and marital status.

Occupational responsibilities

Participants were asked if they were going outside the home for professional activity during lockdown; if yes, does their profession require changing shifts. Two items enquired about work from home and whether participants had to follow a structured time schedule for work from home or left to work as per convenience.

Sleep pattern

They were asked to provide usual bedtime, time to fall asleep, usual wake time, mode of awakening in the morning (self/alarm/other), quality of sleep and daytime naps with duration, total time spent in sleep in a given day before and after lockdown. Although multiple subjective and objective measures are available to assess sleep patterns and sleep patterns longitudinally, for example, sleep diary and actigraphy, use of recall method for sleep pattern

has a moderate correlation with objective methods.^[9,10] Moreover, methods of objective estimation of sleep pattern and duration amount for only 20% variation. Thus, the recall method can reliably be used to estimate the sleep pattern over short periods.

Sleep quality

Sleep quality in this study was assessed based on the subjective report of nighttime sleep after waking up in the morning on a single item. It asked about their subjective feeling of nighttime sleep quality. Single item has been found to have a good correlation with a score of Pittsburgh Sleep Quality Index.^[11]

Screen time

Participants were asked about time spent on screen before and after lockdown each day in hours. Screens involved computers, laptops, smartphones, tablets, and television.

Daily schedule

Participants responded to a question “whether you are following a structured routine after lock-down?” in either yes or no. This question was used to assess the effect of lockdown on the daily routine.

Substance use

Participants were asked if they had used addictive substances such as tobacco, alcohol, cannabis, hypnotics, or any other substance during the past 6 months. They were also asked about changes in the pattern of substance use in the lockdown period.

Other medical comorbidities

Participants were asked if they had any other medical morbidity such as systemic hypertension, diabetes mellitus, cardiac illness, chronic obstructive pulmonary disease, asthma, or any other medical disorders. In addition, they were asked to provide information regarding medications that they were taking.

Diagnosis of insomnia

Insomnia was assessed using the Insomnia Severity Index (ISI).^[12,13] It has seven items that enquire about nighttime sleep as well as daytime functioning and quality of sleep. Each item is scored on a five-point Likert scale with scores ranging between 0 and 28. Score >14 denotes clinical insomnia.^[14] As this instrument was available only in English and Hindi, only scores in these languages are analyzed.

Mood

Depression and anxiety were diagnosed using four-item patient health questionnaire (PHQ-4).^[15] PHQ-4 has been found to have two factors-depression and anxiety (84% variance). Increasing the PHQ-4 score correlates with the use of health-care resources, functional impairment,



and disability. It is an ultra-brief questionnaire to assess depression and anxiety.

Perceived stress scale

To assess the impact of prevailing conditions in emotions, four-item perceived stress scale-4 was used in this study.^[16] It has been validated as a measure of perceived stress among various populations and its score moderately correlates with anxiety and depression scale. It has an internal consistency of 0.74.^[16]

International Physical Activity Questionnaire

A brief version of the International Physical Activity Questionnaire (IPAQ) was used.^[17] This instrument asks the subject to provide information on time spent on exercise in the last 7 days, as well as time spent each day on categories of vigorous physical activity, moderate physical activity, walking, and sitting. This instrument has been shown to generate comparable scores to the longer IPAQ, which has been validated extensively.

Statistical analysis

Statistical analysis was performed using R v 3.6.2, with Standard Packages for the statistical analysis.^[18] Before analysis, participants who had the same IP address were assessed for similarities in demographic characteristics, to exclude duplicates. Categorical responses to multiple-choice questions were summarized with frequency tables, and numerical responses (in relation to age, as well as total sleep time, screen time, and responses to IPAQ questions relating to types of exercise) were summarized using their mean and standard deviation. To study factors associated with changes in routine and sleep measures, these parameters were analyzed across subgroups with a net increase, reduction, or maintenance of sleep schedule. To do so, responses on current and previous bedtimes and waking times were used. These responses were collected on an ordinal scale of 1-hour intervals (between 4 AM and 8 AM for waking time, and between 10 PM and 12 AM for sleeping time). Differences in responses for the current and previous sleeping and waking times were used to identify individuals with later, earlier, and similar schedules. This was then used to recategorize individuals as those with an overall reduction in sleep times (those who had later sleeping times with the same or earlier waking times, or earlier waking times with the same sleep time), an increase in sleep time (an earlier sleeping time and later waking time, or either of these with no change in the other measure). Those individuals who maintained the same sleeping and waking times, or who had a similar direction of change in both were classified as having the same sleep time. Data on various parameters were analyzed across these three groups. The analysis was also conducted by changes in sleep quality between the prelockdown and lockdown periods, with four categories-those with preexisting poor quality sleep that persisted, those with good sleep quality in both

periods, and those whose sleep worsened or improved between these time points.

Data were also compared across groups of occupational categories, namely, health-care workers (doctors and nurses) who were expected to be continuing to work as previously, housewives (who were presumed to be working mostly at home even before the lockdown), and those who did not belong to either of these categories. Bonferroni correction was applied for multiple testing and based on the number of variables, $P < 0.002$ was considered statistically significant.

RESULTS

A total of 1024 completed responses were received during the survey. Out of this, 60 responses were excluded for various reasons, for example, pregnancy, COVID-19 positivity, memory problems, taking sleeping pills and age of participants being <18 years. Nine hundred and thirty-eight participants were from IP addresses in India, with the remaining participants belonging to the USA ($n = 7$), UK and UAE ($n = 4$ each), Canada ($n = 3$), Singapore ($n = 2$), and one each from Australia, Germany, Kuwait, Oman, Qatar, and Saudi Arabia. The Indian respondents were spread across 25 states and from all regions of the country. Although most of the participants responded on all items, responses on some items were missing in some of the forms. However, after ensuring that all missing responses were not localized to some specific respondents, all 958 responses were included in the analysis. Due to missing values on the outcome measure, 958 individuals were included in the analysis on sleep duration, 935 for occupation groups, and 923 for sleep quality assessment.

The average age of participants in the study was 37.32 (± 13.09) years. Two fifths (41.2%) group comprised women, 67% were married and living with their spouse. The rest were either unmarried or living alone. Three-fourth (75.9%) respondents were graduate and 35.9% were health-care workers. Nearly half (47%) of the subjects were working from home and 35.9% were going outside the home for work during lockdown. Nearly half (55%) participants were working as per their convenience while remaining were following daytime shift work. About 16.4% reported that they were engaged in changing shift-work. Nearly 9% were nicotine users, 10.8% were using alcohol and 1.1% reported use of cannabis. Nearly 14% reported that their substance use had reduced during lockdown, while 3.1% reported an increase.

Just over 10% of the group met the criteria for clinically significant insomnia according to ISI, 11.7% reported anxiety and 11.1% reported depression. Other medical disorders were also reported in the group with varying frequency, for example, hypertension (12.3%), 9.4%



diabetes mellitus, 7.2% hypothyroidism, 4.2% had asthma, 1.2% reported coronary artery disease, and chronic obstructive pulmonary disease, each. However, many subjects had more than one disorder.

A change has been noticed in sleep time and wake time after lockdown. Based on bedtime and wake time before and after home confinement, subjects were categorized into three groups-whose sleep duration at night has reduced (16.1%), increased (18.1%), and last, where it remained unchanged [Figure 1a]. These groups were comparable with regard to gender ($P = 0.57$), education ($P = 0.29$), physical activity, working outside

home ($P = 0.17$), working from home ($P = 0.13$), shift working after lockdown ($P = 0.62$), screen time before ($P = 0.90$) and after lockdown ($P = 0.67$), waking up with alarm before ($P = 0.08$), and after lockdown ($P = 0.89$), use of alcohol ($P = 0.28$), tobacco ($P = 0.92$) or any other addictive substance ($P = 0.38$). Other comparing variables are shown in Table 4. Change in sleep quality compared to pre-lockdown state among these groups is depicted in Figure 1b and c shows a comparison of perceived stress among these groups. Figure 1d depicts the change in sleep onset latency after lockdown compared to prelockdown period.

As seen in Table 1, About a quarter (23.4%) reported that sleep quality worsened, in 8.4% it improved and in others remained similar to prelockdown state (pre-lockdown good = 46.9%; prelockdown poor = 20.7%) ($\chi^2 = 64.03$; $P < 0.001$). These groups were comparable with regard to gender ($P = 0.007$), education ($P = 0.07$), occupation ($P = 0.33$), daytime napping before ($P = 0.23$) and after ($P = 0.30$) lockdown. Similarly, working from home ($P = 0.26$) or outside home ($P = 0.91$), regularity of work from home ($P = 0.10$), and shift work ($P = 0.09$) were not different among groups. Physical activity was also comparable among these groups. Table 2 illustrates distribution of other factors in these groups.

Table 3 represents a comparison of demographic, sleep pattern, insomnia, mood, and physical activity among groups based on occupation-health-care workers, homemakers, and others. These groups were comparable with regard to education level ($P = 0.31$), screen time before lock-down, sleep-onset latency before ($P = 0.43$) and after ($P = 0.93$) lockdown, sleep quality before ($P = 0.43$) and after lockdown ($P = 0.52$), and physical activity before and after lockdown.

Table 1: Change in sleep schedule before and during lockdown (n=938)

Sleep pattern	Before lockdown	During lockdown	Test statistic	P
Bedtime				
After 11 PM	451 (48.4)	610 (65.2)	52.98	<0.001
Before 11 PM	480 (51.6)	325 (34.8)		
Sleep onset latency				
<30 min	741 (79.4)	523 (56.6)	132.8	<0.001
>60 min	36 (3.8)	157 (16.99)		
30-60 min	156 (16.7)	244 (26.4)		
Waking time				
After 6 AM	686 (73.6)	748 (80.3)	11.55	0.001
Before 6 AM	246 (26.4)	183 (19.7)		
Mode of waking				
By myself	504 (54.0)	611 (65.7)	80.27	<0.001
Somebody wakes me up	54 (5.8)	113 (12.2)		
With alarm	375 (40.2)	206 (22.2)		
Daytime napping				
<60 min	290 (31.1)	354 (38.0)	129	<0.001
>60 min	86 (9.2)	237 (25)		
No naps	556 (59.7)	340 (37)		
Refreshed sleep on waking				
Nonrefreshed	276 (30)	416 (45)	44.88	<0.001
Refreshed	657 (70)	515 (55)		
Screen time (h)	3.77±2.752	5.522±3.271		<0.001*

*Chi-square test; *Mann-Whitney U-test

Table 2: Comparison of variables associated with change in nighttime sleep after lockdown (n=935)

Variable	Change in Nighttime sleep from pre-lockdown			Test statistic	P
	Reduced (n=151)	Same (n=614)	Increased (n=170)		
Age (years)	37.42±12.6	37.77±13.18	36.12±12.93	30.14	<0.001 [#]
Occupation (%)					
Health-care worker	55 (36.42)	247 (40.22)	63 (37.05)	3.93	0.41
Home-maker	13 (8.60)	47 (7.65)	8 (4.70)		
Other	82 (54.30)	317 (51.62)	99 (58.23)		
Working outside the home after lockdown (%)	61 (40.39)	250 (40.71)	56 (32.94)	3.47	0.18
Sleep-onset latency <30 min before lockdown (%)	123 (81.45)	499 (81.27)	124 (72.94)	6.25	0.04
Sleep-onset latency <30 min after lockdown (%)	74 (49)	351 (57.16)	106 (62.35)	5.95	0.05
Refreshing sleep before lockdown (%)	111 (73.50)	444 (72.31)	105 (61.76)	8.01	0.01
Refreshing sleep after lockdown (%)	68 (45.03)	344 (56.02)	106 (62.35)	10.39	0.005
Daytime napping before lockdown (%)	56 (37.08)	257 (41.85)	66 (38.82)	1.49	0.48
Daytime napping after lockdown (%)	93 (61.58)	400 (65.14)	98 (57.64)	2.82	0.24
Anxiety reported (%)	19 (12.58)	75 (12.21)	13 (7.64)	2.97	0.23
Depression reported (%)	26 (17.21)	66 (10.74)	10 (5.88)	10.62	<0.001
Insomnia (%)	36 (9.92)	6 (8.82)	47 (10.17)	0.122	0.941

[#]Kruskal-Wallis test; Others were Chi-square tests



Table 3: Factors influencing change in sleep quality after lockdown

Variables	Deterioration in Sleep Quality (n=225)	Persistent Poor Quality (n=203)	Improved (n=80)	Good Sleep Persists (n=446)	Test value	P
Age (years)	34.86±12.07	35.03±12.43	32.36±11.84	40.61±13.33	57.47	<0.001*
Bedtime <11 PM before lockdown (%)	109 (48.4)	76 (37.4)	24 (30)	282 (63.2)	56.26	<0.001#
Bedtime <11 PM after lockdown (%)	39 (17.3)	47 (23.2)	31 (38.8)	215 (48.2)	78.72	<0.001#
Sleep onset latency <30 min before lockdown (%)	185 (82.2)	139 (68.5)	60 (75)	374 (83.9)	173.8	<0.001#
Sleep onset latency <30 min after lockdown (%)	57 (25.3)	90 (44.3)	54 (67.5)	338 (75.8)	23.36	<0.001#
Waketime <6 AM before lockdown (%)	52 (23.1)	37 (18.2)	15 (18.8)	147 (33)	21.13	<0.001#
Waketime <6 AM after lockdown (%)	38 (16.9)	28 (13.8)	9 (11.2)	113 (25.3)	18.47	<0.001#
Waking up by self before lockdown (%)	126 (56)	87 (42.9)	29 (36.2)	272 (61)	25.82	<0.001#
Waking up by self after lockdown (%)	130 (57.8)	113 (55.7)	62 (77.5)	316 (70.9)	29.84	<0.001#
Anxiety (%)	47 (20.9)	41 (20.2)	6 (7.5)	19 (4.3)	57.205	<0.001#
Depression (%)	48 (21.3)	36 (17.7)	6 (7.5)	16 (3.6)	59.438	<0.001#
Insomnia (%)	57 (26.8)	5 (1.2)	1 (1.33)	25 (13.66)	112.2	<0.001#

*Kruskal-Wallis test for continuous variables, *X² goodness of fit for categorical variables

Table 4: Comparison of sleep pattern depending upon occupation (n=923)

Variable	Health care workers (n=379)	Homemaker (n=70)	Others (n=509)	Test value	P
Age (years)	35.69±11.43	43.07±11.1	37.77±14.23	168.42	<0.001*
Female gender (%)	175 (46.17)	70 (100)	148 (20.07)	136	<0.001#
Screen time after lockdown (h)	4.82±2.78	3.95±2.6	6.19±3.48	39.03	0.001#
Working outside the home after lockdown (%)	275 (72.55)	1 (1.4)	102 (20.03)	298.3	<0.001#
Shift work after lockdown (%)	121 (31.92)	2 (2.9)	32 (6.28)	115.4	<0.001#
Working from home after lockdown (%)	114 (30.07)	22 (31.42)	316 (62.08)	94.9	<0.001#
Bedtime before 11 PM before lockdown (%)	185 (48.81)	48 (68.57)	259 (50.88)	8.98	0.01#
Bedtime before 11 PM after lockdown (%)	139 (36.67)	25 (35.71)	170 (33.39)	1.05	0.59#
Wake time before 6 AM before lockdown (%)	92 (24.27)	24 (34.28)	136 (26.71)	3.05	0.21#
Wake time before 6 AM after lockdown (%)	80 (21.1)	14 (20)	94 (18.46)	0.95	0.21#
Waking up by self before lockdown (%)	165 (43.53)	37 (52.85)	315 (61.88)	28.28	<0.01#
Waking up by self after lockdown (%)	224 (59.10)	44 (62.85)	358 (70.33)	12.8	<0.01#
Day time napping before lockdown (%)	166 (43.79)	43 (61.42)	177 (34.77)	21.74	<0.001#
Daytime napping after lockdown (%)	242 (63.85)	42 (60)	321 (63.06)	0.41	0.81#
Anxiety (%)	30 (7.91)	7 (10)	76 (14.93)	10.3	0.01#
Depression (%)	31 (7.93)	13 (18.57)	63 (12.37)	7.97	0.02#
Insomnia (%)	20 (14.08)	13 (8.08)	50 (8.82)	4.141	0.1261#
Perceived severity	9.07±4.27	9.21±4.09	9.00±4.15	0.68	0.71#

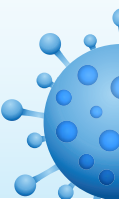
*Kruskal-Wallis test for continuous variables, *X² goodness of fit for categorical variables

However, a greater number of subjects in “other occupations” group were following as-per-convenience work-routine compared to the other two ($P = 0.01$).

DISCUSSION

This study showed that sleep pattern was influenced by lockdown. A shift to later bedtime, delayed sleep onset, reduction in nighttime sleep duration and increased daytime napping was observed. In addition, a significant number of participants reported worsening sleep quality. Although the proportion of insomnia in this sample was similar to population prevalence in the prelockdown period, the proportion of anxiety and the depressive symptom was higher than population estimates. Participants with the change in sleep duration were comparable with regard to most of the parameters except for age.

These findings contrast with those of a recent study from a Greek population, which reported that nearly 38% of participants had clinical insomnia after the COVID-19 outbreak.^[19] However, proportion to clinical insomnia was lower during the present study compared to the Greek population and remained at the level of pre-COVID-19 period.^[20] Voitsidis *et al.*^[19] showed that insomnia in the Greek population was a function of loneliness, uncertainty, depression, and COVID-19-related worries with a major contribution from two factors-depression and uncertainty. Perception of uncertainty and depressive feelings are influenced by a number of factors, for example, age, religious beliefs, availability of family support, to name a few. The study population in this study was younger compared to that included in the present study.^[19] Available literature suggests that resilience increases with age and is positively associated with spiritual beliefs and support of



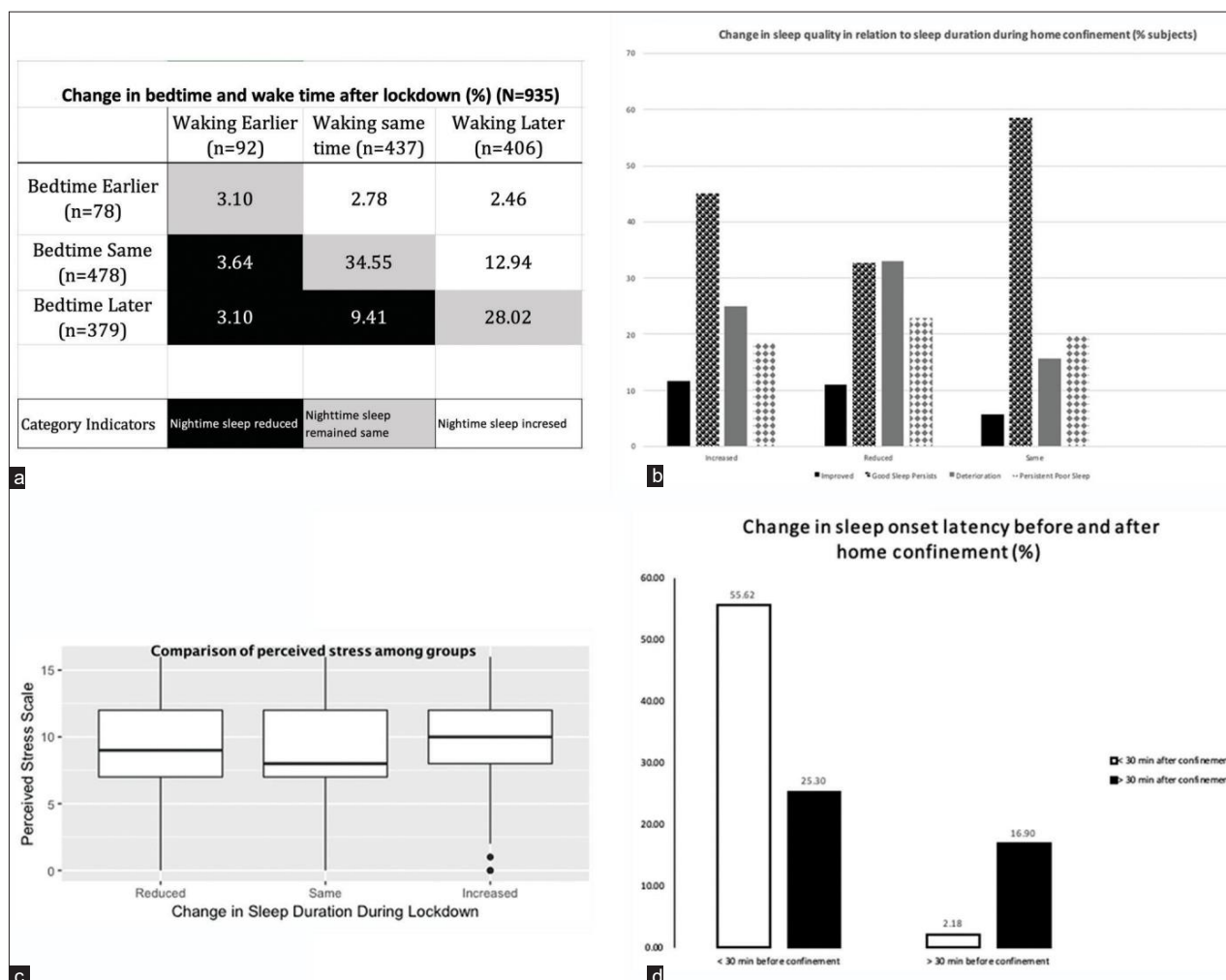


Figure 1: (a-d) Sleep-related variables in subjects during home confinement during COVID-19

family.^[19] Most of the subjects included in the present study were married and living with a spouse (though does not always translate in positive emotional support) that could have resulted in lesser perceived stress and insomnia. It is further strengthened by the finding that perceived stress was comparable among groups with reduced, increased and “no-change” in nighttime duration of sleep after lock-down [Figure 1c].

Lockdown also affected sleep patterns and screen time [Table 3]. Bedtime was delayed, sleep onset latency prolonged, and the proportion of daytime napping increased. A sizable number of subjects were confined to home in the present study, and home confinement is known to produce such effects due to disruption in circadian rhythm.^[3] Daytime napping also reduces the sleep pressure, thus, delays the bedtime and prolongs sleep-onset latency.^[5] Thus, circadian and homeostatic factors regulating sleep are mutually influential and interact to determine the timing and latency of sleep onset.^[5] Moreover, delayed sleep also

reduces the amount of slow-wave sleep owing to circadian factors, and this may result in poor sleep quality, as was seen in the present study.^[5] Other factors that could influence sleep patterns could be screen time, which increased after lock-down. Longer time on screen is associated with shorter sleep and lesser sleep efficiency.^[21]

Owing to the shift of sleep pattern, reduced nighttime sleep compared to prelockdown sleep was observed in 16.1% and longer nighttime sleep in 18.1% [Table 4]. However, the reduction was related to delayed bedtime and prolongation to delayed waking up [Figure 1a]. Shorter sleep duration after lockdown was associated with an increased proportion of longer sleep onset latency and depression after lockdown. In addition, shorter nighttime sleep duration was associated with worsening of sleep quality after lockdown [Table 2]. Although not systematically assessed in the present study, shorter nighttime sleep duration could have resulted in sleep deprivation. This is further reiterated by the fact



that the proportion of poor-quality sleep and daytime napping has also increased in this group [Table 4]. Sleep deprivation is known to produce depressive symptoms, daytime fatigue, and daytime sleepiness.^[22-24] Moreover, the optimal treatment of insomnia also improves depressive symptoms.^[25-27] A dose-response relationship between the proportion of depression with the change in sleep-duration, sleep-quality, and comparable proportions of insomnia supports this notion [Tables 2 and 4]. However, in the present study, change in nighttime sleep duration was not affected by physical activity, occupation, working from home, or going outside home and perceived stress. These findings are contradictory to proposals in a recent paper that suggested plausible mechanisms of sleep changes during home confinement.^[3] It was put forth that confinement may lead to increased stress owing to a multitude of factors, namely, available space, lack of social interaction, absence of work and reduction in physical activity, which ultimately culminates in sleep disruption.^[3] This was not seen in the present study as nearly half of the study population was working from home after lockdown, and social interaction through social media could have been maintained to prelockdown state as depicted by the increment in screen-time after lock-down.

This study indicated that nearly a quarter of participants reported worsening of sleep quality after lockdown. In addition, nearly 21% of participants had poor sleep quality even before the lockdown.

Both proportions are greater than the fraction of poor sleep quality among the Indian population reported earlier.^[28] A number of factors could explain the difference. First, an earlier Indian study was conducted in a limited geographical population using face to face interviews with a validated questionnaire.^[28] On the other hand, the present study was a self-reported survey sent through social media and was dependent on recall-based response. Moreover, sleep quality was determined through a single item rather than using a structured questionnaire. Though single item has been found to have optimal concurrent validity to assess sleep quality, there is a possibility that persons with poor sleep quality have preferred to respond to survey over persons with good sleep quality.^[11] Finally, the prevalence of poor sleep quality was greater than insomnia in the present study because both are different constructs. Considering that sleep quality may be affected by a number of other sleep disorders, besides insomnia, poor sleep quality has been removed from the diagnostic criteria of insomnia disorder.^[29,30]

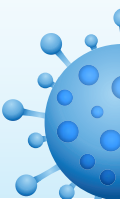
In the present study, groups based on occupation were comparable with regard to sleep quality and delayed in bed-time and wake time compared to prelockdown [Table 1]. Some of the home-makers responded that they were working from home during

lock-down, which could be attributed to part-time home-based professional activities in this group. Home-makers had a maximal shift in sleep-time and wake-time after lockdown. Although increment in the proportion of daytime napping was observed in health-care workers and other professionals, it was not seen in home-makers. Moreover, comparable shifting of sleep schedule and proportion of working after lockdown among three groups also challenge the possibility that work-load could result in stress and consequent sleep problems.^[3] However, interaction among the place of work (from home and outside home) and mood (anxiety and depression) could have influenced sleep quality, which could not be examined in the present study. Health-care workers had the lowest proportions of anxiety and depression compared to the other two groups. This could have resulted from a better understanding of COVID-19 in this group compared to the other two groups.

This study had certain methodological limitations that are inherent to Internet-based surveys. First, all inclusion and exclusion criteria were assessed on the basis of self-report, and therefore some participants who were unaware of their status (e.g., for memory problems or pregnancy) may have been included. Second, cross-sectional collection of data has a recall bias, especially for patterns of sleep and activity assessed for the prelockdown period. Third, as already discussed, response bias could not be ruled out. Fourth, some data was missing in all variables, though the magnitude was limited to 1%–2% of the total number of subjects. As responses were solicited by requests across social media platforms by a snowballing strategy, the subjects recruited may belong to groups that belong to similar strata of society, besides being more likely to be known to each other. This is made evident by the large proportion of health-care workers amongst the respondents ($n = 379$; 39.3%). Internet access, motivation to respond, and comfort with self-reporting emotional and behavioral symptoms, may all have influenced both participation rates, and the responses elicited. Moreover, stresses related to the lockdown are unlikely to be uniformly distributed in the community and are likely to affect those with limited material resources, more than the wealthy. Taken together, these factors affect the generalizability of the results. Fifth, although data is based on self-report on standardized assessment tools wherever available, these have mostly been short screening instruments rather than comprehensive evaluations, as these might limit participation. Finally, it is difficult to ascertain how many individuals received the survey link but did not participate, and thus a response rate could not be ascertained.

CONCLUSIONS

This survey showed that COVID-19 lockdown was associated with poor sleep quality, shift in sleep cycle to delayed phase,



sleep-deprivation based on nighttime sleep, and depressive symptoms in a sizable number of population.

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Conflicts of interest

There are no conflicts of interest.

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CURRENT THEMES

Sexuality, sexual well being, and intimacy during COVID-19 pandemic: An advocacy perspective

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ABSTRACT

The coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome (SARS)-CoV-2, has emerged as a global public health threat. The implications are much beyond just health crisis, and it has long-lasting psychosocial and economic implications. Although the psychological offshoots such as depression, anxiety, posttraumatic stress, and sleep disturbances are being studied in-depth, there is a dearth of literature on the sexual well-being and sexual practices during this pandemic. Considering the physical distancing; travel restrictions; the high human-human transmission rate; misinformation and uncertainty about the sexual routes of transmission for SARS-CoV-2; and fear about intimacy, sexuality, and safe sexual practices have increased significantly. This is more prominent in newly settled or distanced couples and the frontline health workers, with increased risk exposure to the virus. For them, guilt and distress associated with sexual relationships might increase primary psychiatric and sexual disorders. This, in turn, impacts relationships and emotional bonding in couples and affects healthy coping during the pandemic crisis. Although sexual abstinence is the safest practice to prevent transmission, it is not practically feasible in all cases. Risk reduction counseling, sex with quarantined partners, and digital sex are other options that are worth exploring. There are additional concerns of digital safety, unhealthy use of technology, cyber-crimes, and online extortion. Keeping this in the background, this advocacy article glances through the effects of past outbreaks on sexuality, reviews the current recommendations, and proposes methods and approaches for sexual well-being during the COVID-19 pandemic, which is vital for overall public health.

Key words: Coronavirus, COVID-19, intimacy, pandemic, sex, sexuality

INTRODUCTION

The Coronavirus disease 2019 (COVID-19) crisis

Over the last few months, the world has seen the emergence of a new public health threat. The coronavirus disease

2019 (COVID-19) caused by the novel coronavirus severe acute respiratory syndrome (SARS)-CoV-2 has brought the world down to its knees. The medical and psychosocial implications of this large-scale outbreak can potentially long outlast the pandemic itself. Till date, more than three million people have been affected globally and nearly three lakh people have been succumbing to the infection, and the numbers are rising by the day.^[1] The widespread chaos regarding the uncertainty and source of infection has led to fear, panic, apprehension,

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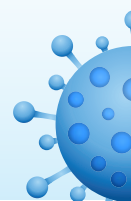
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and mass-hysteria. Grief for loved ones, bereavement, and isolation as a measure of “social distancing” is keeping billions segregated from their loved ones.^[2] Due to the international lockdown imposed on many cities, either the families have got separated for long times or people are having a new experience of staying with their spouses or families, like never before. Physical intimacy and proximity can significantly influence the dynamics of interpersonal relationships and mend them for the better or worse.^[3] The unprecedented changes imposed by COVID-19 and the containment measures have changed the living structure of millions, impacting their relationships and mental health. Research done in China during the first phase of infection shows an increase in acute stress, depressive disorders, obsessive-compulsive disorders, anxiety, panic symptoms, and insomnia. The long-term sequelae are posttraumatic stress, pathological grief, and adjustment disorders, which tend to be chronic.^[4] Social interaction, intimacy, and relationships have shown to boost well-being and serve as critical coping factors during such disasters. The quarantine and travel restriction measures during the COVID-19 pandemic can trigger loneliness and negativity, which prevent healthy coping with the crisis.^[5] Although literature related to this pandemic and mental health is increasing, there is a dearth of discussion on a vital aspect, the sexual and reproductive health. Sexual relations and sexuality have been important determinants of relationships and general well-being.^[6] COVID-19 being a contagious infection has generated a plethora of fears related to couple intimacy, the guilt of transferring the infection to the partners (especially for the frontline workers), altered sexual dynamics and performance in newly married couples or in those who are not used to cohabiting for long periods, and also the serious concerns of domestic abuse and intimate partner violence (IPV).^[7] Pandemics like this can have critical implications on sexual and reproductive health at all levels: individual, systems, or society.

In the absence of enough literature during COVID-19, the authors write this article as an advocacy document based on their clinical experience and relevant research related to past outbreaks. It will discuss the effects that infectious disease outbreaks can have on sexual health and intimacy, with perspectives from the past and present pandemics, and reviews recommendations for ensuring sexual well-being during these times of crisis.

PANDEMICS AND SEXUAL HEALTH: REVISITING THE “PESTILENCES”

“A loveless world is a dead world. The plague makes us crave more for love and the arms of our loved ones.”

- Albert Camus, *The Plague* (La Peste), 1948.^[8]

Since the classical bubonic plague of the 13th century, the world has faced pandemics time and gain, disrupting social

structures. Surprisingly, much literature has focused on the psychosocial constructs of sexuality during this deadly disease. Tsiamis *et al.*^[9] in “Poetic description of the plague” mentions “fear of infection disrupting love and lives.” They mention couples being separated in rooms, not even allowed to talk. The segregation was more for the higher social classes, with separate living arrangements and dining altogether. Cantor^[10] mentions the social perceptions that immorality and illicit sexual relationships were causative of the plague, and physicians advised “physical distancing” and abstinence from all forms of sexual intimacy as it was related to “bad air,” then believed to be responsible for the infection. However, there are also mentions of increase in incest, prostitution, and coercive sexual practices in Europe during those days of the plague.^[11] It seems surprising that when a deadly infection was sweeping off one-thirds of the European population, what is the importance of discussing human relationships. However, contrary to the popular ideas, sexuality and physical intimacy has long been involved in social theories surrounding the classical “black death” in medieval Europe. German physicians advised against jealousy and promiscuity as they open the mind to “bad emotions.”^[12] Religious connotations were attached by the Church as homosexuals were accused of spreading the infection against the “Divine will,” and “sanitary legislation” was proposed based on “moral” laws to have them either publicly flogged or put out of the country.^[13] Salisbury *et al.*^[11] wrote about incest increasing significantly during the bubonic plague. The authors hypothesized that due to the widespread mortality, exogamy (marrying outside the clan or community) turned improbable. Hence, consanguineal marriages increased to preserve the patrimony, especially in the royal families, as many were on the verge of extinction. In *Land, Kinship and Life-Cycle*,^[14] Smith pointed out the increase in the severity of fines for fornication during the middle of the plague period (1349–1350). It is interpreted as a punishment for acts that were seen as morally improper. The Courts blamed the fornicators, as “sexuality” was considered to be a potent medium for infection spread. The idea of sex and intimacy being responsible for all forms of pathogenic spread has been increasing even before the outbreak of plague and peaked in the Victorian era.^[15] This was related to the social taboo, prejudice toward sexuality, and religious antagonism of sexual practices through moral standards. Ironically, there was a spur in the industry of prostitution as the plague waned off. People considered intimacy and sex to be critical coping factors for the pandemic aftermath. Sex-parlors and “royal safeguards” were built to promote safe and consensual sex.^[13] Some consider this as a revolt against the orthodox blame put by the Medieval Church on the society. It has an existential angle too. Hatcher, while describing plague in England, mentioned increase in sexual practices between newly married and elderly couples to deal with the stress.^[16] This was postulated to arise from the uncertainty of life and togetherness during and post the crisis times.



Unfortunately, though social research in pandemics peaked during the “black death,” literature related to sexual health and pandemics declined. The changing public health priorities and more “biological” focus to disease control might be the probable reasons. Furthermore, in the words of Cohn and Cohn,^[17] people were self-stigmatized to consider an immoral topic of sexuality in the face of much more serious issues such as death and disability, though frustration and distress over physical distancing from the partners have played an active role in the social reaction to these pandemics. During the Spanish flu of 1918, social-distancing measures were considered to be oppressive by many.^[18] As the administrative line, “You are your safest sexual partner” gained popularity, so was the common quote, “We want to be quarantined together” by couples that established itself as a landmark romantic comment in many books and movies later in time. Sex steroids for enhancing sexual potency and pregnancy were considered to be risk factors for the influenza outbreak while birth control methods gained importance.^[19] There were reports of discrimination against sexual minorities and increase in violence and abuse in families.^[20] With an increase in the understanding of molecular biology and pathogenesis, fear has grown more about sexual transmission of infections and the degree of permissible intimacy during the outbreaks. There have been debates about the same during the SARS and the Middle East respiratory syndrome (MERS) outbreaks. Chua *et al.*^[21] while studying the psychological effects of the SARS outbreak reported an increase in sexual dysfunction, decreased arousal, and increased marital discord over issues of intimacy. Long-term psychosocial and occupational outcomes of health-care workers dealing with SARS patients showed a rise in erectile dysfunction (ED), premature ejaculation (PME), lack of sexual satisfaction in partners, and heightened performance anxiety. This contributed to the burnout, work stress, absenteeism, substance abuse, and depressive disorders. Substance use also had a positive relationship with sexual dysfunction, anxiety, and partner violence and an inverse relationship with perceived sexual satisfaction in the couples.^[22] SARS and MERS had led to adverse pregnancy outcomes such as miscarriages, abortions, intrauterine growth retardation, and maternal deaths, which is proposed in COVID-19 as well, which generates fear among sexually active couples.^[23] New infections with unknown pathways of transmission always tend to create considerable apprehension about pregnancy and vertical routes of transmission. Hence, the implications of safe sexual practices and sex education become paramount during these times. Ebola outbreak in Africa had a possible sexual mode of spread, which led to significant discrimination based on race, ethnicity, and sociocultural status.^[24] The lesbian, gay, bisexual, transgender (LGBT) community were stigmatized as “carriers” for the same. The psychological models adopted for the Zika outbreak in Brazil and Nipah infection in India involved sex education about the viral transmission among

partners, social connectedness, and focusing on alternative forms of expressing love and intimacy, while observing physical distancing.^[25,26] This becomes vital as sexual well-being has been linked with positivity, hope, personal growth, and overall health, especially at times of disasters.

CORONAVIRUS DISEASE 2019, SEX, AND SEXUALITY

Literature related to sexual health and current COVID-19 pandemic is still in their infancy. The global lockdown has led to marked “physical and social” distancing, and the implications are chronic. Unfortunately, sexual well-being is often neglected at the face of more significant immediate concerns. Given the importance of sexuality in people’s lives and its relationship with quality of life, and psychiatric disorders, physicians need to stay sensitive to this issue, routinely ask or screen for sex-related complaints, and incorporate primary sex education tailored to the present outbreak in their patient counseling. Considering the social stigma attached behind sexuality and the varied sociocultural expression, the dictum that holds true clinically is that “You don’t ask, and they don’t tell.” The summary of the present evidence on COVID-19 suggests that any form of close human–human contact can spread the virus.^[27] The SARS-CoV-2 is much more contagious than its earlier congeners, which is the proposed reason for such speedy global spread. The virus gets easily carried by aerosol and fomites, can remain viable in air for up to 3 days, and survive on various inanimate objects for 2–3 weeks. This further generates fear and frustration related to intimacy. It is all the more for frontline workers against COVID-19 who self-quarantine themselves to prevent interaction with their families. Those who return to their spouses have expressed marked guilt, fear, and apprehension.^[28] This eventually affects the interpersonal relationship, closeness, sexual practices, and an overall lead to discord and emotional distancing in couples.^[29] Looking from the other side, recreational sex when billions are stranded at home, without family planning measures, can lead to increased abortions and population boom with time. Such consequences are unprecedented. Like human rights, sexual and reproductive rights also need to be safeguarded during such biological disasters. Singh and Adhikari while studying the age-structured impact of social distancing on the COVID-19 epidemic in India, have mentioned the emotional distress of the adolescents and younger adults due to separation.^[30] Sentiment analysis from Twitter has shown the lockdown in India to instigate fear, disgust, and stigma. People have reported concerns about physical distancing and traveling to their partners, more so in those who have recently started relationships or got engaged.^[31] Keeping in mind the social situations that might arise due to this pandemic and lockdown, the possible ways in which sexual lives and relationships can get affected are summarized in Table 1.



Table 1: Probable sexuality and intimacy-related issues during the coronavirus disease 2019 pandemic

Effect on sexuality/sexual practices	Contributing factors
Sexual abstinence	Fear related to intimacy Travel history of partners Uncertainty about transmission Physical distancing
Coercive sexual practices/IPV/incest	History of IPV Marital discord/disharmony Couples stranded together away from family (more contact time) Substance abuse Increased pornography use Crowding in joint families (less supervision)
Noncompliance to precautions/lockdown	Frustration and distress associated with prolonged sexual abstinence KAP gap about healthy sex
Increase in paraphilias	History of sexual deviations
Disinterest in sex	Fear/restriction of conventional sexual acts Chronic stress Anxiety, uncertainty related to pandemic Depression, PTSD, and adjustment disorders Guilt Loneliness and isolation
Unhealthy use of technology (pornography addiction, use of dark web)	Isolation/quarantine History of substance abuse, externalizing personality traits, ADHD Compulsive use of technology Lack of partners/social support
Interpersonal issues	Lack of intimacy
Extramarital relationships	Prolonged sexual abstinence
Marital discord/disharmony	Physical distancing Increased sexual appetite/sex addiction
The rise in sexual disorders (erectile dysfunction, premature ejaculation, arousal disorders, etc.)	Preexisting sexual problems Chronic stress Depression, anxiety, psychoses (new onset or exacerbation) Chronic abstinence Interpersonal issues Heightened performance anxiety (fear of infection) Decreased self-esteem
High-risk sexual behaviors	Personality traits The psychological impact of lockdown Poor knowledge about sexual risks and contraception matters
Increased viral spread	Indiscriminate sexual practices without understanding the transmission risk

IPV – Intimate partner violence; KAP – Knowledge-attitude-practice; PTSD – Posttraumatic stress disorder; ADHD – Attention deficit hyperkinetic disorder

SEXUAL ABSTINENCE: A FEASIBLE SOLUTION?

Sexual abstinence is the practice of voluntarily refraining from some or all aspects of sexual activity. It can arise from deliberate ideological or philosophical reasons (chastity and celibacy) or situational reasons (prevention of infection and conception), lack of suitable partners, or to conform to legal provisions.^[32] In infectious disease outbreaks, abstinence is considered to be the safest practice to prevent spread. For decades, the psychological effects of sexual abstinence have been debated in all age groups. The traditional association of abstinence and better “vitality of nerves and brain” has not been scientifically proven.^[33] There are other views related to chastity and puritanism about sexual abstinence, which are beyond the scope of this article. In this discussion, we will stick to the situational need for abstinence during the pandemic, and not refer to the moral or religious connotations of it. Sex is often considered to be a stress

reliever and an indicator of well-being in couples. It also forms an essential parameter of relationship dynamics.^[34] It is vital to understand the difference between asexuality and celibacy. Any obligation to stay abstinent involuntary sexual lives can cause distress. For sexually active couples, not being able to be intimate due to physical distancing or fear of infection can be traumatic. Many might be stranded alone, feeling lonely in the absence of their partners. This becomes more concerning in couples who have just moved in together. Here, by abstinence, we also mean a lack of any form of intimacy, including foreplay, which can impact the self-esteem and well-being of couples. Preexisting marital issues can be amplified as there might be discordance of opinion related to sexual practices between the partners. Sexual frustration and loss of affection are other offshoots. Chronic sexual repression has shown to affect performance anxiety and sexual confidence, which can eventually lead to arousal disorders, anorgasmia, PME, and ED. It can also increase the risk of chronic diseases such



as diabetes, hypertension, and cardiovascular illness.^[35] Studies related to the prevalence of these disorders as the aftermath of pandemics are, however, scarce. Fear of intimacy can lead to emotional distancing from the partner, which leads to loneliness, poor coping, and sleep disturbances, all of which are independent risk factors for depression and anxiety. Although masturbation is often considered to be a replacement for partnered sex, there are significant differences between the emotional processing and perceived satisfaction from both.^[36] Sex has been termed as “emotionally binding,” and it increases the sense of emotional closeness among couples.^[34] Although some studies have shown beneficial effects of abstinence on self-control, spirituality, and well-being, they were on individuals who practiced abstinence as a voluntary lifestyle.^[37] During infectious disease outbreaks, it is more of an “imposed abstinence” to prevent the spread. Bogart *et al.*^[38] studied 1917 adolescents, recruited from mid-school, and assessed them periodically. They found a relationship between sexual abstinence among females and better mental health, which no longer existed once educational variables, family bonding, and conventionality factors were accounted for. In another study, sexually abstinent men were compared with those with high-risk sexual behavior having HIV, and the authors reported that the two groups had similar prevalence of depression, burnout, anxiety, and insomnia.^[39] HIV, however, having entirely different social dynamics and established routes of sexual transmission will be different from other infectious diseases. Psychological distress and sexual abstinence have been shown to share a bi-directional relationship, as increased stress can also induce people to avoid sexual activities altogether. This factor becomes vital during disasters such as COVID-19 as the financial crisis, unemployment, fear of infection, health anxiety, travel restrictions, and uncertainty all can contribute to the collective stress and hence the varied sexual behavior.^[29] Prolonged sexual abstinence might also lead to the emergence of high-risk sexual behavior, substance abuse, gambling, and compulsive self-gratification as harmful coping strategies.^[40] Sexual oppression at the time of emergencies has led to adverse physical and psychological consequences. Considering these factors, total sexual abstinence alone might not be an effective measure to promote sexual well-being during pandemics.

SAFETY OF SEXUAL PRACTICES DURING CORONAVIRUS DISEASE 2019: REVIEWING THE RECOMMENDATIONS

SARS-CoV-2 is present in respiratory secretions and has aerosolized droplet spread. Data so far suggest that the virus can be transmitted through respiratory droplets to the skin and personal objects, from which it can infect the sexual partner.^[27] Hence, any form of in-person sexual activity carries the potential risk. Data related to other

routes of sexual transmission are sparse. The virus was not detected in semen or vaginal samples in two small studies.^[41,42] However, another study detected SARS-CoV-2 by reverse transcriptase-polymerase chain reaction in semen samples of six patients.^[43] Even the detection of the virus in urine samples is equivocal.^[44] Saliva has also been considered to be potential media for cross-contamination in dental practice, and recommendations of testing saliva for viral particles have been suggested.^[45] To summarize, the pathophysiology and epidemiology of COVID-19 are yet extensively studied. Considering the large-scale spread of the infection, it is clinically prudent to consider all of these modes as a source of potential contamination, unless proven otherwise with clear evidence. Many individuals might feel too stressed for sex and prefer to delay it till situation normalizes. It is a normal stress reaction, and their partners need to accept it. Stress responses during pandemics can vary widely.

SAFETY ABOUT SEX/INTIMACY DURING THE CORONAVIRUS DISEASE 2019

The Center for Disease Control and Prevention (CDC) recommends a minimum distance of 6 feet to avoid transmission, which is impossible for intimate relationships.^[46] As mentioned before, any in-person contact carries the potential risk for infection. However, total isolation is not necessary in all cases. Case-by-case safety assessment and decision-making is better. If both the couples are asymptomatic, have been practicing precautions, and have no history of travel or exposure, touching, hugging, kissing, and intercourse are likely to be safe. Sharing the bed with partner and dining together can also be done. After community transmission in many countries, asymptomatic carriers are rising. That always carries a potential risk, which cannot be negated.

SEX/INTIMACY WHEN A PARTNER IS SYMPTOMATIC

Of late, any flu-like symptom generates panic, as it can mimic COVID-19. Although the clear-cut distinction is difficult, high fever, sore throat, respiratory distress, and history of exposure (might not always be present) are useful cues.^[47] The WHO and Indian Council of Medical Research have standard protocols for testing and quarantine, which need to be followed. Ideally, based on CDC recommendations, if any partner is a suspect, self-quarantine is necessary without bed-sharing or any form of intimacy till at least 7–14 days after the symptoms started, or till full resolution of all symptoms, or at least up to 72 h of being fever free without any medications.^[48] For hospitalized patients, negative testing for severe infections is recommended before discharge. A study from Shenzhen, China, had reported 15% transmission in household contacts, which can be minimized using strict hand and respiratory hygiene.^[49]



SEX/INTIMACY FOR FRONTLINE HEALTH WORKERS

Health-care staff, police personnel, delivery executives, or other people involved in essential services have an added vulnerability. Many tend to self-isolate themselves from their spouses, adding to the psychological distress. The most important thing is keeping the partner informed about the risk, using adequate hygiene measures, using a separate set of clothes, having different room for occupational requirements, etc. Based on the degree of risk, isolation can be discussed and decided upon by both the partners. Unilateral decision-making can harm intimacy and relationships. If the partner at risk is asymptomatic, the decision about sexual activities is personal and can be tailored based on mutual preferences and convenience, as there are no evidence-based guidelines for the same. Partner consent is vital in these cases.

There are many who have newly entered relationships or just got married. Many of their partners might be away. For these couples, the challenges might be much more, and the need for continuation of intimacy and digital sexual practices becomes essential. Masturbation, phone or video sex, pornography, and sex toys might be helpful measures.^[50] However, the unhealthy use of technology, pornography addiction, personal and digital safety, and cyber-crimes are often the concerns. Research points out that although pornography can be a self-gratifying replacement for in-person sex, it also tends to be compulsive, can distort ideas about sex, and contribute to partner violence.^[51] The inner anxiety of the pandemic, sexual abstinence, and the resultant psychological distress might contribute to sexual disorders in the postpandemic period. Physicians of all specialties need sensitization and awareness for detecting these problems, offering appropriate sex counseling, and initiating referrals if necessary. Special attention needs to be offered to the sexual minorities, adolescents, and the elderly to prevent them from stigma and prejudice during this pandemic – people who are sexually active need to be advised about contraception and risks to pregnancy if infected. The various sexual approaches during the pandemic (most least to most risky) are summarized in Table 2.

ENSURING HEALTH SEXUALITY AND SEXUAL WELL-BEING: THE WAY FORWARD

Total abstinence and self-gratification can be the safest measures, but not always practically feasible. Abstinence-only approaches have been shown to induce guilt, decrease self-esteem, and increase noncompliance to recommended legal provisions.^[54] Human needs for intimacy need to strike an appropriate balance with personal safety and infection control. The health-care workers need to be empathic and nonjudgmental in these discussions with the couples,

Table 2: Proposed sexual approaches during the coronavirus disease 2019 pandemic

Sexual practice/ methods	Details
Abstinence	Ideal and safest, not always practically feasible
Masturbation/ self-gratification	Low risk for transmission Safe masturbation tips as followed in STD ^[52] (washing hands before touching genitals, clean sex toys, not sharing sex toys, using new condoms each time, nonirritant, and safe lubricant)
Digital sex	Appropriate and mutual consent Sociocultural acceptance Risks of data leakage and theft Sexual extortion Sexual details/images of minors can have legal consequences Risk of cyber harassment and online sexual predation Special counseling for children and adolescents Least risk to others
Sex with a self-quarantined partner	Asymptomatic carriers pose a potential risk Increased risk of multiple sexual partners
Continuation of usual sexual activities	Risk reduction counseling ^[53] Risk of infection and transmission routes, sex education Awareness about performance anxiety, sexual frustration, and symptoms of sexual disorders Reducing the number of sexual partners Identifying COVID-19 symptoms and avoid sexual contact if present Wearing mask, hand and respiratory hygiene before and after intercourse Cleaning of the place of sexual intimacy Avoiding sexual behaviors that can lead to orofecal contact Minimum contact intimacy and regulated frequency of sex, if a suspected risk
Miscellaneous	Informed decision-making Emotional support and bonding Spending quality time Communication; sharing hope and joy “COVID-” free time

STD – Sexually transmitted disease; COVID-19 – Coronavirus disease 2019

as for many, it might be a sensitive and stigma-inducing topic. Many might be hesitant to express it at all. Minors can tend to withhold valuable information (suicidality, high-risk sexual behaviors, abuse, sexual bullying, etc.), if not interviewed in confidence. People can be encouraged to engage in digital sex (such as sexting or video sex), with an eye for the safety concerns. The mutual consent of the partners is, however, an essential consideration. Digital theft has increased during the pandemic, especially with specific platforms such as Zoom, which can lead to leakage of personal data and sexual extortion.^[55] Encrypted and password-protected digital platforms are safer. The risks and legal implications need to be informed and discussed. The administration also needs to be aware of the increased use of digital forums for intimacy and change in cyber security monitoring and policies as necessary. For some minors and others with limited technology access and practice, digital intimacy might not be possible, and other avenues might need to be explored. Telephonic expression



of affection can help closeness and relationships. Being dismissive of the sexual needs during such a crisis might be counter-productive for both the clinicians and the clients. It is especially important to identify any signs of abuse or IPV at the earliest and steps to be taken immediately. The national mental health helplines related to COVID-19 can liaise with related services by the Ministry of Health and Family Welfare, Government of India.^[56] The women, child and elder helplines can also be integrated to help and counsel abuse victims, catering to their safety.

Another safe approach is to self-quarantine with partners if exposure has already occurred with an acceptable degree of risk. In that case, sexual practices can be feasible.^[57] Those who cannot engage in this might continue their sexual relationships in a controlled frequency, with risk reduction counseling. This has helped in reducing the transmission of sexually transmitted diseases (STDs). Indiscriminate sexual practices without understanding the risk of transmission can enable a much faster spread of COVID-19. Unwanted pregnancies need to be prevented and education on the use of contraceptive measures and protection from STDs need to be incorporated in the counseling modules. People affected with HIV form a susceptible section of the population, and the CDC gives particular guidelines about SARS-CoV-2 infection in HIV.^[58] Preexposure prophylaxis needs to be diligently followed. Widespread misinformation has turned COVID-19 into an “infodemic,” which is an added burden to public health. Myths related to sexual transmission can further impair safe sexual practices. Community health workers need to be active for sexual health counseling and exploring the emotional needs during the pandemic; socioculturally appropriate and multilingual infographics providing information-education-communication about sexuality during COVID-19 can help at the primary level. Active liaison of health care with media is necessary for increased penetration at all levels; mainly social media can be a uniquely equipped tool in this field for sexual health communication and promotion.^[59] Authentic sources such as the WHO and CDC are best used for reference. Few websites have useful counseling guidelines for discussion with children about online sexual risk during the pandemic.^[60]

Beyond all the other aspects of intimacy, emotional bond between partners is vital during a global crisis. Sexuality is much beyond just foreplay or intercourse. It involves holistic closeness and emotional bonding between partners. This becomes all the more critical during such pandemics, with various restrictive measures in place. Communication is the key, and informed mutual decision-making can help relationships progress. The lockdown has led many couples to be stranded together for a long time, a chance that was long due. This time can be used for generating love and intimacy, to mend strained relations, and fostering new avenues of trust and hope, that can last long beyond the pandemic threat. Spending quality time together, sharing

happiness, staying away from “information overload,” and cherishing “COVID-” free time every day, can help regenerate the intimacy.^[2] Any form of abuse needs immediate reporting, as otherwise, it tends to become a vicious and recurrent pattern. Another vital issue is the sociocultural acceptance of sexual practices in our country. Traditionally, from the descriptions of Kamasutra to the modern-day literature, intimacy has always been viewed in terms of “personal touch,” and cyber closeness thus becomes a culturally dissonant concept.^[61] Digital sexuality has often been equated with “obscene” or “inappropriate” based on traditional ideas, for which it might be difficult to adapt it even at such times of crisis.^[62] In that context, even with the use of technology for psychosexual well-being, the partners need to discuss and tailor it according to their beliefs, values, and ideals. A discordance in this area can be further damaging.

CONCLUSION

Sexual health and well-being have been extensively spoken about in the early days of “pestilences” and since then, fallen neglected during pandemics, subsumed by other health priorities. New advances might emerge with the innovative use of technology for both social and sexual connectedness. Digital intimacy can be an effective way of closeness in relationships; however, the authors do not intend to advocate that it is mandatory. It is an option that the couples can mutually choose for sexual well-being. Given the many facets of “digital sexuality” discussed above, it is more of a tailored choice and not a generic recommendation.

Antibody testing used to have a prime role in the detection of sexual risk for HIV,^[63] and similar hopes can be expected in COVID-19 too. Antibodies to the causative novel coronavirus might render someone safe as a sexual partner. As research progresses in this field, sexual medicine needs to be integrated into public health as an integral indicator of psychosocial well-being. Mental health counseling at all levels needs adequate sex education tailored to the needs of pandemics. Awareness and knowledge-attitude-practice among the health-care professionals can improve beyond the stigma, prejudice, and taboo related to the discussion about the sexual matter.

Cross-sectional and longitudinal studies need to estimate the prevalence and risk factors of sexual disorders and their sociocultural differences and predictors of the same during a pandemic. Qualitative studies are much-needed assets to understand the in-depth and lived experiences of sexuality in couples and their practices of intimacy and unmet needs. Sexual counseling can be specialized for children, adolescents, the elderly, and LGBT community, who are more vulnerable to social and sexual stigmatization. Sexuality has moved beyond just an emotional requirement



to a “rights-based” approach. Lessons learned now might help psychological preparedness and ensure psychosexual health during futuristic crises. It is high time we discard the “moral” veil of sexuality and start considering it as a natural indicator of human well-being, which needs to be nurtured for healthy relationships. In that sense, COVID-19 might be another chance for us to integrate sexual well-being into broader public health practices for the greater good.

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Banerjee and Rao: Sexual well-being and intimacy during the COVID-19 pandemic

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Impact of the COVID-19 pandemic on psychosocial health and well-being in South-Asian (World Psychiatric Association zone 16) countries: A systematic and advocacy review from the Indian Psychiatric Society

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) has emerged as a global health threat. The South-Asian (SA) countries have witnessed both the initial brunt of the outbreak as well as the ongoing rise of cases. Their unique challenges in relation to mental health during the pandemic are worth exploring.

Materials and Methods: A systematic review was conducted for all the original studies on the impact of COVID-19 and lockdown on psychological health/well-being in the SA countries of the World Psychiatric Association Zone 16. PubMed, Google Scholar, PSYCHINFO, EMBASE, and SCOPUS were searched till June 2020. Studies conducted in the age group of 18–60 years with a minimum sample size of 10, and statistically significant results were included.

Results: Thirteen studies were included in the review. They showed increase prevalence in nonpsychotic depression,


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anxiety, somatic concerns, alcohol-related disorders, and insomnia in the general population. Psychological symptoms correlated more with physical complaints of fatigue and pain in older adults and were directly related to social media use, misinformation, xenophobia, and social distancing. Frontline workers reported guilt, stigma, anxiety, and poor sleep quality, which were related to the lack of availability of adequate personal protective equipment, increased workload, and discrimination. One study validated the Coronavirus anxiety scale in the Indian population while another explored gaming as a double-edged sword during the lockdown in adolescents. Another study from Bangladesh explored psychosexual health during lockdown. Most studies were cross-sectional online surveys, used screening tools and had limited accessibility.

Conclusion: The ongoing COVID-19 crisis and its impact serve as an important period for adequate mental healthcare, promotion, research, and holistic biopsychosocial management of psychiatric disorders, especially in vulnerable groups. Mental healthcare and research strategies during the pandemic and preparedness for postpandemic aftermath are advocated subsequently.

Key words: Advocacy, coronavirus disease 2019, pandemic, psychosocial, review, South Asia, Zone 16 World Psychiatric Association

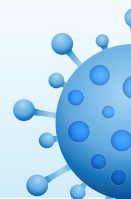
INTRODUCTION

The Coronavirus disease 2019 (COVID-19) has wreaked global havoc in the last 6 months. What started as a Public Health Emergency of International Concern, quickly escalated into a pandemic that took the world by its knees.^[1] Outbreaks like this are far from just being a public health concern. They can have immense psychosocial offshoots that might far outlast the infection itself. Although less fatal than its earlier counterparts Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome, the human-to-human transmission has been exceptionally high for COVID-19, leading to its rapid spread across the world.^[2] Vulnerable groups include the older adults, the socially impoverished (migrants, homeless, etc.), immunocompromised, those with preexisting cardio-pulmonary comorbidities and the gender minorities. They are susceptible to both the physiological as well as psychological effects of the outbreak. Even though each nation faces unique challenges against COVID-19, the common threads of psychosocial comorbidity connect them all. It has been well established by now that this outbreak has not only been causing high mortality but also large-scale psychological effects such as panic, health anxiety, loneliness, isolation, and fear of uncertainty. People with preexisting psychiatric conditions such as depression, schizophrenia, obsessive-compulsive disorders, and dementia have shown exacerbations due to multitude of factors that range from stress-diathesis, lack of access to mental healthcare resulting from lockdown and finally reduced compliance and poor supervision.^[3,4] Unfortunately, in a frantic search for biological cure and vaccines against the virus, these issues are widely neglected, contributing to increased public health burden.

The importance of mental health during the COVID-19 pandemic has been stressed upon by various public health agencies like the World Health Organization (WHO) and the Centre for Disease Control and Prevention. According

to Adhanom Ghebreyesus,^[5] Director general, WHO, integrating mental health needs into public health response will form a vital tool against the ongoing pandemic. The emotional and psychological effects of the outbreak can range from biological factors like the neurotropic effects of SARS-CoV-2 (causative agent of COVID-19) and involvement of the limbic system, psychological factors of fear, discomfort, uncertainty, and addictions as well as socioeconomic issues of isolation, stigma, domestic violence, and loss of livelihoods. Especially the frontline workers, those affected and their families, those in isolation and the socioeconomically deprived population are thought to be at the highest risk for psychiatric comorbidities.^[5] Adverse and distressing circumstances created by biological disasters have historically shown to increase disorders such as depression, posttraumatic stress disorder, generalized anxiety disorder (GAD), and substance use disorders. The impaired process of grieving associated with death, social stigma, prejudice, and discrimination with mass panic can complicate the management of infectious disease outbreaks that happened in the past with the SARS outbreak. Past studies indicated that besides the acute effect, the chronic sequelae of mental and behavioral disorders can also be prevalent that complicate the morbidities and quality of life in the postpandemic aftermath.^[6,7]

Global studies have established by now that COVID-19 has been increasingly associated with neuropsychiatric manifestations such as delirium, anxiety, depressive disorders, insomnia, and increased self-harm. Besides, the incidence of cerebrovascular accidents and seizures have been reported due to the COVID-19 that can have added psychiatric associations.^[8] Plethora of misinformation have added to societal stigma against the patients, their families and frontline health workers. The elderly, those staying alone or in isolation and the migrant workers have often been deprived of their basic living amenities making them doubly vulnerable to the health risks of the pandemics and its social effects. On the other side, those with pre-



existing psychiatric conditions might be at increased risk for the infection due to lack of supervision and inadequate compliance to precautionary measures.^[9] Most studies done till date are online surveys that have used non-specific tools to measure the overall psychological wellbeing, as the world awaits more systematic population-based work to understand the mental health risks that might help design interventions. Various assessment scales have also been used to gauge the psychological parameters specific to the COVID-19 pandemic such as the Coronavirus Anxiety Scale (CAS), Obsession with COVID19 Scale, Fear of COVID-19 Scale (FCV-19S) in Italian, Bangla, Russian and English versions, and the COVID Stress Scale which consists of five Likert subscales.^[10-12] Data on the psychometric properties and widespread use of these scales are still limited though they offer promise in understanding the emotional consequences unique to the COVID-19 pandemic. In this context, mental health professionals can play a unique role in the wellbeing of the general public and bridging the gap in mental health care that becomes all the more apparent at times of crisis in public health infrastructures. Although a global crisis, COVID-19 has differentially affected certain sectors of the world. The South Asian Association for Regional Cooperation (SAARC) countries comprise 23.7% of the world population, and a major proportion of this section is of younger age, who are essentially the working class and hence the economically productive population. In contrast to the other countries in Asia and the west, the South Asian countries (including the SAARC) have a higher rate of COVID-19 infection in the young population, which obviously affects the financial parameters.^[13] Zone 16 of the World Psychiatric Association (WPA) consists of these countries, namely India, Bangladesh, Pakistan, Sri Lanka, Nepal, Bhutan, Thailand, Indonesia, Malaysia, Philippines, and Singapore.^[14] Interestingly, this group consists of nations such as Singapore, Indonesia, and Malaysia, which took the initial hit of the pandemic and are relatively stable at present, as well as the SAARC countries, which have rising cases presently with increased morbidities and fatalities. India, comprising one of the most major and diverse populations in the Zone 16 countries, has a case fatality rate lower than other areas of the world, but the growing number of cases and limited testing can easily overburden the public health infrastructure leading to trying conditions with respect to the psychosocial burden. Jean Gough, the United Nations Children's Fund (UNICEF) Regional Director for South Asia, recently mentioned that the COVID-19 pandemic, containment and prevention measures are complicated by the natural catastrophes of widespread floods, rains, landslides and locust swarms in South Asian countries that can cause significant social and environmental changes.^[15] Added to that, is the mental health gap (mhGAP) that reaches up to 90 percent in low and middle income countries (LMIC), many of which are in South Asia.^[16] The resources are predominantly dependent on grass root health workers and general physicians which

bring in the question of adequate mental health risk communication and community awareness, concepts which become important during public health crises like COVID-19. Keeping this in the background, the authors attempted to review the psychological impact of the COVID-19 crisis and lockdown in the Zone 16 countries and consequently discuss the findings in light of a global picture and advocacy perspectives for mental well-being.

MATERIALS AND METHODS

Search strategy

The search protocol followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines as per Moher *et al.*^[17] The present study was performed by a comprehensive literature search of five electronic databases, namely PubMed, Google Scholar, PsychINFO, EMBASE, SCOPUS, and the last search was done on June 10, 2020. The search keywords for the present study were "COVID-19" OR "Coronavirus" OR "SARS-CoV-2" OR "COVID-19 pandemic" AND "mental health" OR "mental wellbeing" OR "psychiatry" OR "psychosocial" OR "psychiatric" OR "psychosexual" OR "sexual" OR "sexuality" OR "depression" OR "anxiety" OR "psychosis" OR "loneliness" OR "psychological problem," used in varying permutations and combinations, along with extensive cross-referencing. The nine countries of Zone 16 were separately added as keywords to exclude studies from other countries as an initial filter. First, all titles and abstracts were screened for relevance to the study, and the full content of the relevant studies were reviewed.

Identification and selection of studies

Search results were evaluated twice through successive screenings with increasingly stringent criteria. The initial screen was conducted on article abstracts. An article was included if the abstract indicated as a peer-reviewed original research article, written in English, and used online survey and/or cross-sectional and/or longitudinal research study on the impact of COVID-19/SARS-CoV-2 pandemic on mental health or psychological or psychosexual well-being in the population of Zone 16 (South Asian [SA]) countries. Reviews, letters to editors, case reports, and commentaries were excluded. Intervention studies were also excluded. The initial screening of this study applied the following inclusion criteria: (1) sample sizes ≥ 10 participants, (2) studied prevalence/surveys of psychological or psychosocial problems in the WPA Zone 16 countries, (3) investigated prevalence/incidence of psychiatric disorders in general population/frontline workers/COVID-19 affected patients as a consequence of COVID-19 pandemic; (4) used study population of adults age-ranged between ≥ 18 years, and (5) reported significant statistical differences in the studied parameters. The exclusion criteria were selected as: (1) < 10 patients;



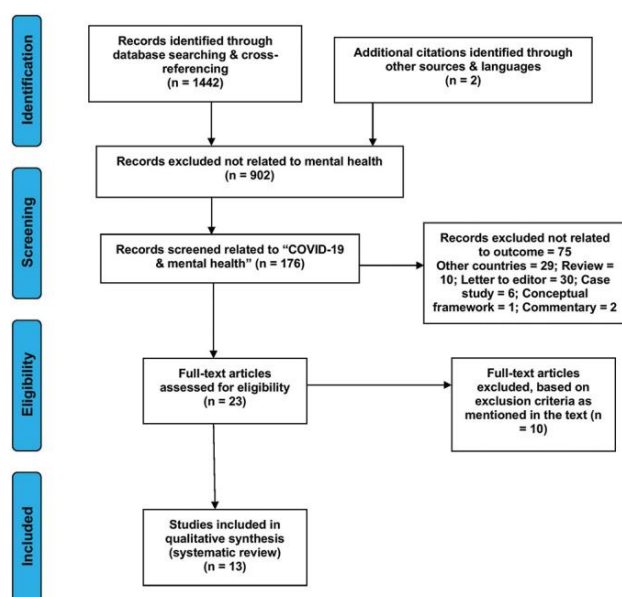


Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart for the systematic review

(2) intervention studies, (3) study with only children and adolescence, and (4) studies from other countries. General perspectives and viewpoint articles, even if related to data within the country, were also excluded.

Data extraction

DB and TSSR performed the initial searches and screened for duplicates. Other reviewers independently screened all unique search results for potential above-mentioned inclusions studied in the Systematic Review with extensive cross-referencing. The articles passing both reviewers' approval and cross-checked by other authors were finally considered for inclusion. Finally, data extraction was done by using a standardized data extraction sheet for extracted data from each study. The authors did not include stringent quality check measures as research in this area is still emerging and too strict inclusion was avoided. The data extraction form included: (1) author name, (2) year of publication, (3) study area, (4) age-groups of the participants, (5) the assessment tools and outcome measures (6) number of participants, and (7) grand mean cross-correlation matrices.

RESULTS

Selection of studies and characteristics of included studies

Figure 1 (PRISMA flowchart) depicts the process of study inclusion and selection for review. In total, 176 citations were obtained after the initial screening, which were on "COVID-19 and mental health." After further screening for original articles based on the outcome of interest, 23 articles were read in full-text, and 10 were excluded

based on the exclusion criteria mentioned earlier. Hence, eventually, 13 articles were included in the systematic review.

As the studies had used different tools and outcome measures related to the COVID-19, they will be briefly described based on their country of origin before moving into the discussion.

India

In the Indian context, Table 1 describes 10 studies on the psychosocial impact of COVID-19. These are briefly discussed as follows:

Varshney *et al.*^[18] studied the psychological impact of COVID-19 and recruited 1106 subjects in a cross-sectional study from 64 cities in India. The mean age of the participants was 41.82 ± 13.85 years and 22% of participants were health-care professionals. One-third of participants had a significant psychological impact based on the Impact of Event-revised (IES-R) score. Higher psychological impact was found in the younger group, females and those with comorbid physical illness, especially liver disease. Regarding psychological impact, most of the participants had minimal (66.8%) or mild (15%) severity (IES-R score 24–32) of impact. Few participants reported moderate (5.5%) (IES-R score 33–36) to severe (12.7%) symptoms (IES-R score >36). The need for tailored mental health interventions were stressed on by the authors.

Khanna *et al.*^[19] conducted an online survey on the psychological impact of COVID-19 between two groups of respondents, namely Practicing Ophthalmologists and trainees Ophthalmologists. The survey included 2,355 participants with mean age of 42.5 ± 12.05 years. Of these, 56.7% were male, 20.2% were still not in practice, 15.5% were single. Nearly half (52.8%) of the participants felt that training or professional work was impaired due to COVID-19, while 37% encountered difficulties to meet living expenses. The mean Patient Health Questionnaire-9 (PHQ-9) score was 3.98 ± 4.65 . One-third (32.6%) of the participants had depressive symptoms, mostly of mild (21.4%) severity, followed by moderate (6.9%) and severe (4.3%) symptoms. Subsequent analysis revealed that the significant predictors of depression were age (younger age), gender, marital status, practicing status, type of service, concerns about the profession, and inability to incur expenses.

Chandu *et al.*^[20] attempted to validate COVID-19-related anxiety scale (CAS) and they studied 307 subjects. According to their study, CAS determined a two-component structure such as: "fear of social interaction" and "illness anxiety." The final scale with seven items showed good internal consistency and reliability (Cronbach's $\alpha = 0.736$) along with moderately negative correlation (Pearson's $r = -0.417$) with self-rated mental health. Interestingly,

Table 1: Indian studies showing impact of coronavirus disease 2019 on mental health

Authors (year)	Place of the study	n (number of subjects)	Methods	Outcome and tools
Varshney <i>et al.</i> , 2020 (FEEL-COVID survey)	Department of Psychiatry, ILBS, New Delhi, India	653	Cross sectional survey and IES-R method	Psychological impact/life events based on IES-R score
Khanna <i>et al.</i> , 2020	LV Prasad Eye Institute, LV Prasad Marg, Hyderabad, Telangana, India	2,355	Online survey	Depression at mild, moderate and severe levels of severity
Chandu <i>et al.</i> , 2020	Sibar Institute of Dental Sciences, Guntur, Andhra Pradesh, India	307	Questionnaire-based survey as per Likert scale	COVID-19 Anxiety Scale and its psychometric properties
Narasimha <i>et al.</i> , 2020	NIMHANS, Hosur Road, Bengaluru, India	96	Hospital-based observational study	Alcohol withdrawal syndrome with seizures, delirium tremens and hallucinations
Roy <i>et al.</i> , 2020	King George's Medical University, Lucknow, Uttar Pradesh, India	662	Cross-sectional, and observational study	Knowledge, attitude, practices and perceived anxiety related to COVID-19
Balhara <i>et al.</i> , 2020	National Drug Dependence Treatment Center, All India Institute of Medical Sciences, New Delhi, India	393	Cross-sectional study	PHQ-9, GAD-7, DSM-IV (to assess depression) and IGDSF-9 for gaming behavior during lockdown
Balhara <i>et al.</i> , 2020	National Drug Dependence Treatment Center, All India Institute of Medical Sciences, New Delhi, India	73	Hospital-based observational study	Psychological distress, alcohol consumption and alcohol withdrawal symptoms
Grover <i>et al.</i> , 2020	Department of Psychiatry, Postgraduate Institute of Medical Education and Research, Chandigarh, India	1685	Multicenter online survey	PHQ-9, GAD-7, WEMWS for anxiety, depression, stress, sleep and other associated psychological parameters
Chakraborty and Chatterjee, 2020	Departments of Psychiatry and Anatomy, College of Medicine and JNM Hospital, Nadia, West Bengal, India	507	Online survey	Self-designed questionnaire for assessing worry about infection, distress, anxiety and sleep disorders
Chatterjee <i>et al.</i> , 2020	Department of Psychiatry, Diamond Harbour Medical College, Diamond Harbour, West Bengal, India	152	Cross-sectional online survey	Knowledge, attitude, behaviour of doctors; DASS-21 for psychiatric morbidities

IES R – Impact of Events Scale Revised; PHQ – Patient Health Questionnaire; GAD – Generalized Anxiety Disorder; IGDSF – Internet Gaming Disorder Short Form; WEMWS – WarwickEdinburgh Mental Well being Scale; DASS 21 – Depression Anxiety Stress Scale 21; ILBS – Institute of Liver and Biliary Science; NIMHANS – National Institute of Mental Health and Neurosciences; COVID 19 – Coronavirus disease 2019; DSM IV – Diagnostic and Statistical Manual IV

the results found significantly higher anxiety scores in the lower educational qualification group. The authors stressed that CAS is a rapid, valid, and reliable test, which might be a useful tool to assess the psychological impact of the pandemic in the Indian population.

Narasimha *et al.*^[21] investigated hospital-based 96 middle-aged participants with an average 46.0 ± 9.0 years and male patients were found suffering from severe alcohol withdrawal syndrome during the lockdown period. Delirium tremens, with or without seizures, was the most common presentation (80%), followed by withdrawal seizures (17%) and withdrawal hallucinosis (12%). Three-fourth (76%) belonged to below the poverty level. All subjects reported heavy alcohol use as per standard use on a daily basis. Majority (95%) subjects reported COVID-19-related lockdown cause for the sudden cessation of alcohol use. This was one of the first Indian studies to explore substance abuse complications as a result of the sudden national lockdown.

Roy *et al.*^[22] assessed the knowledge, attitude, anxiety experience, and perceived mental healthcare need among 662 adult subjects in India during COVID-19. The online survey was questionnaire-based and used non-probability snowball sampling technique. A moderate level of knowledge

about the COVID-19 infection and the least knowledge about prevention were reported. The subjects showed higher levels of anxiety and 80% were preoccupied with the thoughts of COVID-19. The overuse of gloves and sanitizers was reported in 72%. The study indicated sleep difficulties (12.5%), paranoia about acquiring COVID-19 infection (37.8%) and distress related to social media (36.4%) as the common distressing factors. Perceived mental healthcare need was reported by >80% of the sample, which again advocated the need for enhanced psychosocial care during the pandemic.

Balhara *et al.*^[23] conducted a cross-sectional study to know about the gaming behavior of 393 college students during the lockdown period. This study was carried out through social media contact, namely E-mail and WhatsApp messenger using PHQ-9, GAD-7, Diagnostic and Statistical Manual-IV (to assess depression), and Internet Gaming Disorder Short form-9. About half (50.8%) of the participants reported an increase in gaming behavior during the lockdown period. Further analysis indicated that hours of gaming per day increased due to the stress of examination and the participants' belief that gaming helps in stress management. Social isolation and lack of family activities were added factors. The authors suggested "gaming" as a two-edged sword during the lockdown period.



In another study, Balhara *et al.*^[24] studied 73 males with alcohol use disorder of 8.66 ± 6.2 years. Although sale was restricted during the lockdown, 20% of subjects continued procuring alcohol. Two-third (62.5%) of the participants obtained alcohol at higher prices from illicit sources. In addition, about one-fifth of these patients, were at risk of consuming adulterated alcohol. A small proportion (6.6%) participants reported experience of alcohol withdrawal during the starting of lockdown. Only one subject experienced withdrawal seizures. Majority of the subjects could not access health-care facilities to manage their withdrawals. The exacerbated psychosocial effects of alcohol use due to the pandemic situation were once again highlighted in this study.

Grover *et al.*^[25] evaluated the psychological impact of lockdown due to COVID-19 pandemic in 1685 people to assess the prevalence of depression, anxiety, perceived stress, well-being, and sleep. It was an online survey conducted with the Survey Monkey platform, the survey link being circulated using WhatsApp. In this study, PHQ-9, GAD-7, WarwickEdinburgh Mental Well-being Scale were used to assess the various parameters. About two-fifth (38.2%) of the participants had anxiety and 10.5% of the participants had depressive disorder. Among the participants, about 40.5% had either anxiety or depression. Moderate stress and poor well-being were found in 74.1% and 71.7% respectively. Overall two-fifths were experiencing common mental disorders during the COVID-19 situation. This was the first study by the Indian Psychiatric Society (IPS) to assess the psychological impact of the outbreak.

Chakraborty and Chatterjee^[26] in a regional survey evaluated 507 subjects with a mean age of 33.9 ± 8.27 years in West Bengal, India. The 38-item self-designed questionnaire was circulated through WhatsApp. 71.8% and 24.7% showed increased worries and depressive symptoms during the

pandemic. About half (52.1%) of the participants were preoccupied with the idea of contracting COVID-19 and 21.1% wanted testing irrespective of symptoms. About 69.6% were worried of financial loss during the period of lockdown. Slightly less than one-third (30.8%) of the participants perceived health anxiety to be significantly increased and feared that it might not normalize even post lockdown. This study especially showed the importance of uncertainty and panic as factors influencing psychological health.

Chatterjee *et al.*^[27] cross-sectionally assessed the knowledge, attitude, and behavior (KAB) of 152 doctors regarding the pandemic and the influence of depression, anxiety, and stress. KAB of the participants was obtained through semi-structured proforma, and psychiatric morbidity was measured by the Depression, Anxiety, and Stress Scale-21 (DASS-21). Among the participants, 34.9%, 39.5%, and 32.9% were depressed, anxious, and stressed, respectively. Significant predictors of psychological burden were job in the health sector, duty hours, lack of protective measures, and altruistic coping. Stigma and discrimination against the frontline workers were identified as important factors contributing to their stress.

Pakistan

Balkhi *et al.*^[28] [Table 2] studied behavioral changes during COVID-19 pandemic situation among 400 participants in Karachi. It was an online survey through a structured self-administered questionnaire. Majority of participants were aged <35 years, with equal male: female ratio. Everyday fear related to COVID-19 was seen in 62.5%. Participants manifested fear when they visited outdoor (88.8%), were concerned about family's health (94.5%), and felt lack of confidence related to the precautionary measures (71%). Home was not

Table 2: Study in Pakistan showing impact of coronavirus disease 2019 on mental health

Authors (year)	Place of the study	n (number of subjects)	Methods	Outcome and tools
Balkhi <i>et al.</i> , 2020	Jinnah Sindh Medical University, Karachi, Pakistan	400	Descriptive and cross-sectional online survey	Behavioural reactions to pandemic: fear, distress, anxiety, attitudes to social media; self-designed questionnaire

Table 3: Multicenter studies on impact of coronavirus disease 2019 on mental health

Authors (year)	Place of the study	n (number of subjects)	Methods	Outcome and tools
Arafat <i>et al.</i> , 2020	Department of Psychiatry, Enam Medical College and Hospital, Dhaka, Bangladesh	120	Multicenter cross-sectional and cross-national online survey	Sexual behavior for pre, during and post-COVID-19 lockdown; Self-designed questionnaire (Google form)
Chew <i>et al.</i> , 2020	Division of Neurology, Department of Medicine, National University Health System, Singapore and The Department of Neurology, Yashoda Hospital, Secunderabad, India and other departments	480 (India)+426 (Singapore)=906	Multicentre cross-sectional online survey	DASS-21 and the IES-R for psychological problems viz. depression, anxiety, stress, and posttraumatic stress disorder

DASS 21 – Depression Anxiety Stress Scales 21; IES R – Impact of Events Scale Revised; COVID 19 – Coronavirus disease 2019



considered to be safe by most. Majority (82.8%) subjects reported panic due to fake news in social media. A small proportion (14.8%) of subjects had pretended to be sick for avoiding the workplace/educational institute. In addition, 86.5% of participants had restricted their physical contact with people, 74.5% avoided health-care facilities, 84.5% postponed social engagement and 87% showed obsessive washing of hands.

Multicenter studies [Table 3]

The Multicenter studies included in the review are summarized in Table 3. Arafat *et al.*^[29] performed a multicenter online survey to study the effects of lockdown on the sexual life of the participants from three South-East Asian countries (India, Nepal, and Bangladesh). This research was conducted through Google form in the English language among 120 participants. The average age of the participants was 35.42 ± 5.73 years and majority were in the 30–39 years age group. Three-fourth (77.5%) of the participants were male and most subjects had a postgraduate degree. Majority of participants engaged in sexual activity with their partner once to five times a week before (76%) and during lockdown (72%), while 10% showed an increase in sexual interactions during the lockdown period.

Chew *et al.*^[30] investigated the relationship between psychological outcomes and physical symptoms among 906 health-care workers in five major COVID-19 hospitals of India and Singapore. DASS-21 and IES-R were used besides evaluation of demographics factors and medical history. The age range was 25–35 years and about 50.2% were single. The subjects reported common physical symptoms such as headache (31.9%), throat pain (33.6%), anxiety (26.7%), lethargy (26.6%), and insomnia (21.0%). A small proportion (5.3%) had moderate-to-severe depression, 8.7% had moderate-to-extremely severe anxiety, 2.2% had moderate-to-extremely severe stress, while 3.8% had moderate-to-severe levels of psychological distress. Older subjects had more correlation between physical symptoms in the preceding month and depressive symptoms as well as posttraumatic stress. Linear regression indicated that the presence of physical symptoms was related to higher mean scores in the IES-R, DASS Anxiety, Stress and Depression subscales.

DISCUSSION

The reviewed studies mainly show an increase in the prevalence of nonpsychotic depression, anxiety, fear, somatization, insomnia, and alcohol abuse disorders. All the surveys were online except two, which studied a hospital-based sample.^[21,24] This is pragmatic considering the travel restriction during the lockdown. However, multiple studies have stated this as a limitation as only people who were conversant in English could attend to online questionnaires and technologically savvy were

accessed.^[18,19,22,23] Few studies have also used socioculturally relevant surveys, translated in local languages.^[25,27,30] The results resonate with large-scale surveys done in other countries, which bore significant burden of COVID-19. Huang and Zhao collected data from 7236 participants in China and reported increased prevalence of generalized anxiety (35.1%), depressive symptoms (20.1%), and sleep anxiety in the general population.^[31] The health-care workers (HCWs) had the worst sleep quality and decreased total sleep time. Health-related anxiety and guilt were marked in them. A recent study involving 1563 health professionals found that nearly half reported depression, whereas 44.7% and 36.1% reported anxiety and sleep disturbances, respectively.^[32] Two studies from India and one multicenter study assessed physicians for psychological complaints (present in one-third) and reported the anxiety symptoms to be directly correlated with increased duty hours, lack of shift rotations, societal stigma, and inadequate medical protective equipment.^[19,27,30] This is in contrast with the physician stress factors in China and the United Kingdom (U.K.), which were increased witness to death and dying, increased risk of exposure and self-blame, as well as the guilt of spreading the infection to the family members.^[33–35] Liu *et al.*^[36] explored the qualitative perspectives from doctors and nurses in Hubei, China and stated the crucial role of social support, peer counseling and self-management strategies for psychological resilience. Although similar recommendations along with community awareness have been suggested in various of the reviewed studies, the “voices” of the HCW are yet to be heard and explored in SA countries, which is particularly important considering the increasing cases and burdened public health infrastructure. Worsening in preexisting psychiatric disorders has been reported in studies across countries, especially those affected with psychotic, affective, and cognitive disorders. Suicide risk related to socioeconomic crunches have been reported from the United States (U.S.) and Italy.^[37–39] Such studies are probably warranted in the SA countries as they pass through the early stages of pandemic, especially with a high mental illness load and increased mhGAP. Some of the reviewed studies showed the increased correlation of social media exposure with psychological issues, especially sleep deprivation, increase in alcohol withdrawal after the sudden lockdown in India, increased gaming behavior that was inversely related to physical activity in students, and finally, impaired psychosexual health.^[21–24,27,29] The last study was, however, criticized due to the ethical considerations and standardization of the online surveys by multiple other authors. The study from Pakistan pointed out the importance of social distancing as it disrupted rituals, gatherings and was associated with increased social media consumption and enhanced fear as well as anxiety about the infection. Fear related to the infection, avoidance of workplace, and nonspecific panic arising from uncertainty were found to be common in the studies across the Zone 16 countries.^[19,22,25,26] Only one study validated



the Coronavirus anxiety scale (CAS) in India.^[20] Although studies are emerging in this regard, the widespread use of these scales for data collection without appropriate testing of their psychometric properties have raised concerns in research.^[40] It is also important to understand that all these studies are cross-sectional, have used screening tools like PHQ-9, GAD-7, etc., which do not necessarily help in the categorical diagnosis of disorders and have inherent limitations of using online surveys. Many of the surveys are conducted using google forms/WhatsApp, which have been criticized for poor reporting of response rates, nonverification of response sources, appropriate approvals, and standardization.^[41] Furthermore, these studies on the general population miss the acute behavioral effects of the COVID-19 that might possibly elucidate the neurobiological interactions between the virus and the brain. Altered mental status and behavioral changes have been mentioned to be acute effects of the virus, and a putative link between those affected with COVID-19 and long-term psychiatric comorbidities might merit further research.^[8] Nevertheless, even with these caveats, the reviewed studies portray various aspects of the psychological impact of the outbreak on the general population in the Zone 16 countries that can address interventions and policies for mental healthcare.

Advocacy principles for mental health during coronavirus disease 2019

Psychosocial healthcare

Since the time WHO called for a global mental health action related to COVID-19, various National mental health associations like the IPS, the Pakistan Psychiatric Society, Bangladesh Association of Psychiatrists, Singapore Psychiatric Association and even the SAARC Psychiatric Federation (SRF) have sprung into action for promoting psychosocial health and care under the adverse circumstances. Keeping in mind that the LMIC of South Asia can have unique considerations like accessibility to health care, limitation of resources increased population and viral case burden, difficulties in multi-sectoral coordination, outdated legislations in relation to pandemics with poor provision for mental healthcare and finally increased stigma, the estimated psychiatric comorbidities during a biological disaster like COVID-19 tend to get amplified. The IPS, in its official statement, stressed on the paramount importance of assessing the psychological needs of the general population during the pandemic, especially those affected and the frontline workers. Along with the National Institute of Mental Health and Neurosciences (NIMHANS), the IPS brought out the “Mental Health Challenges during COVID-19 pandemic: Guidance for psychiatrists,”^[42] which borrows from the comprehensive guidelines for mental healthcare in psychiatric and general hospital settings, released earlier by NIMHANS.^[43] The document holistically deals with “safe practices” to minimize the psychological and physiological risks of HCWs, the allied professionals, patients, and their families. It covers telepsychiatry, psychopharmacology, and brain stimulation practices during COVID-19, also catering

to special populations like children and adolescents, older adults, perinatal groups, and rehabilitation settings. Various published commentaries from Pakistan, Bangladesh, Thailand, and Singapore also stress on psychological preparedness for the pandemic and warn about the upcoming rise in psychiatric morbidities in the near future.^[44-47]

The role of mental health professionals can be vital in this regard, namely in education, training, encouraging mental health-promoting behaviors, cross-specialty integration, facilitating problems solving approaches, empowering patients and allied professionals, and finally enabling self-care strategies for resilience.^[48] Prepared in lines of the Zika outbreak, a community-based psychosocial

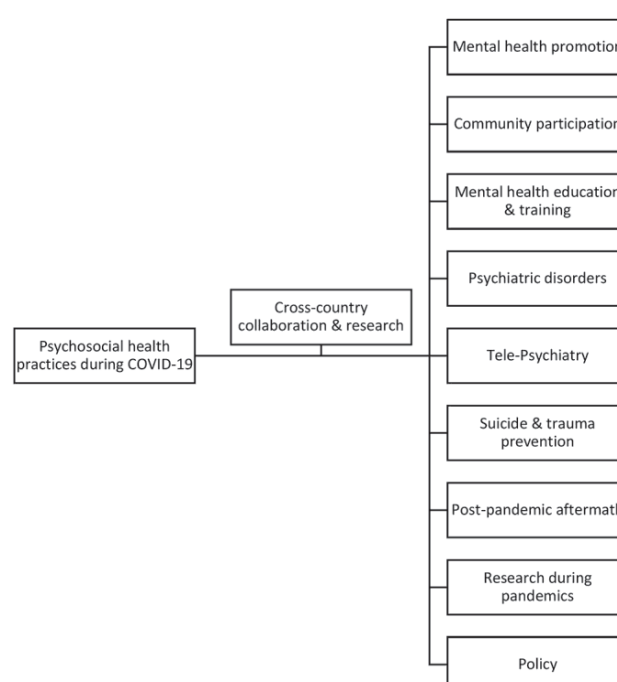


Figure 2: Mental and psychosocial health practices during the Coronavirus disease 2019 pandemic

Box 1: Suggested areas of primary care collaboration in mental health during pandemics

Using technology for supervision and training in identification and treatment of psychiatric disorders
 Involving general physicians, nurses, lay health workers and counselors
 Community programs for mental health awareness
 Local management of stable patients to reduce risk of infection
 Shared resources: Case worker based approach
 Liaising with media for mental health promotion and stigma reduction
 Improving knowledge and beliefs related to pandemic
 Emergency triage planning at district levels: adequate referrals
 Consultation-based care at tertiary centers
 Adequate screening for depression, anxiety and substance use disorders in the community
 Target vulnerable groups for interventions
 Telephonic counseling and support for frontline workers
 Multidisciplinary collaboration: Mental health professionals as advocates

Table 4: Attributes of various mental health practices during the pandemic

Mental healthcare practice	Attributes
Mental health promotion	Improve KAP Fight misinformation Community awareness
Community participation	Integration of care: GPs, AYUSH, primary HCWs, etc. Tele-training and guidance Community screening for SMD and CMD
Mental health education and training	IEC activities Liaison with media/popular figures Anti-stigma interventions Prevention of domestic violence, child and elder abuse
Dealing with psychiatric disorders	Tele-medicine (online platforms, mobile apps, telephonic consultations) Medication availability District mental health teams Coordination of referrals Prompt management of psychiatric emergencies Decreased institutionalization
Tele-psychiatry	Standardization of guidelines/prescribing patterns Legislations Tele-psychotherapy Enabling access for the older adults/minorities
Suicide and trauma prevention	Gatekeeper training Suicide prevention community programs Target vulnerable groups
Post-pandemic aftermath	Digitalization of care and research Preparedness Resource allocation Cross-specialty coordination Epidemiological data to address policies
Research during pandemics	Ethics Validation of new tools specific to COVID-19 Standardization of online surveys Focus on: Neurobiology, acute and long-term neuropsychiatric effects, lived experiences, vulnerable groups, population-based psychiatric risk estimates for various disorders Sharing research Socio-cultural sensitivity
Policy	Enabling the above practices Budget and resource allocation Including mental health in legislations (pandemic acts) National guidelines for safe practice

KAP – Knowledge attitude and practice; GP – General physicians; AYUSH – Ayurveda, Yoga, Unani, Sidda and Homeopathy; HCW – Health care workers; SMD – Severe mental disorders; CMD – Common mental disorders; IEC – Information Education and Communication; COVID-19 – Coronavirus disease 2019

toolkit was proposed by Banerjee and Nair^[49] that target socio-culturally sensitive interventions at different levels to integrate various stakeholders for public awareness, participation, and mental health-care delivery. The role of media integrating it with psychological care for the public has been stressed upon by the authors. Involving

the general physicians, nurses, and primary care workers, as well as qualified practitioners of alternative medicine, are essential for service delivery in the community as many SA countries have an inadequate psychiatrist-patient ratio. Based on this, the Primary Care first (PCP) and Collaborative Care model had been suggested by Türközer and Öngür,^[50] which integrate physical and behavioral care during the outbreak. Certain suggested areas of tertiary-primary collaboration are listed in Box 1. Mental health education can help Information-Education-Communication activities for the public to fight health-related misinformation, stigma and improve the Knowledge-Attitude-Practice gap of the masses. This serves for mental health advocacy and awareness that also help in early detection of cases, psychoeducation, better compliance and suicide prevention. Harnessing technology both for care and training need standard guidelines and prescriptive patterns. It can be a boon during restrictive conditions of an infectious disease outbreak like COVID-19, but at the same time, limited accessibility and poor Internet connectivity in various areas are the real challenges. NIMHANS, in collaboration with the Tele-medicine Society of India and the IPS recently released the tele-mental health guidelines (telepsychiatry, tele-psychotherapy and tele-psychiatric social work) that are first of its kind, are relevant to the current situation and can serve as a model for other countries.^[51] The implementation is, however, fraught with its usual challenges and will serve as a test for time. Above all, suitable legislations are necessary to enable these measures updating the existing Pandemic Acts to suit the present needs and those of any such futuristic crises. Keeping in mind the myriads of challenges involved related to psychosocial needs during the pandemic spanning over dealing with psychiatric disorders to the mental health care needs of the general public and finally education, training and research, Figure 2 and Table 4 summarize the various aspects of mental health services during the pandemic, involving cross-country collaboration and coordination.

Research in mental health during pandemics Implications

The effects of coronaviruses on human central nervous system are a well-known fact. It is worthwhile to explore the psychological, social and neuroscientific underpinnings of COVID-19 and systematic research might help shape interventions and policies. The landmark paper in Lancet on multidisciplinary research priorities in mental health science during the COVID-19 pandemic emphasizes on organized and high quality immediate priorities and long-term research strategies.^[52] Research-driven management will be better suited to address the psychosocial and neuropsychiatric effects of the pandemic and shape guidelines for future. Holmes *et al.*^[52] further raises several important areas of global research on “mental health and COVID-19”: effect of the outbreak on self-harm and suicide, generation of chronic trauma, impact of social distancing and prolonged



lockdown, vulnerabilities of the special groups, harmful effects of repetitive media exposure and misinformation, and finally compliance strategies for mental healthcare. Some of the studies reviewed in this article attempt to answer these questions, though cross-sectionally. Population-based risk estimates, lived experiences of the frontline groups and patients, ethnographic work with the minorities, and community-based heterogeneous mixed-method studies might offer better perspectives. The emerging novel tools specific to COVID-19 such as CAS, FCS, etc., offer promise but need to be better understood in terms of psychometric properties and the cross-country validation will help add value to their use.^[10]

The SAARC countries have numerous ethnocultural and racial variations, and research needs to be sensitive to them. Digital-driven research and standardization of online surveys will be a norm of the post-COVID era, and psychiatric research needs to be prepared for it.^[50] At the same time, ethics is a vital aspect and there needs to be a fine balance between scientific enthusiasm and the principles of benevolence. This is specially applicable for populations with impaired capacity for consent like older adults with cognitive impairment, severe mental disorders, and minors.^[53] The ultimate goal of scientific research is the greater good, but definitely not at the cost of undermining the autonomy and rights of the general population, who are already in the clutches of a pandemic.

CONCLUSION

COVID-19 has created rippling psychosocial effects globally, and the South Asian countries face unique challenges to deal with the same as discussed above. The WPA in its official position statement has highlighted the role of psychiatrists, protection of the mentally ill, and improvising on the quality on psychiatric care and research.^[54] The present review shows an increased prevalence of depression, anxiety, sleep, and alcohol use disorders in the general population as an impact of COVID-19 and lockdown, with the symptoms being related to social isolation, misinformation, social media exposure, fear of infection, and uncertainty. Xenophobia and stigma are other related factors. Mental healthcare and research strategies during the pandemic and preparedness for post-pandemic aftermath are advocated subsequently. It is imperative to mention that recent Indian studies have been published on the state of mental health services in various training centers and sleep quality during the COVID-19 lockdown.^[55,56] They were outside the timeline for the review, but nevertheless holds promise in subsequent analysis and research. The validity of mental health assessment tools specific to COVID-19 and ethical concerns for online surveys are vital areas for consideration. Lessons learnt from this pandemic might help shape interventions and legislations in the near future. "Tremendous interconnectedness" at local and global levels

has been recommended to fight the pandemic.^[57] In that context, the available research forms the anchor and calls for more systematic exploration and multi-disciplinary care in areas of mental health during the ongoing crisis.

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Conflicts of interest

There are no conflicts of interest.

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Comments on psychological impact of COVID-19 lockdown: An online survey from India

Sir,

We thank Singh^[1] and Shukla^[2] for their comments on our article.^[3] Both the authors have raised issues related to the translation of questionnaire to multiple languages. We agree that carrying out the psychometric evaluation of the translated versions in all languages could have added to the whole effort. However, the research was done at the beginning of the COVID-19 pandemic, and carrying out psychometric evaluation of the scales, in the absence of in-person contact, was not feasible, and this itself would have taken lot of time. The other option was to conduct the study by using the available English and the Hindi version of the scales. The Hindi version of the scales has some psychometric data available.^[4-7]

However, to have a wider perspective, we translated the scales into various languages to avoid limiting the study population to those who are able to read only English/Hindi. However, at the end of the survey, we realized that there were few takers for those with local languages. Majority of the responses were received for the English ($n = 1072$; 63.62%), and this was followed by the Hindi (with English version as part of bilingual) version ($n = 213$; 12.64%). Other languages contributed to the remaining 400 (23.73%) responses.

We reduced the time frame for the assessment on perceived stress scale, keeping the timing of the survey. The suggestion of labeling it as a modified version of perceived stress scale is well taken. However, the same was not considered, because, except for the time frame, we did not make other adaptations in the scale. Regarding the Warwick Edinburgh scale and the age norms, the survey actually included subjects aged 18 and above. As already mentioned in the article, we actually intended to exclude all the responses of people aged less than 18 years. Unfortunately, we missed out on 4 responses, 2 from those aged 14 years, 1 aged 15 years, and one aged 16-year-old participant. Accordingly, considering the total number of subjects aged less than 18 years to be 0.25% of the total study sample, this should not be considered as a major issue, which could have influenced the findings. Singh^[1] pointed out a difference in the “frequencies in the variable occupation and profession as retired mentioned are differently documented.” We are aware of the same, and the same can be understood from the perspective that many professionals who had retired formally from their government jobs, marked themselves as retired, but at other place while answering about their profession, marked themselves as per their professional degrees. Hence, we did not alter the responses to align these and presented the responses as such. Unfortunately, the survey questionnaire had no such provision to record the specialty of the healthcare

professionals, which was raised. Considering that this was an online survey and we were not sure about the response rate, we had formally not estimated the sample size. Singh^[1] raised the issue that the “the article did not discuss the effects of lockdown on severe depression and suicide.” We did present the information about the prevalence of severe depression as per the PHQ-9. This study did not aim to evaluate the incidence of completed suicide; hence, this issue is off-placed.

Shukla^[2] has brought out the issue of snowball sampling. It is a pertinent issue, but it needs to be understood that, at the time when the survey was done, the use of other sampling methods could have led to the loss of opportunity to carry out such a survey. In terms of issues related to the face validity of the traditional assessment tools (e.g., PHQ-9 and GAD-7), it is important to understand that the same has been used during the current pandemic across the globe to evaluate the psychological impact on general population and healthcare workers. Hence, this limitation applies to all the surveys carried out during the ongoing pandemic. Shukla^[2] has pointed about the failure to elaborate on the geographical location of the participants of this enormous survey involving several languages. We could not present the breakup of the geographical location of the participants as this variable was not part of the survey. In terms of time to response, the fact that the finding of the current survey of median time to respond to the survey was the 2nd day of the survey itself is understandable, considering the fact that, in most of the surveys, majority of the responses are received during the initial days of the survey. For the variable “level of working,” we have rechecked the data and the total figures do add up to 100%. We did not provide the description of the variable “other,” for which 147 (8.7%) of the responses were given, as the numbers pertaining to each combinations were small, and this was not the major outcome variable.

Further, Shukla^[2] pointed out the issue of SurveyMonkey site not technically supporting one device one response. In response, we would like to say that we verified the responses for the IP addresses to the best of our understanding and no effort was made to purchase the responses. We understand that SurveyMonkey platform has the option of purchasing the responses. If we wanted to utilize all these strategies, we could have used the same to have much more number of responses. As pointed out in the comments of Singh,^[1] we have tried to be very brief in drawing any conclusions. At the end, Shukla^[2] again has misunderstood when we say that the response rate is low. In a snow ball sampling technique, it is not possible to know the denominator; hence, it is not possible to calculate the response rate. When we said that the response rate was low, we basically wanted to put forth the issue that we expected a wider response, from various parts of the country, and we did



not get the desirable level of response. We do not claim that the survey reflects the exact picture at the ground level in every part of the country, as there are many limitations of this survey, as documented in the paper. It is important to understand that every research endeavor will have its limitations and the findings of the same must be interpreted in light of the same.^[8]

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Conflicts of interest
There are no conflicts of interest.


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Recurrent, progressive ventricular tachycardia after electroconvulsive therapy

Sir,
Grover and Aggarwal^[1] reported a case of an adult female with paranoid schizophrenia, who suffered recurrent ventricular tachycardia (VT) during electroconvulsive

therapy (ECT) regimen. We, however, would like to share some concerns regarding the case and the report that emerged from a journal club discussion on the said article.



Perceived Stress, Parental Stress, and Parenting During COVID-19 Lockdown: A Preliminary Study

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Abstract

Background: The outbreak of COVID-19 is a global public health emergency with multifaceted consequences for people's lives and their mental health. Parenting in the time of COVID-19 can be demanding as parents now find themselves in a challenging situation with young, energetic children locked down within the house. However, this issue is not systematically studied.

Aim: The present study examined the stress experienced by parents during COVID-19 lockdown.

Methods: The study was cross-sectional in nature using the online survey method conducted in the month of April 2020. Parents were sent a survey link and were requested to fill the self-designed questionnaire, Parental Stress Scale and Perceived Stress Scale. A total of 227 parents filled in the forms, out of which 196 were complete.

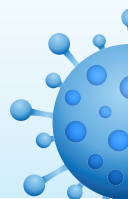
Results: Majority of the parents reported moderate (63%) to high (4%) perceived stress since the COVID-19 lockdown, 37% reported feeling more stressed as a parent after the lockdown, and 8% of the parents said they needed to talk to a counsellor/psychologist. Mothers, parent of children with developmental disorders, and parents who had interpersonal difficulties with spouse and children had significantly higher perceived stress and parental stress compared to parents without these difficulties. Both perceived stress and parental stress were significantly associated with shouting, yelling or screaming, spanking or slapping the child, preoccupation with worries, and difficulty in focusing on parenting and disciplining the child, and excessive time on TV or video games in children.

Conclusions: The results offer preliminary data-based insight into the impact of the COVID-19 pandemic on families in India.

Keywords: Parental stress, Perceived Stress, Interpersonal Difficulties, COVID-19, Stressors, Parenting.

Introduction

The epidemic of the 2019 novel coronavirus SARS-CoV-2, causing the coronavirus disease 2019 (COVID-19), first expanded within the Wuhan region in China and quickly spread to Europe and to rest of the world. The COVID-19 has currently affected over 200 countries. The outbreak of COVID-19 is a global public health emergency, with multifaceted and severe consequences, and has posed a serious threat to global health due to high fatality rate, besides its wide-scale ramifications on socio-economic and psycho-emotional aspects of people's life.[1] In order to contain the spread of the disease, the government of India has employed



public health emergency measures to reduce the spread of the virus such as encouraging the use of facemasks, sanitisation of hands, house, and social distancing, which has led to drastic changes in the day-to-day lives of people. Other restrictions include curfews, quarantine, lockdown, self-isolation, and closure of schools, businesses and universities.

The COVID-19 pandemic situation has the potential for various adverse effects on the mental health of the population across multiple domains. Distress and anxiety can be considered as normal reactions to a situation as threatening and unpredictable as the coronavirus pandemic. Possible stress-related reactions in response to the coronavirus pandemic may include changes in concentration, irritability, anxiety, insomnia, reduced productivity, and interpersonal conflicts.[2]

Parenting in the time of such a pandemic can be specifically taxing as parents now find themselves in a difficult situation with young, energetic and active children locked down within the house. School closures, working remotely from home, physical distancing is a lot to navigate for anyone, and more so for parents, who are struggling with uncertainties about future, balancing work and child care. Parents also need to ensure food, financial, and health security for themselves and their household, and the stress may render some situations and emotions difficult to cope with.[3] Consequently, such difficult conditions at home may deplete personal resources and the ability to manage stress effectively, thereby increasing the risk of parental burnout. Prolonged exposure to high levels of stress in parents and the inability to regulate such debilitating emotions at home may be detrimental for children and may lead to a dramatic increase in child neglect and abuse.[4] Literature has shown that increased parental stress is associated with greater use of harsh parenting styles.[5] Decreased levels of sensitive parenting and greater use of harsh discipline have been linked to the development of behavioural problems.[6][7][8][9] Although the impact of the pandemic on millions of children, adolescents and families is currently being evaluated in several studies worldwide, the presence of this issue and its ramifications in public debate, as well as published literature in India, is not present. Therefore, the present study was carried out to examine the parental stress experienced by parents in during COVID-19 lockdown in India, as well as the factors associated with parental stress. The findings can help mental health professionals address the consequences of the lockdown on mental wellbeing, and develop intervention strategies and policies to help parents deal with the stress.

Methods

Study design

A cross-sectional, online survey design using Google forms was adopted to obtain the data. Google Forms offer the advantage of submitting a response when maintaining anonymity. The survey was initiated during the lockdown, from April 20, 2020, and kept open for responses till May 1, 2020. Inclusion criteria laid for the study included both fathers and mothers from India, with children below 15 years of age. Parents who were unwilling to participate, whose children were older than 15, or who were presently not living with their children were excluded from the study. Following tools were used:

Self-designed questionnaire: A semi-structured self-designed questionnaire was developed for the purpose of the study. It included socio-demographic information such as parent age, gender, location, family type, parent education, work status, marital status, past history of psychiatric illness and physical health conditions in parents and children. The questions also assessed



financial stressors, interpersonal difficulties with spouse and children, stress as a parent during the lockdown, and parental behaviours toward children.

The Parental Stress Scale [10]: The Parental Stress Scale is a self-report measure that contains 18 items representing pleasure or positive themes of parenthood (emotional benefits, self-enrichment, personal development) and negative components (demands on resources, opportunity costs and restrictions). Respondents are asked rate their agreement in terms of their typical relationship with their child/children on a five-point rating scale from strongly disagree (1), disagree (2), undecided (3), agree (4), to strongly agree (5). Eight items are reverse scored so that possible scores on the scale range between 18-90. The scale is intended to be used for the assessment of parental stress for both mothers and fathers, and parents of children with and without clinical problems. It has satisfactory levels of internal reliability (0.83), and test-retest reliability (0.81). The scale demonstrated satisfactory convergent validity with various measures of stress, emotion, and role satisfaction, including work/family stress, loneliness, anxiety, guilt, marital satisfaction, marital commitment, job satisfaction, and social support.

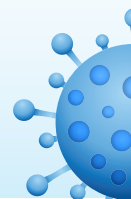
Perceived stress scale [11]: The Perceived Stress Scale is a widely used psychological instrument for measuring the perception of stress. It measures the degree to which each situation is subjectively appraised as stressful by the individual. Items were designed to tap how unpredictable, uncontrollable, and overloaded respondents find their lives. The questions ask about feelings and thoughts during the last month. In each case, respondents are asked how often they felt a certain way – (0) never, (1) almost never, (2) sometimes, (3) fairly often and (4) very often. Some of the items have reverse scoring. Individual scores can range from 0 to 40, with higher scores indicating higher perceived stress. Scores ranging from 0-13 would be considered low stress, 14-26 would be considered moderate stress, and 27-40 would be considered high perceived stress. Studies on psychometric properties of the perceived stress scale have reported high reliability, validity and have concluded that inferences made using the scale scores are valid. [12][13]

Procedure

The self-designed questionnaire, parental stress scale and perceived stress scale were uploaded in Google forms. Google Forms ensure that only one response can be generated using one device. Google Forms with a link were sent using E-mails and WhatsApp to the personal contacts of the investigators. The link was not shared with clinical population or clients, as the target was general population. The link was posted in social media group comprising of Indian parents, with a request to circulate among their contacts. On receiving and clicking the link, the participants got auto directed to the information about the study and informed consent. Once they consent to take the survey, they are directed to the self-designed questionnaire, followed by the parental stress scale and perceived stress scale sequentially. Each participant took about approximately 5-10 minutes to complete the survey. A total of 227 parents filled in the forms, out of which 196 were complete and met the inclusion criteria laid out for the study.

Ethical considerations

1. Institute Ethics Committee (JSS Academy of Higher Education and Research) approval was obtained.
2. The participants received the information sheet and had the full liberty not to respond to the survey.



3. The personal information was kept confidential, and anonymity was maintained
4. The researcher's contact detail was given in case someone wanted to seek help.

Statistical Analysis

The raw scores obtained on all measures were subjected to both descriptive and inferential statistics. The data was analysed using independent samples t-test, one-way ANOVA F-test, Chi-square test and Pearson's correlation in IBM SPSS Statistics (Version 22.0. Armonk, NY: IBM Corp).

Results

The data was examined for normality using the Shapiro-Wilk test and was found to be normally distributed. Hence parametric tests were used for analysis.

Demographic profile, Clinical & Stress related details

Of the 196 participants in the survey, 135 (69%) were mothers (mean age = 35.60 ± 7.1), and 61 (31%) were fathers (mean age = 40.30 ± 5.1) (table 1). A majority (97%) of the participants came from the urban area, and were married (97%). Most of the parents (54%) had postgraduate education suggesting the data was collected mostly from the educated urban strata.

Table-1: Demographic, Clinical & Stress profile of the Participants

Variables	Number (%) / Mean \pm SD
Age	
Father (n=61)	40.30 (± 5.10)
Mother (n=135)	35.60 (± 7.10)
Location	
Urban	171 (87%)
Semi-urban	19 (10%)
Rural	6 (3%)
Marital Status	
Married	190 (97%)
Separated/Divorced	6 (3%)
Education of the parent	
Undergraduate	1 (0.5%)
Graduate	89 (45.5%)
Postgraduate	106 (54%)
Developmental issues in Children	
ADHD	4 (4%)
Autism	1 (0.5%)
Anxiety/depression	2 (1%)
Learning Disability	8 (4%)
Behavioural problems	7 (3.5%)

COVID-19 hotspot	
No	115 (59%)
Yes	54 (27%)
Don't Know	27 (14%)
Perceived stress Scale mean score	15.7 (± 6.03)
Perceived stress Scale score	
Low	65 (33%)
Moderate	124 (63%)
High	7 (4%)
Parental stress Scale mean score	37.87 \pm 8.85
Do you feel more stressed as a parent after the lockdown? – Yes	72 (37%)
Do you need to speak to a counsellor or psychologist to help you with the present challenges? – Yes	16 (8%)
Correlation between perceived stress and parental stress	$r=0.39$ (p value < 0.001)

*Pearson's correlation

Majority of the participants had a single child (57%) and came from nuclear (67%) families (table 2). A small percentage of the participants reported having a past history of chronic physical illness (15%) and psychiatric illness (15%). About 11% of the children had developmental issues (ADHD-4%, Autism -0.5%, Anxiety/depression-1%, Learning Disability-4%, behavioral problems-3.5%). About one-third of the participants (27%) were living in COVID-19 hotspot at the time of the data collection. Majority of the participants came from the states of Karnataka, Telangana, Maharashtra, Uttar Pradesh, Madhya Pradesh, West Bengal, Delhi, Kerala, and Tamil Nadu.

The mean score on the perceived stress scale was 15.7 (± 6.03). Based on the cut off scores on the perceived stress scale, majority of the parents (63%) were found to have moderate perceived stress, and 4% of the parents had high perceived stress in last one month. When asked if they feel more stressed as a parent after the lockdown, 72 (37%) parents reported affirmatively. Further, 16 (8%) parents reported that they needed to talk to a counsellor/psychologist to deal with the present stress (table 1). Mean score on parental stress scale was 37.87 (± 8.85). Parental stress was significantly associated with perceived stress ($r=.39$, $p<.001$), but correlation strength was not strong. This weak correlation between perceived stress and parental stress suggest that these two tools measure different constructs.

Parental stress, Perceived stress and Psychosocial Variables

Mean differences in parental stress and perceived stress was examined using t-test. It was found that mothers ($t=2.06$, $p=.041$) and parent of children with developmental disorders ($t=4.71$, $p<.001$) had significantly higher parental stress when compared to fathers and parent of children without developmental disorder respectively. For perceived stress, it was found that mothers ($t=2.18$, $p=.03$), parents with a history of psychiatric illness ($t=3.35$, $p=.001$), and parents of children with a developmental disorder ($t=2.63$, $p=.009$) had significantly higher perceived stress than fathers, parents, without a history of psychiatric illness and parents whose children did not have a developmental disorder (table 2). Family type, number of children, and history of physical illness did not contribute to perceived stress or parental stress.

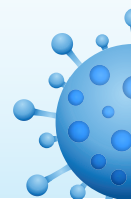


Table-2: Comparison of parental stress and Perceived Stress among Psychosocial Variables

Variables	Numbers (%)	Parent Stress (Mean ± SD)	T	p-value	Perceived Stress (Mean ± SD)	T	p-value
Parent							
Father	61 (31%)	35.95 ± 7.99	2.06	.041	14.34 ± 5.67	2.18	.030
Mother	135 (69%)	38.73 ± 9.11			16.36 ± 6.10		
Children							
1 child	111 (57%)	37.91 ± 8.23	.08	.939	16.14 ± 5.89	1.08	.283
2 or more	85 (43%)	37.81 ± 9.65			15.20 ± 6.20		
Family Type							
Extended	65 (33%)	37.32 ± 9.40	.61	.545	16.03 ± 6.18	.49	.624
Nuclear	131 (67%)	38.14 ± 8.59			15.58 ± 5.97		
History of Physical Illness in Parent							
No	167 (85%)	37.69 ± 9.03	.66	.513	15.53 ± 6.04	1.10	.274
Yes	29 (15%)	38.86 ± 7.76			16.86 ± 5.97		
History of Psychiatric Illness in Parent							
No	166 (85%)	37.57 ± 8.63	1.12	.263	15.13 ±5.86	3.35	.001
Yes	30 (15%)	39.53 ± 9.98			19.03 ± 5.97		
History of Developmental Disorder in Children							
No	174 (89%)	36.86 ± 8.24	4.71	<.001	15.33 ± 6.02	2.63	.009
Yes	22 (11%)	45.82 ± 9.63			18.86 ± 5.26		

Independent samples t test (two tailed), n=196, p < 0.05 is considered significant

Parental stress, Perceived Stress and Stressors

Interpersonal difficulties with spouse: Of the 196 participants, 18 (9%) reported having developed interpersonal issues with their spouse during the lockdown, 69 (35%) reported that their relationship with the spouse had improved during the lockdown, and 109 (56%) responded neutrally that they neither developed interpersonal difficulties nor had improved relationship during the lockdown (table 3). There was a significant difference in mean parental stress ($F=4.32$, $p=.015$) and perceived stress ($F=7.89$, $p=.001$) among the subgroups. On post-hoc analysis (table 3a), it was found that participants who reported improved relationship had significantly lower parental stress when compared to the group of parents who reported interpersonal difficulties ($p=.05$) and even to neutral group which neither had interpersonal difficulties nor had improved relations with spouse ($p=.04$). Perceived stress was also significantly higher among those who reported interpersonal difficulties with spouse compared to neutral group ($p=.001$) and the group which reported improved relationship with spouse ($p<.001$).

Interpersonal difficulties with child: Majority of the parents (53%) reported that the relationship with their child had improved during the lockdown; while, 9% reported having developed interpersonal difficulty with the child during the lockdown, and 39% responded



neutrally that they neither developed interpersonal difficulties nor had improved relationship with their child during lockdown (table 3). There was a significant difference in mean parental stress ($F=13.46$, $p<.001$) and perceived stress ($F=3.78$, $p=.025$) among the subgroups. Post-hoc analysis (table 3a) revealed that, parents who had developed interpersonal difficulties with child had significantly higher parental stress when compared to parents who reported improved relationship with child ($p<.001$) and those who neither developed interpersonal difficulties nor had improved relations ($p<.001$). Perceived stress was also significantly higher among those who reported interpersonal difficulties with child compared to those whose relationship had improved ($p=.043$).

Financial Stress: Financial Stressor was present in 16% of the respondents during the COVID-19 lockdown, and perceived stress was significantly higher among individuals with financial stressor ($t=3.84$, $p<.001$). However, mean parental stress did not significantly differ between individuals with and without financial stressor ($t=1.81$, $p=.073$).

Table-3: Comparison of parental stress among different stressors

Variable	Numbers (%)	Parental Stress			Perceived stress		
		Mean ± SD	F*/t†	P	Mean ± SD	F*/t†	p
Have you developed interpersonal difficulties with spouse since the lockdown?							
Absent	109 (56%)	38.84±9.34	4.32*	.015	15.48 ±5.93	7.89	.001
Present	18 (9%)	40.94±7.08			20.83 ±4.95		
Relationship has Improved	69 (35%)	35.52±7.99			14.80 ±5.87		
Have you developed interpersonal difficulties with your child since the lockdown?							
Absent	76 (39%)	38.03± 8.79	13.46*	<.001	16.42 ±6.24	3.78	.025
Present	17 (9%)	47.47±10.92			18.53 ±6.45		
Relationship has Improved	103 (53%)	36.17±7.48			14.76 ±5.63		
Have you developed financial stress since the lockdown?							
Absent	165 (84%)	37.38±8.62	1.81 †	.073	15.04 ±5.70	3.84†	<.001
Present	31 (16%)	40.48±9.72			19.42± 6.50		

*One-way ANOVA F test, †independent samples t-test, $p < 0.05$ is considered significant

Table-3a: Post-hoc analyses for Parental Stress, perceived stress and stressors

Variables	(I)	(J)	Mean difference in Parental Stress		Mean difference in Perceived Stress	
			(I-J)	P	(I-J)	P
Parental Stress						
Interpersonal difficulty with Spouse	Absent	Present	-2.10	.610	-5.36	.001
		Relationship has improved	3.32	.037	.68	.729
	Present	Absent	2.10	.610	5.36	.001
		Relationship has improved	5.42	.051	6.04	<.001
Interpersonal difficulty with child	Absent	Present	-9.44	<.001	-2.11	.385
		Relationship has improved	1.86	.304	1.66	.156
	Present	Absent	9.44	<.001	2.11	.385
		Relationship has improved	11.31	<.001	3.77	.043

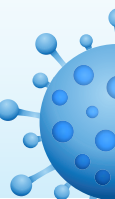


Table 4 shows parental stress, perceived stress and parental behaviours in the sample examined. 18% of the parents reported increased shouting, yelling and screaming at their child since the lock down; 36% reported increased spanking or slapping their child since the lock down, 17% of parents reported being preoccupied with worries and unable to focus on parenting, 61% of the parents reported that their child was watching too much TV or playing video games due to lack of other activities during the lockdown, and 20% reported that they were finding it difficult to discipline the child.

Table-4: Parental Stress and Parental Behaviours

Variable	Numbers (%)	Parental Stress				Perceived Stress			
		Mean ± SD	t	P	g	Mean ± SD	t	P	g
Are you shouting, yelling and screaming more at your child (children) since lock down?									
Absent	161 (82%)	36.31 ± 8.00	5.69	<.001	1.06	14.83 ± 5.54	4.70	<.001	0.88
Present	35 (18%)	45.03 ± 9.13				19.86 ± 6.56			
Have you started spanking or slapped your child (children) since lock down?									
Absent	126 (64%)	36.53 ± 8.93	2.96	.004	0.43	14.59 ± 5.92	3.67	<.001	0.55
Present	70 (36%)	40.27 ± 8.23				17.79 ± 5.71			
Are you preoccupied with worries and unable to focus on parenting?									
Absent	162 (83%)	36.72 ± 7.95	4.11	<.001	0.78	14.85 ± 5.71	4.68	<.001	0.88
Present	34 (17%)	43.32 ± 10.84				19.91 ± 5.87			
Has your child been watching too much TV or playing video games due to lack of other activities?									
Absent	76 (39%)	34.62 ± 7.76	4.27	<.001	0.63	13.92 ± 5.94	3.43	.001	0.50
Present	120 (61%)	39.93 ± 8.91				16.88 ± 5.83			
Are you finding it difficult to discipline the child?									
Absent	157 (80%)	36.24 ± 7.65	5.56	<.001	1.00	14.92 ± 5.97	3.92	<.001	0.70
Present	39 (20%)	44.44 ± 10.30				19.00 ± 5.18			

*Independent samples t test, $p < 0.05$ is considered significant, Hedges' g effect size.

Mean differences in parental stress among specific parental behaviors were examined using on t-test. It was found that parents who reported increased shouting, yelling and screaming ($t=5.69$, $p<.001$, $g=1.06$), spanking or slapping their child($t=2.96$, $p=.004$, $g=0.43$), or those who reported being preoccupied with worries and unable to focus on parenting ($t=4.11$, $p<.001$, $g=0.78$), or had difficulties in disciplining the child ($t=5.56$, $p<0.001$, $g=1.00$) had higher parental stress compared to parents who did not experience these difficulties. Perceived stress



was also associated with increased shouting, yelling and screaming ($t=4.70$, $p<.001$, $g=0.88$), spanking or slapping child ($t=3.67$, $p<.001$, $g=0.55$), preoccupation with worries and difficulty focusing on parenting ($t=4.68$, $p<.001$, $g=0.88$) and in disciplining the child ($t=3.92$, $p<0.001$, $g=0.70$). Further, parents who reported that their child was watching too much TV or playing video games had higher parental stress ($t=4.27$, $p<0.001$, $g=0.63$) and perceived stress ($t=3.43$, $p=0.001$, $g=0.50$). The effect sizes for the differences in parental stress and perceived stress as indicated by Hedges' g was large.

Discussion

This is one of the few studies to examine stress among Indian parents during COVID-19 lockdown. The survey was conducted when the lockdown was strictly implemented all over India. The results indicate that the pandemic had an important effect on parents and parenting. Preliminary evidence suggests that parents experienced perceived stress, financial stressors and interpersonal difficulties with family members during COVID-19 pandemic lockdown. Interpersonal difficulties with spouse were present in 9% of the parents, interpersonal difficulties with the child were present in 9% of the parents, and 16% of the parents reported financial stressors. A large proportion of parents (63%) reported moderate perceived stress, and 4% of the parents reported high perceived stress since last one month after the COVID-19 outbreak, suggesting that pandemic and the associated lockdown was stressful to the parents. Parental stress was significantly associated with perceived stress, but correlation strength was not strong, suggesting that they measured different constructs, and were therefore analysed separately for their association with interpersonal difficulties, financial issues and parental behaviours.

Both perceived stress and parental stress was higher among parents who reported interpersonal difficulties with spouse and child than parents who said that their relationship has improved due to COVID-19 lockdown. Perceived stress was also high among individuals who experienced financial stress during the lockdown. These findings are in accordance with what mental health professionals have been pointing out.[2][3] The present situation can be distressing, especially when individuals are faced with insecurities related to job and finance, and uncertainties about the global economic crisis and the impact it may have on their personal resources. Additional challenges include changes in their daily functioning, especially in their social interactions, physical activity, and time spent working.[14] When family members are forced to stay indoors with limited opportunity to go out for leisure or recreation, and socialization, it is bound to cause stress and lead to interpersonal conflicts, which can further impact their role as a parent. Although there are limited studies that have examined how interpersonal conflicts add to parental stress, it may be assumed that increased conflict among the family members is more likely to add to overall stress, especially parental stress. These stressors can be a potential risk factor for mental health issues such as anxiety or depression if not intervened early. [2]

Both perceived stress and parental stress were found to be higher among mothers than fathers, as well as parents whose children had developmental disorders. The findings from the present study are similar to the results of a recent online survey conducted by University of Oxford, [15] which reported that families with children who have special education needs and neurodevelopmental disorders had higher levels of stress across all areas. Gupta and Nebhinani [16] have also conveyed that parents of a child with mental health issues or developmental disability were struggling due to lack of access to comprehensive medical care or previous treatment options, suggesting the need for clinicians to reach out to parents who were



previously seeking help, or set helpline numbers where parents can easily access them. Parents particularly need support around their child's emotional wellbeing, education and coming out of social isolation. Gender differences in stress found in the present study have been reported by other researchers as well. For example, Widarsson et al. [17] reported that mothers and fathers experience stress differently, with mothers perceiving higher levels of stress than fathers. Healthcare professionals should be aware of the differences in stress that exist between mothers and fathers so that interventions can be sensitized to each parent's need, and they can be adequately prepared to avoid parental stress.

The present study also found a significant relationship between parental and perceived stress, and parental behaviours such as increased shouting, yelling, and spanking and/or slapping the child. Parental and perceived stress was also associated with a preoccupation with worries and inability to focus on parenting as well as with difficulty in disciplining the child. The parents of children who were watching excessive TV or playing video games also had higher parental stress and perceived stress. Several other studies have also reported that chronic stress among parents is related to violent and neglectful behaviour towards one's child.[4][18] Physical and/or verbal abuse and neglect can have serious mental health consequences for the child. In the present study, it was observed that 18% of the parents reported increased shouting, yelling and screaming at their child, and 36% reported increased spanking or slapping their child since the lockdown. Children's exposure to potentially traumatic events is related to negative mental health outcomes, and therefore there is an urgent need to intervene. Studies have also reported that parental stress has a strong direct effect on a child's behavioural and emotional problems, including internalizing and externalizing disorders.[7][8][9] However, parental stress and perceived stress are modifiable factors, and with proper intervention, parents can be able to manage their stress with better coping skills. Systems of care can use this information to encourage the implementation of more family-focused treatments and interventions.[18]

In the present study, 37% of the parents reported that they feel more stressed as a parent after the lockdown. Parenting can be challenging, even on a normal day. However, during these difficult times, it is crucial that parents take steps to help themselves, their child, and their whole family get through this situation. When participants were asked if they needed a counsellor or psychologist to help them deal with the current day challenges, 8% of participants indicated that they needed to talk to counsellors. There is an evident need for mental health professionals to reach out to parents and caregivers, who at the moment may not know how and where to seek help. Therefore, the need of the hour is to set up tele-counselling or video-counselling facilities and helplines, which are easily accessible to all. The interventions can range from minimal psychoeducation and supportive therapy to full-fledged psychotherapy which could be offered online whenever a need is identified. The parents need to be sensitized about parental stress and its impact on their relationship with the child, and adverse consequences it can have on child's developmental outcome, which can be achieved through rigorous programs to educate and sensitize the parents.

UNICEF [19] has issued COVID-19 parenting tips to help deal with COVID-19 parenting challenges, which includes tips on maintaining family harmony, keeping children safe online, keeping calm and managing stress, parenting in crowded homes and communities, parenting teens, parenting a new baby, managing bad behaviours, and parenting children with disabilities. In addition, World Health Organization (WHO) [20] has also issued tips for parents which cover planning one-on-one time, staying positive, creating a daily routine, avoiding bad behaviour, managing stress, and talking about COVID-19. Despite these efforts by international organizations to help parents deal with parental stress, it is doubtful how many parents in India are aware of or have access to these resources. In the present study, 17% of



parents reported being preoccupied with worries and unable to focus on parenting, 61% of the parents reported that their child was watching excessive TV or playing video games due to lack of other activities during the lockdown, and 20% reported that they were finding it difficult to discipline the child. These parents might benefit from parenting tips. Therefore, there is a need for advocacy for positive parenting practices by actively engaging communities through various programmes. Media and social media are also critical in promoting awareness and educating people and may be actively used for the purpose. Mental health professionals can actively set up helplines where they may deliver a set of handy tips to help manage this new situation, and help parents interact constructively with their children during this time.

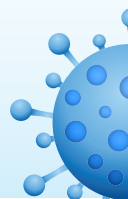
It was also observed in the study that the impact of the pandemic lockdown was not uniform across the sample. A large proportion of parents reported positive impact of the lockdown on the relationship dimension in terms of relationship with spouse and children. Similar findings have been reported by another study in India. [21] The researchers attributed the improved relationship with family members to the availability of more free time, less work pressure and possible fulfilment of long-desired free time during the lockdown.

The present study is not without limitations. The sample size was not calculated beforehand, data collection period was narrow, and despite attempts to circulate widely in all possible social media platforms, the response rate was low, and hence sample size turned out to be relatively small. Most of the participants had post-graduate education, were living in urban areas, and had access to smartphones and the internet, and therefore generalizability of the findings to the entire Indian population is limited. Some of the variables, such as age and gender of the child, were not considered since some families had more than one child. Nevertheless, considering the lockdown situation, where it was not possible to meet parents personally, this was the possibly the best methodology to reach out to the parents in order to understand parental stress during the lockdown period. The results provide an insight into possible issues that parents may be facing during the lockdown as well as pandemic.

To conclude, parents play a major role during the pandemic period to care for their children. The present study is important to understand the current crisis-related experiences of parents and how this crisis is impacting them and their interaction with their children. The outcome of this study has intervention implications, which can help mental health professionals to render appropriate support for the parents going forward. Findings of this study indicated that in the present COVID-19 pandemic, the parents are more vulnerable for increased stress related to parenting which can result in increased physical or verbal abuse and neglect of the child. The important concerns of parents, particularly parents of children with developmental disorders, were also highlighted in this study. Apart from reporting financial and interpersonal difficulties, a significant minority of the parents (8%) verbalized their need to talk to counsellors or psychologists to handle the high stress experienced. Therefore, reaching out to the needy parents who are in distress due to these psychosocial issues is crucial. Psychosocial crisis prevention and intervention models should be urgently developed by the government and mental health care personnel. They may make use of internet-based services, technology, social media and mobile apps to curb both pandemic related fears and deliver information and services.

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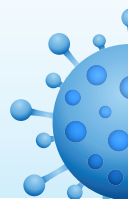
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COVID-19 crisis: Concerns about depression and obesity among adolescents in India

Sir,

India is the second largest country by population with 1.35 billion people, and adolescents constitute about 21%. Adolescence is defined by the World Health Organization as the period in human growth and development that occurs after childhood and before adulthood (10–19 years). This transition from childhood to adulthood is the time when many important psychosocial, biological, and cognitive changes take place in the adolescent's life. These changes along with peer pressure, parental pressure, and students' own expectation can make it a troubled phase. Any mental health disorder during this period could have consequences, and one of the frequent mental health disorders that have an adolescent onset is depression.

The prevalence rates of depression among adolescents range from 3% among school-going adolescents to 11.2% in school dropouts in India.^[1] The problem of adolescent depression is complicated by a variety of symptoms which often overlap with behavior seen in normal adolescence.^[2] The atypical presentation of adolescent depression and decreased awareness makes it difficult to recognize it. Adolescent depression may affect socialization, family relations, and performance at school often with potentially serious long-term consequences. Depression in adolescence increases risk of hospitalizations, recurrent episodes of depressions, psychosocial impairment, abuse of alcohol and/or other substance in early or future life, as well as antisocial behaviors. Moreover, early-onset depression is associated with an increase in comorbidity of other mental illnesses in adult life. There has been an increase in adolescent suicides in the last decade. Multiple factors that can lead to depression listed above also increase the risk of suicide in adolescents. Studies have found a significant association between depression and obesity in adolescents. Obesity in adolescents may lead to feelings of shame, humiliation, negative stigma, low self-esteem, and body image dissatisfaction, all of which can in turn lead to depressed mood.

COVID-19 pandemic is an unprecedented disaster and this can have serious impact on adolescents, affecting their mental health and physical health. In India, current pandemic and earlier lockdown has led to humanitarian

crisis.^[3] Psychological effect in the age group of 14–87 years, as seen in an online study to see the effect of COVID-19 lockdown of 1685 participants, found that 38.2% had anxiety, 10.5% had depression, moderate level of stress was reported in 74.1%, and 71.7% reported poor well-being.^[4] There is, however, a dearth of studies to assess the effect of lockdown on adolescent's mental health. As schools have closed in India since the last week of March 2020 as part of necessary measures, being not able to do everyday activities such as attending school, meeting friends, and going out can become confusing for the younger children and sometimes frustrating to the older adolescents. Constant news and discussion regarding COVID-19 can make one anxious and worry about future.

Children might experience worry, anxiety, and fear, and this can include a fear of dying, a fear of their relatives dying, or a fear of what it means to receive medical treatment. Children may wish to be closer to their parents than before, make more demands on them, and in turn, some parents or caregivers may be under undue pressure themselves.^[5] With schools and colleges shifting to online classes, they are spending more time in online, sometimes without monitoring, and this might lead to their exposure to inappropriate content affecting the mental health. On the other side, for a country like India, learning by digital mode might not be accessible to millions of children from poor socioeconomic strata. This, in addition with parents facing salary cut or losses of jobs due to pandemic, can affect adolescents' mental health at a very young age. Being at home can put some children at increased risk of or increased exposure to domestic violence if their home is not a safe place. There have been reports of increase in child abuse during lockdown worldwide. All these factors can adversely affect mental health of children.

Lockdown and restriction of outdoor activity reduces the opportunity to do physical activity and this could lead to increase in obesity. India already has consistently shown increase in childhood obesity prevalence from 16.3% reported in 2005 to 19.3% in 2010.^[6] When confined to home, one tends to become less active and reduce the physical activity to a minimum. This along with the increase in consumption



Letters to Editor

of food due to boredom can lead to increase in weight and childhood obesity. With most schools closed, children are spending more time in front of the screens which can also increase lethargy. Less recreational activity and lack of peer group for play in the pandemic can further lead to weight gain and predispose to depression. Depression can reduce activity by loss of interest, fatigue, and low mood. Thus, obesity and depression are closely interlinked and can become concern among adolescences during pandemic.

Parents should keenly observe for any emotional changes in children and maintain mental health by listening to them, acknowledging their difficulties, reassuring them, setting a routine, engaging them, and seeking for urgent professional help if required. Monitoring children activity and right food intake in safe environment can sustain required physical activity and appropriate weight.

To conclude, adolescents in India are vulnerable for depression and obesity during the ongoing COVID-19 crisis and its aftermath; more studies are needed to know the magnitude of the problem and for implementing appropriate intervention strategies.

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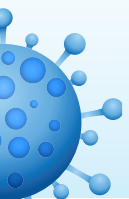
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Combating depression in India, an experiential perspective and its implications in COVID-19 pandemic

According to the World Health Organization by 2030, depression will be the leading cause of global burden of diseases ahead of all health conditions.^[1] Depression is an emerging global epidemic with over 350 million people affected.^[2] Suicide is a major concern in depression and is also the leading cause of death in Indian youths.^[3] India with a population of 1.35 billion and 0.4 psychiatrist/100,000 people has inadequate professionals to cater mental health services.^[4] It should also be noted that not a single skill in psychiatry is mandatory part of licensing to become doctor under the undergraduate competency-based medical curriculum. This impairs Indian doctors' ability to manage common mental health problems such as depression at primary health centers which are the pillars of health-care services in India. Hence, to address this unique Indian scenario, we have to look at all possible ways and means to combat depression. When the plan of having a first national conference on "combat depression" in India began in 2018 under the aegis of Indian Psychiatric Society, it was set out with the following objectives described. The possible processes and approach to achieve those objectives have been mentioned in the first section of this article and its implication in COVID-19 pandemic has been discussed in later part.

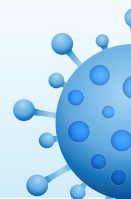
To address the issue of combating depression at earliest phase of life and among the most vulnerable, it is important to focus on the school teachers and college lecturers who can play a key role in creating awareness about depression. There are more than 1.6 million schools, 60,000 colleges, 30 million schoolteachers, and four million lecturers in India.^[5] Studies have reported that 20%–50% of students report depressive symptoms.^[6] The focus was to develop and standardize a training module for schoolteachers and college lecturers to combat depression among students. That enables the teachers and lecturers in the prevention–identification–help-seeking process. To design the module in a meaningful manner, representative schoolteachers and lecturers were involved right from the beginning. There was also a separate module for schoolteachers and college lecturers. It was also planned to submit a proposal and network with the Ministry of Human Resources and University Grant Commission at the central and similar institutions at the state level government. The

module prepared was used for exclusive workshop for teachers and lecturers during the conference with positive feedback.^[7]

Addressing the issue of misdiagnosis or under treatment of patients with depression in India, training of medical practitioners is crucial. Studies indicate that more than 20% of patients presenting to doctors may have comorbid mental health condition.^[8] Hence, it was decided to develop and standardize a module for training physicians and general practitioners on combating depression (identification–treatment–referral). There are more than a million doctors in India; hence, their training becomes important in combating depression. The module was presented at the local chapter of Physician Association of India and it was planned to be implemented with collaboration of Indian Medical Association.^[9] Based on the feedback from physicians, a prototype mobile application-based awareness module that helps users was made available after the conference.^[10]

As depression is considered common in women and women meet obstetricians and gynecologists at a vulnerable phase of their life, enhancing skills of obstetrics and gynecology (OBG) practitioners in combating depression are required. Nearly 10%–13% of women develop depression during pregnancy and postpartum period.^[11] It is, thus, important to engage OBG professionals in India to develop and standardize a module for training OBG professionals on combating depression that enables them in identification–treatment–referral when needed. This module was incorporated with crucial input from senior OBG faculty and module was presented in an exclusive workshop for OBG professionals during the conference.^[12] It was decided to network with OBG Society of India and thus making it a useful upgradation of OBG clinical services.

Similarly, pediatricians play an important role in the mental health of children in India. Studies suggest that nearly 18%–25% of those in the pediatric age group are found to be depressed.^[13] Hence, it was decided to develop and standardize module for training pediatricians in combating depression in children (identification–treatment–referral). The module was prepared with input



from pediatricians and presented as exclusive workshop for pediatricians at the conference.^[14] Considering, the constructive feedback it was decided to network with Indian Academy of Pediatrics for wider dissemination of the module content.

Involvement of professionals from health and allied sciences cannot be undermined in combating depression in India. Psychologists and social workers can play an important role. There are more than 700 colleges offering under graduation and postgraduation in these disciplines in India. The number of professionals from these disciplines may be more than 10,000.^[15] They can work for spreading the awareness, identification, and counseling people with depression. A mental health team involving psychologists and social workers was formed to look at designing a module for training the psychology and social work students at earliest in such skills that help in combating depression. The group conducted an exclusive workshop for students at the conference.^[16]

Pharmacists account for 11.2% of India's health workforce.^[17] There are more than one million pharmacists registered with pharmacy council of India.^[18] They can play an important role in creating awareness about depression, antidepressant medications, and adherence to medication. Hence, a module for training pharmacists was planned with involvement of pharmacist and an exclusive workshop was conducted.^[19] It is important to network with Pharmacy Council of India for further enhancement of such collaborations.

Similarly, in India, nursing profession play a key role in health-care services. There are more than two million nurses in India.^[17] Their involvement can be invaluable in combating depression. Capacity building in identification, creating awareness, and management skills in hospital and community care is important for nurses. Hence, a module of training was planned with involvement of nurses working in government and private hospitals including faculty from school of nursing and college of nursing. An exclusive workshop for nursing professionals was conducted during the conference.^[20] It was proposed to network with Nursing Council of India for further capacity building exercise.

Combating depression in vulnerable population such as engineering students and information technology (IT) professionals is also important for India. Studies indicate that 30%–40% of individuals in software industry are at risk of developing depression and 40% of suicide in India is in the age group below 30 years, and engineering students formed major subgroup according to National Crime Report Bureau 2014.^[21,22] There are more than 10 million people working in the Indian IT sector and 1.5 million engineering students graduate every year.^[23]

The profession has many risk factors for depression such as a highly competitive environment, erratic work schedules, impairing sleep and food habits, and increasing use of alcohol and tobacco use. Hence, there has to be training module for engineering profession, where faculty members from engineering institutions and representatives from IT industry are involved along with mental health professionals. Efforts along these lines were made during the conference and an exclusive workshop was conducted for IT professionals.^[24] Based on the positive feedback, it was proposed to network with All India Council for Technical Education and National Association of Software and Services Companies for combating depression by awareness, early identification, risk reduction, and help seeking.

Interestingly combating depression in India also means that medical students and doctors are aware of depression. India has 529 medical colleges with more than 70,000 students passing out every year and more than 10,00,000 registered doctors.^[25] Suicide among doctors is 2.5 times more than general population.^[26] Hence, not only a training module for combating depression in medical students and doctors was proposed but also another for training the psychiatry faculty in imparting theoretical and clinical skills on art of teaching depression was proposed. Both the modules were presented as workshop for specific purpose during conference. The team also included medical students as they are stakeholders.^[27,28] It was planned to submit the module to Medical Council of India or the proposed National Medical Council for incorporation of module at various levels and also to network with Indian Medical Association.

Combating depression also incorporates emphasis on research in basic sciences to improve our understanding of depression. There has been interesting finding about micronutrients and minerals.^[29] The conference also provided glimpse into advance research in the brain and a team was entrusted to look at possible areas of research.^[30]

Depression has numerous socioeconomic–cultural determinants that play an important role beyond the biopsychological factors and it is necessary to consider them in combating depression.^[31] The concern regarding glamorization of depression or medicalization of normal sadness as depression should be made aware for public and professionals. The modules presented at the conference incorporated this issues.^[32]

Yoga in depression has shown numerous benefits but there are some limitations which are rarely discussed.^[33] A presentation on benefits and limitation of yoga in depression was held at the conference.^[34] An e-book on yoga in combating depression is being prepared by the



experts in yoga and mental health to be made available free for the public.

Combating depression can only be successful if the community is involved at every stage in India and hence it was proposed to have audio video competition for public to create awareness. The emphasis was given to all segments such as 20 s audio clips, 20 s video clip, 1–2 min video clip, and short movie section of 5–10 min slot. To make it more inclusive, the audio-video clips could be made in English/Hindi or vernacular language (Kannada). This enhanced the reach of the goals in combating depression among the public. Some of the videos have already attracted thousands of viewers in YouTube platforms.^[35] Community reach is also important through the street plays and theater that connect well with public and these have to be incorporated more often in Indian scenario, which the conference did. Involving nongovernmental organizations (NGO) is important in community and interestingly an NGO sponsored the conference to an extent. Press and media play an important role in community for dissemination of mental health issues, particularly so about depression and suicide, they have to be partnered at the earliest. The preconference programs involved journalists in a seminar on responsible reporting of suicide.

With availability of mobile phones, the e-books have wider reach in community. Hence, self-help e-book on combating depression for armed forces and police personnel, women, medical students, IT professionals, and geriatric population was also proposed and is considered for free circulation. A concept e-book for emergency medicine professionals was released and is already made available.^[36]

It is important for India to have such national conference once in 4 years and enable all stake holders to come together and deliberate on addressing depression in India. The 2 days national conference ensured all stakeholders participation with delegate fee of Rs. 500 that included breakfast, lunch, and high tea on both days largely due to institutional sponsorship and expert speakers, who ensured that no additional cost is added expenditure of the conference. The future conferences can also be held in online platforms.

Combating depression in India during COVID-19 pandemic and its aftermath: COVID-19 pandemic is humanitarian disaster.^[37] More than 500,000 people have died worldwide and nearly 20,000 in India due to COVID-19 infection.^[38] The impact of disaster on the mental health is immense during the crisis and its aftermath. In India, from 1685 people aged 14–87 years surveyed during lockdown, more than 10% reported depression.^[39] The number is likely to increase as the

pandemic engulfs India, more importantly in the aftermath of pandemic. There is a need for additional resources to enable people to cope with psychological issues.^[40] Unless every subsection of the society is considered and specific manpower is targeted like schoolteacher, lecturers, doctors, pharmacists, nursing professionals, engineers, and IT professionals as mentioned above in the tailored multidisciplinary manner, the pandemic will have devastating effect on millions even after disaster.

To conclude, combating depression in India should be the joint efforts of all and not just the mental health professionals. It involves a multidimensional approach to understand depression and varied strategy to combat depression in India. COVID-19 pandemic and its aftermath is a challenging time which reaffirms the need.

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REVIEW ARTICLE

Coronavirus disease 2019 and the elderly: Focus on psychosocial well-being, agism, and abuse prevention – An advocacy review

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ABSTRACT

Age and agism are significant vulnerabilities for the coronavirus disease 2019 (COVID-19). While the number of cases and fatalities rises throughout the globe, the elderly are prone both to the physiological and psychosocial aftermaths of the infection. As the focus on management is predominantly directed toward precautionary measures and searching for a biological cure, the mental well-being of this vulnerable population is unfortunately neglected. Besides being prone to isolation, loneliness, stress, grief, depression, and anxiety during the lockdown, the seniors are also victims of stigma, prejudice, and abuse, stemming from agism. Substance abuse-related complications and cognitive disorders are added concerns. Elder abuse in every form has particularly been concerning during the present pandemic. Especially those staying alone, those with sensory or cognitive impairment, and those institutionalized are at a greater risk. Considering the increasing number of aging population, such biological disasters can have notable acute and long-term consequences on overall health and well-being of the seniors, if not adequately cared for. A holistic care based on biopsychosocial model needs to be in force for elderly mental health care during the pandemics, supplemented by research to shape policies. Keeping this in background, the advocacy review glances at the unique challenges that the older adults face during COVID-19 with special focus on psychosocial well-being, agism, and abuse. It also highlights the important facets for elderly care and abuse prevention during such crises.

Key words: Coronavirus, coronavirus disease 2019, elderly, pandemic, psychosocial, stigma

CORONAVIRUS DISEASE 2019: THE PROBLEM STATEMENT

The world is facing a new global health threat. The coronavirus disease 2019 (COVID-19) has emerged as a “life-changer” for human civilization. Various nations have closed down their borders, global economies have been slashed and travel has been restricted worldwide. Billions are quarantined at their own residences in an attempt to control the outbreak.^[1] These unprecedented times have struck heavily on daily lives of millions, especially the vulnerable sections. One such population are the elderly, who ironically are susceptible to both the infection and the lockdown imposed to control it. Already predisposed to the severity and fatality of COVID-19

due to age, the psychosocial implications also tend to be more significant for them.^[2] Isolation, neglect, lack of autonomy, and risks of abuse are the few commonly observed offshoots of this pandemic. Social distancing can impact their mental well-being, increasing the risk of psychiatric disorders. With a rapidly aging world, when the number of people above 60 years is greater than that of under-five children,^[3] ensuring the holistic safety of seniors is of utmost importance during such biological disasters. Lessons from past pandemics show that the elderly are at the highest risk for both acute and long-term consequences. Data from the classical “pestilences” of the bubonic plague in the 13th century, the Spanish flu of

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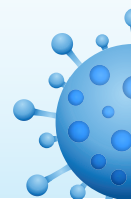
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1918, the Asiatic cholera, and the severe acute respiratory syndrome (SARS) show the increased vulnerabilities of the elderly besides increased case fatality rates.^[4,5] As the world is still in the early clutches of the COVID-19 pandemic, it might be worthwhile to take prompt steps to decrease the morbidity and protect the quality of life of the older population. Keeping this in background, this commentary glances at the unique challenges faced by the aged, the social implications, and attempts to highlight the ways forward.

“AGE AND AGISM”: THE TWO COMMON VULNERABILITIES

Nearly four million have been affected globally with COVID-19 and almost three lakhs succumbed to it, the numbers rising as we speak.^[6] The World Health Organization (WHO) has rightly declared it as a “Public Health Emergency of International Concern” within a month of its origin, as an outbreak of such a large scale affecting every aspect of life has not been seen in modern times. The causative agent of COVID-19, novel coronavirus SARS-CoV-2, is definitely less fatal than its earlier congeners (SARS and Middle East respiratory syndrome) but much more contagious with increased human-human transmission risk.^[7] One of the reasons being that the viability of the virus in aerosol and various surfaces is up to 2 weeks, though the exact scientific consensus on that is yet to be established. Majority of infections are mild, but few have pneumonia and acute respiratory distress syndrome, which can eventually lead to mortality. Furthermore, the severity and fatality of the infection is higher in the elderly, immunosuppressed patients, and people with preexisting respiratory illnesses, chronic medical problems as well as under-detection of symptoms.^[8] The elderly are at an unique risk of all these vulnerabilities together. During the first wave of infection in China, 20% of deaths were aged above 60 years.^[8] Chinese Centre for Disease Control and Prevention has reported a fatality rate of 3.6% in 60–69 years’ age group which can rise up to 20% above 80 years.^[9] Similar findings have been resonated in countries with high COVID-19 deaths such as Italy, Spain, South Korea, Iran, and the United States.^[10] It has also been seen that in old age, there can be mortalities even without lung involvement. It is related to nonspecific multi-organ failure and septicemia.^[9] An age-wise comparative study done by Liu *et al.* among hospitalized cases of COVID-19 showed that the elderly group (above 55 years) had increased duration of hospital stay, delayed clinical recovery, increased lung involvement, faster progression of the illness, and eventually increased fatalities.^[11] The need for mechanical ventilation and oxygen therapy was doubled in the elderly age group, and their blood also showed decreased lymphocytes and C-reactive protein, both of which are markers of adequate immune response to the virus.

Issues with mobility, chronic uncontrolled illnesses (such as diabetes, hypertension, pneumonitis, osteoarthritis, and cognitive decline), multiple medications, and increased need for hospitalizations due to various other factors further increase the susceptibility of the elderly. Connective tissue

disorders, endocrinopathies, cerebrovascular accidents, osteoarthritis, and other inflammatory conditions have been shown to alter immune response and complicate the course of COVID-19 infection.^[12] The prevalence of these disorders increases with age, thus adding to the risk. Studies have also shown the psychosocial burden of the elderly due to the pandemic. Prolonged social isolation has been mentioned as a “serious public health concern” for the elderly as it increases the risks of cardiovascular, autoimmune, neurocognitive, and mental health-related disorders.^[13] A longitudinal mediation analysis had shown that social disconnectedness increases the prevalence of depression, anxiety, stress, and insomnia in older adults.^[14] While isolating them is essential for their own physical safety, enforcing it without supervision will increase loneliness, worsen mood state, compromise their autonomy, and affect their overall well-being.

The unique vulnerabilities of the elderly predisposing them to the pandemic threat are:

1. Frailty (the age-related sum-total biological and psychosocial vulnerability of the individual) that is related to movement restriction, malnutrition, and poor immunity^[15]
2. Loneliness, neglect, isolation, and poor nutrition (more so in old care homes and institutionalized setups)
3. Sensory problems (difficulties in vision and hearing) that can prevent them from taking adequate precautions
4. Chronic illness, polypharmacy, increased health-care need, and physical support
5. Impaired cognitive abilities (memory, processing speed, thinking, and language) that worsen with age can prevent them from comprehending and adhering to the precautionary instructions. People affected with dementia might have behavioral problems and wandering tendencies that can add to challenges of keeping them isolated at times of such outbreak
6. Social distancing might not always be possible (multiple people in various roles are involved in their care, including domestic help for those who stay alone). Older adults often live by habits developed over years that form an important part of their day. Sudden disruption of this schedule can be traumatizing. Daily walks in the park or to meet peer group and need to obtain daily essentials can lead to increased exposure to the infection and hence increased fear. Many older adults find it quite challenging to psychologically accept the “restrictive” regulations of mobility issued by the government for containing the outbreak, even if they understand the need
7. The elderly might not be aware and updated about the authentic information related to infection, amid the plethora of “information pollution” that is already prevalent. Confusion and misconceptions might result in noncompliance to precautionary measures, faulty treatments, and overmedication
8. Inadequate COVID-19 testing and consequently less detection can risk them to be asymptomatic carriers of this highly contagious infection
9. Existential issues of “what after me” and “what about my family” due to the fear of death are common in



older adults. Self-neglect can result from a willful surrender to pandemic situations, misconstruing the risk of infection and overestimating the threat. The other concern in older adults is that of a dignified death, which is threatened during the ongoing lockdown, travel restrictions, and social distancing. A pertinent fear arises of a sudden and lonely death in solidarity and loneliness, away from the family, devoid of the last wishes that one had. Essentially, the context of the apprehended “death” becomes a greater worry than death itself, which can affect the emotional well-being. Spirituality is an important coping factor for the elderly,^[3] and the interruption of religious rituals as a part of last rites for the demised can prevent healthy grieving

10. Psychosocial vulnerability, especially at times of lockdown and quarantine: loneliness, anxiety, and uncertainty can give rise to depressive disorders, insomnia, and chronic stress. Grief and bereavement due to loss or distancing from their loved ones can be significant and chronic. They are also at increased risk for posttraumatic stress syndrome, if the stress is prolonged. Alarming, suicide risk is also two to three times more in the elderly population and is often underreported.^[16] A nationwide mental health survey in China during the present pandemic showed that one-third of those above 60 years suffered from grief, depression, anxiety, and insomnia^[17] (mentioned further in a later section)
11. COVID-19 has brought about a distinct change in the epidemiology and treatment gap of addiction disorders.^[18] Alcohol abuse, alcoholism, and stress-related drinking have increased globally secondary to the pandemic crisis. It has been hypothesized that ethanol reduces adaptive immunity and upregulates the angiotensin-converting enzyme-2 receptors, which are the targets of SARS-CoV-2 infection.^[19] The sudden lockdown in India has led to increase in complicated withdrawals, which can be fatal if untreated, especially for the elderly. Consumption of adulterated alcohol and methanol are other life-threatening risks.^[20] Opioid substitution treatment can get hampered, and excessive smoking can further worsen the preexisting pulmonary conditions of the older adults predisposing them to the infective effects of COVID-19. Importantly, self-care and precautionary measures get impaired with poor treatment seeking adding to the vicious cycle of substance abuse, which has much more detrimental health effects in the seniors
12. Lack of domestic help and basic living amenities in those living alone due to the lockdown can make survival a greater problem than the threat of infection. Considering that the domestic helpers cater to multiple houses with unknown standards of hygiene and safety, they run the risk of being asymptomatic carriers of the infection. This often adds to the uncertainty and fear experienced by the elderly whom they serve. This is a “dual-edged sword” as the seniors residing alone are often dependent on their daily help, but at the same time apprehensive and fearful about contracting infection.^[21] This serves

an important source of vulnerability, both physical and emotional

13. Difficulty in digital connectivity: Due to various reasons such as lack of familiarity, cognitive or sensory deficits, and difficulties in adapting to a new practice, many senior citizens might not be proficient enough to stay in touch with their loved ones through social networking (WhatsApp, Facebook, etc.) and video-conferencing methods, which are recommended worldwide during the COVID-19 crisis for social connectedness. Especially the older adults residing alone might not have the required assistance when they want to connect virtually with their families. This can add to the frustration and helplessness. Even though digital connection appears to be a rational substitute, it has been shown in earlier studies that the elderly prefer personal communication and care, rather than virtual interactions.^[22] During the current pandemic situation, staying physically “segregated” adds to their loneliness and social isolation.

MENTAL HEALTH AND CORONAVIRUS DISEASE 2019: RELEVANCE FOR THE ELDERLY

The COVID-19 crisis is an unprecedented one globally. All the abovementioned risk factors add to the mental health burden of the elderly and can have detrimental effects on the quality of life. Unfortunately, research related to this field is still scarce. Few commentaries have glanced at the need of special advocacy for the elderly mental health, mentioning digitalization of connections as a priority and warning about loneliness and social disintegration as the major offshoots of the pandemic and resultant lockdown.^[2,23] Besides the fear, risk of abuse, and discrimination during COVID-19, many seniors reside miles away from their children. Western countries such as the United States (U. S.) and United Kingdom (U. K.) have been disproportionately affected by the pandemic with increased mortality rates.^[6] The elderly whose children reside in these countries stay in a constant state of worry, apprehension, and helplessness. On the other side, the inability to receive their physical presence and care if ill or hospitalized during this global lockdown can add to the emotional frailty. As mentioned earlier, virtual association, though an option, cannot be a substitute for a “loving touch” from family. Furthermore, demise or loss of their spouse or children due to the infection, with lockdown hindering adequate last rites, can further compound the grief. All of these can be independent risk factors for late-life depression, which can be clinically polymorphic, underdetected during other priorities during pandemics also increasing the risk for suicides. An online survey conducted in 1074 people from Hubei, China, showed decreased mental well-being, increased depression, and poorer quality of sleep in the elderly (age >55 years), compared to substance use and anxiety which were more in the younger population.^[24] Another prospective longitudinal study conducted on 1738 participants from 190 Chinese cities reported a higher rate of physical (somatic) symptoms associated with anxiety, increased trauma scores, and decreased sleep, which increased with age and were related to isolation,



perceived stress, and dissemination of health information by media.^[25] On the contrary, a study by Huang and Zhao mentioned younger people having more depressive and anxiety symptoms than their elder counterparts.^[26] A study from Northern Italy stated individual factors (sensory and cognitive deficits, comorbidities, and polypharmacy), infective factors (neurotrophic effects of the virus, immunocompromised state, and frailty), and environmental factors (social isolation, institutionalization, and intensive care admissions) as the important risks for psychosocial condition of the elderly and reported 30%–50% neuropsychiatric associates of COVID-19 to be delirium, agitation, and depression, though the exact prevalence of each was not reported.^[27] A multinational (Brazil, Portugal, and Norway) report on the mental health of the elderly during COVID-19 cautioned against increased hospitalization, fear of death, stigma, age-related prejudice, and distancing from family as the factors for increasing psychiatric comorbidity in this age group.^[28] Risk minimization, physical safety, and social integrity were the suggested steps by these authors based on the case vignettes that they have discussed. Special at-risk sections within the elderly are those with poor social support, residing alone, with preexisting mental disorders and homeless. Substance abuse-related complications as mentioned earlier can increase both morbidity and mortality. A position paper on “COVID-19 and substance use disorders” by the International Society of Addiction Medicine raises the concern of addictive behaviors adding to the public health burden and identifies adults >60 years old at significantly higher risk.^[29] Baker and Clark recently recommended a biopsychosocial approach to deal with their social isolation during the pandemic by reducing the infective risk, supportive counseling sessions, psychoeducation of the families, and their continued involvement in care.^[30]

STIGMA OF “AGISM:” THE PRECURSOR TO ABUSE

There is another aspect to it, the stigma of agism. Often, the elderly are marginalized population. Even though traditionally humans are taught to respect and take care of the older generation, the innate fear of “aging,” “losing vitality,” and death have made “agism” a prevalent “social evil.” The WHO defines agism as “the stereotyping, prejudice, discrimination against people based on their age.”^[31] Society equates aging with loss of “charm and beauty” of the youth and hence has given the risk to various forms of old-age abuse. Such stigma and abuse can flare up at times of an outbreak which has an age-specific vulnerability.^[32] A recent systematic review by Chang *et al.*^[33] has linked agism with multiple negative physiological and psychosocial consequences. Common conversational content during this pandemic, like “*Oh, you are mostly a target, you need to be safe,*” “*It is the old who are dying, so you better stay separate lest you get infected*” or “*you need to take more care, or else you might infect others*” seem apparently benign but laden with reproach and stigma. The elderly are prone to have chronic bronchitis, obstructive lung disease, common cold leading to chronic cough, sore throat and flu-like symptoms which are easily mistaken for those of COVID-19. This can

lead to social segregation, stigma and impaired mental well-being. Overcrowding, neglect, and poor self-care in old-age homes are other contributing factors. Stress has an independent impact on immunity and hence can increase the proneness to any infection. Autonomy and self-dignity can be hampered during the worldwide lockdown that they are experiencing, which might further impair their mood, appetite, and sleep.^[34] Many of them live alone and are struggling with basic amenities such as food, domestic utilities, and hygiene along with the lingering fear of the pandemic. The latent agism and preexisting stigma can manifest as violence and abuse against the elderly, especially during entrapment and lockdown situations when many families are spending significant unbuffered time, like never before. Aggression, substance abuse, irrational reasoning, and familial power hierarchy can get amplified during pandemics. This can potentiate elder abuse, a serious concern of the COVID-19 crisis.

ELDER ABUSE AND CORONAVIRUS DISEASE 2019: THE DUAL VULNERABILITY

The WHO defines elder abuse as a single, or repeated act, or lack of appropriate action, occurring within any relationship where there is an expectation of trust, that causes harm or distress to an older person.^[35] This includes both acts of omission and commission. It can range from physical, psychological to financial abuse and even frank neglect. Since the time COVID-19 started, incidents of family violence and abuse have been increasing against the elderly, and public warnings have been issued related to the same by the American Bar Association.^[36] In the guidelines for care in the elderly during COVID-19, the WHO and Centers for Disease Control and Prevention (CDC) have both mentioned the risks of abuse and the urgent necessity to prevent and mitigate it.^[37,38] At certain times, restriction of autonomy and noninvolvement in decision-making done in good faith can also impair the rights of the elderly and lead to marginalization. Abandonment, neglect, and denying access to information can be the other offshoots, more so for the institutionalized seniors. To explain the abuse risk during the COVID-19 pandemic, Mosqueda *et al.* have proposed a theoretical model called the Abuse Intervention/Prevention Model.^[39] The model focuses on a triad of intersecting factors, namely the vulnerabilities of the elderly during the pandemic, the “trusted other,” and the context of abuse. The unique vulnerabilities of “age and agism” have already been discussed above, the trusted person might be a family member, a paid caregiver, a domestic help, or the old-age institutional management. The contexts are mostly situational and sometimes individualistic during pandemic situations.

Elder abuse tends to be more common in communities where both the victims and perpetrators lack mental health treatment or social care support in community. Lockdown has increased demands for all essential services, and the elderly have difficulty in accessing many of them as most have moved online. Barriers to access of care lead to underreporting, self-stigma, and normalization of abuse. The helplines at our tertiary care have received frequent calls for help regarding restriction of mobility, neglect, inability to



connect to loved ones, and overcrowding without face masks and adequate sanitary facilities in care homes and hospitals. People with dementia, especially those away from family, are at an increased risk. In the COVID-19 situation, with increased digital exchange, financial scams and exploitation of the elderly are common by opportunistic strangers.^[40] Even research in the elderly population during the time of pandemics, without appropriate informed consent, can be considered to be violation of their rights and dignity. The coronavirus has instigated agism in thoughts and remarks right from its initiation in China. With time, as the case fatality rate has increased in the aged, unfortunate and utilitarian comments have been passed regarding “needs of the many versus needs of the few.”^[41] In a similar context, it is ironic that the elderly population is rapidly growing and emotional well-being is a prime requirement for their healthy longevity.

CARING FOR THE ELDERLY DURING CORONAVIRUS DISEASE 2019: THE WAY FORWARD

Awareness about the special needs of the elderly during such crises and sensitivity to their vulnerabilities are the premise on which help can be provided. Caring for them needs to be a collective responsibility at all levels. Few important facets are highlighted below:

1. “Physical distancing” needs to be implemented rather than social distancing. Regular telephonic/digital contact needs to be maintained with them to ensure they have adequate emotional support. Every individual has their “special” loved ones which can be grandchildren, children, spouse, or even pets. Meeting them frequently over video-conferencing helps foster hope and happiness
2. Considering their vulnerability, it is better for them to avoid going out or meeting too many people. Additional effort is necessary to supervise whether their hand and respiratory hygiene are ensured. Simple directions (written or recorded) in their language are appropriate for those for stay away from the families
3. Hospital visits are best avoided during the pandemic. Tele-consultations have been started by most institutes. Technology access might be a challenge in some, and adequate guidance is necessary. Emergency medical or psychiatric consultations can always be availed, should need arise. The availability of common psychotropics needs to be ensured at the district levels
4. All elective surgeries such as cataract, hernia, or knee replacements (unless complicated) are better postponed
5. Bulk of statistics does not mean much to them, however, the elderly have all the rights to be updated for their own safety. The status of the pandemic and necessary precautions needs to be explained in simple terms, especially for those with sensory or cognitive difficulties. “Digital screen time” needs to reduce to avoid panic and confusion
6. The older adults in isolation or quarantine need special care: ensuring support through telephonic counselling, virtual contact with their loved ones and maintaining adequate nutritional needs are vital
7. Family members need to be sensitive to the early symptoms of COVID-19 and testing if needed should be promptly done. This, however, should not give rise to panic, self-isolation, and stigma. Medical advice is the best choice for any clarification
8. It is for the best interest not to medicate the elderly with any drug (antivirals, hydroxychloroquine, any herbal supplement, or advertised quick remedy) as a preventive or curative strategy for COVID-19. They can be life-threatening. It is always better to seek professional help^[42]
9. Authentic guidance sources by public health agencies (WHO, CDC, and Ministry of Health and Family Welfare, Government of India) have clear guidelines for elderly care during the pandemic. They can be advocated and adhered to
10. Essential service-delivery helplines (food, water, medications, and other necessary amenities) are helpful for those stranded alone
11. Psychosocial issues are vital, and families need to be sensitive to them. It is natural to be stressed, but signs of excessive panic, depression, sleep problems, or suicidality need urgent attention from a qualified mental health professional. Suicidality is already an added risk in the elderly, and more attempts tend to be successful. Late-life depression can be polymorphic and hard to detect, which further increases the risk of self-neglect and self-harm. Substance abuse and associated comorbidities need prompt detection and treatment. Harm reduction approaches might be helpful
12. The elderly are best involved in decision-making even at times of crisis. They need to have their rights, self-respect, and dignity preserved and protected. Their will to quarantine, intimacy, and sexual autonomy are to be respected
13. Digital literacy for older adults: Digitization of existing services means little unless there is provision for penetrance into older populations, where only 18%–25% of respondents in surveys have access to smart devices and the wherewithal to operate them meaningfully.^[43] This can also be achieved for those with mild cognitive deficits. Recently, a novel study looked into the effects of a television-based assistive integrated technology TV-AssistDem (TeleVision-based ASSistive Integrated Service to support European adults living with mild dementia or mild cognitive impairment) and found it to be comparable to the control groups on reducing sleeping problems, improving psychological well-being, greater social involvement, and better activity structuring^[44]
14. Targeted welfare interventions for minorities and vulnerable subgroups among the elderly, namely the gender and sexual minorities, refugees, migrants, the internally and externally displaced, racial, ethnic, religious and caste minorities, the disabled, persons with dementia, persons living in long-term care facilities, and socioeconomically underprivileged
15. Prevention of abuse needs special priority and considerations [Box 1].



Box 1: Elder abuse prevention during pandemics

Multiple communication methods for awareness, integrating COVID-19 helplines with elder care services
Training general physicians, nurses, and primary health-care workers in identifying elder abuse during COVID-19 (utilizing teleservices)
Advocacies for elderly and systematic outreach for monitoring
Those with history of abuse, neglect, and violence need proactive follow-up
Training the local authorities like police for crisis response and interventions
Community awareness for promoting KAP, related to autonomy and independence in older adults
Increased representation of the elderly in public and private sectors during the pandemic for safeguarding their rights
Using the social media, religious and nonprofit organizations to fight agism
Mental health care and placement for the abuse victims
Hassle-free legislation by policy-makers, increasing penalties for elder abuse

KAP: Knowledge-attitude-practice, COVID-19: Coronavirus disease 2019

CORONAVIRUS DISEASE 2019, THE ELDERLY, AND MENTAL HEALTH: SPECIAL IMPLICATIONS FOR INDIA

India reported its first COVID-19 case on January 30, 2020. After a slow initial phase, as of today, it has the largest number of confirmed cases in Asia, with more than 2.7 lakhs infected and 7745 succumbing to the infection.^[45] India's case fatality rate, however, is 2.8%, which is much lower against the global 6.13%. Decreased testing rate compared to the population and selective testing of the symptomatic individuals have been proposed as a reason by some researchers for this figure.^[1] Overall, the mortality rate appears to be lower and age being a significant risk factor for the same like the rest of the world, though the majority of the affected Indians are in the younger population. These statistics, however, hint little at the public health burden of a country that is predicted to reach 1.7 billion population by 2050, with the elderly likely to form 20% of them.^[46] Besides, the lack of adequate mental health services and service utilization, prevalent stigma, and knowledge-attitude-practice gap toward mental health compound the challenges related to the psychosocial comorbidities during the COVID-19 pandemic.^[47] The sudden lockdown has also increased substance abuse-related complications, which act as a "double blow" to both their mental health and physiological risk to the virus.^[23] The fear and vulnerabilities of the elderly exist, along with the challenges of digitalization and accessing telemedicine services unlike the other developed countries. Even simple telephonic access for consultations and online prescriptions are difficult in a country where majority are not adequately equipped for technology use. Furthermore, physicians face challenges in evaluating the elder adult through the online media. An age-structured impact of social distancing during the four-phased lockdown in India shows increased psychosocial burden above the age of 50 years, with increased loneliness and decreased social interaction.^[48] Taking care of their needs in a sociocultural context will be important, tailored to their requirements. Personal "touch," empathy, and validation of their distress have been shown to improve their psychological resilience.^[22] In the varied sociocultural contexts of India, helping their personal social connections, improving their company, doorstep delivery of essentials, respecting their dignity and autonomy as well as scheduling their day with preserved mobility, will help in their psychosocial care. Their

physical safety needs supervision, and spirituality can be a vital source of coping during such times of distress. Agism and stigma have been prevalent in India during the pandemic, added by the effect of social media. Fighting misinformation, involving the seniors in decision-making, and keeping them adequately informed can enhance their perceived sense of safety.^[49] The Indian Pandemic Act, 1897 is already set for an overhaul in the face of COVID-19, and incorporating the mental health needs of the elderly will be vital. As the caseload peaks in the next few months in the subcontinent, systematic research on the elderly and their mental health will help us understand population-based risk, their lived experiences and unmet needs, that can shape policies and improve the preparedness for such futuristic crises.

CONCLUSION

The older adults might have a range of challenges during the pandemics, but most are preventable. COVID-19 is still in its early times. Much more psychosocial morbidity is expected in the months to follow, and the health services need to be prepared for the same. The Indian Pandemic Act, 1897 needs an update in the true sense. This might be a good opportunity to include the protection and well-being of the older adults during the pandemics. The vulnerabilities of the elderly and their dependencies need to be collectively addressed with organized and systematic efforts at all levels. Cross-sectional and longitudinal research into their psychosocial issues and lived experiences during the pandemic will help estimate population-based risk and shape policies. The seniors might be vulnerable and frail due to age, but they are not weak. To quote Albert Camus "The old can go through every plague" from his classical *La Peste* (The Plague),^[50] the resilience of the elderly can be amazing, if adequately cared for and the young can borrow from their strengths. How one treats their seniors during a disaster, shapes what treatment they receive in futuristic crises. COVID-19 delivers yet another opportunity for the same.

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Conflicts of interest

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Sexual Behavior in the Days of COVID-19

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Coronaviruses comprise a very large family of viruses, many of which have been identified to cause minor and major illnesses in humans and animals. In humans, several coronaviruses can cause symptoms resembling the common cold. However, 2 coronaviruses are responsible for more severe respiratory illnesses: Severe Acute Respiratory Syndrome (SARS) and Middle-East Respiratory Syndrome (MERS). The coronavirus that is responsible for the current pandemic has been named SARS coronavirus 2 (SARS-CoV-2); this virus causes coronavirus disease 2019, abbreviated as COVID-19.¹

COVID-19 started in Wuhan, China, and has now been identified in all parts of the world. As of July 04, 2020, more than 11 million people have tested positive for the virus and more than 525,000 patients have died of the disease. Countries in North America and Europe were initially the worst affected, but now Brazil and India have moved up on the list.

Almost every medical journal now contains articles on COVID-19; in some issues of some general medical journals, articles on the disease outnumber articles on all other subjects combined. Specialty journals, such as psychiatry journals, discuss the immediate and delayed impact of COVID-19 on their respective fields.^{2,3} In this context, not COVID-19, per se, but the lockdown imposed to limit the spread of COVID-19 is likely to impact sexual behavior, as we will examine in the rest of this article.

Lockdown refers to government-placed and government-enforced restrictions on citizen movement. Total lockdown in China was responsible for the containment of the epidemic in that country. Following the same model, total lockdown was imposed in India on March 24, 2020. Less harsh versions of lockdown have been set in place in other parts of the world, as well.

Lockdown, and especially total lockdown, forces couples into prolonged, inescapable proximity. For some, this could present favorable opportunities. For example, there are couples today who work in different cities, or who work in the same city but in different shifts, or who work in the same city and in the same shift but are too tired by the end of the day for intimacy. For all these couples, therefore, lockdown could be an opportunity for improving intimacy. This could improve

the quality of marital and sexual relationships and could also result in a spurt in the pregnancy and abortion rates.^{4,5}

The prolonged proximity could have an adverse impact, too. Nobody is perfect, and no relationship is perfect, and so imperfections and interpersonal frictions could increase during lockdown, because couples in prolonged, forced proximity have ample time and opportunity to observe weaknesses in each other and in their relationships. This could result in quarrels that escalate into marital disharmony that could impair the quality of sexual relationships. Disharmony could reduce partner sexual attractiveness and result in partner-specific sexual dysfunction. And, of course, disharmony could later cause a spurt in the divorce rates. It should not be forgotten that disharmony associated with inescapable proximity could also result in intimate partner violence.^{6,7}

Time hangs heavily on one's hands during lockdown, even if one works from home. This could result in increased viewing of visual entertainment on internet-connected devices such as smartphones, tablets, laptops, and desktops, and on cable television. This could, in particular, result in increased time and opportunity to view online pornographic materials. Excessive viewing of pornography could overtly change partner expectations in terms of sexual performance and behavior; if the partner is unwilling to or incapable of exhibiting the desired change, this could result in stressed relationships. Expectations could also be changed unconsciously, as in wanting a picture-perfect or idealized partner; because this is never possible in real life, dampened expectations could also adversely affect the quality of sexual and emotional relationships.⁸ It is also possible that there will be a rise in porn addiction as a special form of internet addiction.⁹

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During lockdown, increased viewing of entertainment channels, such as movies on television, could be accompanied by increased eating. Compounding this is the lack of opportunity for exercise when one is not permitted to leave home. As a result, weight could increase. This would have long range adverse effects on the risks for overweight and obesity, diabetes, hypertension, and cardiovascular disease, all of which are associated with impaired sexual functioning, most especially with erectile dysfunction.¹⁰ Who would imagine, 2 to 3 decades in the future, that new onset sexual dysfunction had a pathophysiological contribution from the COVID-19 lockdown imposed in 2020.³

Lockdown, forced proximity, anxiety about work and finances, and other stresses could trigger new onset psychiatric disorders and worsen the existing ones. Psychiatric disorders and many psychopharmacological interventions are well known to be associated with sexual disturbances. For example, D2 dopamine receptor antagonist drugs elevate serum prolactin and decrease libido. Drugs with anticholinergic action impair erection and drugs that block alpha adrenergic receptors impair ejaculation. Drugs that inhibit the reuptake of serotonin delay or prevent ejaculation. Sedating drugs have a generally dampening effect on sexual functioning; a sleepy subject is unlikely to be interested in sex. Thus, a large number of antianxiety, antidepressant, and antipsychotic drugs used in the treatment of psychiatric disorders triggered by lockdown and other COVID-19 stresses may result in sexual dysfunctions such as decreased libido, erectile dysfunction, and ejaculatory delay or anorgasmia.^{11,12}

In this context, it should be remembered that, even in the absence of a psychiatric diagnosis, stress is itself related with disturbances in sexual functioning, and so lockdown-related stressors can result in such disturbances even in persons who are psychiatrically stable.

The bottom line is that healthy sexual functioning is not something that arises in isolation. Healthy sexual functioning requires a sound mind, a sound body, and (as we now learn) a sound environment, and not merely a sound reproductive system!

Declaration of Conflicting Interests

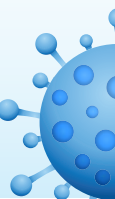
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ACCELERATED RESEARCH

Psychological impact of COVID-19 lockdown: An online survey from India

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ABSTRACT

Background: The COVID-19 pandemic has led to a complete shut-down of the entire world and almost all the countries are presently in a “lockdown” mode. While the lockdown strategy is an essential step to curb the exponential rise of COVID-19 cases, the impact of the same on mental health is not well known.

Aim: This study aimed to evaluate the psychological impact of lockdown due to COVID-19 pandemic on the general public with an objective to assess the prevalence of depression, anxiety, perceived stress, well-being, and other psychological issues.

Materials and Methods: It was an online survey conducted under the aegis of the Indian Psychiatry Society. Using the Survey Monkey platform, a survey link was circulated using the Whatsapp. The survey questionnaire included perceived stress scale, Patient Health Questionnaire-9, Generalized Anxiety Disorder-7, Warwick-Edinburgh Mental Well-being Scale to assess perceived stress, anxiety, depression, and mental well-being, respectively. The survey link was circulated starting from April 6, 2020 and was closed on April 24, 2020.


Results: During the survey, a total of 1871 responses were collected, of which 1685 (90.05%) responses were analyzed. About two-fifth (38.2%) had anxiety and 10.5% of the participants had depression. Overall, 40.5% of the participants

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had either anxiety or depression. Moderate level of stress was reported by about three-fourth (74.1%) of the participants and 71.7% reported poor well-being.

Conclusions: The present survey suggests that more than two-fifths of the people are experiencing common mental disorders, due to lockdown and the prevailing COVID-19 pandemic. This finding suggests that there is a need for expanding mental health services to everyone in the society during this pandemic situation.

Key words: Anxiety, COVID-19, Depression, Stress

INTRODUCTION

One of the extreme challenges for survival is facing a pandemic of an infectious disease of the COVID-19 type.^[1] The World Health Organization (WHO) declared COVID-19 as a pandemic on March 11, 2020 and as on March 24, 2020, more than 3.5 lakhs cases have been confirmed and more than 14,000 deaths have been reported, affecting 190 countries worldwide (WHO website dated March 24, 2020 at 21:00 pm Indian standard time)^[2] and these figures have exponentially increased to about 27.19 lakhs cases with about 1.9 lakhs deaths in 1 month time (WHO website date April 25, 2020 at 05:30 pm Indian standard time).^[3]

To tackle the rapid rise of cases in India and to curb the community spread, national level “lockdown” was declared starting from midnight of March 25, 2020 initially for 21 days, which was later extended up to May 3, 2020, with assurance that the basic needs of the general public will be taken care of.^[4]

“Lockdown” is an emergency protocol that prevents public from moving from one area to the other. Complete lockdown further means that persons should stay where they are currently and no entry/exit movements would be allowed further. It can be both a preventive and an emergency strategy in order to save the lives of the vulnerable or at-risk persons. In this scenario, all educational institutions, shopping arcades, factories, offices, local markets, transport vehicles, airports, railways, metros, and buses are completely shut down except hospitals, police stations, emergency services like fire station, petrol pumps, etc., and groceries. In recent times, lockdown had been very well documented during September 9/11 attacks in New York (3 day lockdown) and during riots in several countries. As social distancing is an important public health solution to tackle the spread of COVID-19, many affected countries such as China, Italy, the United States, France, and Malaysia have also enforced lockdowns of public spaces effectively.^[5,6]

While lockdown can be a significant and effective strategy of social distancing to tackle the increasing spread of the highly infectious COVID-19 virus, at the same time, it can have some degree of psychological impact on the

public. It is well known that quarantine/isolation for any cause and in the context of a pandemic (Severe Acute Respiratory distress Syndrome, 2003) has been associated with significant mental health problems ranging from anxiety, fear, depressive symptoms, sense of loneliness, sleep disturbances, anger, etc., in the immediate few days of isolation, and later with symptoms of posttraumatic stress disorder and depression after discharge from the hospital.^[7] However, the psychological impact of lockdown on the general public has not been studied yet. Man being a social animal, such restrictions on free movements can lead to anger, frustration, loneliness and depressive symptoms. There can be fear/apprehension among the public related to supply of basic amenities like groceries and milk supplies, medicines, care of previously sick persons in the family due to other medical causes, elderly persons staying alone, restriction of free movements, having a prevailing sense of being imprisoned in one's own house or “being in house arrest,” etc., Moreover, lockdown can lead to a “panic” mode of stockpiling of essential commodities without maintaining social distancing as advised by the government.^[8]

Lockdown can have different effects on different age groups. It may be difficult to engage the children at home throughout the day. This can be a source of stress to the parents. Similarly, due to the vulnerability of elderly for COVID-19 infections, others would avoid to meet the elderly, which can be a major source of distress, both for the elderly and their family members.

Unlike western countries, Indians are thought to be more social and have more social networks, engage in several religious festivals, and get-togethers across the year.^[9] This can be attributed to India's diverse culture and traditions.^[10] In this regard, a complete lockdown can have a downgrading effect on the psyche of the general public. It can also have a long lasting effect on the economy, farming and daily wage earners of the country. While it is an utmost necessary step to be taken at present to combat the COVID-19 infection, steps should be taken to mitigate the possible psychological impact of lockdown in the general public.

Moreover, recent reports suggest that the government's sudden enforcement of lockdown has created many hurdles to the economically disadvantaged populations



as evident from the mass exodus of migrant workers and concerns about starvation among people in slum areas.^[4] A recently published sentiment analysis of lockdown through twitter (analysis as evident from tweets extracted from 25th to 28th March 2020; $n = 24,000$ tweets) reported that the prominent sentiment was positive and trust on the government; further, many respondents reported sadness and worries about the problems of daily wage laborers during lockdown.^[11] However, no national-wide data on the psychological impact of lockdown in India are available. Therefore, the current study was planned with an aim to evaluate the psychological impact of lockdown on the general public with an objective to assess the fear, perceived stress, and psychological problems related to lockdown due to COVID-19 infection in India.

MATERIALS AND METHODS

It was an online survey conducted under the aegis of Research, Education and Training sub-Committee of Indian Psychiatric Society. Using the Survey Monkey platform, a survey link was circulated using the Whatsapp. The survey questionnaire was translated into 11 Indian languages (Hindi, Odia, Bengali, Marathi, Tamil, Telugu, Kannada, Malayalam, Punjabi, Gujarati, and Urdu) besides being used in English. The link was designed in such a way, that only 1 response can be generated using one device. The survey questionnaire consisted of the following instruments:

Demographics and personal characteristics

A basic information sheet which included information about the subject's age, gender, marital status, educational qualifications, and current work profile.

A questionnaire to evaluate the effect of lockdown on relationship with family members/neighbors/significant others and how lockdown had affected one's emotions, feelings, and behaviors in different aspects of life.

The Warwick-Edinburgh Mental Well-being Scale^[12]

It is 14-item scale covering both hedonic and eudaimonic aspects of mental health including positive affect (feelings of optimism, cheerfulness, and relaxation), satisfying interpersonal relationships and positive functioning (energy, clear thinking, self-acceptance, personal development, competence, and autonomy). It has good content validity and high test-retest reliability.^[12] The total score was determined by adding the score of all the 14 items. A higher score indicates greater positive well-being. A score of ≤ 40 has been reported to indicate high risk for depression.^[13,14]

Patient Health Questionnaire-9

The Patient Health Questionnaire (PHQ) is a self-administered version of the PRIME-MD diagnostic instrument for common

mental disorders.^[15] The PHQ-9 is the depression module, which scores each of the 9 Diagnostic and Statistical Manual-IV criteria as "0" (not at all) to "3" (nearly every day). This questionnaire is found to have excellent reliability and validity, and sensitivity and specificity of 88% for major depression.

Generalized Anxiety Disorder-7 Scale

It is a 7-item anxiety scale with good reliability as well as criterion, construct, factorial, and procedural validity. Cutoff points of 5, 10, and 15 are interpreted as representing mild, moderate, and severe levels of anxiety on the Generalized Anxiety Disorder (GAD)-7.^[16] Increasing scores on the scale are strongly associated with multiple domains of functional impairment. Although GAD and depression symptoms frequently co-occurred, factor analysis confirmed them as distinct dimensions. Moreover, GAD and depression symptoms have differing but independent effects on functional impairment and disability. There is good agreement between self-report and interviewer administered versions of the scale. This study employed self-reported version.

Perceived stress scale

It is a 10-item scale widely used to assess the perception of stress. It is a measure of the degree to which situations in one's life are appraised as stressful. Items were designed to tap how unpredictable, uncontrollable, and overloaded respondents find their lives. The scale also includes a number of direct queries about current levels of experienced stress.^[17] The questions are of a general nature and hence are relatively free of content specific to any subpopulation group. The questions in the perceived stress scale (PSS) ask about feelings and thoughts during the last month. It has adequate psychometric properties.^[18] For this survey, we had reduced the time limit to 15 days.

The survey link was circulated in 12 Indian languages starting from April 6, 2020, i.e. after 10 days of declaration of lockdown, and the survey was closed on April 24, 2020. The link was circulated by the Exponential Non-Discriminative snowballing method, people receiving the message were requested to complete the survey and then forward the link to their close contacts in various Whatsapp group, Facebook, and Twitter platforms.

The study was approved by the Ethics Committee of the Indian Psychiatric Society, for the research purposes. Descriptive statistics were applied and the data collected was analyzed using SPSS 20.0 version. Pearson's co-relation co-efficient and Spearman's co-relation co-efficient were used to find the association between different variables.

RESULTS

During the survey, a total of 1871 responses were collected of which 1685 (90.05%) responses were analyzed (which were complete in all aspects, except for information on age available



for 1653 participants only). The median duration of completing the survey was 12th day of the lockdown period (mean: 12.84, standard deviation [SD]:2.04; Range: 11th day to 21st day).

The mean age of the participants (1653 responses) was 41.26 (SD: 13.67) years. About three-fifths of the participants (63.7%) were male, about three-fourth were married (72.6%), three-fifth had completed postgraduation (61.8%), majority were employed (self-employed/employed in government sector or private sector) (78.9%). With regard to profession, slightly less than half of the responders (47.1%) were health-care workers (HCWs). In terms of current level of working during lockdown, about one-fifth of responders (21.1%) were not going to work and rest were either working from home for few hours (17.7%) or for usual hours (8.5%) and some were going for work for few hours (16.6%) [Table 1].

Perceived stress, anxiety, depression, and mental well-being during lockdown

The mean PSS score for the study participants was 16.56 (SD - 5.60) and about 70% of the participants reported moderate level of stress and one-fourth reported mild stress after the onset of the lockdown period. The mean GAD-7 score was 4.14 (SD - 4.84) and about one-fourth participants (23.7%) fell into the category of moderate symptom severity. The mean PHQ-9 score of the participants was 3.63 (SD - 4.81) with majority of the participants reported "no or minimal depressive symptoms" but 18.5% reported mild depressive symptoms and a small proportion of the participants reported moderate (5.8%) and moderate-to-severe depression (3.0%). The mean Warwick-Edinburgh Mental Well-being Scale (WEMWBS) score for the study participants was 43.92 (SD - 8.79). When the cut off for high risk of depression (i.e., score ≤ 40) was applied, about 70% of the participants (71.7%) had score ≤ 40 , suggesting poor mental well-being [Table 2].

Comparison of anxiety, depression, stress, and well-being of health-care workers and non health-care workers

As about a half of the responders were HCWs (47.1%), we compared the data of the HCWs and those who were not HCWs. Compared to HCWs, non-HCWs had significantly higher mean PHQ-9 score, higher proportion of them had depression, if mild depression is taken into account, and lower proportion of them had poor mental well-being. Details are mentioned in Table 2.

Effect of lockdown on relationships

Nearly half of the responders reported marked improvement in their relationships with their spouse/partner (47.4%), children (44.2%), and with parents (47.3%) after the beginning of lockdown period. Further, about three-fifth of the participants reported marked improvement in their relationship with their neighbors (61.8%) and office colleagues (59.6%) during the lockdown period [Table 3].

Table 1: Sociodemographic profile (n=1685)

Variables	Frequency (%)/ mean (SD)
Age (n=1653)	41.26 (13.67); range: 14-87
Sex	
Male	1074 (63.7)
Female	611 (36.3)
Marital status	
Married	1223 (72.6)
Unmarried	401 (23.8)
Widowed	16 (0.9)
Divorced/separated	22 (1.3)
Others	11 (0.7)
Details not available	12 (0.7)
Educational qualification	
Less than matriculation	7 (0.4)
Matriculation	21 (1.2)
Intermediate/+2	57 (3.4)
Graduate	539 (32)
Postgraduate	1041 (61.8)
Diploma	20 (1.2)
Occupation	
Self-employed	410 (24.3)
Employed in government sector	413 (24.5)
Employed in private sector	511 (30.3)
Home maker	86 (5.1)
Unemployed	77 (4.6)
Retired	99 (5.9)
Student	83 (4.9)
Others	6 (0.4)
Profession	
Doctor	764 (45.3)
Nurse	30 (1.8)
Engineer	117 (6.9)
Lawyer	40 (2.4)
Bureaucrat	38 (2.3)
Businessman	103 (6.1)
Business management consultant	65 (3.9)
Home maker	87 (5.2)
Politician	4 (0.2)
IT professional	30 (1.8)
Student	10 (0.6)
Retired	5 (0.3)
Teaching	64 (3.8)
Others	328 (19.5)
Level of working	
Not going to work	490 (21.1)
Working from home for few hours	299 (17.7)
Working from home for usual hours	143 (8.5)
Working from home for more than usual hours	92 (5.5)
Going to work for few hours	279 (16.6)
Going to work as usual	160 (9.5)
Going to work and doing work, more than usual hours	67 (4.0)
Others	147 (8.7)
Details not available	8 (0.5)

SD – Standard deviation

Effect of lockdown on one's emotions, feelings and various aspects of life

The effect of lockdown on one's emotions, feelings, and various aspects of life was evaluated on likert scale with the following options "no change," "slightly increased," "markedly increased," "slightly decreased," "markedly decreased," and "can't



Table 2: Perceived stress, anxiety, depression, and mental well-being during lockdown and comparison of these variables between health care workers and nonhealth-care workers

Variables	Whole sample (n=1685) Mean (SD)/frequency (%)	Non-HCWs (n=891), n (%)	HCWs (n=794), n (%)	t-test/Mann-Whitney U-value/Chi-square test (P)
Mean PSS-10 score, range (median)	16.56 (5.60), 0-37 (17.0)	16.61 (5.40)	16.51 (5.81)	0.356 (0.722)
Severity of stress				
Low stress (0-13)	437 (25.9)	225 (25.3)	212 (26.7)	1.351 (0.509)
Moderate stress (14-26)	1181 (70.1)	634 (71.2)	547 (68.9)	
Severe stress (>27)	67 (4.0)	32 (3.6)	35 (4.4)	
Mean GAD-7 score, range (median)	4.41 (4.84), 0-21 (3.0)	4.61 (4.93)	4.19 (4.73)	U=334575.0 (0.052)
Severity of anxiety				
Normal (0-4)	1042 (61.8)	535 (60.0)	507 (63.9)	5.612 (0.132)
Mild (5-9)	400 (23.7)	216 (24.2)	184 (23.2)	
Moderate (10-14)	147 (8.7)	79 (8.9)	68 (8.6)	
Severe (≥15)	96 (5.7)	61 (6.8)	35 (4.4)	
Mean PHQ-9 score, range (median)	3.62 (4.81), 0-27 (2.0)	3.90 (4.93)	3.33 (4.66)	U=328912.5 (0.011)*
Severity of depression				
Minimal (1-4)	1197 (71.0)	613 (68.8)	584 (73.6)	10.275 (0.036)*
Mild (5-9)	311 (18.5)	173 (19.4)	138 (17.4)	
Moderate (10-14)	98 (5.8)	55 (6.2)	43 (5.4)	
Moderate severe (15-19)	50 (3.0)	36 (4.0)	14 (1.8)	
Severe (≥20)	29 (1.7)	14 (1.6)	15 (1.9)	
Mean mental well-being score, range (median)	43.9 (8.8), 14-56 (45.0)	43.42 (8.94)	44.48 (8.60)	-2.465 (0.014)*
Number of participants with WEMWBS score ≤40	1208 (71.7)	617 (69.2)	591 (74.4)	5.562 (0.018)*
Overall prevalence				
Percentage of responders reporting GAD score ≥5	643 (38.16)	356 (40.0)	287 (36.1)	2.581 (0.108)
Percentage of responders reporting PHQ-9 score ≥10	177 (10.5)	105 (11.8)	72 (9.1)	3.296 (0.069)
Percentage of responders reporting only GAD score ≥5 but PHQ-9 <10	506 (30.0)	275 (30.9)	231 (29.1)	0.627 (0.429)
Percentage of responders reporting PHQ-9 score >10 but GAD-7 <5	40 (2.4)	24 (2.7)	16 (2.0)	0.834 (0.361)
Percentage of responders reporting both GAD score ≥5 + PHQ-9 score >10	137 (8.1)	81 (9.1)	56 (7.1)	2.335 (0.127)

*p<0.05. SD – Standard deviation; HCWs – Health-care workers; PSS – Perceived stress scale; GAD – Generalized anxiety disorder; WEMWBS – Warwick-Edinburgh Mental Well-being Scale; PHQ – Patient health questionnaire

say” [Table 3]. In most of the areas, majority of the participants reported no change, yet about one-third of the study participants reported slight worsening (increase) of negative emotions such as sadness (30.7%), anxiety (36%), irritability (32.2%), frustration (32.3%), and fear and apprehension (33.8%). About one-fifth of the participants reported increase in feelings of loneliness (21.3%) and fear of death (20.8%). Another 10%–15% of participants reported marked worsening of these negative emotions. Slight increased in social connectedness was reported by 18.7% and marked increase in use of social media was reported by about one-third (35.1%) of the participants.

Regarding somatic symptoms, sleep, appetite and fatigue, there was slight worsening (increase) in these features in about one-fifths of responders [Table 4]. About one-third to about three-fifth of the participants reported slight or marked increase in activities such as exercise, faith in God, watching movies, internet gaming, playing indoor games, sexual activity, reading books, painting, cooking, and cleaning [Table 4]. There was marked reduction in shopping and spending in a significant proportion of the participants.

Stress due to COVID-19 infection

More than one-third of the participants (38.5%) had fear of getting infected with COVID-19 infection, always wore masks and protective equipment even in open spaces (37.9%),

invested majority of their time reading or watching COVID-related facts (38.5%), and had anxiety when dealing with febrile patients/family members (38.8%). One-fourth of the responders reported feelings of pessimism or hopelessness (23.3%), feeling detached from others (24.0%), feeling exhausted (24.3%) and had trouble falling asleep/frequent awakenings (27.7%). Further, about one-fifth of the responders reported having avoided COVID-19-related information (20.8%), had anxiety/palpitations (19.3%) and had deterioration in the work performance (19.3%). About 30% of the participants reported of feeling irritated and angry on self or others, and with the uncertainty about frequent modifications of infection control procedures (32.0%). About one-fourth of the participants also reported fear of going out of home, because of fear of infecting family members. Only 10% of the responders reported experiencing stigma and rejection in neighborhood because of working in the hospital/being kept in quarantined facility, and a similar proportion was reluctant to work or considered resignation after discharge [Table 5].

Relationship between anxiety, stress, sadness, mental well-being, and duration of lockdown period

Higher level of stress, depression, and anxiety correlated positively with each other and negatively with the well-being. It was further seen that there was significant



Table 3: Effect of lockdown on relationships

Variables	Frequency (%)				
	No change	Slightly improved	Marked improved	Slightly worsened	Markedly worsened
Relationship with family members	661 (39.2)	563 (33.4)	304 (18.0)	122 (7.2)	35 (2.1)
Relationship with your spouse/partner	277 (16.4)	476 (28.2)	799 (47.4)	121 (7.2)	12 (0.7)
Relationship with children	387 (23.0)	477 (28.3)	744 (44.2)	56 (3.3)	21 (1.2)
Relationship with parents	274 (16.3)	544 (32.3)	797 (47.3)	57 (3.4)	13 (0.8)
Relationship with your neighbors	123 (7.3)	424 (25.2)	1042 (61.8)	82 (4.9)	14 (0.8)
Relationship with your office colleagues	123 (7.3)	411 (24.4)	1004 (59.6)	127 (7.5)	20 (1.2)

Table 4: Effect of lockdown on one's emotions, feelings, and various aspects of life

	Frequency (%)					
	No change	Slightly increased	Markedly increased	Slightly decreased	Markedly decreased	Cannot say
Sadness	613 (36.4)	518 (30.7)	181 (10.7)	175 (10.4)	96 (5.7)	102 (6.1)
Anxiety	509 (30.2)	606 (36.0)	218 (12.9)	203 (12.0)	98 (5.8)	51 (3.0)
Irritability	595 (35.3)	545 (32.3)	213 (12.6)	184 (10.9)	97 (5.8)	51 (3.0)
Frustration	59 (35.2)	545 (32.3)	231 (13.7)	146 (8.7)	101 (6.0)	69 (4.1)
Loneliness	709 (42.1)	359 (21.3)	248 (14.7)	160 (9.5)	127 (7.5)	82 (4.9)
Social connectedness	579 (34.4)	315 (18.7)	167 (9.9)	295 (17.7)	268 (15.9)	61 (3.6)
Social isolation	527 (31.3)	378 (22.4)	385 (22.8)	176 (10.4)	139 (8.2)	80 (4.7)
Fear and apprehension	575 (34.1)	569 (33.8)	222 (13.2)	165 (9.8)	91 (5.4)	63 (3.7)
Fear of death	893 (53.0)	351 (20.8)	176 (10.4)	73 (4.3)	60 (3.6)	132 (7.8)
Sleep	652 (38.7)	367 (21.8)	225 (13.4)	285 (16.9)	104 (6.2)	52 (3.1)
Appetite	880 (47.5)	378 (22.4)	182 (10.8)	261 (15.5)	39 (2.3)	25 (1.5)
Pain	1103 (65.5)	190 (11.3)	158 (9.4)	97 (5.8)	37 (2.2)	100 (5.9)
Fatigue	836 (49.6)	372 (22.1)	162 (9.6)	157 (9.3)	98 (5.8)	60 (3.6)
Exercise	569 (33.8)	376 (22.3)	193 (11.5)	247 (14.7)	248 (14.7)	52 (3.1)
Substance use, including alcohol	1009 (59.9)	173 (10.3)	125 (7.4)	78 (4.6)	157 (9.3)	143 (8.5)
Use of social media	323 (19.2)	489 (29.0)	591 (35.1)	140 (8.3)	108 (6.4)	34 (2.0)
Faith in god	844 (50.1)	308 (18.3)	358 (21.2)	74 (4.4)	67 (4.0)	34 (2.0)
Watching movies	515 (30.6)	534 (31.7)	436 (25.9)	107 (6.4)	58 (3.4)	35 (2.1)
Internet gaming	913 (54.2)	311 (18.5)	269 (16.0)	57 (3.4)	50 (3.0)	85 (5.0)
Playing indoor games (without using the gadgets)	813 (48.2)	417 (24.7)	227 (13.5)	69 (4.1)	54 (3.2)	105 (6.2)
Sexual activity	945 (56.1)	241 (14.3)	165 (9.8)	109 (6.5)	112 (6.6)	113 (6.7)
Shopping	477 (28.3)	196 (11.6)	61 (3.6)	188 (11.2)	707 (42.0)	56 (3.3)
Spending	377 (22.4)	160 (9.5)	60 (3.6)	370 (22.0)	681 (40.4)	37 (2.2)
Reading books	599 (35.5)	529 (31.4)	264 (15.7)	133 (7.9)	114 (6.8)	46 (2.7)
Drawing/painting	1018 (60.4)	252 (15.0)	211 (12.5)	23 (1.4)	33 (2.0)	148 (8.8)
Cooking	596 (35.4)	461 (27.4)	449 (26.6)	72 (4.3)	42 (2.5)	65 (3.9)
Cleaning	380 (22.6)	603 (35.8)	505 (30.0)	118 (7.0)	52 (3.1)	27 (1.6)

positive correlation between the perceived stress and severity of depression with the duration of lockdown period [Table 6].

DISCUSSION

With no alternative ways to escape from the COVID pandemic, almost all the countries have adopted the lockdown strategy as a potentially effective strategy to fight against the COVID-19. India was also quite early in its response to impose lockdown, as early as, within 2 weeks of declaration of COVID-19 as a pandemic, i.e., March 25 (WHO declared COVID-19 to be pandemic on March 11, 2020). Even though this strategy is an important measure to tackle the exponential rise of COVID cases, it has widespread impact on the economy, psyche, and daily living of the public. In this regard, the current study was

planned to evaluate the psychological impact of lockdown on the general public with an objective to assess the fear, perceived stress, and psychological problems related to lockdown due to COVID-19 pandemic in India.

Some of the strengths of the survey were that it was translated into 11 Indian languages along with English. Further, the survey questionnaires also included the evaluation of impact of lockdown on relationship with significant others and how the lockdown affected one's emotions and feelings. Besides, the use of some self-designed questionnaire, the survey also included well-validated scales usually used for community surveys such as GAD-7, PHQ-9, PSS, and WEMWBS (for well-being).^[19-22]

The prevalence rates of depressive symptoms and anxiety symptoms based on cut off scores of PHQ-9 and GAD-7



Table 5: Stress due to coronavirus disease-19 infection

Variable	Frequency (%)		
	Yes	No	Not applicable
Feared getting infected more severely with corona virus	648 (38.5)	900 (53.4)	137 (8.1)
Feeling pessimism or hopelessness	393 (23.3)	1172 (69.6)	120 (7.1)
Absence of emotional response - feeling numb/no happiness or sadness	324 (19.2)	1162 (69.0)	199 (11.8)
Feeling exhausted	409 (24.3)	1119 (66.4)	157 (9.3)
Reduced awareness or being in a daze/feeling confused/unable to think clearly	311 (18.5)	1249 (74.1)	125 (7.4)
Feeling detached from others	404 (24.0)	1155 (68.5)	126 (7.5)
Always wore mask and protective equipment even in open spaces	639 (37.9)	940 (55.8)	106 (6.3)
Invest majority of free time reading or watching corona virus-related information	649 (38.5)	968 (57.4)	68 (4.0)
Anxiety when dealing with febrile patients/family members	653 (38.8)	781 (46.4)	251 (14.9)
Avoided corona virus related information	350 (20.8)	1186 (70.4)	149 (8.8)
Had anxiety/palpitations	325 (19.3)	1284 (76.2)	76 (4.5)
Felt irritated/angry on self or others	526 (31.2)	1087 (64.5)	72 (4.3)
Had trouble falling asleep/frequent awakening	467 (27.7)	1156 (68.6)	62 (3.7)
Uncertainty about frequent modification of infection control procedures	540 (32.0)	1001 (59.4)	144 (8.5)
Poor concentration and felt indecisive	409 (24.3)	1156 (68.6)	120 (7.1)
Afraid to go to home because of fear of infecting family	402 (23.9)	1013 (60.1)	270 (16.0)
Deteriorating work performance	325 (19.3)	1103 (65.5)	257 (15.3)
Reluctant to work or consider resignation after discharge	163 (9.7)	1109 (65.8)	413 (24.5)
Depressed mood - feeling low most part of the day	276 (16.4)	1238 (73.5)	171 (10.1)
Stigmatization and rejection in neighborhood because of hospital work/being kept in quarantined facility	173 (10.3)	1069 (63.4)	443 (26.3)

Table 6: The association between day of response of lockdown with reported perceived stress, sadness, anxiety, and mental well-being during lockdown

Variables	Total PSS score, <i>r</i> (<i>P</i>)	Total GAD score, <i>r</i> (<i>P</i>) [#]	Total PHQ-9 score, <i>r</i> (<i>P</i>) [#]	Total well-being score, <i>r</i> (<i>P</i>)
Total GAD score	0.528 [#] (<0.001)***			
Total PHQ-9 score	0.321 [#] (<0.001)***	0.448 [#] (<0.001)***		
Total well-being score	-0.469 (<0.001)***	-0.481 [#] (<0.001)***	-0.391 [#] (<0.001)***	
Days of response of lockdown	0.062 (0.011)*	0.031 (0.197)	0.053 (0.029)*	-0.006 (0.810)

[#]Spearman correlation coefficient. GAD – Generalized anxiety disorder; PSS – Perceived stress scale; PHQ – Patient health questionnaire

were 10.5% and 38.2%, respectively. A comparison of our findings with those of the National Mental Health Survey (NMHS)^[23] shows that psychiatric morbidity of common mental illnesses may be higher in our study (40.5%) than the estimated prevalence of 10% in the NMHS.^[24] It can be argued that the significantly higher prevalence of psychiatric morbidity in the present study compared to the NMHS may be due to the use of different sampling methods and use screening instruments (whereas NMHS employed Mini International Neuropsychiatric Interview), but the screening instruments have been found to have high sensitivity and specificity against the diagnosis made by mental health professionals.^[25,26] Thus, the difference in the prevalence rates cannot be completely attributed to the difference in the methodology. Hence, it is possible that lockdown period has led to a significant increase in the mental morbidity of mostly milder intensity in the general public. A web-based survey from China, which evaluated the psychological problems among the Chinese people (*n* = 1074) close to the COVID-19 epidemic peak and subsequent lockdown, reported anxiety (mild/moderate/severe as evident from Beck's Anxiety Inventory) in 29% of participants and depression (mild/moderate/severe as evident from Beck's Depression Inventory) in 37% of participants, and poor mental well-being in one-third of its participants.^[27] The prevalence

of anxiety found in the present study is comparable to the previous study from China, but the prevalence rate of depression is lower. The lower rate of depression in the present survey, compared to the study from China, could be due to the difference in the timing of the study, in terms of the number of COVID-19 cases in the country. The present survey was done at the beginning of the epidemic in the country, compared to the survey from China, which was done, close to the peak of epidemic. The association of higher prevalence of depression, close to the peak of the epidemic, can be understood by the fact that the COVID-19 was associated with higher mortality rate in China, compared to current statistics from India. In the present study too, the association of depression and longer duration of lockdown was seen, which could be an indicator of increase in prevalence of depression with an increase in the number of cases of COVID-19 infection. The prevalence of mild-to-moderate anxiety and depression, in 40.5% of the participants in the present survey indicate that the pandemic and the lockdown is having a big toll on the mental health of people in the country and suggest an urgent need to address the same. The Indian Psychiatric Society took a lead in this direction, in the early stages of the lockdown, by providing free mental health aid to the people desirous of seeking mental health care.



In the present survey, 47.1% of the participants were HCWs and when the prevalence of psychiatric morbidity was compared between the HCWs, when the mild depression (i.e., PHQ-9 score of 5-9) was also included as an indicator of depression. However, when the cut-off of ≥ 10 was used for depression, there was no significant difference between the 2 groups. and non-HCWs, it was seen that the prevalence of depression to be significantly higher among the non-HCWs. Existing literature on the mental health problems faced by the HCWs in China during the COVID-19 crisis suggests a significant proportion of HCWs (36.9%) suffered from subthreshold mental health disturbances (as assessed by PHQ-9, GAD-7, Insomnia Severity Index)^[28] and about 22.4%–50% of HCWs reported experiencing depression, anxiety, significant distress and insomnia.^[29] Our findings are comparable to these studies among HCWs, if mild anxiety and mild depression are taken into account.

In the present study, in general, majority of the participants reported positive impact of the lockdown on the relationship dimension in terms of relationship with parents, children, spouse, colleagues, and neighbors. The improved relationship could be attributed to the availability of more free time, less work pressure and possible fulfillment of long desired free time. Findings of the present study are supported by many available websites/blogs, which have reported positive aspects of lockdown such as improvement in air quality/healing of nature,^[30] making people realize value of re-connecting with families^[31] and improvement in love/dating and family relationships.^[32] However, the improved relationship dimensions could also be attributed to the fact that, when everyone is fighting a common enemy, the interpersonal relationship issues are forgotten, which is possibly reflected as improved relationships.^[33,34] Another explanation for the improved relationship could be a fear of death, which often makes people perceive themselves as weak, and hence, have less initiative to fight with others.^[35]

However, despite improvement in the interpersonal dimension, there was increase in the prevalence of negative emotions such as sadness, loneliness, anxiety, frustration, and fear and apprehension in about one-third to nearly half of the participants. These findings again support the possible increase in the prevalence of depression and anxiety, in the wake of the pandemic. When asked about the COVID-19 infection *per se*, about one-fourth to one-third of the participants reported presence of symptoms related to possible COVID-19 infection to be stressful. Some of the other reported areas for which a significant proportion of participants reported significant stress were fear of getting infected with COVID-19 infection, always wore masks and protective equipment even in open spaces, invested majority of their time reading or watching COVID related facts, had anxiety when dealing with febrile patients/family members, feelings of pessimism or hopelessness, feeling detached from others, feeling exhausted and had trouble falling

asleep/frequent awakenings, avoiding COVID-19-related information, having anxiety/palpitations, deterioration in the work performance and some experiencing stigma and rejection due to their profession related to HCWs or due to being under quarantine. All these findings reflect the fear of infection of contracting COVID-19. While fear of contracting COVID-19 can be considered as justified, considering the worldwide mortality and infection rates, but these could also be attributed to the issues such as media hype and prevailing myths related to COVID-19 infection.

This survey has certain limitations. Despite attempts to circulate widely in all possible social media platforms, wider participation was expected. Accordingly, it can be said that the response rate for the survey was low. About half of the participants were doctors, which suggest that the survey did not have the desired snowballing effect, as much as it was expected. A majority of the participants were postgraduates, which was possibly again influenced by the higher proportion of participants being doctors. The survey was limited to those, who had access to a smart phone device and it can be said that the study participants may not be representative of people from various strata of the country. However, considering the situation, this was the possible best methodology to reach to the people to understand the psychological impact. These limitations suggest that the findings may not be generalizable to every strata of the society.

CONCLUSIONS

To conclude, the present survey suggests that more than two-fifth of the people are experiencing anxiety and depression, due to lockdown and the prevailing COVID-19 pandemic. This finding suggests that there is a need of expanding the mental health services to everyone in the society during this pandemic situation.

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Conflicts of interest

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CURRENT THEMES

Sexuality, sexual well being, and intimacy during COVID-19 pandemic: An advocacy perspective

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ABSTRACT

The coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome (SARS)-CoV-2, has emerged as a global public health threat. The implications are much beyond just health crisis, and it has long-lasting psychosocial and economic implications. Although the psychological offshoots such as depression, anxiety, posttraumatic stress, and sleep disturbances are being studied in-depth, there is a dearth of literature on the sexual well-being and sexual practices during this pandemic. Considering the physical distancing; travel restrictions; the high human-human transmission rate; misinformation and uncertainty about the sexual routes of transmission for SARS-CoV-2; and fear about intimacy, sexuality, and safe sexual practices have increased significantly. This is more prominent in newly settled or distanced couples and the frontline health workers, with increased risk exposure to the virus. For them, guilt and distress associated with sexual relationships might increase primary psychiatric and sexual disorders. This, in turn, impacts relationships and emotional bonding in couples and affects healthy coping during the pandemic crisis. Although sexual abstinence is the safest practice to prevent transmission, it is not practically feasible in all cases. Risk reduction counseling, sex with quarantined partners, and digital sex are other options that are worth exploring. There are additional concerns of digital safety, unhealthy use of technology, cyber-crimes, and online extortion. Keeping this in the background, this advocacy article glances through the effects of past outbreaks on sexuality, reviews the current recommendations, and proposes methods and approaches for sexual well-being during the COVID-19 pandemic, which is vital for overall public health.

Key words: Coronavirus, COVID-19, intimacy, pandemic, sex, sexuality

INTRODUCTION

The Coronavirus disease 2019 (COVID-19) crisis


Over the last few months, the world has seen the emergence of a new public health threat. The coronavirus disease

2019 (COVID-19) caused by the novel coronavirus severe acute respiratory syndrome (SARS)-CoV-2 has brought the world down to its knees. The medical and psychosocial implications of this large-scale outbreak can potentially long outlast the pandemic itself. Till date, more than three million people have been affected globally and nearly three lakh people have been succumbing to the infection, and the numbers are rising by the day.^[1] The widespread chaos regarding the uncertainty and source of infection has led to fear, panic, apprehension,

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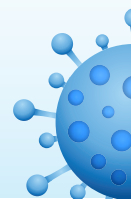
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and mass-hysteria. Grief for loved ones, bereavement, and isolation as a measure of “social distancing” is keeping billions segregated from their loved ones.^[2] Due to the international lockdown imposed on many cities, either the families have got separated for long times or people are having a new experience of staying with their spouses or families, like never before. Physical intimacy and proximity can significantly influence the dynamics of interpersonal relationships and mend them for the better or worse.^[3] The unprecedented changes imposed by COVID-19 and the containment measures have changed the living structure of millions, impacting their relationships and mental health. Research done in China during the first phase of infection shows an increase in acute stress, depressive disorders, obsessive-compulsive disorders, anxiety, panic symptoms, and insomnia. The long-term sequelae are posttraumatic stress, pathological grief, and adjustment disorders, which tend to be chronic.^[4] Social interaction, intimacy, and relationships have shown to boost well-being and serve as critical coping factors during such disasters. The quarantine and travel restriction measures during the COVID-19 pandemic can trigger loneliness and negativity, which prevent healthy coping with the crisis.^[5] Although literature related to this pandemic and mental health is increasing, there is a dearth of discussion on a vital aspect, the sexual and reproductive health. Sexual relations and sexuality have been important determinants of relationships and general well-being.^[6] COVID-19 being a contagious infection has generated a plethora of fears related to couple intimacy, the guilt of transferring the infection to the partners (especially for the frontline workers), altered sexual dynamics and performance in newly married couples or in those who are not used to cohabiting for long periods, and also the serious concerns of domestic abuse and intimate partner violence (IPV).^[7] Pandemics like this can have critical implications on sexual and reproductive health at all levels: individual, systems, or society.

In the absence of enough literature during COVID-19, the authors write this article as an advocacy document based on their clinical experience and relevant research related to past outbreaks. It will discuss the effects that infectious disease outbreaks can have on sexual health and intimacy, with perspectives from the past and present pandemics, and reviews recommendations for ensuring sexual well-being during these times of crisis.

PANDEMICS AND SEXUAL HEALTH: REVISITING THE “PESTILENCES”

“A loveless world is a dead world. The plague makes us crave more for love and the arms of our loved ones.”

- Albert Camus, *The Plague* (La Peste), 1948.^[8]

Since the classical bubonic plague of the 13th century, the world has faced pandemics time and again, disrupting social

structures. Surprisingly, much literature has focused on the psychosocial constructs of sexuality during this deadly disease. Tsiamis *et al.*^[9] in “Poetic description of the plague” mentions “fear of infection disrupting love and lives.” They mention couples being separated in rooms, not even allowed to talk. The segregation was more for the higher social classes, with separate living arrangements and dining altogether. Cantor^[10] mentions the social perceptions that immorality and illicit sexual relationships were causative of the plague, and physicians advised “physical distancing” and abstinence from all forms of sexual intimacy as it was related to “bad air,” then believed to be responsible for the infection. However, there are also mentions of increase in incest, prostitution, and coercive sexual practices in Europe during those days of the plague.^[11] It seems surprising that when a deadly infection was sweeping off one-thirds of the European population, what is the importance of discussing human relationships. However, contrary to the popular ideas, sexuality and physical intimacy has long been involved in social theories surrounding the classical “black death” in medieval Europe. German physicians advised against jealousy and promiscuity as they open the mind to “bad emotions.”^[12] Religious connotations were attached by the Church as homosexuals were accused of spreading the infection against the “Divine will,” and “sanitary legislation” was proposed based on “moral” laws to have them either publicly flogged or put out of the country.^[13] Salisbury *et al.*^[11] wrote about incest increasing significantly during the bubonic plague. The authors hypothesized that due to the widespread mortality, exogamy (marrying outside the clan or community) turned improbable. Hence, consanguineal marriages increased to preserve the patrimony, especially in the royal families, as many were on the verge of extinction. In *Land, Kinship and Life-Cycle*,^[14] Smith pointed out the increase in the severity of fines for fornication during the middle of the plague period (1349–1350). It is interpreted as a punishment for acts that were seen as morally improper. The Courts blamed the fornicators, as “sexuality” was considered to be a potent medium for infection spread. The idea of sex and intimacy being responsible for all forms of pathogenic spread has been increasing even before the outbreak of plague and peaked in the Victorian era.^[15] This was related to the social taboo, prejudice toward sexuality, and religious antagonism of sexual practices through moral standards. Ironically, there was a spur in the industry of prostitution as the plague waned off. People considered intimacy and sex to be critical coping factors for the pandemic aftermath. Sex-parlors and “royal safeguards” were built to promote safe and consensual sex.^[13] Some consider this as a revolt against the orthodox blame put by the Medieval Church on the society. It has an existential angle too. Hatcher, while describing plague in England, mentioned increase in sexual practices between newly married and elderly couples to deal with the stress.^[16] This was postulated to arise from the uncertainty of life and togetherness during and post the crisis times.



Unfortunately, though social research in pandemics peaked during the “black death,” literature related to sexual health and pandemics declined. The changing public health priorities and more “biological” focus to disease control might be the probable reasons. Furthermore, in the words of Cohn and Cohn,^[17] people were self-stigmatized to consider an immoral topic of sexuality in the face of much more serious issues such as death and disability, though frustration and distress over physical distancing from the partners have played an active role in the social reaction to these pandemics. During the Spanish flu of 1918, social-distancing measures were considered to be oppressive by many.^[18] As the administrative line, “You are your safest sexual partner” gained popularity, so was the common quote, “We want to be quarantined together” by couples that established itself as a landmark romantic comment in many books and movies later in time. Sex steroids for enhancing sexual potency and pregnancy were considered to be risk factors for the influenza outbreak while birth control methods gained importance.^[19] There were reports of discrimination against sexual minorities and increase in violence and abuse in families.^[20] With an increase in the understanding of molecular biology and pathogenesis, fear has grown more about sexual transmission of infections and the degree of permissible intimacy during the outbreaks. There have been debates about the same during the SARS and the Middle East respiratory syndrome (MERS) outbreaks. Chua *et al.*^[21] while studying the psychological effects of the SARS outbreak reported an increase in sexual dysfunction, decreased arousal, and increased marital discord over issues of intimacy. Long-term psychosocial and occupational outcomes of health-care workers dealing with SARS patients showed a rise in erectile dysfunction (ED), premature ejaculation (PME), lack of sexual satisfaction in partners, and heightened performance anxiety. This contributed to the burnout, work stress, absenteeism, substance abuse, and depressive disorders. Substance use also had a positive relationship with sexual dysfunction, anxiety, and partner violence and an inverse relationship with perceived sexual satisfaction in the couples.^[22] SARS and MERS had led to adverse pregnancy outcomes such as miscarriages, abortions, intrauterine growth retardation, and maternal deaths, which is proposed in COVID-19 as well, which generates fear among sexually active couples.^[23] New infections with unknown pathways of transmission always tend to create considerable apprehension about pregnancy and vertical routes of transmission. Hence, the implications of safe sexual practices and sex education become paramount during these times. Ebola outbreak in Africa had a possible sexual mode of spread, which led to significant discrimination based on race, ethnicity, and sociocultural status.^[24] The lesbian, gay, bisexual, transgender (LGBT) community were stigmatized as “carriers” for the same. The psychological models adopted for the Zika outbreak in Brazil and Nipah infection in India involved sex education about the viral transmission among

partners, social connectedness, and focusing on alternative forms of expressing love and intimacy, while observing physical distancing.^[25,26] This becomes vital as sexual well-being has been linked with positivity, hope, personal growth, and overall health, especially at times of disasters.

CORONAVIRUS DISEASE 2019, SEX, AND SEXUALITY

Literature related to sexual health and current COVID-19 pandemic is still in their infancy. The global lockdown has led to marked “physical and social” distancing, and the implications are chronic. Unfortunately, sexual well-being is often neglected at the face of more significant immediate concerns. Given the importance of sexuality in people’s lives and its relationship with quality of life, and psychiatric disorders, physicians need to stay sensitive to this issue, routinely ask or screen for sex-related complaints, and incorporate primary sex education tailored to the present outbreak in their patient counseling. Considering the social stigma attached behind sexuality and the varied sociocultural expression, the dictum that holds true clinically is that “You don’t ask, and they don’t tell.” The summary of the present evidence on COVID-19 suggests that any form of close human–human contact can spread the virus.^[27] The SARS-CoV-2 is much more contagious than its earlier congeners, which is the proposed reason for such speedy global spread. The virus gets easily carried by aerosol and fomites, can remain viable in air for up to 3 days, and survive on various inanimate objects for 2–3 weeks. This further generates fear and frustration related to intimacy. It is all the more for frontline workers against COVID-19 who self-quarantine themselves to prevent interaction with their families. Those who return to their spouses have expressed marked guilt, fear, and apprehension.^[28] This eventually affects the interpersonal relationship, closeness, sexual practices, and an overall lead to discord and emotional distancing in couples.^[29] Looking from the other side, recreational sex when billions are stranded at home, without family planning measures, can lead to increased abortions and population boom with time. Such consequences are unprecedented. Like human rights, sexual and reproductive rights also need to be safeguarded during such biological disasters. Singh and Adhikari while studying the age-structured impact of social distancing on the COVID-19 epidemic in India, have mentioned the emotional distress of the adolescents and younger adults due to separation.^[30] Sentiment analysis from Twitter has shown the lockdown in India to instigate fear, disgust, and stigma. People have reported concerns about physical distancing and traveling to their partners, more so in those who have recently started relationships or got engaged.^[31] Keeping in mind the social situations that might arise due to this pandemic and lockdown, the possible ways in which sexual lives and relationships can get affected are summarized in Table 1.

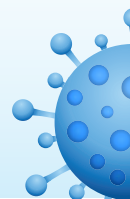


Table 1: Probable sexuality and intimacy-related issues during the coronavirus disease 2019 pandemic

Effect on sexuality/sexual practices	Contributing factors
Sexual abstinence	Fear related to intimacy Travel history of partners Uncertainty about transmission Physical distancing
Coercive sexual practices/IPV/incest	History of IPV Marital discord/disharmony Couples stranded together away from family (more contact time) Substance abuse Increased pornography use Crowding in joint families (less supervision)
Noncompliance to precautions/lockdown	Frustration and distress associated with prolonged sexual abstinence KAP gap about healthy sex History of sexual deviations
Increase in paraphilias	Fear/restriction of conventional sexual acts
Disinterest in sex	Chronic stress Anxiety, uncertainty related to pandemic Depression, PTSD, and adjustment disorders Guilt Loneliness and isolation Isolation/quarantine History of substance abuse, externalizing personality traits, ADHD Compulsive use of technology Lack of partners/social support Lack of intimacy Prolonged sexual abstinence Physical distancing Increased sexual appetite/sex addiction Preexisting sexual problems Chronic stress Depression, anxiety, psychoses (new onset or exacerbation) Chronic abstinence Interpersonal issues Heightened performance anxiety (fear of infection) Decreased self-esteem Personality traits The psychological impact of lockdown Poor knowledge about sexual risks and contraception matters
Unhealthy use of technology (pornography addiction, use of dark web)	Indiscriminate sexual practices without understanding the transmission risk
Interpersonal issues Extramarital relationships Marital discord/disharmony	
The rise in sexual disorders (erectile dysfunction, premature ejaculation, arousal disorders, etc.)	
High-risk sexual behaviors	
Increased viral spread	

IPV – Intimate partner violence; KAP – Knowledge-attitude-practice; PTSD – Posttraumatic stress disorder; ADHD – Attention deficit hyperkinetic disorder

SEXUAL ABSTINENCE: A FEASIBLE SOLUTION?

Sexual abstinence is the practice of voluntarily refraining from some or all aspects of sexual activity. It can arise from deliberate ideological or philosophical reasons (chastity and celibacy) or situational reasons (prevention of infection and conception), lack of suitable partners, or to conform to legal provisions.^[32] In infectious disease outbreaks, abstinence is considered to be the safest practice to prevent spread. For decades, the psychological effects of sexual abstinence have been debated in all age groups. The traditional association of abstinence and better “vitality of nerves and brain” has not been scientifically proven.^[33] There are other views related to chastity and puritanism about sexual abstinence, which are beyond the scope of this article. In this discussion, we will stick to the situational need for abstinence during the pandemic, and not refer to the moral or religious connotations of it. Sex is often considered to be a stress

reliever and an indicator of well-being in couples. It also forms an essential parameter of relationship dynamics.^[34] It is vital to understand the difference between asexuality and celibacy. Any obligation to stay abstinent involuntary sexual lives can cause distress. For sexually active couples, not being able to be intimate due to physical distancing or fear of infection can be traumatic. Many might be stranded alone, feeling lonely in the absence of their partners. This becomes more concerning in couples who have just moved in together. Here, by abstinence, we also mean a lack of any form of intimacy, including foreplay, which can impact the self-esteem and well-being of couples. Preexisting marital issues can be amplified as there might be discordance of opinion related to sexual practices between the partners. Sexual frustration and loss of affection are other offshoots. Chronic sexual repression has shown to affect performance anxiety and sexual confidence, which can eventually lead to arousal disorders, anorgasmia, PME, and ED. It can also increase the risk of chronic diseases such



as diabetes, hypertension, and cardiovascular illness.^[35] Studies related to the prevalence of these disorders as the aftermath of pandemics are, however, scarce. Fear of intimacy can lead to emotional distancing from the partner, which leads to loneliness, poor coping, and sleep disturbances, all of which are independent risk factors for depression and anxiety. Although masturbation is often considered to be a replacement for partnered sex, there are significant differences between the emotional processing and perceived satisfaction from both.^[36] Sex has been termed as “emotionally binding,” and it increases the sense of emotional closeness among couples.^[34] Although some studies have shown beneficial effects of abstinence on self-control, spirituality, and well-being, they were on individuals who practiced abstinence as a voluntary lifestyle.^[37] During infectious disease outbreaks, it is more of an “imposed abstinence” to prevent the spread. Bogart *et al.*^[38] studied 1917 adolescents, recruited from mid-school, and assessed them periodically. They found a relationship between sexual abstinence among females and better mental health, which no longer existed once educational variables, family bonding, and conventionality factors were accounted for. In another study, sexually abstinent men were compared with those with high-risk sexual behavior having HIV, and the authors reported that the two groups had similar prevalence of depression, burnout, anxiety, and insomnia.^[39] HIV, however, having entirely different social dynamics and established routes of sexual transmission will be different from other infectious diseases. Psychological distress and sexual abstinence have been shown to share a bi-directional relationship, as increased stress can also induce people to avoid sexual activities altogether. This factor becomes vital during disasters such as COVID-19 as the financial crisis, unemployment, fear of infection, health anxiety, travel restrictions, and uncertainty all can contribute to the collective stress and hence the varied sexual behavior.^[29] Prolonged sexual abstinence might also lead to the emergence of high-risk sexual behavior, substance abuse, gambling, and compulsive self-gratification as harmful coping strategies.^[40] Sexual oppression at the time of emergencies has led to adverse physical and psychological consequences. Considering these factors, total sexual abstinence alone might not be an effective measure to promote sexual well-being during pandemics.

SAFETY OF SEXUAL PRACTICES DURING CORONAVIRUS DISEASE 2019: REVIEWING THE RECOMMENDATIONS

SARS-CoV-2 is present in respiratory secretions and has aerosolized droplet spread. Data so far suggest that the virus can be transmitted through respiratory droplets to the skin and personal objects, from which it can infect the sexual partner.^[27] Hence, any form of in-person sexual activity carries the potential risk. Data related to other

routes of sexual transmission are sparse. The virus was not detected in semen or vaginal samples in two small studies.^[41,42] However, another study detected SARS-CoV-2 by reverse transcriptase-polymerase chain reaction in semen samples of six patients.^[43] Even the detection of the virus in urine samples is equivocal.^[44] Saliva has also been considered to be potential media for cross-contamination in dental practice, and recommendations of testing saliva for viral particles have been suggested.^[45] To summarize, the pathophysiology and epidemiology of COVID-19 are yet extensively studied. Considering the large-scale spread of the infection, it is clinically prudent to consider all of these modes as a source of potential contamination, unless proven otherwise with clear evidence. Many individuals might feel too stressed for sex and prefer to delay it till situation normalizes. It is a normal stress reaction, and their partners need to accept it. Stress responses during pandemics can vary widely.

SAFETY ABOUT SEX/INTIMACY DURING THE CORONAVIRUS DISEASE 2019

The Center for Disease Control and Prevention (CDC) recommends a minimum distance of 6 feet to avoid transmission, which is impossible for intimate relationships.^[46] As mentioned before, any in-person contact carries the potential risk for infection. However, total isolation is not necessary in all cases. Case-by-case safety assessment and decision-making is better. If both the couples are asymptomatic, have been practicing precautions, and have no history of travel or exposure, touching, hugging, kissing, and intercourse are likely to be safe. Sharing the bed with partner and dining together can also be done. After community transmission in many countries, asymptomatic carriers are rising. That always carries a potential risk, which cannot be negated.

SEX/INTIMACY WHEN A PARTNER IS SYMPTOMATIC

Of late, any flu-like symptom generates panic, as it can mimic COVID-19. Although the clear-cut distinction is difficult, high fever, sore throat, respiratory distress, and history of exposure (might not always be present) are useful cues.^[47] The WHO and Indian Council of Medical Research have standard protocols for testing and quarantine, which need to be followed. Ideally, based on CDC recommendations, if any partner is a suspect, self-quarantine is necessary without bed-sharing or any form of intimacy till at least 7–14 days after the symptoms started, or till full resolution of all symptoms, or at least up to 72 h of being fever free without any medications.^[48] For hospitalized patients, negative testing for severe infections is recommended before discharge. A study from Shenzhen, China, had reported 15% transmission in household contacts, which can be minimized using strict hand and respiratory hygiene.^[49]



SEX/INTIMACY FOR FRONTLINE HEALTH WORKERS

Health-care staff, police personnel, delivery executives, or other people involved in essential services have an added vulnerability. Many tend to self-isolate themselves from their spouses, adding to the psychological distress. The most important thing is keeping the partner informed about the risk, using adequate hygiene measures, using a separate set of clothes, having different room for occupational requirements, etc. Based on the degree of risk, isolation can be discussed and decided upon by both the partners. Unilateral decision-making can harm intimacy and relationships. If the partner at risk is asymptomatic, the decision about sexual activities is personal and can be tailored based on mutual preferences and convenience, as there are no evidence-based guidelines for the same. Partner consent is vital in these cases.

There are many who have newly entered relationships or just got married. Many of their partners might be away. For these couples, the challenges might be much more, and the need for continuation of intimacy and digital sexual practices becomes essential. Masturbation, phone or video sex, pornography, and sex toys might be helpful measures.^[50] However, the unhealthy use of technology, pornography addiction, personal and digital safety, and cyber-crimes are often the concerns. Research points out that although pornography can be a self-gratifying replacement for in-person sex, it also tends to be compulsive, can distort ideas about sex, and contribute to partner violence.^[51] The inner anxiety of the pandemic, sexual abstinence, and the resultant psychological distress might contribute to sexual disorders in the postpandemic period. Physicians of all specialties need sensitization and awareness for detecting these problems, offering appropriate sex counseling, and initiating referrals if necessary. Special attention needs to be offered to the sexual minorities, adolescents, and the elderly to prevent them from stigma and prejudice during this pandemic – people who are sexually active need to be advised about contraception and risks to pregnancy if infected. The various sexual approaches during the pandemic (most least to most risky) are summarized in Table 2.

ENSURING HEALTH SEXUALITY AND SEXUAL WELL-BEING: THE WAY FORWARD

Total abstinence and self-gratification can be the safest measures, but not always practically feasible. Abstinence-only approaches have been shown to induce guilt, decrease self-esteem, and increase noncompliance to recommended legal provisions.^[54] Human needs for intimacy need to strike an appropriate balance with personal safety and infection control. The health-care workers need to be empathic and nonjudgmental in these discussions with the couples,

Table 2: Proposed sexual approaches during the coronavirus disease 2019 pandemic

Sexual practice/ methods	Details
Abstinence	Ideal and safest, not always practically feasible
Masturbation/ self-gratification	Low risk for transmission Safe masturbation tips as followed in STD ^[52] (washing hands before touching genitals, clean sex toys, not sharing sex toys, using new condoms each time, nonirritant, and safe lubricant)
Digital sex	Appropriate and mutual consent Sociocultural acceptance Risks of data leakage and theft Sexual extortion Sexual details/images of minors can have legal consequences Risk of cyber harassment and online sexual predation Special counseling for children and adolescents
Sex with a self-quarantined partner	Least risk to others Asymptomatic carriers pose a potential risk Increased risk of multiple sexual partners
Continuation of usual sexual activities	Risk reduction counseling ^[53] Risk of infection and transmission routes, sex education Awareness about performance anxiety, sexual frustration, and symptoms of sexual disorders Reducing the number of sexual partners Identifying COVID-19 symptoms and avoid sexual contact if present Wearing mask, hand and respiratory hygiene before and after intercourse Cleaning of the place of sexual intimacy Avoiding sexual behaviors that can lead to orofecal contact Minimum contact intimacy and regulated frequency of sex, if a suspected risk
Miscellaneous	Informed decision-making Emotional support and bonding Spending quality time Communication; sharing hope and joy “COVID-” free time

STD – Sexually transmitted disease; COVID-19 – Coronavirus disease 2019

as for many, it might be a sensitive and stigma-inducing topic. Many might be hesitant to express it at all. Minors can tend to withhold valuable information (suicidality, high-risk sexual behaviors, abuse, sexual bullying, etc.), if not interviewed in confidence. People can be encouraged to engage in digital sex (such as sexting or video sex), with an eye for the safety concerns. The mutual consent of the partners is, however, an essential consideration. Digital theft has increased during the pandemic, especially with specific platforms such as Zoom, which can lead to leakage of personal data and sexual extortion.^[55] Encrypted and password-protected digital platforms are safer. The risks and legal implications need to be informed and discussed. The administration also needs to be aware of the increased use of digital forums for intimacy and change in cyber security monitoring and policies as necessary. For some minors and others with limited technology access and practice, digital intimacy might not be possible, and other avenues might need to be explored. Telephonic expression



of affection can help closeness and relationships. Being dismissive of the sexual needs during such a crisis might be counter-productive for both the clinicians and the clients. It is especially important to identify any signs of abuse or IPV at the earliest and steps to be taken immediately. The national mental health helplines related to COVID-19 can liaise with related services by the Ministry of Health and Family Welfare, Government of India.^[56] The women, child and elder helplines can also be integrated to help and counsel abuse victims, catering to their safety.

Another safe approach is to self-quarantine with partners if exposure has already occurred with an acceptable degree of risk. In that case, sexual practices can be feasible.^[57] Those who cannot engage in this might continue their sexual relationships in a controlled frequency, with risk reduction counseling. This has helped in reducing the transmission of sexually transmitted diseases (STDs). Indiscriminate sexual practices without understanding the risk of transmission can enable a much faster spread of COVID-19. Unwanted pregnancies need to be prevented and education on the use of contraceptive measures and protection from STDs need to be incorporated in the counseling modules. People affected with HIV form a susceptible section of the population, and the CDC gives particular guidelines about SARS-CoV-2 infection in HIV.^[58] Preexposure prophylaxis needs to be diligently followed. Widespread misinformation has turned COVID-19 into an “infodemic,” which is an added burden to public health. Myths related to sexual transmission can further impair safe sexual practices. Community health workers need to be active for sexual health counseling and exploring the emotional needs during the pandemic; socioculturally appropriate and multilingual infographics providing information-education-communication about sexuality during COVID-19 can help at the primary level. Active liaison of health care with media is necessary for increased penetration at all levels; mainly social media can be a uniquely equipped tool in this field for sexual health communication and promotion.^[59] Authentic sources such as the WHO and CDC are best used for reference. Few websites have useful counseling guidelines for discussion with children about online sexual risk during the pandemic.^[60]

Beyond all the other aspects of intimacy, emotional bond between partners is vital during a global crisis. Sexuality is much beyond just foreplay or intercourse. It involves holistic closeness and emotional bonding between partners. This becomes all the more critical during such pandemics, with various restrictive measures in place. Communication is the key, and informed mutual decision-making can help relationships progress. The lockdown has led many couples to be stranded together for a long time, a chance that was long due. This time can be used for generating love and intimacy, to mend strained relations, and fostering new avenues of trust and hope, that can last long beyond the pandemic threat. Spending quality time together, sharing

happiness, staying away from “information overload,” and cherishing “COVID-” free time every day, can help regenerate the intimacy.^[2] Any form of abuse needs immediate reporting, as otherwise, it tends to become a vicious and recurrent pattern. Another vital issue is the sociocultural acceptance of sexual practices in our country. Traditionally, from the descriptions of Kamasutra to the modern-day literature, intimacy has always been viewed in terms of “personal touch,” and cyber closeness thus becomes a culturally dissonant concept.^[61] Digital sexuality has often been equated with “obscene” or “inappropriate” based on traditional ideas, for which it might be difficult to adapt it even at such times of crisis.^[62] In that context, even with the use of technology for psychosexual well-being, the partners need to discuss and tailor it according to their beliefs, values, and ideals. A discordance in this area can be further damaging.

CONCLUSION

Sexual health and well-being have been extensively spoken about in the early days of “pestilences” and since then, fallen neglected during pandemics, subsumed by other health priorities. New advances might emerge with the innovative use of technology for both social and sexual connectedness. Digital intimacy can be an effective way of closeness in relationships; however, the authors do not intend to advocate that it is mandatory. It is an option that the couples can mutually choose for sexual well-being. Given the many facets of “digital sexuality” discussed above, it is more of a tailored choice and not a generic recommendation.

Antibody testing used to have a prime role in the detection of sexual risk for HIV,^[63] and similar hopes can be expected in COVID-19 too. Antibodies to the causative novel coronavirus might render someone safe as a sexual partner. As research progresses in this field, sexual medicine needs to be integrated into public health as an integral indicator of psychosocial well-being. Mental health counseling at all levels needs adequate sex education tailored to the needs of pandemics. Awareness and knowledge-attitude-practice among the health-care professionals can improve beyond the stigma, prejudice, and taboo related to the discussion about the sexual matter.

Cross-sectional and longitudinal studies need to estimate the prevalence and risk factors of sexual disorders and their sociocultural differences and predictors of the same during a pandemic. Qualitative studies are much-needed assets to understand the in-depth and lived experiences of sexuality in couples and their practices of intimacy and unmet needs. Sexual counseling can be specialized for children, adolescents, the elderly, and LGBT community, who are more vulnerable to social and sexual stigmatization. Sexuality has moved beyond just an emotional requirement



to a “rights-based” approach. Lessons learned now might help psychological preparedness and ensure psychosexual health during futuristic crises. It is high time we discard the “moral” veil of sexuality and start considering it as a natural indicator of human well-being, which needs to be nurtured for healthy relationships. In that sense, COVID-19 might be another chance for us to integrate sexual well-being into broader public health practices for the greater good.

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of affection can help closeness and relationships. Being dismissive of the sexual needs during such a crisis might be counter-productive for both the clinicians and the clients. It is especially important to identify any signs of abuse or IPV at the earliest and steps to be taken immediately. The national mental health helplines related to COVID-19 can liaise with related services by the Ministry of Health and Family Welfare, Government of India.^[56] The women, child and elder helplines can also be integrated to help and counsel abuse victims, catering to their safety.

Another safe approach is to self-quarantine with partners if exposure has already occurred with an acceptable degree of risk. In that case, sexual practices can be feasible.^[57] Those who cannot engage in this might continue their sexual relationships in a controlled frequency, with risk reduction counseling. This has helped in reducing the transmission of sexually transmitted diseases (STDs). Indiscriminate sexual practices without understanding the risk of transmission can enable a much faster spread of COVID-19. Unwanted pregnancies need to be prevented and education on the use of contraceptive measures and protection from STDs need to be incorporated in the counseling modules. People affected with HIV form a susceptible section of the population, and the CDC gives particular guidelines about SARS-CoV-2 infection in HIV.^[58] Preexposure prophylaxis needs to be diligently followed. Widespread misinformation has turned COVID-19 into an “infodemic,” which is an added burden to public health. Myths related to sexual transmission can further impair safe sexual practices. Community health workers need to be active for sexual health counseling and exploring the emotional needs during the pandemic; socioculturally appropriate and multilingual infographics providing information-education-communication about sexuality during COVID-19 can help at the primary level. Active liaison of health care with media is necessary for increased penetration at all levels; mainly social media can be a uniquely equipped tool in this field for sexual health communication and promotion.^[59] Authentic sources such as the WHO and CDC are best used for reference. Few websites have useful counseling guidelines for discussion with children about online sexual risk during the pandemic.^[60]

Beyond all the other aspects of intimacy, emotional bond between partners is vital during a global crisis. Sexuality is much beyond just foreplay or intercourse. It involves holistic closeness and emotional bonding between partners. This becomes all the more critical during such pandemics, with various restrictive measures in place. Communication is the key, and informed mutual decision-making can help relationships progress. The lockdown has led many couples to be stranded together for a long time, a chance that was long due. This time can be used for generating love and intimacy, to mend strained relations, and fostering new avenues of trust and hope, that can last long beyond the pandemic threat. Spending quality time together, sharing

happiness, staying away from “information overload,” and cherishing “COVID-” free time every day, can help regenerate the intimacy.^[2] Any form of abuse needs immediate reporting, as otherwise, it tends to become a vicious and recurrent pattern. Another vital issue is the sociocultural acceptance of sexual practices in our country. Traditionally, from the descriptions of Kamasutra to the modern-day literature, intimacy has always been viewed in terms of “personal touch,” and cyber closeness thus becomes a culturally dissonant concept.^[61] Digital sexuality has often been equated with “obscene” or “inappropriate” based on traditional ideas, for which it might be difficult to adapt it even at such times of crisis.^[62] In that context, even with the use of technology for psychosexual well-being, the partners need to discuss and tailor it according to their beliefs, values, and ideals. A discordance in this area can be further damaging.

CONCLUSION

Sexual health and well-being have been extensively spoken about in the early days of “pestilences” and since then, fallen neglected during pandemics, subsumed by other health priorities. New advances might emerge with the innovative use of technology for both social and sexual connectedness. Digital intimacy can be an effective way of closeness in relationships; however, the authors do not intend to advocate that it is mandatory. It is an option that the couples can mutually choose for sexual well-being. Given the many facets of “digital sexuality” discussed above, it is more of a tailored choice and not a generic recommendation.

Antibody testing used to have a prime role in the detection of sexual risk for HIV,^[63] and similar hopes can be expected in COVID-19 too. Antibodies to the causative novel coronavirus might render someone safe as a sexual partner. As research progresses in this field, sexual medicine needs to be integrated into public health as an integral indicator of psychosocial well-being. Mental health counseling at all levels needs adequate sex education tailored to the needs of pandemics. Awareness and knowledge-attitude-practice among the health-care professionals can improve beyond the stigma, prejudice, and taboo related to the discussion about the sexual matter.

Cross-sectional and longitudinal studies need to estimate the prevalence and risk factors of sexual disorders and their sociocultural differences and predictors of the same during a pandemic. Qualitative studies are much-needed assets to understand the in-depth and lived experiences of sexuality in couples and their practices of intimacy and unmet needs. Sexual counseling can be specialized for children, adolescents, the elderly, and LGBT community, who are more vulnerable to social and sexual stigmatization. Sexuality has moved beyond just an emotional requirement



to a “rights-based” approach. Lessons learned now might help psychological preparedness and ensure psychosexual health during futuristic crises. It is high time we discard the “moral” veil of sexuality and start considering it as a natural indicator of human well-being, which needs to be nurtured for healthy relationships. In that sense, COVID-19 might be another chance for us to integrate sexual well-being into broader public health practices for the greater good.

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It is indeed with immense pleasure and happiness that I pen down these lines!

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The Indian Psychiatric Society (IPS), established in 1947, is the single largest professional body of mental health professionals in India, having more than 7000 psychiatrists as its members, many of whom are on leading fronts in the country. As the last semester of this year has marked an unprecedented threat in the global landscape in the form of coronavirus disease 2019 (COVID-19), challenges in psychosocial health have emerged as a concerning factor in public health worldwide. Pandemics are far from just biological phenomena. The implications that such a widespread biological disaster has on mental health and well-being can outlast the infection itself. India has faced unique challenges during the ongoing crisis, with recently the case load crossing one million mark. Besides the usual risk of neuropsychiatric effects of the SARS-CoV-2 virus, a plethora of factors can influence the psychological state of the general public in the present times. Fear of infection, uncertainty, mass panic, stigma, xenophobia, national and international tension, isolation and loneliness arising out of social distancing, as well as exacerbation of preexisting psychiatric disorders, all can impact the mental health during the ongoing crisis and in the long run. The frontline workers, those affected with COVID-19 and their families, those in quarantine, the age and gender minorities, and finally the migrants and socioeconomically impoverished classes are much more vulnerable and at an increased risk to both the physiological and the psychosocial offshoots of COVID-19. Psychiatrists all over India under the guidance of the IPS are trying their best to avoid holistic care in the biopsychosocial model anticipating the upcoming mental health-related morbidities.

In April 2020, various global public health agencies such as the World Health Organization and the Centers for Disease Control and Prevention have emphasized on the urgent need for mental health promotion and care as an integral

measure of public health responses to the pandemic. In line with it, the IPS in May 2020 in its official statement called for a national action at all levels to maintain and enhance the standard of psychological health-care services. Multiple publications have followed from the IPS subsequently related to guidelines for psychiatrists in the management of psychosocial comorbidities during COVID-19, mental health challenges of the frontline health-care workers, and finally standardization of telepsychiatry. This special issue of *Indian Journal of Psychiatry*, the official publication of the IPS, intends to bring in a similar endeavor compiling global research on "COVID-19 and mental health" to obtain bird's eye perspectives on holistic care, management, exploration, and understanding of the unprecedented impact of the pandemic on mental and emotional health.

Optimism and humanity have always succeeded amidst all the odds. With these hope and prayers, I wish this special issue a huge success to enlighten the dark ways ahead.

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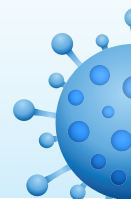
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Healthy Sexuality

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and T.S. Sathyanarayana Rao*

Abstract

Sexuality is one of the basic instincts which determine the behavior of an individual. Though it is one of the basic drives, it is under researched. Sexuality has biological, psychological and social dimensions. Sexuality is a developmental phenomenon; from childhood to old age it has several implications. Exercise, sleep, nutrition, marriage, divorce and diseases have their own impact on sexuality. Sexuality is one of the key components in determining the quality of life. In this article, we have tried to explore various dimensions of sexuality.

Keywords: sexuality, healthy sexuality, psychological, social, fantasy

1. Introduction

The fundamental drive behind every thought, feeling and behavior is Sexuality. The way an individual projects himself psychologically and socially is defined by sexuality. Sexuality is the best example of mind body harmony. The world goes around sex. The basis of babies bonding, teens flirting, and adults having babies is sexuality. Our dressing sense, sense of humor and the way we talk is influenced by sexuality; sex defines who we are. Sexuality has been addressed in holy books of great religions.

Karl Pribram, a Neuropsychologist described four drives which motivates us to accomplish our goals. These drives included fighting, feeding, fleeing and sex. These drives are essential for physical and psychological health. The least understood as well as least studied drive is sex [1].

2. History of scientific research in human sexuality

History of human sexuality is as ancient as human history. Some of the artifacts from ancient cultures are thought to be fertility totems. Kama Sutra (400 BC–200 BC), a Hindu epic describes about love, pleasure and desire; in fact about life in general. It is also a manual for sexual intercourse. Quran, Bible, Torah also have rules, advice and stories about sex.

Scientific research on sexuality started only around 150 years ago. Henry Havelock Ellis, an English physician used case study method to scientifically study sexuality. He published a seven volume book titled Psychology of Sex in which he tried to address different topics of sexuality which included arousal and masturbation. He emphasized that the sexuality of transgender is different from homosexuals. He advocated equal sexual rights for women and sex education at public schools [2].

Father of Psychiatry Sigmund Freud linked sex to health development. He recognized sexuality throughout the life span. Freud gave five stages of psychosexual development which includes oral, anal, phallic, latent and genital. According to Freud, each individual should pass all these stages. If the child's needs are unsatisfied or over-satisfied in these stages, either fixation or regression happens. This means child shows attachment to the previous stage, problems from that stage even persists into the adulthood. By keen observation of the individual behavior, one could recognize the psychosexual stage the adult had fixated or regressed [3, 4].

Alfred Kinsey, commonly referred to as Father of human sexuality research, believed most of the sexuality knowledge is guess work and there is lack of unbiased research. He had set a goal to interview around 100,000 people about sexual histories. Though he fell short of his goal, he could collect 18,000 interviews. Most of the contemporary scientists work on "behind closed door" behaviors were based on Kinsey's seminal work [5].

3. Sexual health

Sex describes means of biological reproduction. Sex also describes sexual organs both external as well as internal which defines individual to be male or female. According to the WHO, sexual health must be considered as "a state of physical, emotional, mental, and social well-being related to sexuality; it is not merely the absence of disease, dysfunction or infirmity. Human sexuality emerges in the body, but, like other human phenomena, it simultaneously unfolds in mental landscapes, social relations, and cultural spheres. Sexuality is closely linked to personal integrity, identity, body image, bonding, and social curiosity. Physiological and psychosocial determinants contribute significantly to sexual health."

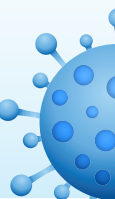
Healthy sexuality is a dynamic equilibrium, whereby adversity is balanced by personal agency and available resources. Sexual health is not mere absence of sexual dysfunction, it is individual's ability to navigate through problems. Clinical and research experience indicate there is no correlation between subjective well-being and objective strains. Sexual health like any other health is contextual and multifactorial [6].

4. Gender and orientation

The term gender represents psychological and sociological representation of biological sex, which includes gender identity as well as gender role. Though Gender and sex are important aspects of person's identity, it does not tell anything about orientation. Gender orientation refers to persons' sexual attraction to others. Sexual attraction refers to persons' capacity to arouse interest in others. One must be comfortable with their chosen gender and sex role and accept themselves without shame, guilt or fear. Be able to maintain good relationships with both sexes, regardless of whether they are platonic or intimate [7].

5. Attitude towards sex

Associations between general health and sexuality are diverse and intricate, and the two can interact in both positive and negative ways. Culture significantly determines our attitude towards sex. Culture influences our beliefs about what is normal and what is deviant in sexuality. Based on cultural attitude towards sex;



Cultures can be broadly classified into sex positive and sex negative cultures. Sex negative cultures which include India and Asian subcontinent believe that sex is for procreation while sex positive cultures which include western cultures consider sex beyond procreation. Sexual knowledge is usually acquired from someone in charge which may include parents, siblings, religious authorities, school, rumors from friends and mass media. One significant experience or stimulus that matches our fantasy would have long lasting impact on our attitude towards sexuality. Upbringing, witnessing parental interaction and intimacy shapes our life and beliefs [8].

6. Myths about sexuality

About female sexuality

- People think sex is dirty.
- Sex is sweet only during second decade of women's life.
- Sex during menstruation is harmful
- Bigger the breast-better sexuality
- Orgasm is a must in all sexual encounters
- Only vaginal and clitoral sex leads to orgasm
- A women's "no" convey "yes"
- Women never masturbate
- Sexual desire decrease dramatically after menopause

About Male Sexuality

- Erectile dysfunction is inevitable and incurable
- If a man does not get immediate erection he is not aroused
- If a man does not get aroused by mere site of partner he is not able to perform
- Masturbation leads to impotence
- Semen is a special cargo [9]

7. Sexual response cycle

Sexual response cycle which consists of desire, excitement and orgasm, have been classified by various authors in different ways. One of the simplest classifications is given by Kaplan, which is called DEOR model. D stands for desire, E stands for excitement, O stands for orgasm and R stands for resolution. Desire phase has biological, social and psychological component. Biological component



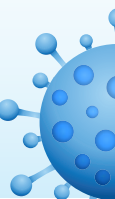
is the drive, sexual motivation is the psychological component and sexual wish is the social component. Excitement phase is characterized by penile tumescence in males and vaginal lubrication in female. Orgasm phase is characterized by heightening of sexual pleasure and resolution phase is characterized by disgorgement of blood from genital organs. Any impairment in any of these stages constitutes dysfunction [10].

8. Childhood sexuality

A strong emotional response is expected socially, whenever this topic is raised. Discussion on sexual behavior in children is obviously going to raise many eyebrows. Sexuality forms part of the personality and is a normal aspect of growing up. On one hand we resist talking to children regarding sexuality and on the other they get exposed to various sexual behaviors through the media. This makes it difficult for children to make right decisions during their adolescence. It is important to understand that the concept of normal sexual behavior in children is likely to vary with change in society's attitude. Research in the area of childhood sexual knowledge and behavior is scarce. Methodical issues are important during research as many of these rely on parental interviews leading to inconsistent results [11]. Sexual behavior is related to the age of the child, maternal education, family sexuality, family stress and violence, and hours spent in day care. For the clinician to understand the relationship between sexual abuse and sexual behaviors, it is important to understand normative childhood sexual behavior [12].

Much important psychosexual development occurs during childhood. Sexual development starts from birth and as the child develops the knowledge of gender identity during the first 2 years of life, genital exploration begins. Sexual knowledge is a child's basic understanding of sexual acts. It varies with the child's age and the education level of the parents [13]. A child learns labeling of body parts including genitals and experiences genital pleasure during this time. They may use slang labels and touch other children's genitals or take off clothes in public. The physiology related to sexual arousal and orgasm is present in children at birth or even before that. Fetuses suck fingers/toes and penile erection or vaginal lubrication is seen in new born males and females. Sexual arousal is associated with REM (Rapid Eye Movement) sleep in infants and young children similar to adults. However infants and young children lack cognitive capacity to understand this autoerotic behavior which is more of "pleasure seeking" and is a reflex behavior. Sexual development occurs throughout early years but except for during puberty none of these sexual development milestones have been clearly defined [13].

During 3–5 years of sexual development, gender is permanently established and gender differences are clearly understood. The child has only little information regarding pregnancy and delivery. The child may use slangs for sexual parts of the body. During the preschool years (2–6 years) many overt sexual behaviors are seen. The child may masturbate for pleasure and experience orgasm either in public or private. Nudity is enjoyed and removing clothes in public may be noticed. Sex play with peers (mimicking dating behavior, using naughty words even if they do not understand the meaning) self-genital exploration and that of others, attempted intercourse may be noticed. Sitting close to others, touching breasts of mother or other females (in males), trying to view peer or adult nudity may be noticed. Masturbation is likely the most commonly observed sexual behavior in children. It has been noted in infants as young as 7 months, which is initially based on curiosity about one's body but gradually the pleasure obtained becomes a decisive act. Friedrich et al. [15] has reported that some of the behaviors like inserting objects



into vagina/ anus, putting mouth on sex parts and masturbating with objects may rarely be seen in children aged 2–12 years. Many parents may react negatively to this and punish their children for this behavior. Caregiving and nurturing provide the first sensual and erotic encounters to the new born and these experiences of physical affection are critical for healthy development of the child [14, 15].

During 6–12 years the child understands genital basis of gender. The child is able to label sex parts but uses slang. The child is able to understand sexual aspects of pregnancy; with increasing knowledge of sexual behavior, children may masturbate in private. Sex games with peers (like girlfriend/ boyfriend, truth or dare, playing family) role plays and sexual fantasy may be seen. Developmentally appropriate behavior includes touching their own genitals, trying to view another person's genitals or breasts and standing too close to other persons. Young children, who are yet to learn culturally appropriate distance, may rub against people, or casually touch their mother's breasts or father's genitals [16]. Sexual behaviors become more covert after 5 years of age [18]. Gundersen reported in 1981 that among preschool children aged 3–7 years sexual play was common including body exploration, genital manipulation and attempts at sexual intercourse. Kissing is part of normal sexual development. Exhibitionistic behavior in children, showing body parts to other children or adults, may be part of "playing doctor" [17]. About 85% of college women recalled engaging in sexual games during childhood in a study done by Lamb and Coakley in 1993. Over 40% reported fantasy sexual play including sexual stimulation, intercourse, rape, prostitution and strip shows. Over one third of the games involved genital fondling. These games are due to curiosity, however some children find them a source of sexual excitement. Coercive childhood sexual games are considered to be "normal" especially as boys and girls usually play together. Children may develop anxiety when parents or adults show affection towards each other. The frequency of childhood sexual behaviors when retrospectively recalled by adults may differ from the frequency reported by parents; recollection bias and personal acceptance of sexual behaviors as normal, differs. Educated mothers are likely to report more sexual behaviors in their children [18].

Sexual encounters between siblings are very similar to those seen with friends in terms of the activities occurring, motivations associated, age and perception of them being positive or negative. Finkelhor in 1981 reported that younger children are more likely to exhibit their genitals whereas older children are more likely to engage in attempted or actual intercourse. Younger children show a broad range of sexual behaviors which decrease with the growing age. Sex between siblings occurs much less frequently than between friends. Sexual encounters in siblings range from 9 to 13%. Lower reported rates of sexual encounters between siblings may be either due to age difference or biased retrospective reporting due to incest taboo. However frequency of coercive sexual encounters is almost similar to that with friends and girls are predominantly the victims. Young children are likely to explore their sexuality more at home than in structured and monitored settings among children. The results reported may not represent full range of sexual behaviors seen in children due to ethnic differences in subjects on which research is conducted. Women who have had sibling sexual experiences (positive or negative) are more likely to be sexually active as adults. Sexual sibling experiences before the age of 9 with large difference of age between siblings led to lower sexual self-esteem. Sexual experiences between friends or siblings suggest that normal sexual contact occurs on a continuum and differentiation between sexual play and abuse is not always clear [19].

The child gains knowledge of physical aspects of puberty by age 10. The child shows modesty and embarrassment and tries to hide sex games as well as masturbation from adults. Masturbation most likely increases before puberty especially



among boys. There are few physical changes associated with sexual development before the onset of puberty. Just before the teenage years body changes begin, menstruation starts in females and boys may experience wet dreams; fantasizing about sex, interest in media sex, using sexual language with peers is observed [19].

9. Adolescent sexuality

Adolescent sexuality has received much attention in comparison to childhood sexuality. Teens are sexually active but they are hardly prepared for developing responsible sexual behavior. Adolescents reach physical maturity but they are cognitively immature to handle it. A teenager's primary source of exposure to sexuality related information is his or her peer group. Family dynamics may not be strong enough to guide the teenagers in developing healthy and non-risky sexual behavior [20].

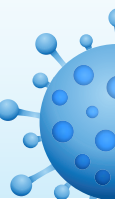
Puberty is the time when sexual development can be much clearly delineated especially the physical changes. There is variation in age at which puberty begins although the onset is typically 18–24 months earlier when compared to boys [21]. The average age of first ejaculation in boys is 14 years (range 14–16 years). However, girls' breast development begins between 8 and 13 years of age; menarche starts at an average age of 13 years (age range 10–16.5 years). Adolescents acquire knowledge about sexual intercourse, contraception and sexually transmitted diseases. Adolescents get fondness for dating, kissing and petting; sexual fantasies are common. The issue of greatest concern for parents has been the age at which teens engage in sexual intercourse. The average age of first sexual contact has decreased rapidly. They may make sexual contacts including mutual masturbation and first sexual intercourse may occur in 75% by the age of 18 years. However in India as per National Family Health Survey (NFHS), males are mostly likely to have their first sexual intercourse between 20 and 24 years, whereas in females, the peak age at first sex is lower between 15 and 19 years [5].

Early onset of sexual intercourse affects the psychosocial development. Early onset sexual activity has been linked to delinquent behavior. Chances of unintended pregnancy are higher in teens who engage in sexual activity earlier. Teenage parents are at an economic disadvantage and are more likely to drop out of school. Authoritarian parents, poor communication regarding sexuality and having older siblings who are sexually active can facilitate early sexual activity. Rutter and Rutter refer to early sexual activity as a "turning point" which can change the course of a teenager's life. Understanding early sexual activity can help in planning intervention programs. Other factors which are associated with adolescents who are sexually active include: (1) less educated mother, (2) lower educational expectation, (3) presence of a boyfriend or girlfriend, and (4) higher age. Adolescents are at cross roads as far as sexuality is concerned. A wrong decision can have strong and negative economic and social consequences for the society at large and for the individual in particular. Sex education is an important area which needs to be taken seriously particularly for the adolescent age group [22, 23].

10. Other factors influencing sexuality

10.1 Nutrition and sexuality

Mediterranean diet which includes fruits, nuts, legumes, monounsaturated fats from olive oils, vegetables and whole grains is gaining popularity in the last few



decades. Studies have shown that these groups of foods improve or at least diminish the progression of sexual dysfunctions. Paleolithic diet which is an ancestral diet, before agricultural revolution is gaining more attention in the recent past. Paleo diet which includes lean meat, fruits, legume, plant based foods, restricted consumption of dairy, salt and sugar similar to Mediterranean diet have shown to be beneficial, but well-designed studies are not available. Vegetarian or vegan diet which can be classified as pesco-diet (absence of all animal products except fish), lacto-ovo-vegetarian diet (absence of all animal products except egg and dairy products), ovo-vegetarian diet (absence of all animal products except egg) and vegan-diet (absence of all animal products). Vegetarian diet has shown to reduce morbidity due to vascular causes, which in turn may help in healthy sexual functioning. Vegetarian or vegan diet may cause protein and vitamin B12 deficiency which can be prevented through careful monitoring and supplementation [24].

10.2 Intelligence and sexuality

There is evidence for correlation between intelligence and the age at the first sexual contact. There is inverse correlation between intelligence quotient and the age at first sexual intercourse. Though there is evidence that more intelligent people have more sexual desire, but the frequency of intercourse is less. Emotional intelligence plays a key role in marital relationship. Knowledge, self-competence, secured attachment, emotional processing and self-compassion were few aspects which determined good marital satisfaction [25].

10.3 Job, vocation and sexuality

Job stressors have significant impact on sexuality. It majorly depends upon the role the individual is having in the job. It depends on working ability of individual for that job. Work ability includes physiological and psychological ability of the individual to cope with the specific type of the job. The managerial and organizational support also played important role in job stress. Job stress significantly affected desire, arousal and orgasm phases of sexual response cycle [26].

10.4 Exercise and sexuality

Exercise releases hormones called endorphins, which has a feel good component as well as analgesic effects. Exercise may be acute as well as chronic exercise. Acute exercise increases metabolic rate, causes muscle activation and increases blood flow. Chronic exercise causes long lasting adaptation and improves performance. Acute exercise improves physiological sexual arousal through increasing sympathetic nervous system activity and endocrine factors. Chronic exercise increases sexual satisfaction by maintaining autonomic flexibility. Autonomic flexibility helps in maintaining cardiovascular health as well mood. Chronic exercise also gives positive body image which in turn gives sexual well-being. A couple of small studies have shown the effectiveness of exercise as intervention for dysfunctions [27].

10.5 Sleep

Adequate sleep is essential for normal sexual activity. Quality of sleep has significant impact on various phases of sexual response cycle. Desire is a motivational state which drives the individual to search for sexual activity, while arousal prepares individual physically and psychologically for sexual activity. Rapid eye



movement sleep (REM) deprivation increases unstimulated sexual arousal but does not have any effect on desire. Sleep deprivation can also have impact on endocrine factors [28].

10.6 Fantasy

Fantasy both during masturbation as well as sexual intercourse enhances sexual responsiveness dramatically. Sometimes it may be perplexing for some individuals while having sex with someone. Sexual fantasies indicate person's sexual values that may not be overt in their behavior. Source of fantasies is not always obvious, it may be something one has read or seen or may be totally imaginary. Sexual fantasies can arouse sexual excitement and vice versa is also true, sexual excitement arouses sexual fantasy. Women and men who fantasize are more likely to experience orgasm during intercourse. Individuals who report frequent sexual fantasies are less likely to develop sexual dysfunctions. Themes of sexual fantasies are varied, imagining of having sexual intercourse with someone whom you love, having sexual encounters with strangers, having multiple sexual partners simultaneously, forcing someone to have sex or you being forced, being found sexually irresistible by someone, having sex with someone famous and many more. There are gender differences in sexual fantasies, men have more sexual fantasies than women. Even the content also varies, men fantasize an active role in sexual encounter while women more a passive role. Women fantasies' have more of emotional or romantic theme, revolves around current or previous partner, thoughts and feelings about love and devotion. Men usually fantasize impersonal sexual behavior, implicit visual sexual imagery, specific parts of partner's body, group sexual activity and focus on specific sexual activity [29].

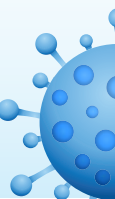
10.7 Masturbation

Masturbation is genital self-stimulation with some anticipation of rewarding erotic feelings, though it is not a necessity that to achieve orgasm genital stimulation is required, some women achieve orgasm even with breast stimulation. Autoeroticism conveys a different meaning, it involves self-stimulation which may or may not involve external physical stimulation. It refers to personal sexual perception and feelings.

There are lots of myths and misconceptions about masturbation. Lot of cultural and religious myths surrounds masturbation. There is a misconception that masturbation is a dismal alternative to sexual intercourse. Professor NN Wig, an Indian psychiatrist described a syndrome called "Dhat Syndrome" which is characterized by "undue concern about debilitating effects of passage of semen". It has been included in International classification of disease (ICD 10) both under neurotic disorder and culture specific disorder. There is cultural myth that semen is made up of "Dhat" (Elixir), when individual loses semen either through masturbation or wet dreams, they start feeling apprehensive about loss of vitality. Though this syndrome is prevalent worldwide, it is more common in Indian subcontinent.

There are gender differences in masturbation. The frequency of masturbation is more in men when compared to women. Studies show that individuals who report masturbating more frequently, are more open minded about sexuality and have more satisfactory sexual relationship with the partners.

People who believe masturbation as second best mode of sexual expression, get perplexed finding a place for masturbation in relationship. Age, illness, boredom and interpersonal issues influence frequency and intensity of sexual relationship among couples. Masturbation is not always problematic in relationship. Men and



women view masturbation differently in a relationship. Men view it as a supplement to pent up sexual energy, while women view masturbation as a substitutive role.

Vibrators and Dildos are not synonyms. Dildos are erect “penis-like” objects which may or may not vibrate. Though vibrators are not substitutes for nurturance, love and sexual attachment, it helps to explore oneself about their sexual response cycle, remove inhibitions and enhance knowledge about themselves [30].

10.8 Marriage

Religious prohibitions prevalent in the society results in restrictive upbringing. Effect of mass media leads to unrealistic sexual expectations. This leads to a conflict, which in turn causes guilt. Lack of communication, exhaustion and unusual expectation can lead to sexual problems during honeymoon. Interaction patterns among couples play an important role in sexual relationship. Hostility, power struggle and conflicts are few of the destructive interaction patterns. Sex at times can be used as a weapon where one partner may forego sexual pleasure rather than give satisfaction to the other. Emotions like anger, anxiety can act as antierotic stimuli [31].

10.9 Pregnancy

Pregnancy and childbirth are both the part of woman's sexual life. Positive experiences of female sexual functioning (as measured by dimensions including sexual desire, arousal, and satisfaction) were negatively correlated with the experience of stress, anxiety, and depression, and positively correlated with general quality of life during pregnancy. Moreover, experiencing fulfilling sexual experiences during pregnancy has been shown to promote well-being and maintain partner-intimacy, while low sexual functioning during pregnancy has been linked to poor body image [32].

Changes occurring in every trimester of pregnancy have significant influence on the sexual behaviors. A number of physiological and psychological changes occur in pregnancy with surge of hormones like estrogen, progesterone and prolactin that ultimately affect not only the frequency but also the quality and the outcome of sexual intercourse. Duration of coitus decreases over the length of pregnancy due to unfounded fears that intercourse may hurt the health of mother or baby or cause premature labor [33].

Sexual satisfaction correlates with the feeling of happiness resulting from being pregnant. Pregnant women prefer the following types of sexual activity: non-genital fondling, stimulation of the clitoris, vagina and breasts, oral and anal stimulation and masturbation. However females and their partners are under informed on sexual life in pregnancy [34]. Many authors emphasize, that the pregnancy is a stimulus for partners to search for ways to maintain mutual emotional bond, close physical affinity and satisfy sexual needs not necessarily finished with an intercourse. As the pregnancy progresses patients report frequent dyspareunia, decline in orgasm and poor self-image. Anatomical changes during pregnancy compel couples to attempt abnormal uncomfortable positions. For a number of couples, pregnancy becomes a stimulus to search for new ways of pleasing each other in love play, which does not necessarily culminates with intercourse.

Mode of delivery also impacts sexual functioning. Patients who delivered vaginally even after 6 months postpartum may experience dysfunction in all phases of sexual cycle compared to women who deliver by caesarian section. Women who deliver vaginally have weakened pelvic floor muscles and may also have discomfort due to rectocele and cystocele. Kegel exercises are advised early in postpartum



period to strengthen pelvic floor muscles. The eventual benefits of cesarean delivery on sexual function do not last longer than a few months after childbirth.

The research makes it evident, that experiencing sexual satisfaction by pregnant women improves their self-esteem, facilitates mutual relationship between partners and tightens the marital bond. There are various factors that may be influencing the lack of dialog initiated by prenatal health-care providers with their pregnant patients and partners regarding sexual activity during pregnancy. For one, our society at large often deemphasizes the sexuality of pregnant women, finding the discussion of sex during pregnancy to be a taboo. Moreover, Hinchcliff et al. noted that prenatal care providers may avoid discussing sexuality proactively as it is a complex issue and requires sensitivity [35].

11. Marriage after living together

After marriage, couple's start taking one another for granted. At times when marriages happen due to social pressure, couple may start taking one another for granted after marriage. When marriage happens after a period of open relationship due to social pressure, they may feel trapped [36].

11.1 Divorce

The rates of divorce have increased in all age groups in the recent times. Life after divorce requires emotional, social and sexual adjustment. Individuals spending most of their lives in wedlock, finds it difficult to adjust to singlehood. Many people are so adjusted to think their adult life as couple, they take time to get used to singlehood. It is confusing and perplexing for people to learn divorced role. Divorce leads to decline in life style in some people while in others it may lead to sexual liberty. Spiritual values and Literacy levels determines the number and frequency of partners [36].

11.2 Remarriage

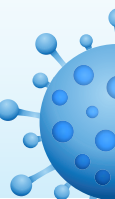
Multitude of factors influences the likelihood of remarriage. Younger the person, there is more probability of remarriage. About 89% who separate under the age of 25 remarry, it decreases to 31% after 40 years. Shorter the duration of first marriage, there are more chances of remarriage. Other factors are the age at first marriage, younger a person at first marriage, more probability of remarriage [36].

11.3 Families

The attitude of parents about sexuality has a significant impact on sexual well-being. Attitude of parents as well as siblings about nudity, masturbation, willingness to discuss about sex and homosexuality all contributes to the development of sexuality of an individual. Relationship of the parents with the individual as well as the partner also influences sexuality. Distorted intrafamilial relationship, lack of discipline, overcrowding, lack of warmth, unusual helplessness and withdrawal from society may lead to certain deviant sexual behavior [36].

12. Sexuality in geriatric population

Sexuality is an important aspect in Geriatric population. Elderly individuals look sexuality as a means of expression of passion, love, admiration and loyalty.



Furthermore sexuality acts as a means of affirming physical functioning, sense of identity and self-confidence. Though desire may remain the same, there may be alterations in other phases of sexual response cycle [9].

12.1 Sexuality and spirituality

The popular belief is that sexuality and spirituality exists in opposition, but in reality spirituality and sexuality go hand in hand. If we look at different geographical areas, there is lot of literature in Chinese Taoist tradition about practices bringing Yin (Feminine) and Yang (Masculine) in harmony. In Indian literature there is mention about energy generated in the pelvic region moving upwards through chakras to the crown, where one enters the cosmic orgasm generated eternally by union of Shakti and Shiva. In psychotherapeutic perspective, people believe that sexuality is something sin and it should be removed or cured. What spirituality should do is to help these people move from the belief that sexuality is sin to enjoying it as an integrated energy for passionate living [37].

12.2 Medical illness and sexuality

Looking at sexuality from the biological perspective, neurological, vascular and endocrine systems contribute significantly for normal sexual functioning. Neurological disorders like stroke, epilepsy, multiple sclerosis, traumatic brain injury and spinal cord disorders lead to sexual problems. Endocrine disorders like androgen deficiency, hyperprolactinemia, diabetes mellitus can produce sexual dysfunctions. Vascular disorders like hypertension and atherosclerosis, prostatic illness, carcinomas all can lead to sexual dysfunctions. Prevalence of sexual dysfunctions among these psychosomatic disorders is around 20–70%. Sex and intimacy are likely to be powerful providers of salutogenesis in both the chronically and critically ill patients. Sexual encounters can serve as a refuge in an otherwise chaotic and turbulent situation, and intimate relations might constitute engines of meaningfulness and coherence in a context of meaninglessness and incoherence that so often dominate the everyday life of patients with chronic illnesses [38].

12.3 Psychiatric illness and sexuality

Substance use disorders have varying effects on sexual functions. Alcohol at a smaller quantity may have some stimulatory effect, at higher quantity decreases both desire as well arousal through its effect on testosterone. Cannabis causes detrimental effect on initiation as well as maintenance of erection. Cannabis historically has aphrodisiac effect, but current evidence shows mixed results. Long term use of cannabis has detrimental effect on testosterone. Similarly opioids delay ejaculation in men and improve vaginismus in women, but long term use decreases testosterone as well as luteinising hormone.

The rates of sexual dysfunction in people suffering from schizophrenia, mood disorders, personality disorders, anxiety disorders and eating disorders is very high. In these disorders illness itself can have effect various stages of sexual response cycle, and also medication used can have adverse effects on sexuality. One of the major psychiatric disorder schizophrenia has negative symptoms like blunted affect, anhedonia and avolition itself causes impedance in enjoying sexual life. Loss of libido is one of the symptoms in major depressive disorder. Anxiety disorders are usually associated with premature ejaculation. Mania is associated with increased libido during the episode, at times disinhibited sexual behavior leads to high risk sexual behavior [39].



13. Conclusion

Sexuality is one of the key factors for wellbeing. There are more myths than adequate knowledge about sexuality. It plays an important role in molding the personality during childhood and adolescence, while it contributes to self-esteem throughout life. Various bio psychosocial factors may influence sexuality. It is one area where research is lacking. In this chapter we have tried to explore some of the key areas influencing sexuality. More research and evidence based data is needed in this area.


Author details

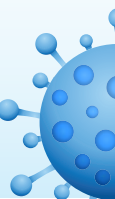
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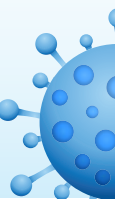
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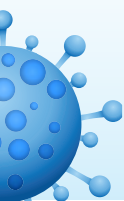
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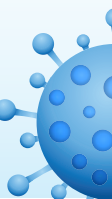
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6. Infodemic of Pandemic

SI No	Title	SDG IMPACT
52	Coronavirus19 pandemic: Time to defuse misbelief and build trust, Dr Praveen Kulkarni., Dr Narayana Murthy M.R., Archisman Mohapatra, International Journal of Health and Allied Sciences, 9, 97-98, 2278-4292	Goal 3: Good health and wellbeing
53	COVID -19- Infodemic overtaking Pandemic? Time to disseminate facts over fear, Dr Praveen Kulkarni., Dr. Sunil Kumar D., Balaji Ramraj., Sudhir Prabhu, Indian Journal of Community Health, 32, 265-268, 0971-7587	Goal 3: Good health and wellbeing
54	Effect of False News on Knowledge, Attitude, and Practice toward COVID-19 Pandemic among Educated of Karnataka, India, Amogha Shree., N Chandan., Dr Shwethashree M., Dr Narayana Murthy M.R., Annals of Community Health, 9, 254-262, 2347-5455	Goal 3: Good health and wellbeing
55	COVID-19 infodemic: Unveiling the root causes through public perspectives, Jose Jom Thomas., Dr Praveen Kulkarni., Dr. Sunil Kumar D., Dr Prakash B., Dr Narayana Murthy M.R., International Journal of Health and Allied Sciences ,9, 31-37, 2278-4292	Goal 3: Good health and wellbeing
56	Psychology of misinformation and the media: Insights from the COVID-19 pandemic, Debanjan Banerjee., Dr Sathyanarayana Rao T.S., Indian Journal of Social Psychiatry, 36, 131-137, 0971-9962	Goal 3: Good health and wellbeing



Coronavirus-19 pandemic: Time to defuse misbelief and build trust

“Raising awareness versus raising alarm; the public can’t be better informed if the information isn’t better.”

— T.K. Naliaka

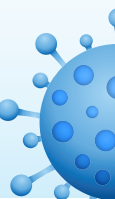
The novel coronavirus-19 (COVID-19) “pandemic” (WHO, March 11, 2020) calls for concerted national and international effort for containment.^[1] Since its emergence in Wuhan (China), the virus has rapidly spread to at least 143 countries across the globe despite concerned efforts. As on March 11, 2020, 153,517 confirmed cases and 5735 deaths have been reported globally.^[2] After China lived through its worse, Europe has become the new epicenter of the pandemic.^[3] Beyond health, the impact on other sectors and overall development is perceived to be huge. Worldwide stock indices have reacted to the sentiment and have taken nose-dives. With travel restrictions and work-from-home recommendations, international businesses are likely to have slowed down. It is estimated that the COVID-19 pandemic could cost \$2 trillion globally, push several households below the poverty line, and may derail the Sustainable Development Goals agenda. On the other hand, evidence is accruing day by day on the COVID-19 epidemiology, risk predictions, and potential combat strategies. There is hope that we may be able to find a drug that works against the virus or manage to develop a vaccine but that is unlikely before 2021.

Available evidence suggests that COVID-19 is transmitted through droplets; 81% of cases are mild and self-limiting. The case fatality rate (proportion of cases who die due to the infection) ranges at around 3%–5% and increases exponentially in the elderly (possibly due to comorbidities and a weaker immune system). Children are mostly protected against adverse outcome though even newborns have been tested positive, with the virus raising questions whether the infection was transmitted intrauterine or peripartum. The secondary attack rate, which is the measure of transmissibility of disease in one incubation period, is around 3%–10%. Basic reproduction number (R_0), which is a measure of average number of new infections generated from a single-infected, person is around 2.4. These numbers are expected to change as the pandemic progresses through different stages and according to the country’s level of preparedness.^[4] There

have been reports of those declared as “cured” being “reinfecting” – something that needs to be investigated amidst the chances of being wrongly declared as “cured” or as false positives (due to test or human error).

India reported its first laboratory-confirmed case of COVID-19 on January 30, 2020 – a student from Kerala who had returned from Wuhan provinces of China. Since then, the total count has risen to 84 with two deaths as on March 14, 2020 – a female in Delhi and a male in Karnataka, both elderly and with comorbid conditions, likely leading to complications.^[5,6] Of the 84 cases, 67 are Indian nationals and 17 are foreigners; 10 have been declared cured, whereas the remaining are under isolation and observation. Local transmission of COVID-19 (infection among those with no travel history to affected countries) has been reported in the following five states: Delhi, Karnataka, Kerala, Maharashtra, and Uttar Pradesh. In a resource-constrained country of 1.3 billion people with grossly inadequate health logistics and skilled personnel and an unsure capacity for rapid scaling up of diagnostic and health services, delaying the spread of infection within the country seems to be a “war that must be won.”

By dwarfing the epidemiological curve, we are likely to be better prepared, and from historical experience with pandemics, likely incur lesser human loss to the pandemic. The Government of India (GOI) is fast responsive to the situation. The outbreak combat has been through a series of aggressive measures by the central and state governments. The GOI has declared COVID-19 outbreak in the country as a “notified disaster.” Health being a state subject, several states have invoked the provisions under Section 2 of the Epidemic Disease Act 1897, which gives “power to take special measures and prescribe regulations as to dangerous epidemic disease.” Screening of all the international passengers at airports, suspending all the visas (with few exceptions), strict quarantine of suspected cases, designing and disseminating standard operating guidelines for the management of cases, and knowledge resources for general public awareness materials are a few to name.^[5] Social distancing; cough etiquette; hand hygiene; not touching the eyes, nose, and mouth with unclean hands; avoiding crowded places; withholding foreign travels; judicious use of face masks; self-quarantine in case of exposure; seeking immediate health care in need; spreading awareness prevention and control measures;



and preventing social gatherings are the measures to be undertaken for effective containment of this pandemic, and these are being actively circulated through various channels to the public and even implemented with administrative strong-handedness (Section 144 of IPC has been applied in several places across India which disallows congregation of people; failure to register on part of any one returning from abroad has been made punishable by the Government of Odisha).^[7] Face masks and sanitizers have been included in the list of most essential drugs, and their export has been blocked.

There are certain indigenous insights emerging from the COVID-19 situation in India. The felt need is shifting from tertiary care and health insurance toward disease prevention. Political commitment has gradually matured to political accountability and apolitical pragmatism. For instance, the government had announced cash compensation to the next of kin of COVID-19 victims (demonstrating empathy and commitment to ensure health security to all), but was quick to reverse the same (thus showing that the government's responsiveness is rooted in reality and with purpose). The present pandemic of COVID-19 has also seen an unprecedented media attention – both the organized sector and in the social media. Notwithstanding the rumors, mispropaganda and fear this might have led to, this has seemingly led to rapid on-boarding of the public *en masse* in terms of some awareness on the topic, thanks to the penetration of technology. Our demographic structure (being predominantly a young country) and climate conditions (a hot summer) may be of help – an optimistic speculation that only the times to come will clarify.

Outbreaks pose challenges, and they also open plenty of opportunities to understand the finer details of epidemiology and dynamics of disease transmission. The present pandemic is not an exception for this. Across the world, we are learning new lessons, adapting new strategies, sharing our experiences, exchanging ideas, and helping each other for being disease free in this situation of crisis. This validates the philosophy of “*Vasudhaiva Kutumbakam*,” which means that the whole world is just one family – in health and in disease!

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COMMENTARY

COVID -19- Infodemic overtaking Pandemic? Time to disseminate facts over fear**Praveen Kulkarni¹, Sudhir Prabhu², Sunil Kumar D³, Balaji Ramraj⁴,**¹Associate Professor, Department of Community Medicine, JSS Medical College, JSS Academy of Higher Education & Research, Mysuru, Karnataka; ²Associate Professor, Department of Community Medicine, Father Muller Medical College, Mangaluru, Karnataka; ³Associate Professor, Department of Community Medicine, JSS Medical College, JSS Academy of Higher Education & Research, Mysuru, Karnataka; ⁴SRM Medical College Hospital and Research Centre, Chennai[Abstract](#) | [Introduction](#) | [Methodology](#) | [Results](#) | [Conclusion](#) | [References](#) | [Citation](#) | [Tables / Figures](#)**Corresponding Author**Dr Praveen Kulkarni, Associate Professor, Department of Community Medicine, JSS Medical College, SS Nagara, Mysuru-570015, Karnataka
E Mail ID: praveenkulkarni@jssuni.edu.in**Citation**

Kulkarni P, Prabhu S, Dumar SD, Ramraj B. COVID -19- Infodemic overtaking Pandemic? Time to disseminate facts over fear. Indian J Comm Health. 2020;32(2-Special Issue):264-268.

Source of Funding: Nil **Conflict of Interest:** None declared**Article Cycle****Received:** 08/04/2020; **Revision:** 12/04/2020; **Accepted:** 13/04/2020; **Published:** 20/04/2020This work is licensed under a [Creative Commons Attribution 4.0 International License](#).**Abstract**

Coronavirus (COVID-19) is a humanitarian emergency. World Health Organization (WHO) and National Governments are making their best efforts to prevent the spread of disease. But a global epidemic of misinformation which is rapidly spreading through social media platforms and other outlets is posing serious problem to the public health interventions. This rapid spread of all sorts of information pertaining to the epidemic which makes its solution difficult is termed as infodemic. Infodemic creates fear, confusion and stigmatization among people and makes them more vulnerable to practice the measures which are not evidence based and scientifically sound. Hence there is an urgent need to identify the source of misinformation and prevent them from further spreading. WHO and the government of India have taken several steps in controlling this problem but there is a need for active involvement of social media companies, professional bodies, health care providers and general public in identification of misinformation and combating its spread.

Keywords

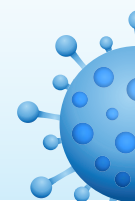
COVID -19; Infodemic; Pandemic

In the last week of December 2019, China reported unusual increase in the number of pneumonia cases in Wuhan province of China and neighboring areas.(1) The novel SARS-Corona virus was isolated from these patients and the organism was named as COVID-19.(2) Considering the alarming spread of infection, severity of disease and inaction exhibited by various countries, in combating the condition, COVID-19 was declared as Pandemic on 11th March 2020.(3)

First confirmed case of COVID-19 in India was reported on 30th January 2020 at Kerala in one of the

medical student who returned from Wuhan province of China.(4) Subsequently the disease has spread to almost entire country with the shift in the pandemic phase from stage 2 to stage 3. Government of India declared complete lock down from 25th of March 2020 as a firm step to prevent the community spread of infection and flatten the epidemic curve.

The current pandemic has posed serious challenge to the public health professionals due to rapid spread of both virus and misinformation related to it (Infodemic). The present paper discusses the



concept, causes, consequences and prevention of infodemic related to COVID-19.

The concept of Infodemic

Every epidemic is associated with a tsunami of information but also within this information there exists ample expanse of misinformation and rumors. Even the epidemics which took place in middle age had similar phenomenon, but the difference in present pandemic is the presence of social media.(5) Social media platforms, if used judiciously can act as a very important source of information. Their popularity, wider use, user friendliness, visual impact, interactivity can make any message spread to 'N' number of people in a very short span of time. Hyperactive and overenthusiastic social media platforms can potentially amplify the information leading to faster and further spread of misinformation, rumors, and misconceptions. WHO defines infodemic as a rapid spread of all kinds of information concerning a problem such that the solution is made more difficult.(6) COVID-19 seems to be a true social media infodemic compared to previous viral outbreaks. Though the previous pandemics like SARS and MERS caused worldwide panic, the current pandemic due to CoV 19 have been particularly exaggerated by social media.(7)

U.N. Secretary-General Antonio Guterres expressed his deeper concern on this issue and said that "the world is not only fighting the "common enemy" of the coronavirus "but our enemy is also the growing surge of misinformation" about COVID-19 disease. To overcome the virus, "we need to urgently promote facts and science" and "promote hope and solidarity over despair and division."(8)

Root causes of COVID Infodemic- Fish bone

We have tried to explain the root cause analysis of COVID-19 through fish bone diagram ([Figure-1](#)). The root or the tail is represented by the social media related components, the body represents four broad areas around which most of the misinformation revolves and the tip is represented by the outcome viz. Infodemic and the consequences associated with it.

1. Social media usage and spread of misinformation

There is exponential growth of internet users in both rural and urban parts of India over the last decade. With the introduction of much ambitious Digital India Initiative added by wider internet penetration has resulted in growth of digital population in India to the extent of 688 million as on January 2020. It is worthy to note that major proportion of this digital

population is constituted by mobile internet users. Social media users in India have increased from 142.2 in 2015 to 376.1 million in 2020.(9) Social media platforms like, facebook, whatsapp, youtube, twitter, instagram, telegram, TikTok are quite active in spreading both information and misinformation on the current pandemic.

Any message in the form of a text or a video that is rolled out through these media platforms will reach large number of people in a very short span of time and gets viral. Misinformation that flows through these media may be a totally wrong information, partially right information or correct information which is projected in a wrong way. People spread this kind of information to impose their own bias/thoughts on the people, to gain publicity, to promote their self-interest or ignorance of right information. The last set of people may be of intension to help society but they cannot filter the right and wrong information due to their lack of knowledge. There are some instances where the wrong messages are falsely tagged with names of professional and international health related organizations in order to make people believe those messages.(10)

2. Epidemiology related aspects

Novel nature of the COVID-19 virus has attracted the attention of social media. The domains like structure, infectivity, pathogenicity, mutation, effect of temperature and humidity on the multiplication and spread of virus has given major scope for spread of information and misinformation. Non availability of specific treatment and vaccine for the prevention of infection has also added to this pool.

3. Policy related aspects

As the disease is a novel one, the entire country is in the process of developing new policies and guidelines. Differences in the content of guidelines, serial evolution of policies, each state or province designing their own policies and strategies have influenced the development of misinformation

4. Behavioral issues

Indians are voracious social media users. The lockdown announced by the government and work from home have resulted in extensive use of the social media platforms. People indulge in spreading the information and misinformation received through the social media without fact check. Often, they pick the most extreme pictures which totally manipulate the scenario and make it viral to gain publicity. Noncompliance towards cyber related



rules, ignorance about correct information and ability to differentiate between the sources of right and wrong information can act as a major factor influencing spread of misinformation.

5. Health care system related issues

Delayed and inadequate risk communication by the health care providers was a major drawback which has resulted in spread of misinformation. Hospital based care being given more focus at initial phase of epidemic giving rise to panic on PPEs and ventilators have further raked up the chances of spread of misinformation. Inadequate knowledge on the concept of quarantine, its difference with isolation, lack of quarantine facilities have further fueled this risk

Misinformation on COVID-19

Since the beginning of COVID-19 pandemic, the spread of misinformation has become rampant. The messages carrying misinformation are usually tailored on the prevalent socio-cultural norms of the community in which they are rolled out. For example consumption of garlic, cow's urine (Gou mutra), turmeric powder are common culturally accepted practices in India, which are also reflected in messages related to COVID-19. Looking at the trend of misinformation in social media platforms, they can be categorized as those related to, ([Table 1](#))

Apart from the ones mentioned in the table, many non-health related misinformation pertaining to duration of lockdown period, economic slowdown, non-availability of essential commodities in the market, military being called to control the situation, exhaustion of food and agricultural products in the country etc are flowing in full swing across the media.

Consequences of infodemic

Infodemic causes fear, panic and confusion among general population. It influences people to indulge in practices which have no role in prevention of infection and its spread. Eventually people lose trust on the health care delivery system and evidence based interventions. Reinforcement of wrong information through social media will lead to mental health problems like anxiety, stress and depression among people. Rampant spread of wrong information will force the health care workers to shift their attention from prevention of infection to prevention of spread of this information. Practicing wrong things will provide a sense of security among people, which may adversely affect the response to preventive interventions.(10)

Steps taken to prevent the spread of misinformation

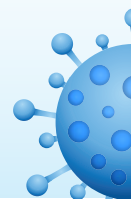
Brainard and Hunter through their agent based model for prediction of spread of infectious diseases based on human behavior found that that by reducing the amount of harmful advice circulating online by just 10% or making at least 20% of the population unable to share fake advice, reduced the severity of disease outbreak. Thus we need to take active steps in preventing the spread of misinformation through social media.(11)

World Health Organization has taken a step to publish mythbusters in their website and disseminated them through information leaflets across the world.(12) It has also made a positive attempt in convincing the social media companies in keeping a check on the correctness of the messages being circulated through their platforms. Government of India has also advised the states to undertake necessary steps to curb this menace. Government of Karnataka, by exercising its powers under Epidemic Diseases Act 1897 released 'The Karnataka Epidemic Diseases, COVID-19 Regulations, 2020'. While these regulations largely deal with the obligations of hospitals and laboratories, they also stipulate that no person, institute or organization should use any print or electronic media for spreading mis-information regarding the Coronavirus. Employers are strongly advised to make sure that their employees do not, deliberately or otherwise, engage in any conduct which may be construed as spreading mis-information about the Coronavirus.(13) Messages are being circulated in social media as legal actions will be taken on the people who are involved in spread such information [Using Infodemic to control Infodemic].

What else needs to be done?

The government should ensure people receive updates only from credible sources which include scientists and researchers in the field of infectious diseases, community medicine, microbiology and emergency medicine etc. Announcements from the WHO, Centres for Disease Control USA and the Indian Council of Medical Research should receive paramount importance. Any information that comes out through any media houses or social media platforms should compulsorily cite the primary source.

Apart from regulatory approach, there is a need to adapt stringent fact checking mechanism by the social media companies. They have to actively screen



all the messages that pass through their channels and block the ones which are not based on scientific evidence. It is a responsibility of people also not to blindly send the forwarded messages without checking for their correctness. Behaviour Change Communication shall be emphasized through the social media. The government and health care providers should implement trust based, bi-directional risk communication (RC) strategies. An appropriately designed and efficiently implemented RC can bridge the gap between what experts think people to know, what actually people want to know and what they already know.

Summary

Infodemic is one of the several challenges posed by COVID-19. In the era of digital revolution it is extremely important to understand the source, spread and impact of misinformation that spreads through the social media. Misinformation not only creates confusion and panic among people but also makes control of pandemic a different task. Thus it is important to differentiate between right and wrong information to prevent these consequences. There is a need to have a structured strategy to combat this menace through regulatory and behavior change communication strategies. Evidence based, bidirectional risk communication can find a help in achieving better control.

Authors Contribution

All authors have contributed equally.

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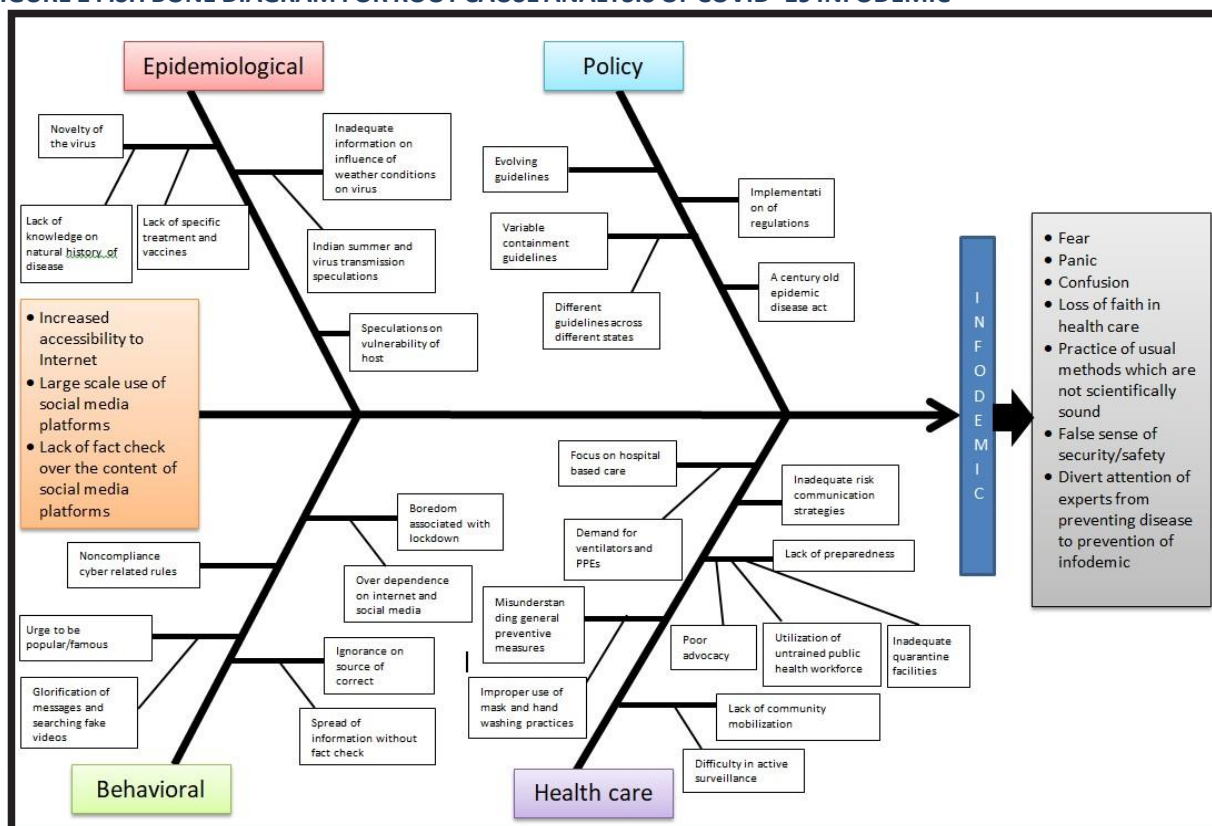


Tables

TABLE 1 CLASSIFICATION OF MISINFORMATION RELATED TO COVID 19

Transmission	Effect of weather conditions	Prevention	Treatment and cure	Miscellaneous
Consumption of meat	Indian summer can be protective	Consumption of garlic, turmeric powder, cow's urine and application of mustard oil to nose	There is no cure for COVID-19	God or spiritual powers will protect
Mosquito bites	Cold weather and snowfall can prevent multiplication of virus	Consumption of alcohol	Once affected with COVID, the person remains infected for life	COVID-19 is a biological warfare
Handling the news papers		Regular rinsing of nose with saline	If infected with COVID death is certain	Virus is killed when it comes in contact with lamps (Deepam)
		Taking hot water bath	Antibiotics can protect against COVID	Government is hiding the number of cases and showing us less in the media
		Taking vaccines against pneumonia and can prevent COVID	Holding the breath or cough for 10 seconds can cure COVID infection	
		Spraying alcohol and chlorine all over the body		
		Tying neem leaves and placing turmeric outside the house		

Figures

FIGURE 1 FISH BONE DIAGRAM FOR ROOT CAUSE ANALYSIS OF COVID -19 INFODEMIC


ORIGINAL ARTICLE

Effect of False News on Knowledge, Attitude, and Practice toward COVID-19 Pandemic among Educated of Karnataka, India

Amogha Shree, N. Chandan, M. Shwethashree, M. R. Narayana Murthy

ABSTRACT

Background: COVID-19 pandemic has taken millions of lives across the globe. Preventive measures in developing country like India were affected by fake news at some point of time. This created lots of confusion among public which in turn affected their knowledge, attitude, and practice (KAP) toward COVID-19 pandemic. With this context this study was taken up to assess the KAP toward COVID-19 and also to assess the effect of false news on KAP of educates.

Materials and Methods: Web-based cross-sectional study was conducted among educates of Karnataka. Google form was sent through WhatsApp and email to collect data. Analysis was performed using IBM SPSS 25.0. **Results:** A total of 421 participants took part in the study. Major source of information was TV (82.9%) followed by family and friends (71.5%). Mean knowledge, attitude, and practice scores were 12.5 ± 2.49 , 3.0 ± 0.67 , and 4.7 ± 0.66 , respectively. Among the participants 230 (54.6%), 336 (79.8%), and 329 (78.1%) had good knowledge, attitude, and practice scores, respectively. Nearly 60% of participants with good knowledge did not believe in false news and this was found to be statistically significant. **Conclusions:** Among our participants regarding COVID-19 knowledge score was moderate to low and in contrast attitude and practice scores were good.

Key words: COVID-19, False news, Knowledge, Attitude, Practice, Pandemic

INTRODUCTION

Novel coronavirus disease (COVID-19) is an emerging respiratory infectious disease, caused by the coronavirus subtype SARS-CoV-2. It was first detected in Wuhan, China, in December 2019 and currently spreading across the globe resulting in lakhs of deaths. In response to this situation, World Health Organization (WHO) declared it as a public health emergency of international concern (PHEIC) on January 30, 2020, and called for collaborative efforts of all countries to prevent the rapid spread of COVID-19.^[1] Deeply concerned both by the alarming levels of spread and severity, and by the alarming levels of inaction, WHO made the assessment that COVID-19 can be characterized as a pandemic on March 11.^[2] Following this Indian prime minister declared nationwide lockdown on March 25 initially for 3 weeks and it has been further extended to May 31, 2020. During this period, public was requested to adopt and follow various preventive measures

such as frequent hand washing with soap and water, using hand sanitizer often, maintaining social distancing, wearing mask, not to touch face, eyes, and nose and to stay at home.^[3]

Unreliable and false information started spreading across the world and this was putting lives at risk, promoting some with the symptoms to try unproven remedies in the hope of curing themselves. It was spreading so much so that ranging from origin of coronavirus, preventive measures till the treatment for infection. Efforts were made to counter falsehoods and promote the facts about virus and preventive measures. Because of the scale of the problem, the WHO added a

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“myth busters” section to its online coronavirus advice pages which refutes a staggering array of myths, including claims that drinking potent alcoholic drinks and exposure to high temperatures can kill the virus, those in warm climates or countries where summer is on its way, do not need to worry too much.^[3]

Despite of various efforts by the WHO, Government of India and mass media, this false information are spreading through various social media platforms and people are noted to believe the same without checking for the source and same being forwarded to others which might have affected the knowledge, attitude, and practice (KAP) among educates. In this context, this study was taken up among educates of Karnataka, India.

Objectives

The objectives are as follows:

1. To assess the knowledge, attitude, and practice about COVID-19 among educates of Karnataka, India.
2. To find the association between socio-demographic profile and knowledge, attitude, and practice among educates of Karnataka, India.
3. To find the association between false news and knowledge, attitude, and practice among educates of Karnataka, India.

MATERIALS AND METHODS

Web-based cross-sectional study was conducted among educated of Karnataka state, India. Google form was created which consisted question related to demographic details like district, age, education, and occupation and also question related to knowledge, attitude, and practice towards COVID-19. The knowledge questionnaire consisted 18 questions regarding the clinical characteristics, prevention measures, and questions related to false news. Assessment of attitude and practices toward COVID-19 included questions on preventive measures. Snow ball sampling technique was used to collect data. Study was conducted between March to May 2020. Google form was developed in two languages English and Kannada (local language). Google forms were sent to the known people through email and WhatsApp. They were asked to fill the form and were requested to share the link to their contacts. Study participants who were more than 18 years and those with gadgets with internet connectivity took part in the study.

Operational Definition of Educates

A person can read and understand either English or Kannada language.

Sample size was calculated assuming good knowledge among educates to be 50% with 95% confidence level and

5% absolute precision, minimum sample size to be studied was 384. As more responses were obtained than the required sample size, all the 421 responses were included in the study. Data were analyzed using SPSS version 25 (Licensed to JSS AHER). Age, knowledge, attitude, and practice scores are expressed as mean and standard deviation. Questions about knowledge, attitude, and practices were expressed as frequencies and percentages. Chi-square test was used to find out the association between KAP scores and socio-demographic profile, KAP scores and false news. $P < 0.05$ was considered statistically significant.

KAP Scoring

For every correct answer a score of 1 was given and score of 0 for every wrong answer and the mean score and standard deviation was calculated for knowledge, attitude, and practice. The participants who had scored more than mean scores were considered as good and less than mean score was considered poor.^[4]

RESULTS

Mean age of the study participants was 31.3 ± 12.7 years and majority (58.2%) belonged to the age group of 18–30 years. Where in majority were females (58.4%) and graduates (61%). By occupation majority of them were professionals/semi-professionals (43.5%), followed by students (30.9%). Source of information was mainly from Television (82.9%), followed by information from Family and Friends (71.5%), WHO/Govt websites (52.7%), Newspaper (49.4%), and through Social media such as WhatsApp, Facebook, and Instagram (47.5%) [Table 1].

In our study, nearly 50% (210) of the participants knew that rinsing the nose with saline will not help in protecting against coronavirus infection. Similarly 87.2% (367) knew that corona virus will not spread from mosquitoes and 39% (164) knew that eating garlic will not prevent the infection. Drinking alcohol does not protect against COVID-19 infection was the opinion from 81% (341). Likewise 66.7% (281) and 57.7% (243) responded that taking hot bath and exposing to temperature higher than 25°C does not prevent infection, respectively [Figure 1].

Assessment of Knowledge toward COVID-19 Pandemic

Correct knowledge about causative agent, mode of spread and age group affected was present in 97.6%, 86%, and 77% of the participants, respectively. Most of the clinical features were known by 25.7% of the participants whereas 73.9% knew one or the other clinical features. Similarly, 78.1% knew the safeguards of COVID-19 and remaining 21.9% of the participants were aware of one or the other safeguards. Around 72.7% were aware that eating or contact with wild

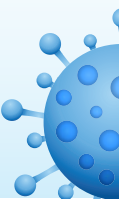


Table 1: Socio-demographic characteristics of study participants

Socio-demographic characteristics	Number	Percentage
Age (Years)		
18–30	245	58.2
31–50	128	30.4
51–70	46	10.9
>70	02	0.5
Gender		
Male	175	41.6
Female	246	58.4
Place of residence		
Urban	258	61.3
Rural	163	38.7
Education		
Primary school	1	0.2
High school	15	3.6
PUC/Diploma	51	12.1
Graduation	257	61
Post-graduation	97	23
Occupation		
Unemployed/retired	42	10
Home maker	27	6.4
Student	130	30.9
Unskilled workers	8	1.9
Semi-skilled workers	30	7.1
Skilled workers	1	0.2
Professional/semi professionals	183	43.5
Source of Information		
Television	349	82.9
Newspaper	208	49.4
Family and friends	301	71.5
Social Media (WhatsApp, Instagram, and Facebook)	200	47.5
WHO/ Government websites	222	52.7

animals will not result in infection and 98.3% participants believed that infection can be prevented by avoiding crowded places. About the vaccine 74.1% correctly reported it is not available whereas 21.6% think that there is a specific food/drink/drug for treatment of COVID-19. Regarding mask etiquette 46.6% thought that it is necessary for all whereas 35.6% says mask is not advisable if the person is not having any symptoms related to COVID-19. Knowledge about social distancing was good in 67.5% of the study participants. Regarding good knowledge about the period of quarantine was 77.7% of the study and 75.5% knew COVID-19 helpline numbers [Table 2].

Assessment of Attitude toward COVID-19 Pandemic

While assessing the attitude, 98.3% felt that taking precautions reduces the transmission and 84.3% showed positive attitude of taking all the necessary measures if they had symptoms. About 46.8% thought wearing mask might help in preventing the infection. About 59% of the participants did not wanted to go to hospital for non COVID-19 conditions due to lockdown (12.2%) and also for fear of acquiring COVID-19 (38.4%). Facts shown in the news channel are not cent percent true was the opinion of 70.8% of the participants [Table 2].

Assessment of Practices towards COVID-19 Pandemic

About 91.2% of study participants practiced hand washing regularly and 97.1% maintained social distancing. They even wore mask (89.5%) to avoid transmission and most of them wore cloth mask (52.7%) and majority of them avoided crowded places [Table 2].

KAP Scoring

Mean scores of knowledge, attitude, and practice among study participants were 12.5 ± 2.49 out of 18.3 ± 0.67 out of 4 and 4.7 ± 0 out of 5, respectively.

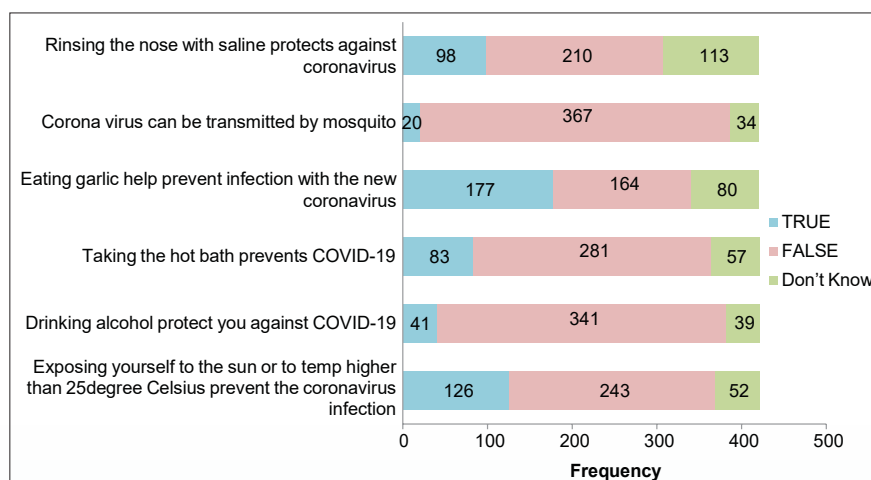
**Figure 1:** Knowledge based questionnaire on false news

Table 2: Knowledge, attitude, and practice of the study participants regarding COVID-19

Practice question	Response	Percentage
Causative agent of COVID-19 is a?		
Bacteria	3	0.7
Virus	411	97.6
Air	6	1.4
Do not know	1	0.2
COVID-19 is a disease spreads from?		
Shaking hands with infected person	26	6.2
Staying with infected person	31	7.4
Both of the above	362	86
Do not know	2	0.5
Which age groups are affected by COVID-19?		
Less than 5 years and > 50 years	82	19.5
15 years and above	12	2.9
All age group	324	77
Do not know	3	0.7
What are the signs and symptoms of COVID-19?		
Fever, sore throat, dry cough, shortness of breath	108	25.7
Any one or combination of above but not all	311	73.9
Do not know	2	0.5
What are the safeguards from COVID-19?		
Washing hands >20s, using hand sanitizer, social distancing, not touching face, eyes	329	78.1
Any one or combination of above but not all	92	21.9
Eating or contact with wild animals would result in infection by the COVID-19		
True	61	14.5
False	306	72.7
Do not know	54	12.8
To prevent infection by COVID-19, individual should avoid going to crowded places such as bus/train stations and avoid taking public transport		
True	414	98.3
False	5	1.2
Do not know	2	0.5
Which of the following is true about COVID-19?		
Vaccine not available	312	74.1
Vaccine not available + specific food/drinks/drug can cure the disease	91	21.6
Do not know	18	4.3
Medical mask are not advisable for?		
Person not having symptoms	150	35.6
Everyone should wear mask	196	46.6
Health workers taking care of COVID-19 patients + visitors	56	13.3
Do not know	19	4.5
Suspected patients should be quarantined for _____ days		
14 days	327	77.7
21 days	31	7.4
28 days	61	14.5
What is the help line number for COVID-19 in Karnataka?		
100	5	1.2
104	318	75.5
108	60	14.3

(Contd...)

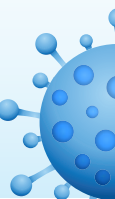


Table 2: (Continued)

Practice question	Response	Percentage
Do not know	38	9
Social distancing means?		
Maintaining distance of >1 m	284	67.5
Maintaining distance of >1 m + wearing mask + not attending functions + hand hygiene	107	25.4
Wearing mask + not attending functions + hand hygiene	30	7.1
Attitude Question	Response	Percentage
Do you feel that taking precautions such as hand washing, isolation, Quarantine, social distancing, and wearing a mask will reduce the transmission?		
Yes	414	98.3
No	4	1.0
Don't know	3	0.7
What should you do if you have symptoms of COVID-19?		
Self-isolate	12	2.9
Consult your family physician	3	0.7
Contact state helpline or Government of India helpline	51	12.1
All or any of the above	355	84.3
Do you think wearing mask will help in preventing the disease?		
Yes	150	35.6
No	69	16.4
May be	197	46.8
I don't know	5	1.2
Do you prefer going to hospital for non-COVID-19 condition?		
Yes	172	40.9
No	249	59.1
If no, Reason for not going to hospital? (n=172)		
Due to lockdown	21	12.2
Not advisable/risk of acquiring COVID-19	66	38.4
No particular reason	85	49.4
Do you think, facts shown in news channel about COVID-19 are 100% correct?		
Yes	76	18.1
No	298	70.8
I don't know	47	11.2
Practice Question	Response	Percentage
Do you wash your hands with soap and water regularly?		
Yes	384	91.2
No	3	0.7
Sometimes	34	8.1
Have you been maintaining social distancing?		
Yes	409	97.1
No	1	0.2
Sometimes	11	2.6
Are you wearing mask to avoid transmission?		
Yes	377	89.5
No	4	1.0
Sometimes	39	9.3
Don't remember	1	0.2
In recent days, have you worn a mask while leaving home?		
Yes	404	96
No	9	2.1

(Contd...)



Table 3: Association between socio-demographic details, false news with knowledge, attitude, and practice among general population

Socio-demographic details	Knowledge (%)		P value
	Poor	Good	
Age (years)			
18–30	124 (50.6)	121 (49.4)	0.016
31–50	43 (33.6)	85 (66.4)	
51–70	23 (50)	23 (50)	
>70	1 (50)	1 (50)	
Resident			
Urban	101 (39.1)	157 (60.9)	0.001
Rural	90 (55.2)	73 (44.8)	
Education			
Primary	0	1 (100)	0.003
High school	8 (53.3)	7 (46.7)	
PUC/Diploma	31 (60.8)	20 (39.2)	
Graduation	123 (47.9)	134 (52.1)	
Postgraduation	29 (29.9)	68 (70.1)	
Occupation			
Students	74 (56.9)	56 (43.1)	<0.001
Home maker, Retired, Unemployed	36 (52.2)	33 (47.8)	
Employed	81 (36.5)	141 (63.5)	
Socio-demographic details	Attitude		P value
	Poor	Good	
Resident			
Urban	36 (14)	222 (86)	<0.001
Rural	49 (30.1)	114 (69.9)	
Socio-demographic details	Practice		P value
	Poor	Good	
Resident			
Urban	46 (17.8)	212 (82.2)	0.012
Rural	46 (28.2)	117 (71.8)	
False news	Knowledge		P value
	Poor	Good	
Rinsing the nose with saline protects against coronavirus			
No	128 (39.6)	195 (60.4)	<0.001
Yes	63 (64.3)	35 (35.7)	
Corona virus can be transmitted by mosquito			
No	172 (42.9)	229 (57.1)	<0.001
Yes	19 (95)	1 (5)	
Eating garlic helps prevent infection with the new coronavirus			
No	86 (35.2)	158 (64.8)	<0.001
Yes	105 (59.3)	72 (40.7)	
Taking the hot bath prevents the disease			
No	121 (35.8)	217 (64.2)	<0.001
Yes	70 (84.3)	13 (15.7)	
Drinking alcohol protect you against COVID-19			
No	154 (40.5)	226 (59.5)	<0.001
Yes	37 (90.2)	4 (9.8)	



Table 3: (Continued)

Socio-demographic details	Knowledge (%)		P value
	Poor	Good	
Exposing yourself to the sun or to temp higher than 25° centigrade prevent the coronavirus infection			
No	97 (32.9)	198 (67.1)	<0.001
Yes	94 (74.6)	32 (25.4)	
False news	Attitude		P value
	Poor	Good	
Drinking alcohol protect you against COVID-19			
No	70(18.4)	310 (81.6)	0.006
Yes	15 (36.6)	26 (63.4)	
False news	Practice		P value
	Poor	Good	
Eating garlic helps prevent infection with the new coronavirus			
No	43 (17.6)	201 (82.4)	0.014
Yes	49 (27.7)	128 (72.3)	

other clinical features. COVID-19 spreads by shaking hands and staying with infected person was answered by 86% of study participants. Hand washing for more than 20 second with soap and water was considered protective against COVID-19 by 91.2% of the study participants. Most of the respondents (72.7%) believed that eating or contact with wild animals will not result in the infection.

In a study conducted among Indian population 29.5% answered that the virus spreads through multiple modes such as touching, kissing, sneezing, and food. Furthermore, 56% negated the notion of pets transmitting the virus. Most participants (97%) acknowledged that washing hands frequently could stop the spread of infection. Only 18.2% regarded fever as a symptom of COVID-19, which is known to be a major symptom.^[6] Most of the findings are consistent with our study findings.

In a study done among US and UK population cough, fever, and shortness of breath were common symptoms of COVID-19 according to 79.8% and 84.6% of the study participants', respectively.^[7] Findings are similar to our study.

In the present study, 98.3% felt that taking precautions reduces the transmission of COVID-19 and 84.3% showed positive attitude of taking all the necessary measures if they had symptoms, including self-isolation (77.7%). Around 46.8% thought wearing mask might help in preventing COVID-19 and majority (67.5%) of them practiced social distancing.

In a study done among Indian population more than 96% of the participants agreed to quarantine/isolate themselves if they had fever and cough. Most (98%) of the participants thought social distancing is essential to stop the virus from spreading.^[6] The findings are different from our study probably due to wide geographic distribution of the study participants across many states in this study.

Mean scores of knowledge, attitude, and practice among our study participants were 12.5 ± 2.49 out of 18, 3 ± 0.67 out of 4 and 4.7 ± 0.66 out of 5, respectively. Knowledge score significantly varied across age, education, occupation, and place of residence regarding COVID-19 pandemic. Out of 421 study participants, 54.6% had good knowledge and remaining 45.4% had poor knowledge about COVID-19 whereas nearly 80% had good attitude (79.8%) and followed good practice (78.1%).

The mean COVID-19 knowledge score in a study done in China was 10.8 ± 1.6 . Knowledge scores significantly differed across genders, age-groups, categories of marital status, education levels, and residence places ($P < 0.001$).^[8]

In our study, statistically significant association was found for age ($P = 0.016$), place of residence ($P = 0.001$), education ($P = 0.003$), and occupation ($P \leq 0.001$) with the knowledge of the participants. There was statistically significant association between attitude and place of residence ($P \leq 0.001$). Practice was also found to be statistically significant with place of residence ($P = 0.012$).

In the present study, nearly 50% (210) of the participants knew that rinsing the nose with saline will not help in protecting against coronavirus infection. Similarly, 87.2% (367) knew that corona virus will not spread from mosquitoes and 39% (164) knew that eating garlic will not prevent the infection. Drinking alcohol does not protect against COVID-19 infection was the opinion from 81% (341). Likewise 66.7% (281) and 57.7% (243) responded that taking hot bath and exposing to temperature higher than 25°C does not prevent infection respectively. Hence, the knowledge among our study participants was not much affected due to false information which was being circulated in various types of media.



CONCLUSION

Knowledge regarding COVID-19 is moderate to low among our study participants. In spite of a moderate to low knowledge score, attitude, and practice scores towards COVID-19 prevention are good. Furthermore, there was significant variation of knowledge scores across age, place of residence, education, and occupational status. Even though, there is lot of false news being circulated in social media and other forms of media our study participants are not much affected and overall have a rational knowledge, attitude and practice toward COVID-19.

Recommendations

Repeated communications and cautions against false news must be communicated through mass media and inter personal communications. Also people should be stressed to utilize only authentic sources of information such as WHO, MOHFW, Government of India, and respective state's instructions, guidelines, and announcements.

Limitations

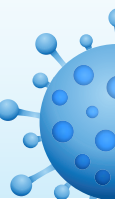
Due to current situation of COVID-19 pandemic and risk of infection to the person going to the field is more and country wide lockdown we decided to do an online survey using Google form. People who have certain amount of knowledge, literates and one with access to gadgets with internet connectivity could only take part in the study. Hence, the results might not be generalizable.

ACKNOWLEDGMENTS

We are thankful to our study participants.

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COVID-19 infodemic: Unveiling the root causes through public perspectives

Jose Jom Thomas, Praveen Kulkarni, D Sunil Kumar, B Prakash, M R Narayana Murthy

Abstract:

INTRODUCTION: The novel coronavirus pandemic raises great concern due to its spread and collateral effects on the society. Nearly 30,000 cases are reported from India by the beginning of May 2020. The current pandemic is associated with a sudden surge of false information termed as infodemic. This study attempts to understand the root causes of COVID-19 infodemic.

METHODS: This cross-sectional online study was conducted from April 20, 2020, to April 30, 2020, to collect information on the possible causes of COVID-19 infodemic. A fishbone diagram was developed from the data through iterative process to illustrate the root causes of the infodemic.

RESULTS: The total of 179 people responded to the online survey. Among them, 99 were health-care professionals and 75 were representatives of the general public. The mean age of the respondents was 28.93 ± 9.99 years. The root causes for the COVID-19 infodemic were classified into five domains, namely, social media-associated causes, behavioral aspects, the novelty of the virus and related challenges, causes due to lacunae in policies and health systems, and difficulties in the verification of information.

CONCLUSION: A comprehensive action plan has to be developed to contain the infodemic through adequate education of all stakeholders, warnings and legal actions, improvements in policy and health systems. The authorities should brainstorm to design activities that contain the spread of false information through social media at the origin itself.

Keywords:

COVID-19, infodemic, root cause analysis

Introduction

With more than 3 million cases worldwide and over 22,000 deaths by the 1st week of May, COVID-19 has become a major health emergency modern world has seldom witnessed. First reported in Wuhan city of China, COVID-19 has affected 215 countries, areas, or territories across the world in a relatively short span of 4 months.^[1] The novelty of the virus along with its high infection rates, lack of knowledge about its specific symptoms, and varying mortality rates has caused severe

stress on public health systems across the world.^[2] India reported the first confirmed case of COVID-19 on January 30, 2020, from Kerala state, following which nearly 30,000 cases are reported from various states and union territories as on the 1st week of May.^[3]

The inevitable preventive measures such as country-wide lockdown and containment efforts have exacerbated the economic crisis in the country.^[4] The falling market and rising unemployment rates along with the panic about the pandemic further added to this crisis. Along with the COVID-19 pandemic, we are facing an unusual phenomenon of

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“infodemic” which is an epidemic of false information.^[5] Experts consider social media as one of the most important channels of infodemic. The easy access and the higher amplification rates of information in social media make its transmission dynamics difficult to tackle.^[6]

Researchers have identified the rise of “misinformation: unintentionally false information,” “dis-information: deliberately misleading information,” and “mal-information: reconfigured true information” regarding COVID-19.^[7] The spread of misinformation is associated with fear, panic, loss of confidence on health-care delivery system; following of irrational practices which can further spread the disease, and provision of false sense of security among people.

Thus, it is important to understand the nature of the information and reasons for spreading such information for the effective management of infodemic. The initial surveys show unsatisfactory levels of awareness and attitudes even among health-care professionals.^[8,9] The rise if infodemic will have an add on effect to this, making the already-exhausting containment measures even more difficult.

The reasons for infodemic have to be analyzed in the Indian context for better management of the misinformation. The initial attempt by Kulkarni *et al.* illustrates the root causes of COVID-19 infodemic under the themes of social media usage, epidemiological factors including the novelty of disease and associated limitations, behavioral issues, and policy and health-care system aspects.^[10] Analyzing the perspectives of both technically sound population such as medical professionals and less technically informed general public on the origin and spread of misinformation will provide better insight into the root causes of Infodemic. In this background, the current study was undertaken to understand perspectives of the public as well as the medical community on possible causes, consequences, and ways to prevent the Infodemic.

Methods

This cross-sectional study was conducted through an online survey to collect the perspectives about information handling and factors associated with information sharing among the general public and health-care professionals for a period of 11 days from April 20–30, 2020. The information was retrieved through convenient sampling using a questionnaire prepared using Google Forms, which was circulated among the people from nonmedical and medical backgrounds, in the contacts of the principal investigator. All the respondents above the age of 18 years were considered for data acquisition.

The questionnaire

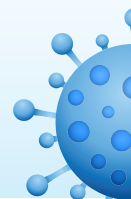
Responses were collected using a semi-structured questionnaire which was face validated by subject experts, and content validation was done by a pilot study among ten respondents representing the medical community and the general public. Based on the inputs from the pilot study, suitable modifications were made. The final 30-item questionnaire was divided into three sections. The first section included demographic characters such as age, gender, residence, education, and occupation of the respondents. The second section was containing questions regarding the social media usage patterns, frequency of sharing information, fact-checking, behavioral aspects of information sharing, frequency and hindrances in information verification, etc., The final section was consisting of seven questions designed as Likert's scale. Respondents' views about policy and health system factors in infodemic were assessed in the third section. Both section two and three were provided with a final column for the respondents to describe their additional views and perspectives on the respective sections.

Data collection

The Google Forms' link was shared in different social media platforms including WhatsApp, Facebook, Instagram, and E-mails. A description of the pandemic, concept of infodemic, and purpose of the study was attached with the link. The researchers shared the link through their accounts and used the help of others in sharing to attain a wider reach for the survey. The first page of the Google survey sheet contained a detailed description of the study including the time required for filling the survey form. The respondents could proceed to the questionnaire only after marking their informed consent. All the questions were made compulsory to avoid the submission of incomplete responses. A note of thanks and acknowledgment was provided to each respondent after filling the details. The link was allowed to be shared for 11 days, a total of 174 responses were obtained, and all the responses were considered for further analysis.

Data analysis

The data were collected as a.csv file and were later coded and recorded in a Microsoft Excel sheet. The analysis was performed using SPSS-version 23 licensed to JSS Academy of Higher Education and Research, Mysuru. The categorical data were measured in percentages and were represented using tables and a multiple bar diagram. The continuous variable such as age was represented using mean and standard deviation. Few categorical data were compared across the general public and health professionals by Chi-square test or Fisher's exact test.



A fishbone diagram was developed from the data through iterative process to illustrate the root causes of the infodemic.

Results

Among the 174 respondents, 99 (56.89%) were health-care professionals and 75 (43.10%) represented the general public. There was almost an equal representation of both the genders. The mean age of the respondents was 28.93 ± 9.99 years. Majority of the respondents were graduates (57.47%), and half of the respondents were professionals (35.63%). More than two-thirds of the respondents were belonging to Kerala (67.24%), while 17.81% belonged to Karnataka, 4.59% belonged to Tamil Nadu, and 7.47% to rest of the Indian states. Five respondents were either nonresidential Indians or overseas citizen of India [Table 1].

Patterns of media usage and handling of information

The major sources of information regarding COVID-19 were social media (68%), online or printed news sources (66.6%), and television (TV) (65.3%) for the general public. Only 29.3% of the respondents representing the general public used official resources by the government or international agencies. For the health-care professionals and health science students, news agencies followed by official websites were the main

sources of information. Among the 104 respondents who used social media as one of the sources of information, WhatsApp followed by Facebook and Instagram were the main resources. Two of the respondents commented that "TikTok" also is a potential source of information as the videos show and share the perspectives of the users [Table 2].

Nearly 68.9% (70.2% of the general public and 68.6% of the health-care professionals) reported an increase in social media usage after the announcement of lockdown [Table 3]. Among the respondents, 2.8% always, while 2.8% often, 33.9% sometimes, and 43.1% rarely share messages in social media. A significant difference was observed between the general public and health-care professionals in the pattern of message sharing in social media [Table 4].

False information sharing and fact verification practices

Out of the 174 respondents, 14.8% of the public respondents and 14.1% of the health-care professionals admitted that they have forwarded at least one piece of information and later realized that it was false. An alarmingly high proportion of 45.3% of the public and 42.4% of the health-care professionals believed messages spread by unauthentic sources at least once during the pandemic period [Table 3]. The fact-checking pattern among health-care professionals was significantly different from that of the general public. Only 36% of the public respondents reported a habit of doing fact-checking always. Almost 10.6% of the respondents in the general public category never did a fact-checking. More than 50% of the health-care professionals verify all the information they receive in nonacademic channels of information [Table 4].

The common site for fact checking for medical professionals was government or WHO websites and guidelines and that for general public was TV/newspaper followed by Google search and official websites. Other sources include social media pages run by the authorities and direct clarification from health professionals [Figure 1]. On an inquiry on the common hindering factors for fact checking, majority opined that it is difficult to do a fact checking using the available resources (57.1%). Few of the respondents observed it time-consuming (31.4%), while two respondents considered it unnecessary due to various factors such as trust in social media and lack of trust in the official resources of information (25.7%).

Behavioral aspects of the infodemic

A total of 122 (84.7%) respondents mentioned that they share the COVID-19-related information on social media platforms because it benefits others

Table 1: The demographic characteristics of the respondents

Demographic characteristics	n (%)
Category	
Health professionals/students	99 (56.89)
General public	75 (43.10)
Gender	
Female	85 (48.85)
Male	89 (51.14)
Education	
HSC/diploma	11 (6.32)
Graduation	100 (57.47)
Postgraduation	58 (33.33)
PhD/fellowships	5 (2.87)
Occupation	
Students	46 (26.43)
Business	17 (9.77)
Semi-professional	26 (14.94)
Professional	62 (35.63)
Unemployed	23 (13.21)
State of permanent residence	
Kerala	117 (67.24)
Karnataka	31 (17.81)
Tamil Nadu	8 (4.59)
Other Indian states	13 (7.47)
NRI/OCI	5 (2.87)

NRI=Nonresident Indians, OCI=Overseas citizen of India



Table 2: The sources of information regarding COVID-19 based on multiple responses by the study participants

Source of information	General public (75) (%)	Medical profession (99) (%)	Total (174) (%)
General sources of information			
Social media	51 (68)	53 (53.5)	104 (59.7)
Online/printed newspapers/magazines	50 (66.6)	82 (82.8)	132 (75.8)
TV	49 (65.3)	47 (47.4)	96 (55.1)
Friends/family	25 (33.3)	24 (24.2)	99 (56.8)
WHO/government websites/trusted online trainings	22 (29.3)	60 (60.6)	82 (47.1)
Source of information	General public (51) (%)	Medical profession (53) (%)	Total (104) (%)
Social media platforms for information (104 respondents; general public: 51; health professionals:53)			
Facebook	29 (56.8)	25 (47.1)	54 (51.9)
WhatsApp	37 (72.5)	33 (62.2)	70 (67.3)
Instagram	19 (37.2)	21 (39.6)	40 (38.4)
Telegram	3 (5.8)	1 (1.8)	4 (3.8)
Twitter	7 (13.7)	4 (7.5)	11 (10.5)
YouTube	4 (7.8)	1 (1.8)	5 (4.8)

WHO=World Health Organization, TV=Television

Table 3: Distribution of respondents based social media usage and spread of infodemic

	General public, n (%)	Health workers, n (%)	Total, n (%)
Frequency and usage of social media after the lockdown			
Increased	52 (70.2)	68 (68.6)	120 (68.9)
Did not increase	23 (31)	31 (31.4)	54 (31.1)
Forwarded false information at least once (unintentionally)			
Yes	11 (14.8)	14 (14.1)	25 (14.3)
No	64 (85.2)	85 (85.6)	149 (85.7)
Believed unauthentic source of information at least once			
Yes	34 (45.3)	42 (42.4)	76 (43.6)
No	41 (54.7)	57 (57.6)	98 (56.4)

Table 4: Frequency of information sharing and fact verification by the respondents

Information handling	Always (%)	Often (%)	Sometimes (%)	Rarely (%)	Never (%)	P*
Forwarding information in social media						
General public	5 (6.6)	5 (6.6)	27 (36)	26 (34.6)	12 (16)	0.002
Health-care professionals	0	0	32 (32.3)	49 (49.4)	18 (18.1)	
Total	5 (2.8)	5 (2.8)	59 (33.9)	75 (43.1)	30 (17.2)	
Fact checking of received information						
General public	27 (36)	13 (17.3)	14 (18.6)	11 (14.6)	8 (10.6)	<0.001
Health-care professionals	58 (58.5)	27 (27.2)	9 (9.09)	2 (2.02)	3 (3.03)	
Total	85 (48.8)	40 (22.9)	23 (13.2)	13 (7.4)	11 (6.3)	

*Fisher's exact test

as it is a "good deed" (70%). Others' intension of sharing information was entertainment (4%), habitual practice (3.4%), method of socializing (6.32%), wish for appreciation (2.3%) from the receivers, and popularity (1.72%). The behavioral pattern of social media message sharing was similar in the both categories. The common reason for believing unauthentic sources of information among the general public was lack of epidemiological data to correctly explain the disease dynamics by the authorities (65.2%) and lack of adequate scientific knowledge 39%. Nearly 7% reported a lack of trust in modern medicine as it is not able to provide a vaccine or specific treatment for the disease.

Majority of the respondents agreed that the health systems and policy factors such as the lack of uniform guidelines, the difference in practice between the states, lack of preparedness by the public health systems, need for legal actions to control infodemic, misunderstanding of preventive measures by the public, need for more efficient communication strategies by the governments, and the lack of community involvement are contributing to the infodemic [Table 5].

Preventing the infodemic

Among the study participants, 64% of the general public and 70% of the health-care professionals opined that all the information about the disease should be



Table 5: Distribution of responses based on the policy-related reasons for infodemic

Query	Strongly agree (%)	Agree (%)	Neutral (%)	Disagree (%)	Strongly disagree (%)
Lack of unique guidelines is causing confusion in prevention/management	5 (2.8)	43 (24.7)	76 (43.6)	34 (19.5)	16 (9.1)
Difference in practices followed between states in causing confusion	7 (4)	58 (33.3)	60 (34.4)	37 (21.2)	12 (6.8)
More preparedness was required by the public health system	32 (18.3)	76 (43.6)	40 (22.9)	18 (10.3)	32 (18.3)
More stringent actions are required to control fake news	77 (44.2)	68 (39)	22 (12.6)	5 (2.8)	2 (1.1)
Preventive measures are often misunderstood by the general public	23 (13.2)	75 (43.1)	42 (24.1)	26 (14.9)	8 (4.5)
The communication of information by the government is not sufficient	22 (12.6)	65 (37.3)	46 (26.4)	34 (19.5)	7 (4)
More community involvement is required in information handling	26 (14.9)	77 (44.2)	52 (29.8)	13 (7.4)	6 (3.4)

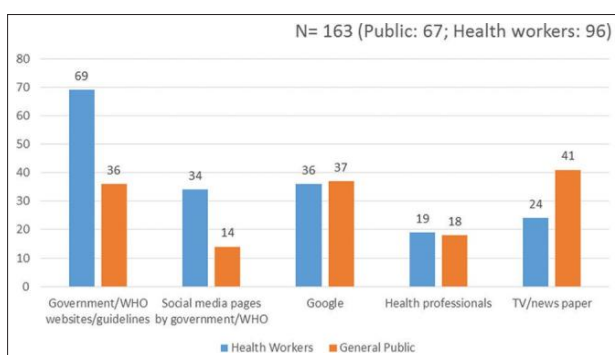


Figure 1: The sources for verification of received information used by the study respondents (based on multiple responses)

handled by the government alone. The points suggested by the respondents to prevent the infodemic can be classified into three domains. A total of 120 (68.9%) respondents suggested health educational measures, 98 (56.32%) mentioned warnings and freezing of social media accounts if proved of sharing false information, and 102 (58.6%) suggested legal actions to contain the infodemic.

Qualitative inputs from the respondents

The descriptions and narratives given by the participants align in par with the already-discussed findings of the study. The fear, panic, and confusions associated with the pandemic were shown as a root cause for infodemic by majority of the participants. A respondent suggested that *"the false information has to be identified and managed at the origin itself as controlling a message later in social media is very difficult."* Another was of opinion that *the scope of artificial intelligence in identification of false information should also be examined.* The banning on social media was generally discouraged by the respondents. One of the responses was *"There are a lot of mimetic going on in social media. The ban on it would make people go crazy since it's the only one keeping them sane during this isolation."*

Discussion

The results of the study can be discussed under six broad themes. We attempt to classify the root causes under these themes and derive at a fishbone diagram illustrating the root causes of COVID-19 infodemic.

The unchecked spread of information through social media

The increased access and usage of social media platforms is an opportunity for the unchecked proliferation of infodemic. Majority of the times, general public heavily depends on social media for the updates on pandemic. As the information rolling through social media is difficult to track, fact check, and regulate, it definitely increases the chances of the infodemic.

Behavioral aspects

Most of the respondents share information through social media with a good dead. However, it has the potential to lead to the infodemic of "misinformation" unless some mechanism to do the fact check is implemented. Other behavioral aspects such as entertainment, habitual practice, method of socializing, wish for appreciation from the receivers, and seeking popularity also lead to the spread of information through social media. The fear, panic, and confusion among the public is also a reason for the fast spreading of information.

The novelty of the virus/disease

The lack of epidemiological data and evidence on disease dynamics and unavailability of vaccine and specific treatment has led to the rise of conspiracy theories and affected the trust of the general public in modern medicine to a certain extend. People's faith on home remedies in alternative systems of medicine also encourages the rapid spread of unverified information.



Health system and policy

The lacunae in public health systems and lack of preparedness have affected the public's trust in the system. The fast upgrading guidelines and different practices across different territories/states can cause confusions about the ideal practices among the general public and medical community. Majority opine that the communications of the governments have to improve to transfer the correct information to the public. Community involvement of larger extent is required to manage this crisis.

Easing the process of fact checking

Easy and more accessible sources should be available to the public for better fact checking. At least a few respondents find the true information through the existing sources as exhaustive and time-consuming. More innovative methods should be introduced from the perspectives of the general public who are the main stakeholders.

Preventive mechanisms

The major preventive checks for the infodemic according to the respondents are the education of the public,

legal actions, and warnings. The information should be checked and verified at the origin as the containment of the spread of information in social media is a difficult task.

Figure 2 shows the fishbone diagram in the root cause analysis of the COVID-19 infodemic from the study. The fishbone diagram unveiled through the perspectives of the general public and the health-care professionals is comparable to that of Kulkarni *et al.*^[10] The study also categorizes the causes under the headings of epidemiological, behavioral, policy, and health system factors. Thus, our study findings are affirmative of the descriptions in a previous study.^[10]

Limitations

A scientific calculation of the sample size could not be done and the study was limited to a small sample size and short study period due to the pandemic situation. The study should be reproduced in a wider sample population with more rigorous sampling techniques to generate more solid evidence on the subject. Even though

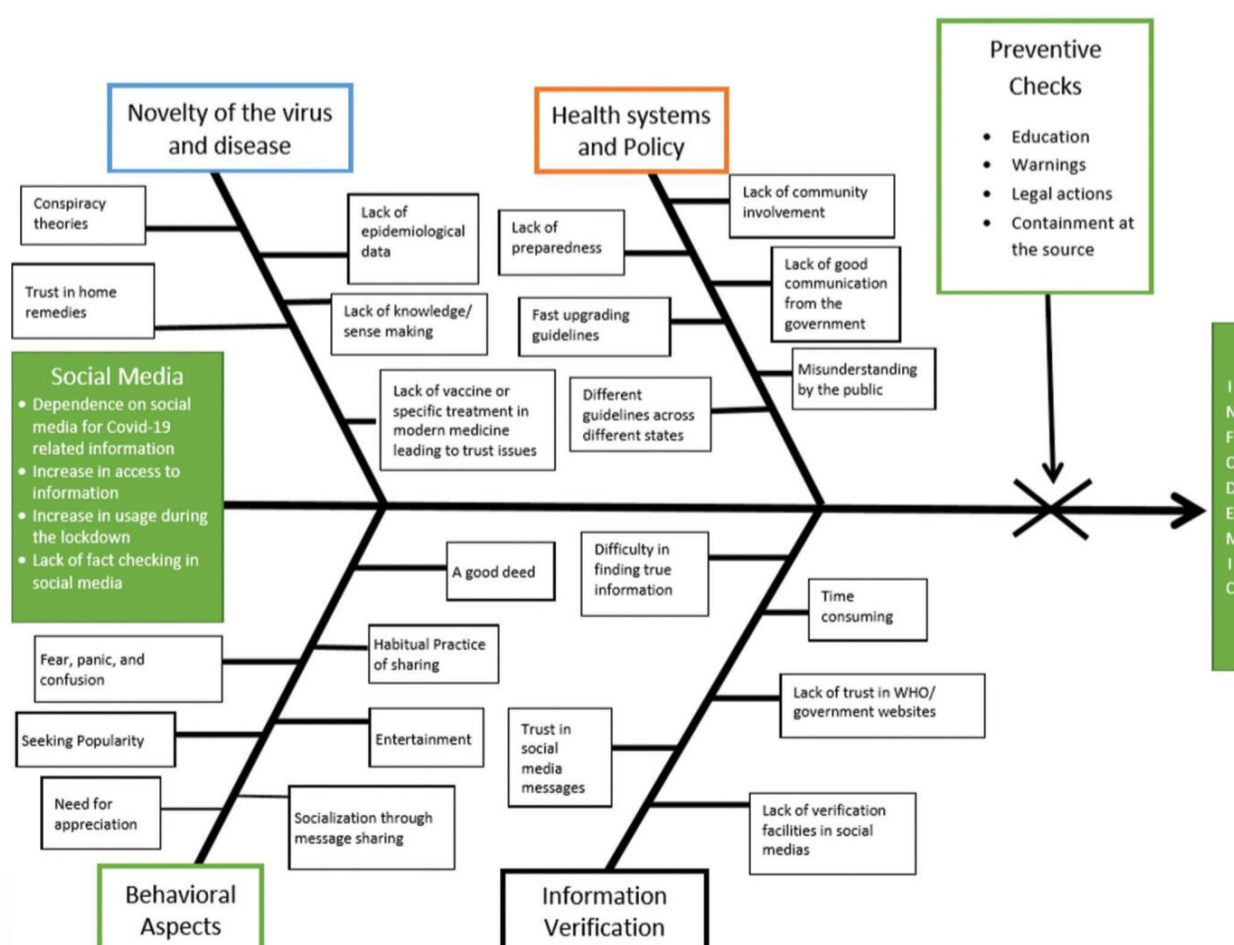


Figure 2: Version of fishbone diagram developed by Kulkarni *et al.* showing the root causes of COVID-19 infodemic testified by the observations from the study^[10]

the study reveals the root causes of the infodemic, the degree and mechanisms of causality cannot be assumed from our findings and hence the policy implications of the study are limited. A more detailed qualitative inquiry will be required for the same.

Conclusions

The root causes for the COVID-19 infodemic can be classified into five domains of social media-associated causes, behavioral aspects, the novelty of the virus and related challenges, causes due to lacunae in policies and health systems, and difficulties in the verification of information. A comprehensive action plan has to be developed to contain the infodemic through adequate education of all stakeholders, warnings and legal actions, and improvements in policy and health systems. The authorities should brainstorm to design activities that contain the spread of false information through social media at the origin itself.

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Conflicts of interest

There are no conflicts of interest.

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Invited Perspective

Psychology of Misinformation and the Media: Insights from the COVID-19 Pandemic

Abstract

The coronavirus disease 2019 (COVID-19) pandemic has emerged as a significant and global public health crisis. Besides the rising number of cases and fatalities, the outbreak has also affected economies, employment, and policies alike. As billions are being isolated at their homes to contain the infection, the uncertainty gives rise to mass hysteria and panic. Amid this, there has been a hidden epidemic of “information” that makes COVID-19 stand out as a “digital infodemic” from the earlier outbreaks. Misinformation and fake news are invariable accompaniments to this “information pollution” which can add to the anxiety, fear, uncertainty, and agitation and lead to faulty treatments, noncompliance to precautionary measures, prejudice, and stigma. Research shows that distress and panic during pandemics can propagate and promote misinformation in various ways along with increased digital screen time and unhealthy use of technology. In that context, media is considered to be a “double-edged sword” and can either add to the misinformation burden or aid in the awareness and health communication during such a biological crisis. Lessons from past outbreaks portray media, especially social media, as a useful tool to promote health literacy and control the outbreak. This article looks at the impact of information during COVID-19, the psychology behind spread of misinformation, and finally, a balanced view of the role of media in such disasters, proposing ways for its healthy integration into public and social health.

Keywords: Coronavirus, coronavirus disease 2019, health, media, misinformation, pandemics, social media

“Whoever controls the media, controls the mind.”

(Jim Morrison)

Introduction

While the last few months witnessed a global health threat named coronavirus disease 2019 (COVID-19), the spread of information about the pandemic was much faster than the virus itself. There has not been 1 day since the World Health Organization (WHO) declared COVID-19 as a “public health emergency” that people have not come across messages, memes, or videos related to COVID content, going widely viral on the social media.^[1] Added to that is the plethora of information about the outbreak statistics (number of cases and causalities in every single geographical distribution), being fed daily to the common masses. As billions are isolated or quarantined at their homes, in an attempt to contain the infection,

“digital screen time” exposure has increased with much more penetration of media.^[2] Subsequent to the same, every single day “information pollution” about COVID-19 adds to the already existing uncertainty and panic about the virus and lockdown. In our daily lives, we have seen people with eyes glued to their television, laptop, or mobile screen busy consuming news feeds related to the coronavirus. This often assumes a “compulsive” nature, with the need to stay updated on every single facet about the illness, that further increases the psychological discomfort and physical unrest.^[3] Keeping this in background, this review looks at the significance of information during COVID-19, the psychology behind spread of misinformation, and finally, perspectives on a balanced role of media in such disasters, proposing ways for its healthy integration into public and psychosocial health.

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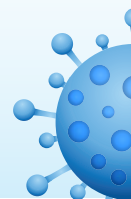


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Information and Coronavirus Disease 2019: Role of Media

Contrary to popular belief, COVID-19 is not the first “digital infodemic.” In the recent past, the outbreaks of Zika in Brazil, Ebola in Africa, influenza in Europe, and Nipah in India had similar bidirectional relationships with media.^[4,5] However, the degree of “media panic,” the amount of media consumption, and the consequent change in public reaction have been paramount during COVID-19, especially considering that the modern world has been unprepared for such a large-scale biological disaster. Harding in “*Pandemics, Plagues and Panic*”^[6] highlights how the spread of an outbreak and the resultant human behavior can be influenced significantly by the flow and vectors of information. Any piece of news attaching an existing belief or theory to the ongoing “topic of interest” can serve as a potential vector (for example: during COVID-19, the well-known antiviral effect of garlic according to Ayurveda has been generalized to garlic being considered as an antidote of coronavirus, which is definitely a false news propagating vector). Identifying such vectors is useful in debunking misinformation. Health communication and understanding of public health depends a lot on how the data about an illness are interpreted by the masses.^[7] Within every bit of news, there can be a potential admixture of “fake information” with the major challenge being teasing out both separately. This health-related misinformation becomes all the more crucial during a pandemic like COVID-19 when the “fear of an unknown infection without a definitive cure” mixed with “an anxious mind” tends to easily accept “fast solutions and theories,” irrespective of visible loopholes in their logic and reasoning.^[8] One senseless forward of a wrong message in wrong hands can snowball the spread, increasing the acceptability as it moves along the chain. Often, names of credible public health agencies such as the WHO and Centers for Disease Control and Prevention are tagged along wrongly to make the piece of false news more credible and acceptable.^[9] Similar things were being circulated during the first wave of infection in China, implicating “biological weaponry” in the manufacture of coronavirus. It unfortunately remained viral on various social media platforms for more than 2 weeks till the WHO finally discredited it.^[10]

Misinformation and Rumors: Mechanism of Spread

There is a certain price we pay for being social beings. This includes the continued sharing of misperception and faulty interpretations of information. Like the Aesop’s Fables where a boy starts chasing a crow after hearing from a stranger that the crow has his ear, we all tend to follow lucrative and hope-generating information in times of fear and crisis, irrespective of the authenticity of evidence. Fake news or rumors are sometimes socially useful half-truths

with strong emotional overtones that help it spread fast, gripping human minds to create “common” consciousness and agency, but with dire social consequences.^[7]

Health-related misinformation has been studied extensively in health communication and cognitive psychology. Jamuna Prasad, a social psychologist, was the first to establish a relationship between high levels of anxiety and the spread of false news.^[11] Later, multiple studies have established the link between various forms of disasters, human-made or biological, and rumor mongering.^[12,13] At times of uncertainty, people rely on knee-jerk speculation and prejudice. Based on the theories summarized by a systematic review of literature on health-related misinformation,^[14] here are some psychological perspectives as to why the snowballing of fake news occurs, with examples from the current pandemic.

1. False but commonly held beliefs: A message on social media that ginger and turmeric can cure COVID-19 went viral after an accidental text. Although it is a commonly held belief that ginger has antiviral properties, there is no evidence about its effectiveness in fighting coronavirus
2. Generalization of other false beliefs to the current crisis: A common false belief is that the consumption of hot water helps combat multiple illnesses. Not surprisingly, it is wrongly believed that hot water can kill coronavirus
3. Cultivation theory: Repetitive exposure to consistent and regular news (fake or true) can “reiterate, confirm, and modify” values, beliefs, and perceptions of reality. How the news is portrayed is important. This is commonly how advertisements work
4. Social learning theory: New behaviors can be fostered by imitating and observing popular or idealized others in the media. Certain stereotypes, mannerisms, and choices of celebrities tend to get popular in community cultures through this mechanism
5. Theory of negativity bias: The prohibition or negation of certain acts is often accepted as preventive measures. For instance, decreased consumption of chicken or seafood has led to a marked reduction in their sales. This is more acceptable as a preventive strategy to most people than wearing masks or maintaining good hand hygiene
6. Modeling of rumor: A hearsay or rumor becomes a learned behavior for fear of social deprivation. If a majority of members in one’s social network are doing something, it is easier to blindly follow them
7. Overanalysis and faulty interpretation of science: Phenyl/cresol/autoclave is known to kill viruses. The same logic is being used for coronavirus without any evidence. Furthermore, there are half-baked theories about reptiles and birds spreading the virus. The widespread hoarding and use of hydroxychloroquine (HCQ) immediately after it came



in news has led to many inadvertent side effects and mortality^[15]

8. Motivated reasoning: Human beings, usually, accept things in keeping with their culture and traditions. For instance, Indians are more likely to believe that herbal remedies made of tulsi (holy basil) and triphala (ayurvedic herbal formulation) are effective, even if there is little scientific evidence to support the claim. Similarly, religious or local customs often compound the practices related to the disease outbreak
9. Fear reasoning: Human beings fear the “unknown” or “uncertain.” In such cases, the anxious mind cooks up its own remedies and tends to accept the most irrational or logically bizarre facts. That explains why antibiotic sale has increased considerably due to self-medication and prescriptions, even though they have no efficacy against coronavirus. Hoarding of protective medical equipment, antivirals, and sanitizers has not only led to panic but also their unavailability for hospitals and patients who need them
10. Boomerang effect of social media: Hundreds of fake videos about the outbreak in India, mass burials in China, virus spreading through cattle, etc., on various social media platforms bear testament to the perils of senseless sharing. Conspiracy theories like coronavirus being used as a biological weapon or biowaste may make for stimulating debates, but eventually, they add to the global panic and hysteria.

The Impact of Information during Pandemics

“We have sold our priced jewelry to go to this treatment camp. They charge high for each vial of medicine. It is also far from our house. Many people from our village told it works and we can prevent corona infection. Now my son is so ill after taking this tonic. Doctors are not able to help much” (mentioned by a lady from rural Assam).

“People don’t talk to me anymore. They move away when they see me. My neighbors give me a strange look. I fail to explain them my role in the whole process. It makes me frustrated when I return home” (from a doctor working in a COVID-19-designated hospital in Karnataka).

“I was too scared. I just wanted to get the medicine to save my elderly mother. It was all over the news. I got lot of messages that it must be taken by all at risk to stay safe” (son of a senior citizen, who had cardiac arrest after taking inadvertent dose of HCQ in West Bengal).

These excerpts have been slightly modified for anonymity and reproduced with informed consent from the individuals. They are obtained from the crisis calls made to the National Institute of Mental Health and Neurosciences COVID-19-related mental health helpline.

The excerpts mentioned above are both from general public in urban and rural areas as well as frontline health workers,

all of whom were the victims of misinformation and related stigma.

The impact that information or misinformation can have on human behavior is remarkable. It can range from faulty treatment, noncompliance to precautionary measures, panic, mass hysteria, agitation, and competition for health-care resources.^[16] On the other hand, relevant and timely information has shown to improve preparedness for infectious diseases and strengthen public health infrastructure.^[17] One of the main related platforms, social media, thus can be a “double-edged sword.” A review by Kadam and Atre^[18] points out that social media reach has risen three times during the lockdown period in India, with COVID-19-related search spiking significantly. The inherent insecurity and lack of daily structure that strikes people during lockdown makes them feel inadequate without the constant feed of health-related information. It is indeed extremely challenging to ensure a fine balance between the “toxic overuse” of technology and the healthy and systematic harnessing of health data. Many distress calls that the helplines of our tertiary mental health-care center cater to nowadays are related to compulsive use of the Internet and social media leading to health anxiety, somatic complaints, anxiety, depressive disorders, agitation, and insomnia. On a different note, children and adolescents being exposed to more “online time” tend to develop technology and gaming addiction. It is vital to remember that certain unhealthy habits will long outlast the pandemic to cause continued problems in life. Furthermore, anxiety and apprehension about an unknown illness might increase irrational decisions and inadvertent self-medication. One such popular example is the selective appearance of HCQ in the media as a “life-saving” drug against COVID-19 which has overshadowed the strictly prescribed guidelines for its use and the weak scientific evidence for its widespread use against the coronavirus.^[15] Such a selective portrayal of scientific literature generalizing the effects of treatment in its early phases, especially during a crisis like pandemic, can quickly generate a “false hope” with overuse against the recommended safety guidelines. Furthermore, social media-related “blame” can also lead to stigma, marginalization, communalism, and violence, especially at such times of crisis.^[19] In India, people from the North East, certain religious communities, and lower socioeconomic classes like the migrants and homeless have already been victims of such stigmatization related to COVID-19 in our country.^[20] This labeling of “outsiders” in these polarized populations can further increase the social unrest during the already difficult situations. Furthermore, the generation of “self-stigma” in the minority groups increases stress, delays the detection and treatment of mental comorbidities, and perpetuates the vicious cycle of social prejudice.^[19]



“Digital Balance”: The Integrative Role of Media and Technology

Information dissemination definitely has its own merits. It cannot be looked into as an “all-or-none” process. History has proven that continued and timely liaison between media personnel and scientific community can help immensely for the information-education-communication outreach in the community.^[21] The increased use of social media can be a powerful tool for debunking misinformation itself. The linkage of various media platforms with scientific databases such as PubMed and Google Scholar can provide appropriate search guidance, and content analysis of the

search data gives useful information about the search trends, the popular “sought for” information, and the unmet need for data.^[22] Those can then be harnessed for authentic updates and fighting false news. Social media owing to its increased penetration, popularity, and consumption is uniquely equipped to aid public and mental health during such times. Various proposed ways of this integration are summarized in Table 1.

Awareness for healthy use of technology can be spread by social media itself with administrative reforms regulating unnecessary forward and rumormongering related to the ongoing pandemic.^[2] In the short run, such regulations

Table 1: Role of social media during pandemics

Role of the social media during pandemics	Processes involved
Fighting false news and misinformation	Using diagnostic and referral health tool (example: Facebook preventive health tool) Individualized approach for evaluation, testing, and counseling based on reported symptoms Highlighting and debunking rumors and providing relevant data Integrating data from search engines (like Google QHub) to understand and study trends of misinformation
Enabling digital health literacy	Prevent information overload and content related to xenophobia, stigma, and prejudice Video conferences and webinars Live platforms (like Facebook and Instagram) for awareness campaigns Liaison between journalists and physicians
Helping research during crisis	Search data can be pooled and studied to understand the unmet needs Community public health research
Resource and psychological preparedness during pandemics	Liaising with public health platforms (WHO, CDC, ICMR, etc.) and forums like “Worldometer” to update statistics and trends of ongoing infection Integrating essential service location and contact tracing using special applications Counseling, mental health crisis intervention, and suicide prevention
Crisis communication	Identifying priorities, providing relevant facts, and precautionary measures
Fighting stigma	Assisting community awareness campaigns through advertisements and promotion Incorporating popular/public figures in the media IEC activities
Facilitating public health needs	Socioculturally and linguistically sensitive infographics Geolocation facilities for identifying hotspot zones and caseloads “COVID-free” content for recreational purpose Special services for those in quarantine
Addressing mental health	Training and health communication between tertiary and primary health care Social connectedness in community and enhancing mutual support Mitigating loneliness Increasing “COVID-free” content to reduce panic Fostering optimism and hope Humanizing mental illness Providing authentic information of mental disorders and treatment Advocating and promoting mental well-being through media programs (especially for the vulnerable groups and those with preexisting psychiatric disorders) Counseling using cyberspace
Aiding healthy use of media	Sensitive reporting of suicides (including celebrity suicides) Advocate healthy use of technology Regulated timelines and content

IEC=Information-education-communication, CDC=Centers for Disease Control and Prevention, WHO=World Health Organization



are imperative. In the long run, destigmatizing pandemics, preventing prejudice in community, and addressing the collective anxiety need to be the goals of the government. Recently, the Regional Outreach Bureau of the Ministry of Information and Broadcasting, Government of India (GOI), had launched a digital media and messaging campaign drive related to COVID-19 for the rural areas.^[23] The messaging service focused on the following targets: maintaining

good personal hygiene, abiding by the lockdown rules, ensuring social distancing, targeting mental and physical health, prevention of rumormongering, and downloading the Aarogya Setu app. The messages were also made in local languages and dialects to cater to the sociolinguistic diversity of the country. The audio version of the same was popularized by all the telecommunication companies which played the message compulsorily during any call

Table 2: Proposed channels of media communication during a pandemic

Channel	Benefits	Challenges
Radio and television	Widespread High consumption	Takes time to get the warnings Limited use at night
Telephone (fixed and mobile)	Messages delivered quickly Simplest method of communication	Problems of authenticity Does not reach many areas Network connectivity issues Difficulty for some groups in telephonic expression of distress
SMS	Quick Messages can be sent to groups	Congestion Does not reach nonusers Local language problems
Cell broadcasting	No congestion Can address a group simultaneously	Elaborate discussion/detailed communication is not possible Frequent network interruption Does not reach nonusers Local language problems
Satellite radio	High penetration	Cannot be used to educate masses Only good for specific points
Amateur/community radio	Excellent for rural, poor, and remote communities	Not widespread People lose interest if used only in case of disaster
Internet/web network	Interactive Multiple sources can be checked for accuracy of information Increasing penetration	Not widespread (limited penetration into rural areas) Bandwidth issues Issues with handling of technology More prone to misinformation bias (less filters) Difficult without technical assistance in sensory and cognitive impairment

Table 3: Responsible reporting of suicides by media

Preferred ways of reporting	Practices to be avoided
Accuracy of information	Personal assumptions, biases, and “tales” of suicide
Authentic sources of help-seeking	Conspiracy theories
Facts and risks of suicide	Detailed and repetitive reporting
Suicide prevention methods	Sensationalizing, fantasizing, or normalizing suicides
Vulnerable groups at risks for suicide	Reporting self-harm as “heroic” or “constructive”
Expert opinions for qualified professionals/ first-person accounts of coping	Generation of fear, stress, and panic
Sensitive and humane interviewing of the bereaved	Extensive debate and discussion with multiple professionals about the same incident, which generates confusion
Peer debriefing and support among the media personnel to deal with trauma	Avoid using “catchy” or sympathetic headlines/phrases
Factual reporting of the suicide event (especially celebrity suicide)	Coercive questioning of the bereaved on camera
	Avoid visual content (photographs, videos, social media links, etc.) whenever possible
	Excessive emphasis of personal life and contextual information
	Judgmental comments
	Explicit details of methods used

Modified from WHO (2017). Preventing suicide: A resource for media professionals, update.^[30] WHO=World Health Organization



and also appropriate advertisement on audiovisual and print media. The Aarogya Setu (Health Bridge) application, developed by the National Informatics Center, was introduced by the GOI to spread awareness and connect essential COVID-19-related health services to the people of India.^[23,24] It is a tracking app that uses smartphone's global positioning system (GPS) and Bluetooth features to track the coronavirus infection. It tries to determine the risk if one has been in the proximity of a COVID-19-infected person, using geolocation and containment zone data. Although debates have persisted about the "coercive nature" of its use and security concerns, it has definitely been a novel use of technology during the pandemic for the greater good. The various modalities of media with their respective challenges are summarized in Table 2.

The pandemic has also led to increase in suicidality and self-harm attempts. Although systematic studies are yet to emerge, various reports have been published globally including India.^[25,26] Besides the usual psychological impact of stress, isolation, and panic on suicide, media reporting can also have a significant effect on suicide prevention efforts. Extensive coverage, portrayal of information, fantasizing suicide in vulnerable groups, and drawing inconclusive evidence between the pandemic and suicidality can all lead to misinterpretation and public chaos. The "Werther effect" is already a well-known manifestation of "copycat suicides" in vulnerable consumers of media. Studies have consistently found a relevant association between how suicide is portrayed in the media and the effects on the viewers/readers. On the other hand, the protective effect of media is paramount in suicide prevention.^[27] Also known as "Papageno effect," this involves responsible reporting of suicides (especially during disasters and for popular figures), educating the audience about prevention strategies, raising awareness about the early signs of self-harm, encouraging prompt detection and management, targeting at-risk population during the pandemic, and finally, enhancing care for those already suffering from psychiatric disorders.^[28] Liaison between the media outlets and suicide prevention helplines along with those for woman, child, and elder safety can not only decrease self-harm but also age- and gender-based abuse that has increased during the ongoing crisis. It is also important to remember that media professionals themselves get affected with suicide reporting and vivid visual content, with studies showing a high prevalence of insomnia, acute stress, depression, and complex posttraumatic stress disorder in them.^[29] Hence, peer support, counseling, and managerial sensitivity are prime necessities at all hierarchical levels in media organizations. Public health agencies like the WHO has clear guidelines for suicide reporting by the media, especially in sensitive situations.^[30] Few facets of the same are highlighted in Table 3. These are, however, more commonly overlooked than implemented.

Conclusion

Irrespective of profession or socioeconomic background, it becomes the collective responsibility of stakeholders at all levels to join the fight against health-related false news that can have devastating public health and social consequences. Societies can never be fully informed or secure, so rumors are inevitable, particularly during the present times. However, providing active and relevant rebuttal will help in tackling this "unwarranted fatalism" of information. Importantly, we need to understand that we do need information, but "loads of statistics" about every single aspect of "the virus" make no sense to the masses. They will do more harm than good. Maintaining a conscious and informed distance from social media can help increase the "COVID-free" time which is so necessary for the mental well-being.^[31] Technology can rather be used for social connectedness than isolating people in their own "digital spaces" that can add to loneliness, isolation, and depression. When the viral caseload is peaking globally, the most desired plan is obviously to prevent COVID-19 from invading our "mental peace." In keeping with those lines, "digital distancing" can be best practiced through these words of Abraham Lincoln, "Discipline is choosing between what you want now and what you want most."^[32]

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Conflicts of interest

There are no conflicts of interest.

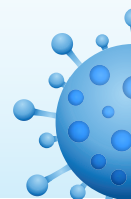
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NOTE: The data and views in this Perspective are updated, and accurate, to the best of knowledge of the Authors as of August 3, 2020.



7. Diagnostic modalities

SI No	Title	SDG IMPACT
57	COVID-19: Chest CT Imaging Patterns in Assessment of Disease Progression and Severity, Sachin Thammegowda, Sudha Kiran Das, Raghu Ramachandra, Shashikiran Ramachandraiah, Shashank Honnegowda, International Journal of Anatomy, Radiology and Surgery, 10, 13-16	Goal 3: Good health and wellbeing Goal 9: Industry innovation and infrastructure



COVID-19: Chest Computed Tomography Imaging Patterns in Assessment of Disease Progression and Severity

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ABSTRACT

Introduction: Chest Computed Tomography (CT) plays an important role in the diagnosis and management of Corona Virus Disease (COVID-19) infection. A better understanding of the chest CT imaging findings in COVID-19 disease may help in accurate diagnosis and staging of the disease. The temporal changes in the chest CT imaging findings follows a specific pattern which helps in identification of disease progression or recovery from the illness.

Aim: To evaluate the chest CT imaging findings of COVID-19 patients during the course of disease.

Materials and Methods: This was a retrospective observational study in which 110 hospitalised patients with COVID-19 disease were evaluated for chest CT imaging findings and severity of the infection. Chest CT findings with respect to duration of symptoms onset were divided into early phase disease (<5 days of symptom onset), intermediate phase (5-12 days) and late phase disease (>12 days of symptom onset). Based on visual assessment, CT severity score was given depending on the percentage of each lobe involved in bilateral lung parenchyma. Descriptive statistics were expressed using percentage, range, means and Standard Deviation (mean±SD).

Results: A total of 110 COVID-19 positive patients (79 males and 31 females) with mean age of 48.33±9.18 years (range between 22-84 years) were included in the study. CT chest was performed during the different time periods of hospital stay ranging from 2 to 16 days. Early phase disease constituted 53 (48.18%) patients,

21 (19.09%) patients in the intermediate phase and 36 (32.72%) patients were in the late phase. Nineteen (17.27%) patients in the early phase disease (<5 days) had a normal scan. Out of 91 chest CT positive patients, 13 patients (14.28%) were asymptomatic and 78 patients were symptomatic (85.71%). Among the CT positive patients, early phase disease constituted 34 (37.36%) patients, 21 (23.07%) patients were in the intermediate phase and 36 (39.56%) patients in the late phase disease. Early phase disease was predominantly characterised by Ground Glass Opacities (GGOs) which were seen in 27 patients (79.41%), gradual conversion of these GGOs into consolidations during the intermediate phase. Consolidations with fibrotic bands were predominant imaging patterns during the late phase disease seen in 21 patients (58.33%). Mean CT severity score during the early, intermediate and late phase diseases were 4.14±2.12, 14.71±4.80 and 11.08±4.68, respectively. Along with few existing signs described in COVID-19 disease, two signs during the late phase disease were observed such as target sign in 5 patients (13.88%) and centipede sign in 13 patients (36.11%). Splenomegaly was an additional extrapulmonary finding seen in 27 patients (24.5%) which has not been described previously.

Conclusion: Specific imaging patterns during the course of COVID-19 illness provide an information regarding the stage of the illness and disease severity. Ideal timing of chest CT is found to be during the intermediate phase of disease (5-12 days of symptom onset), since most of the lesions evolve in this period and provide accurate disease severity which in turn helps in treatment planning.

Keywords: Consolidations, Computed tomography severity score, Ground glass opacities, Splenomegaly

INTRODUCTION

COVID-19 infection is an acute respiratory disease caused by Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2). COVID-19 infection is highly contagious and an exponential increase in the number of cases has been observed in the last few months [1,2]. Concerns regarding rapid identification of moderate and severe disease patients help in reducing the mortality associated with this infection. The diagnosis of COVID-19 infection is made by Reverse-Transcription Polymerase Chain Reaction (RT-PCR) technique by collection of nasopharyngeal/throat swab samples. With increase in the daily number of cases, the number of RT-PCR tests done for COVID-19 infection is limited. In the present scenario, Chest CT is found to be more sensitive and an important imaging modality for rapid identification of COVID-19 infection [3]. Considering the wide range of COVID-19 symptoms, early detection of the disease with assessment of severity is crucial. SARS-CoV-2 shares a similar genomic sequence with SARS-CoV and MERS-CoV (family of corona viruses), leading to the development of similar clinical manifestations. Diverse imaging findings ranging from focal lung lesion to extensive

interstitial inflammation and consolidations have been described [4]. Previous studies on COVID-19 pneumonia have described GGOs and consolidations as predominant CT chest findings [5,6].

A better understanding about the imaging finding of COVID-19 pneumonia will help to identify the stage of the disease. Initiation of antiviral therapies in the early stages of the disease decreases the duration of illness and prompts early recovery [7]. In the present study, imaging findings were analysed during different phases of COVID-19 infection and severity using CT severity score was assessed.

MATERIALS AND METHODS

This was a retrospective observational study conducted at Hassan Institute of Medical Sciences, Hassan, Karnataka, India from July-August 2020 for a period of two months. The study was approved by the Institutional Ethical Committee (IEC/HIMS/RR171) and the need for informed consent was waived. The study included 110 patients who were positive for COVID-19 infection by RT-PCR test and were admitted in the hospital. The duration of hospital stay during which the CT chest was performed ranged from 2 to 16 days.

Inclusion Criteria

RT-PCR positive patients with COVID-19 disease who had undergone at least one chest CT during the hospital stay. CT chest was performed as per the clinician decision (based on clinical assessment) and suspicion for COVID-19 infection on chest x-ray which was performed for all hospitalised patients in their respective COVID wards.

Exclusion Criteria

Patients with pre-existing lung disorders were excluded. Based on the duration of onset of symptoms to the time of CT scan, the sample population was divided into. Early phase (<5 days), Intermediate phase (5-12 days duration), Late phase (>12 days after the date of symptom onset). The CT imaging characteristics in these different phases were evaluated. CT was performed using 16-slice Multi Detector Computed Tomography (MDCT) scanner (Philips MX-16). All patients underwent non-contrast CT scan of the thorax in supine position and during end inspiration. The following parameters were used: Tube voltage of 100-120 kV; tube current-exposure time product of 200-300 mAs; and section thickness of 1.25 mm. The CT imaging patterns were described according to the internationally standard nomenclature defined by the Fleischner Society and peer-reviewed literature on viral pneumonia [8,9]. The CT images were evaluated for the presence of GGO, consolidation, reticular pattern, mixed pattern (combination of GGO and consolidation), fibrotic bands, and other findings. Various chest CT signs described in COVID-19 infection were also observed in the present study [10]. Target sign is seen as a ring like peripheral opacity with central small ground glass attenuation [11]. Centipede sign is seen in late phase of the disease represents resolving subpleural curvilinear consolidation of varying length with small reticular shadows on either side which has not been described previously.

CT severity score: A semi-quantitative scoring system was used to assess the percentage of lung involvement in each of the five lobes [12]. Depending on the percentage of lung parenchymal involvement, each of the five lung lobes will be visually scored on a scale of 0 to 5, with score 0 indicating no involvement; 1 for <5% involvement; 2 indicating 5%-25% involvement; 3 for 26%-49% involvement; 4 signifies 50%-75% involvement; and 5 indicating more than 75% involvement. The total CT score was determined as the sum of lung involvement, ranging from 0 (no involvement) to 25 (maximum involvement). The severity of lung parenchymal involvement on CT scan was classified on a three-point ordinal scale: grade one with score of 1-8, grade two with score of 9-15 and grade three with score of 16-25 [13].

STATISTICAL ANALYSIS

Quantitative and Qualitative data were recorded using Microsoft Excel Spread Sheet (2010). Descriptive statistics for quantitative data were expressed using percentage, range, means and standard deviation (mean±SD).

RESULTS

A total of 110 COVID-19 positive patients with mean age of 48.33±9.18 years (range between 22-84 years) were included in the study. Thirty one of the 110 patients (28.18%) were females and 79 patients (71.81%) were males. Thirteen patients (11.8%) were found to be asymptomatic. Among symptomatic patients, the most common presentations were fever (46.36%) and cough (40.90%) followed by breathlessness (32.72%) [Table/Fig-1].

Nineteen (17.27%) patients in the early phase disease had no chest CT findings. Out of 91 chest CT positive patients, 13 patients (14.28%) were asymptomatic and 78 patients were symptomatic (85.71%). The imaging findings observed in CT positive patients is depicted in [Table/Fig-2]. Among the CT positive patients, early phase disease constituted 34 (37.36%) patients, 21 (23.07%) patients were in the intermediate phase and 36 (39.56%) patients in the late phase

Characteristics	Number (n=110)
Age (years)	
Mean±SD	48.33±9.18
Range	22-84 years
Sex	
Male	79 (71.81%)
Female	31 (28.18%)
Symptoms*	
Asymptomatic	13 (11.8%)
Fever	51 (46.36%)
Cough	45 (40.90%)
Breathlessness	36 (32.72%)
Others (myalgia, sore throat and diarrhea)	18 (16.36%)
Phase of illness (Based on the duration of symptom onset)	
Early phase <5 days	53 (48.18%)
Intermediate phase (5-12 days)	21 (19.09%)
Late phase (>12 days)	36 (32.72%)

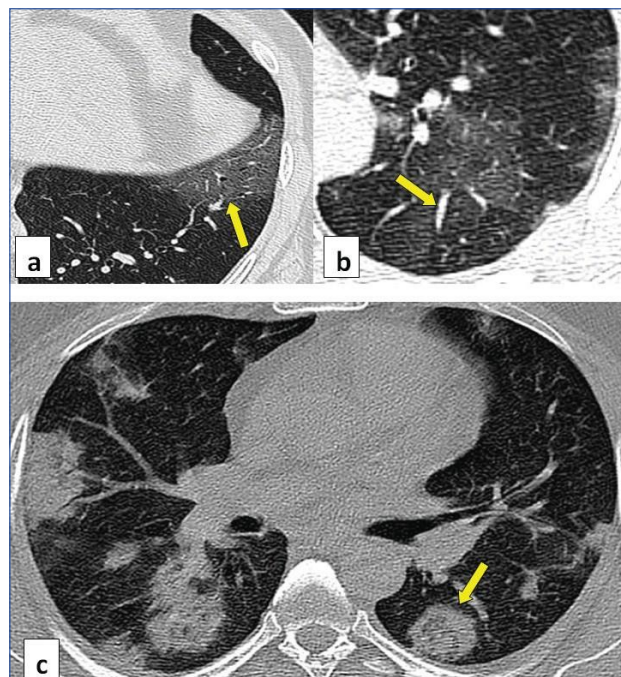
[Table/Fig-1]: Demographic and clinical characteristics of the study group.
*more than one symptom present

Characteristics (CT positive patients)	Number
Pattern of lesion distribution (n=91)	
Peripheral	57 (62.63%)
Both central and peripheral	34 (37.36%)
Lesions observed in each phase	
Early phase (n=34)	
Peripheral	28 (82.35%)
Both central and peripheral	6 (17.64%)
Ground glass opacities alone	27 (79.41%)
Ground glass opacities + Consolidations	7 (20.58%)
Intermediate phase (n=21)	
Ground glass opacities alone	2 (9.52%)
Ground glass opacities + Consolidations	10 (47.61%)
Consolidations alone	7 (33.33%)
Consolidations + Fibrotic bands	2 (9.52%)
Late phase (n=36)	
Ground glass opacities alone	5 (13.88%)
Ground glass opacities + Consolidations	10 (27.77%)
Consolidations + Fibrotic bands	21 (58.33%)
Signs during the early phase (n=34)	
Microvascular dilatation	15 (44.11%)
No sign	19 (55.88%)
Signs during the Intermediate phase (n=21)	
Organising pneumonia	9 (42.85%)
No sign	12 (57.14%)
Signs during the late phase (n=36)	
Subpleural transparent line	18 (50%)
Target sign	5 (13.88%)
Centipede sign	13 (36.11%)
Mean CT severity score	
Early phase (<5 days)	4.14±2.12
Intermediate phase (5-12 days)	14.71±4.80
Late phase (>12 days)	11.08±4.68

[Table/Fig-2]: Chest CT imaging characteristics of the study group.

disease. Early phase disease was predominantly characterised by GGO which was seen in 27 patients (79.41%), gradual conversion of these GGOs into consolidations during the intermediate phase [Table/Fig-3]. Microvascular dilatation sign was observed during the early

phase disease in 15 patients (44.11%) [Table/Fig-3]. Consolidations with well-defined rounded margins representing nodular pattern of organising pneumonia were observed during the intermediate phase [Table/Fig-3]. Consolidations with fibrotic bands were predominant imaging patterns during the late phase disease seen in 21 patients (58.33%) [Table/Fig-4]. Along with subpleural transparent line seen in 18 patients (50%) and two new signs were observed during the late phase disease such as target sign in 5 patients (13.88%) and centipede sign in 13 patients (36.11%) [Table/Fig-4].



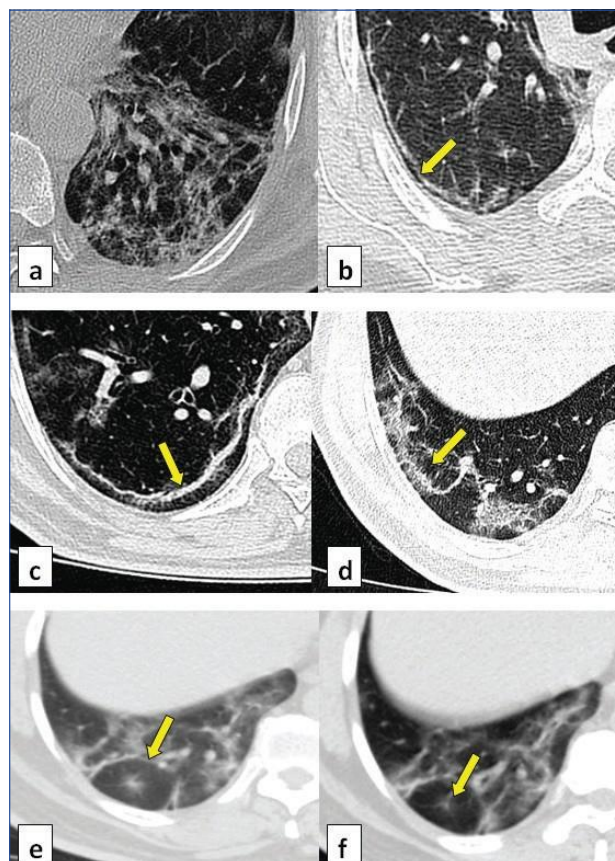
[Table/Fig-3]: (a) Axial sections of the CT thorax shows focal area of ground glass opacity (arrow) in left lower lobe with; (b) Microvascular dilatation sign (arrow) during early phase disease; (c) Multifocal round consolidations (arrow) in bilateral lung representing the nodular pattern of organising pneumonia seen during intermediate phase of illness.

Out of total 91 CT chest positive patients, 31 patients (91.17%) in the early phase had a CT severity score of less than 8 indicating mild disease and three patients (8.82%) had CT scores in the range of 8-15. Eleven patients (52.38 %) in the intermediate phase had severe disease with a severity score of more than 15, seven patients (33.33%) had scores in the range of 8-15 and three patients (14.28%) had a score of less than 8. Seventeen patients (47.22%) in the late phase had moderate disease with signs of absorptive phase. Eleven patients (30.55%) in the late phase had a score of less than 8 and severe disease with score of more than 15 was seen in eight patients (22.22%). The mean CT severity score was more during the intermediate and late phases of disease as summarised in [Table/Fig-2].

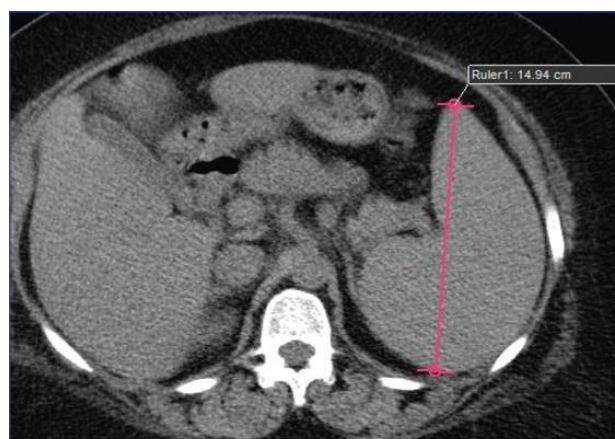
Splenomegaly was an additional extrapulmonary finding seen in the upper abdominal sections of 27 patients (24.5%) which has not been described previously [Table/Fig-5].

DISCUSSION

In this study, chest CT findings were retrospectively evaluated to determine the stage and severity of COVID-19 disease. Present study results suggest that the infection was less severe during the early phase and progresses during the intermediate and late phase of disease. Specific signs have been described to accurately identify the stage of the disease. Nineteen patients (17.27%) in the early phase disease (<5 days) had no chest CT findings. Similar negative chest CT findings were seen in other studies during the early phase of illness [Table/Fig-6] [14-16]. Ideal timing of chest CT appears to be after 5 days of symptom onset since all the patients in intermediate



[Table/Fig-4]: (a) Axial sections of the CT thorax shows mixed resolving consolidations and fibrotic changes in left lower lobe; (b) Subpleural transparent line (arrow) just adjacent to linear consolidation band; (c) Subpleural curvilinear consolidation (arrow); (d) Reticular shadows (arrow) on either side representing centipede sign; (e) Target sign seen as a peripheral ring like opacity (arrow); (f) Central small ground glass attenuation representing a dilated microvasculature (arrow).



[Table/Fig-5]: Visualised upper abdominal section of the CT thorax shows mildly enlarged spleen.

Early phase CT findings	Bhandari S et al., [14]	Hu Q et al., [15]	Pan F et al., [16]	Present study
No CT findings	36.25%	4.34%	16.66%	17.27%
Peripheral location	52.94%	65.22%	54.16%	82.35%
Ground Glass Opacities (GGO)	49.01%	39.13%	75%	79.41%

[Table/Fig-6]: Comparison of early phase CT findings with previous studies [14-16].

phase shows lung involvement. Semi-quantitative CT scoring helps to know the severity of different phases of COVID-19 disease. A previously validated CT severity scoring system was used which is based on the extent of lobar involvement as reported by Pan F et al.,

[16]. A three-point ordinal scale was derived to grade the CT severity score based on the results given by Francone M et al., [13]. Mean CT severity score in mild, severe and critical categories were 8.7 ± 4 , 17.4 ± 3.1 and 20.3 ± 3 , respectively [13]. Two grades were used by Bhandari S et al., to classify patients into mild and severe group with scores less than 15 indicating mild infection and severe disease with scores more than 15 [14]. The intermediate phase between 5-12 days of symptom onset is crucial and is characterised by expansion of the GGOs with consolidations and increasing severity score. The typical findings in this stage include nodular pattern of organising pneumonia. This stage in particular is important for initiation of antiviral therapies and close monitoring [15].

Patients who had recovered from COVID-19 pneumonia presented with severe disease on CT at approximately 10 days after initial onset of symptoms indicating peak stage. Absorptive stage with improvement in chest CT signs began at approximately 14 days after the onset of initial symptoms [16]. Signs in the each of these three different phases has been described indicating the evolution of the lesions from early to late stage. Along with subpleural transparent line, target sign and centipede sign are indicative of late phase of infection. The temporal changes of the radiological manifestations followed a specific pattern, which might indicate the progression and recovery of the illness [17]. A long term follow-up of moderate and severe disease patients is required to know the duration of radiological recovery and whether there is persistence of fibrotic changes.

Limitation(s)

Relatively small sample size in different phases of COVID-19 disease, warrants further study with larger study group. Only hospitalised patients were included resulting in possible selection bias. Follow-up of the patients was not included.

CONCLUSION(S)

Being familiarised with the chest CT findings of COVID-19 pneumonia will help to identify the stage of the disease and assess severity. Chest CT imaging is found to be useful in identification of disease progression or signs of improvement. Patients can be categorised based on the CT severity score and patients with severe disease can be started on early antiviral therapy.

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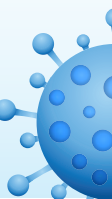
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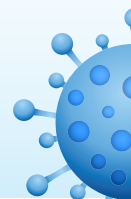


8. Therapeutic Dimension

SI No	Title	SDG IMPACT
58	PCV81 Virtual Anticoagulation Clinic Care a Telehealth MODEL to Deliver Continuity of Anticoagulation Care during the COVID 19 Pandemic: Insights from Southern India, O GONA., SUNIL KUMAR S., R MADHAN, Value in Health, 23, 1098-3015	Goal 3: Good health and wellbeing Goal 9: Industry innovation and infrastructure
59	THE MYSTERY OF HYPOXIA IN COVID-19, Varsha Konyala., Raghavendra Bhat, International Journal of Surgery and Medicine, 6, 85-94, 2367-7414	Goal 3: Good health and wellbeing
60	Antiviral and immunomodulatory activity of curcumin: A case for prophylactic therapy for COVID-19, Dr B Suresh., Dr Rajesh Kumar Thimmulappa., DR KIRAN KUMAR M N., Dr Chandan S., K J Thirumalai Subramaniam., Arun Radhakrishnan., GowthamarajanKuppusamy, Heliyon, 7, 2405-8440	Goal 3: Good health and wellbeing Goal 9: Industry innovation and infrastructure
61	Management of leprosy in the context of COVID-19 pandemic: Recommendations by SIG leprosy (IADVL academy), Santoshdev Rathod., SujaiSuneetha., Tarun Narang., Shagufta P Rather., Vikas Shankar., Sridhar Jandhyala., Abhishek Bhardwaj., Sunil K Gupta., Sushruth G Kamoji., Dr Ashwini P.K., Swetalina Pradhan., Satyadarshi Patnaik., P Narasimha Rao., Sunil Dogra, Indian Dermatology Online Journal, 11, 345-348, 2229- 5178	Goal 3: Good health and wellbeing
62	Perceptions, Experiences, and Challenges of Physicians Involved in Dementia Care During the COVID-19 Lockdown in India: A Qualitative Study, Banerjee D., Vajawat B., Varshney P., Rao T.S.S., Frontiers in Psychiatry, 11, 1664-0640	Goal 3: Good health and wellbeing Goal 8: Decent work and economic growth



63	COVID-19 infection: The prospects of pharmacotherapy, Prithvi S Shirahatti., Shashank M Patil., V B Chandana Kumari., S Sujay., M Tejaswini., Lakshmi V Ranganath., Dr Jayanthi M.K., Dr RamithRamu, International Journal of Health and Allied Sciences, 9, 111-113, 2278-4292	Goal 3: Good health and wellbeing Goal 9: Industry innovation and infrastructure
64	Proposed drug interventions for SARS CoV 2 infection, Pranshu Mehta., Dr Bharathi M.B., International Journal of Research in Medical Sciences, 8, 1950-1956, 2320-6071	Goal 3: Good health and wellbeing Goal 9: Industry innovation and infrastructure
65	Pharmacotherapy of COVID-19: A Perspective of Pathogenicity and Life Cycle, Prithvi S Shirahatti., Shashank M Patil., V B Chandana Kumari., S Sujay., M Tejaswini., V Lakshmi Ranganatha., C Mallikarjunaswamy., Dr Jayanthi M.K., Dr RamithRamu, Biomedical and Pharmacology Journal, 13, 1579-1594, 0974-6242	Goal 3: Good health and wellbeing Goal 9: Industry innovation and infrastructure
66	Implementation and Evaluation of Virtual Anticoagulation Clinic Care to Provide Incessant Care During COVID-19 Times in an Indian Tertiary Care Teaching Hospital, Dr Sunil Kumar S., Dr Shyam Prasad Shetty.B., Oliver Joel Gona., Nagaraj Desai., Dr Madhu B., Dr Ramesh Madhan., Revanth V, Frontiers in Cardiovascular Medicine, 1-7, 2297- 055X	Goal 3: Good health and wellbeing Goal 9: Industry innovation and infrastructure
67	Assessment of Clinical Pharmacists' Assistance for Patients With Established Cardiovascular Diseases During the COVID-19 Pandemic: Insights From Southern India, Oliver Joel Gona , Ramesh Madhan and Sunil Kumar Shambu ,Frontiers in Cardiovascular Medicine, December 2020, Volume 7	Goal 3: Good Health and Wellbeing



PCV79

CURRENT BARRIERS TO MARKET ACCESS OF ALIROCUMAB IN ITALIAN REGIONS

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Objectives: Prescription of proprotein convertase subtilisin/kexin-type-9 inhibitors (PCSK9i) under the Italian AIFA's reimbursement scheme is limited to specialized Centers/physicians appointed by the Regions and Autonomous Provinces. Patient access to PCSK9i is still very limited and varies considerably across Regions. Our aim was to analyse updated records from AIFA Registry to understand determinants of alirocumab uptake at the regional level. **Methods:** We analysed regional distribution of patients enrolled in the alirocumab registry (April/19-March/20) in correlation with: number of prescribing centers and units appointed by each Region; number of previous hospitalizations (from published Ministry of Health statistics) for Acute Myocardial infarction (AMI) and number of percutaneous transluminal coronary angioplasty (PTCA) in 2018 and 2016-2018. Classical statistics were performed (max-min-SD-RSQ) and data were plotted as XY graphs. **Results:** As of 30/03/20, a total of 325 centers and 541 operational units are appointed for prescription of PCSK9i in the Italian Regions with wide distribution disparities: statistics per million population (PMP) show the number of centers per Region varies from 2.23 to 20.87 PMP with mean (SD) 8.03 (4.32) PMP and median 7.39 PMP; statistics by operational units: mean 11.9 (5.96) PMP median 9.81, range (25.04 – 2.89) PMP. No correlation was shown between number/100.000 residents of alirocumab patients enrolled and number/PMP of appointed centers or operational units; similarly, no correlation was shown with number/PMP of AMI or PTCA hospitalizations. **Conclusions:** Correlation between patient enrollment on PCSK9i and number of appointed centers and operating units in Italy, is far from being established: this may depend on local infrastructural diversities (geographical distribution, location and accessibility of centers), as well as on specific regional healthcare strategies and policies. Further research should investigate correlation of local coverage and prescription for new, innovative anti-hyperlipidemics, with definition and enforcement of structured pathways in post-CV event management.

PCV80

CHARACTERIZATION OF THE CLINICAL PATHWAY AND TREATMENT PATTERNS FOR POST-MYOCARDIAL INFARCTION PATIENTS: A PHYSICIAN SURVEY

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Objectives: Describe lipid-lowering therapy (LLT) treatment patterns in post-MI patients and adherence to 2019 ESC/EAS dyslipidemias guidelines. **Methods:** A cross-sectional survey was conducted in France, Germany, Italy, Netherlands, Spain, and United Kingdom (UK). A stratified sample of 60 physicians (cardiologists and general practitioners [GPs]) were surveyed in each country. **Results:** Of 360 physicians surveyed, 233 (64.7%) were secondary care cardiologists and 127 (35.3%) were primary care physicians (PCPs). 13.5% of cardiologists and 18.9% of PCPs reviewed LLT for all patients within 12 weeks of discharge after MI. 82.0% of cardiologists and 55.1% of PCPs stated that they consulted ESC/EAS guidelines, 42.9% of cardiologists and 55.1% of PCPs consulted national guidelines. Most physicians (86.9%) used LDL-C to assess lipid profile. Total cholesterol was mostly used in the UK, where 80.0% of GPs used that measure. For patients not achieving recommended lipid levels at 12 weeks, 90.6% of cardiologists would change LLT regimen immediately, 7.6% would wait longer, and 1.8% would take no action. Among PCPs, 51.6% would change LLT regimen immediately, 47.6% would wait longer, and 0.8% would take no action. Evaluating fictitious cases of post-MI patients whose LDL-C target recommended by ESC/EAS guidelines could not be reached using statins and ezetimibe, 23.0% of cardiologists and 6.3% of PCPs indicated that they would prescribe PCSK9 inhibitors. **Conclusions:** Less than one fifth of physicians follow the recommendations of ESC/EAS guidelines and review all post-MI patients in their care within 12 weeks of discharge. When LDL-C goals are not reached, almost all cardiologists and approximately half of PCPs would change LLT. A small proportion of physicians use intensive LLT with PCSK9 inhibitors for post-MI patients, as recommended by ESC/EAS guidelines. These data suggest that education of physicians treating MI patients may be warranted.

PCV81

VIRTUAL ANTICOAGULATION CLINIC CARE A TELEHEALTH MODEL TO DELIVER CONTINUITY OF ANTICOAGULATION CARE DURING THE COVID-19 PANDEMIC: INSIGHTS FROM SOUTHERN INDIA

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Objectives: COVID-19 pandemic is a disaster which has affected the entire world. Nationwide lockdown during this pandemic rendered healthcare inaccessible to many. Patients taking oral anticoagulants need continuity of care. Hence, we aimed to study the impact of Virtual anticoagulation clinic initiative on the quality of anticoagulation and patient satisfaction during COVID-19. **Methods:** Prospective observational study was conducted on patients enrolled in to the VAC. Of 508 patients receiving dedicated Anticoagulation clinic in southern India, 379 patients consented to receive anticoagulation care virtually. Patients were followed

up for 3 months (March 2020 to June 2020). Digital platforms like WhatsApp, email and voice call/ SMS was used. Patients were monitored for anticoagulation related parameters like Time in Therapeutic Range (TTR), Percentage of International Normalized Ratio in Range (PINRR) and adverse events. Descriptive and Inferential statistics have been executed where appropriate using SPSS version 25.0. **Results:** Mean age was 59.51

61.22 years with 61% men. Hypertension (60.5%) and diabetes (40.5%) were the most common comorbidities. Atrial fibrillation (72%) was the most common indication. Acenocoumarol (92.9%) was the most common VKA used. Mean TTR was 75.46 8.9%. PINRR was 66.76 9.47%. 1.8% of INRs were in extreme range. WhatsApp (73%), email (19%) was the most common digital platform used. Voice call and SMS was used by 8% of patients. One patient had minor lower gastrointestinal bleed. None of the patients had major adverse events. 12 patients were scheduled for in person visit. 74% were extremely satisfied with overall VAC care and 82% of patients were extremely satisfied to continue virtual care as assessed by 5-point Likert scale **Conclusions:** Virtual anticoagulation clinic can deliver optimal quality of anti-coagulation in patients with chronic VKA therapy. This care model can be ideal not only during this COVID-19 pandemic and even beyond in India.

PCV82 CHARACTERISTICS AND OUTCOMES OF PATIENTS WITH CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (CTEPH) TREATED WITH RIOCIQUAT: A RETROSPECTIVE, OBSERVATIONAL COHORT STUDY

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Objectives: To describe characteristics, treatment patterns and outcomes of patients treated with riociguat in France. **Methods:** An observational retrospective cohort study – RIAD (Retrospective Adempas® study) – was conducted within the French pulmonary hypertension network. Data of patients initiated with riociguat between 14/01/2015 and 31/12/2016 were collected. Patients were followed-up for 2 years. Dosing regimen and treatment patterns were recorded at riociguat initiation and during follow-up. Other measures including time-on-treatment and changes from baseline to 24 months (M24) in 6-minute walk distance [6MWD] and NYHA functional class (FC) were assessed in patients still receiving riociguat. **Results:** Overall, 173 patients were included in 18 centres: 63% were female, mean age was 71.46 12.4 years, 80.3% were in NYHA FC II/III. All had CTEPH (75.7% inoperable, 20.8% persistent/recurrent after surgery, 3.5% not available). At riociguat initiation, median 6MWD

was 323.5 m (min-max: 60–650), median right atrial pressure was 7 mmHg (0–22), mean pulmonary artery (PA) pressure was 43.06 11.4 mmHg, median PA wedge pressure was 9 mmHg (1–17), median cardiac output was 4 L/min (1.9–9.2) and median pulmonary vascular resistance was 7 WU (2–29). At the time of initiation of riociguat, 93.1% of patients were receiving anticoagulants and 83.2% were not receiving concomitant specific treatments. Riociguat was initiated at 1 mg ter in day (tid) in 85.5% of patients and 82.1% were receiving 2.5 mg dose tid at M24. The maximal daily dose reported was 2.5 mg tid. At M24, 78.8% of patients were still on riociguat, with a mean time-on-treatment of 20.16 0.5 months per patient. Both mean 6MWD and NYHA FC improved at M24 (6MWD increased by a mean of

+31.16 89.2 m; 54.1% of patients improved by at least one FC). No new safety signals were recorded. **Conclusions:** In real-world clinical practice in France, riociguat was administered in accordance with current recommendations and summary of product characteristics.

PCV83 THE VALUE OF POLYPILL IN THE CARDIOVASCULAR DISEASE: AN ITALIAN MULTIDISCIPLINARY DELPHI PANEL CONSENSUS

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THE MYSTERY OF HYPOXIA IN COVID-19

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ABSTRACT The COVID-19 pandemic has caused untimely deaths of many people. Predominantly, many of those who have been infected, have had an uneventful recovery. However, for those with co-morbidities, advanced ages, the story has been different. This review aims to highlight various pathogenesis of SARS-CoV-2 through the lens of hypoxia. The review consolidates information about virus induced hypoxia, neuroinvasive cause of hypoxia, thromboembolic cause of hypoxia, bradykinin and cytokine storms contributing to hypoxia. It brings out aspects of immune response which is aided by both coagulation cascade and the complement. In conclusion, we suggest care providers to be on the look out for asymptomatic hypoxia. We implore physicians and researchers to revisit and acutely look at the behaviour of the virus in vivo and the resulting immune response to be well equipped in this fight against the SARS-CoV-2 virus.

KEYWORDS Happy hypoxia, Cytokine storm, Bradykinin storm, Neuroinvasive SARS-CoV-2, SARS-CoV-2, COVID-19

Introduction

SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus 2) is the notorious agent implicated in the rampantly spreading COVID-19 (Coronavirus disease 2019) pandemic.[1] Like other coronaviruses, SARS-CoV-2 predominantly affects the respiratory system. The enteric, neurological system has also been reported to be affected.[2] The clinical features of this disease is a spectrum between asymptomatic to severe. Majority of the symptomatic patients complain of fever, cough, fatigue, dyspnea.[3] Nausea, vomiting, anorexia are features of enteric system involvement.[4] Loss of smell and taste have also been reported.[5] Of interest is a cohort of patients that present with 'Happy Hypoxia'. [6] In this review, we aim to talk about this phenomenon. We also extend the discussion to understand the development of hypoxia in COVID-19 patients. Amongst the various etiologies proposed for hypoxia, we address the concepts of 'Neuroinvasive SARS-CoV-2', 'Virus-induced Hypoxia', 'Bradykinin Storm', 'Cytokine Storm', 'Thromboembolic cause of Hypoxia'. These concepts are still evolving. This review gives a bird's eye glimpse

of COVID-19 pathophysiology in the hope of having a positive impact on prognosis and timely treatment protocols.

SARS-CoV-2: The novel virus

Coronaviruses have a single-stranded RNA (Ribonucleic acid) genome, and an envelope defines its outer surface. These viruses are present ubiquitously among humans, avians and other mammals. While most coronaviruses typically cause mild respiratory illnesses, SARS-CoV (Severe Acute Respiratory Disease Corona Virus) and MERS-CoV (Middle Eastern Respiratory Syndrome Corona Virus) cause severe disease. Genomic analysis shows that SARS-CoV-2 is part of the betacoronavirus clade. SARS-CoV and SARS-CoV-2 share nearly identical genetic makeup. It shouldn't be of any surprise then, to know that SARS-CoV-2 shares similar infective strategies with SARS-CoV. In fact, the entry of SARS-CoV-2 into human host cells is with the same receptor as SARS-CoV, i.e. ACE2 (Angiotensin Converting Enzyme 2)[1,7,8,9,10,11].

Pathogenesis of SARS-CoV-2

The virus has a spike glycoprotein S, made of 2 subunits namely, S1 and S2. S1 binds to the host cell receptor, ACE2. ACE2 is widely present in the cell membranes of cells belonging to respiratory, cardiovascular, enteric and central nervous systems to name a few. The S2 subunit, fuses with the host cell membrane. TMPRSS2 (Transmembrane Serine Protease 2) is a transmembrane protease which allows entry of the virus into the

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cells. It works by two mechanisms: as S1 is binding to ACE2, TMPRSS2 cleaves ACE2 rendering it dysfunctional. It then acts on S2 and facilitates fusion of the virus to the host membrane allowing it to enter the cell seamlessly.[12,13]

Defining dyspnea

Dyspnea is a sensation of uncomfortable, difficult, or laborious breathing and occurs when the demand for ventilation is out of proportion to an individual's ability to tackle this discomfort. Tachypnea or fast breathing and hyperpnea or increased ventilation are used interchangeably with dyspnea but are separate phenomena. [14,15] Respiration is regulated at the higher levels through the respiratory centre (RC) which is in the medulla oblongata and pons areas of the brainstem.[6]

Mechanisms of Dyspnea

There are several known features contributing to dyspnea. Of importance are the chemoreceptors. Largely, PaO₂ (Partial gas pressure of dissolved oxygen in the blood) acts at peripheral chemoreceptors while PaCO₂ (Partial gas pressure of dissolved carbon dioxide in the blood) acts at the central chemoreceptors. Central chemoreceptors are present in the medulla, whereas peripheral receptors are the carotid and aortic bodies.[16,17]

In hypercapnia, central and peripheral receptors relay the message to the RC. This centre then sends efferents to the respiratory system allowing an increase in the drive to respire and an increase in the amount of air entering the lungs per minute, also known as minute volume ventilation.[6] Similarly, when there is a decrease in the PaCO₂, the RC decreases the ventilation in order to restore normal PaCO₂. The central chemoreceptors and hypercapnia are the most important factors implicated in dyspnea.[16,17] Likewise, a similar mechanism is in play for hypoxemia. But, hypoxemia is a minor contributor to dyspnea, with dyspnea only occurring at dangerously low levels of PaO₂. The Nucleus Tractus Solitarius (NTS) meanwhile also relays all afferent data received to higher sensory and motor cortices and the insula.[18] It has been found that this cortical projection produces the unpleasant sensation of dyspnea.[19]

The paradox of hypoxemia in COVID-19

Normal values of PaO₂ is 75-100mmHg. Studies have shown that the quantity of hypoxemia needed to increase ventilatory capacity is the same as the amount needed to experience dyspnea. Hypoxemia and ventilation are related by a hyperbolic curve. In fact, as the partial pressure of oxygen falls to 60mmHg, there are negligible changes in ventilation. However, further decline shows a drastic increase in ventilation. Since the physiological response to hypoxemia is a rise in minute ventilation, both the number of breaths per minute and the volume of air entering the lungs is increased. Increased respiratory rate (tachypnea) and tidal volume (hyperpnea) initially, are, therefore, the most important early clinical signs of eventual hypoxemic respiratory failure[6].

Viral pathogenic changes have shown features of ARDS (Acute Respiratory Distress Syndrome).[14] These changes indicate that there is a diffusion defect which leads to hypoxia or decreased PAO₂ (Partial gas pressure of oxygen at the alveoli).[14]

So, to see a patient with tachypnea, hyperpnea, and in severe hypoxemia, presenting with dyspnea is the norm. What is as-

tounding, however, is the lack of dyspnea in patients even with severely low PaO₂ levels.[14,19]

Reports from Wuhan have shown that 62.4% of severe cases and 46.3% of cases on respiratory support and even the dead did not present dyspnea. Not surprisingly, findings with SARS-CoV infections also show that a mere 34.8% of severely affected patients reported dyspnea. These numbers are grim in contrast to other viral respiratory infections such as RSV (Respiratory Syncytial Virus) (95%) and influenza (82%) where dyspnea is frequently encountered.[18] Apart from viral pathogenic features which hinder the awareness of dyspnea, one may not see dyspnea in a SARS-CoV-2 patient because of confounding factors such as the following: Tobin et al. argue that the ODC (Oxygen dissociation curve) shows a rightward shift. Of concern in the setting of SARS-CoV-2 infection is fever which is the most common symptom in these patients.[3,19] Fever raises the core body temperature and allows the shift of the oxygen dissociation curve to the right. This means that for the same PaO₂, the SaO₂ (Oxygen saturation in the blood) will be low, i.e. at a body temperature of 37 degrees and 40 degrees, the PaO₂ could be at 60mmHg, but SaO₂ will read 91.1% and 85.8% respectively. Similarly at a PaO₂ of 40mmHg, at and below which dyspnea is expected to occur, the SaO₂ is 74.1% at 37 degrees and 64.2% at 40 degrees. These shifts produce evident desaturations with not much change in the chemoreceptor input (this is so because carotid bodies respond only to PaO₂ and not SaO₂).[19]

Meanwhile, Dhont et al. give a contrasting explanation. They say that the ODC in fact shifts to the left, possibly in response to the respiratory alkalosis (drop in PaCO₂) that develops in hypoxemia associated high minute volume ventilation. When PaCO₂ is reduced, the affinity of Hb (Haemoglobin) for oxygen increases and so SaO₂ increases for a given PaO₂. This explains the well-preserved SpO₂ (Oxygen saturation measured by pulse oximetry) even when there is dangerously low PaO₂. [6]

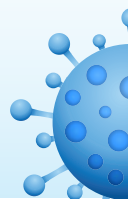
It has also been theorised that direct viral interaction with the heme group of Hb allows harmful iron (Fe³⁺) to be available and lead to inflammation and cell death. In response to this, the body produces large amounts of ferritin to bind the free ions.[18] So, with the diminished amount of Hb molecules to carry oxygen, the body would lap up any oxygen molecules that it may encounter due to the now increased affinity of Hb for oxygen. Therefore, oxygen may not be released to the tissues. This gives a falsely elevated SpO₂. It also gives the physician an impression that the patient does not have any dyspnea.

Another confounding factor could be pulse oximeter readings. The pulse oximeter measures SpO₂. The principle of pulse oximetry lies in the illumination of the skin and measuring the differences in the amounts of light absorption of oxyhaemoglobin and reduced Hb. SpO₂ can differ from true SaO₂ measured with a CO-oximeter by about 4%. Pulse oximetry has also known to be less accurate at SaO₂ of less than 80%. [19]

There are a wide number of patients with COVID-19 who are elderly and diabetic. The physiological response to hypoxia is down by almost 50% in patients who are 65 years or older. People with diabetes to have an attenuated response to hypoxemia.[19]

Both these factors attenuate the response of the respiratory centre to hypoxia.

In conclusion, SpO₂ should be interpreted considering hyperventilation, arterial measurements of PaO₂, measuring the alveolar to arterial oxygen gradient, i.e. A-a gradient and keeping in mind the age of the patient, co-morbid conditions and



supplemental oxygen.[6]

The above discussion allows us to elaborate on happy hypoxia. *Happy hypoxia* is a state of apparent normalcy in terms of breathing, i.e. there is no perception of difficult breathing or uncomfortable breathing to the patient, and the patient seems comfortable despite the PaO₂ levels being subnormal.

Neuroinvasive SARS-CoV-2 & hypoxia

Neurotropic property of CoVs has been documented for many of the β CoVs (Beta Corona Viruses), including SARS-CoV, MERS-CoV.[20,21] It is possible that SARS-CoV-2 could behave in a similar neuroinvasive fashion. The entry of SARS-CoV-2 into the nervous system could be explained by both retrograde neuronal or hematogenous routes.[22]

The ACE2 receptors in the nasal mucosa and the chemoreceptors are one of the potential areas which SARS-CoV-2 may target. The SARS-CoV-2 virus could be gaining entry into the CNS via the olfactory mucosa to reach the cribriform plate, the olfactory bulb and finally to the olfactory neurons. Here there could be a possible transsynaptic transfer of the virus, and it reaches the brain stem where the RC is encountered.[22] Here, it causes the breakdown of the RC leading to its dysfunction in a manner where hypoxia is present. However, because it has collapsed, there is no further projection of this message to the cortex and insula leading to the absence of any perception of discomfort in breathing or dyspnea. The virus could also enter the CNS via hematogenous route, in which endothelium could be the culprit.[22]

Three mechanisms can explain the hematogenous route of viral transmission into neural tissues. The virus attacks endothelial cells of the blood-brain barrier directly to allow itself access to neural tissue. It could mimic the Trojan horse model, as is seen in HIV (Human Immunodeficiency Virus) infections. In this, infected immune cells are introduced into the neural tissues. Another mechanism is via transcytosis wherein the virus crosses the endothelial cells with the help of endocytic vesicles.

There is a need for more clarity in the hematogenous spread of neurotropic SARS-CoV-2.[22] Another example to support the cause of neurotropism causing happy hypoxia is the development of hyposmia/anosmia in SARS-CoV-2 infected patients. This could be because the virus reaching the olfactory neurons damages them, which leads to the presentation of impaired smell sensation. Studies have shown that after exposure to SARS-CoV by inhalation, it was detected at the olfactory bulb and higher neural tissues a few days later. Similar observations were made with another virus of the betacoronavirus family. Another study showed that disconnecting the olfactory pathway did not allow coronavirus to reach higher neural tissues in an animal model.[23]

So, going by the high homology between SARS-CoV and SARS-CoV-2, the general nature of coronaviruses to have an affinity towards neural tissue and evidence shown in animal studies, one may not be wrong to assume that SARS-CoV-2 is indeed neuroinvasive. Moreover, it may also be one of the mechanisms driving happy hypoxia.

Happy hypoxia is being reported very frequently in literature in association with COVID-19.[14,19,24,25,26] Apart from neuroinvasive cause of happy hypoxia there has been accumulating evidence of several other contributing factors to happy hypoxia.

On the basis of many factors, Gattinoni et al. have proposed the presence of 2 phenotypes: The L phenotype has been defined for a lung which has low elastance or high compliance, low V/Q

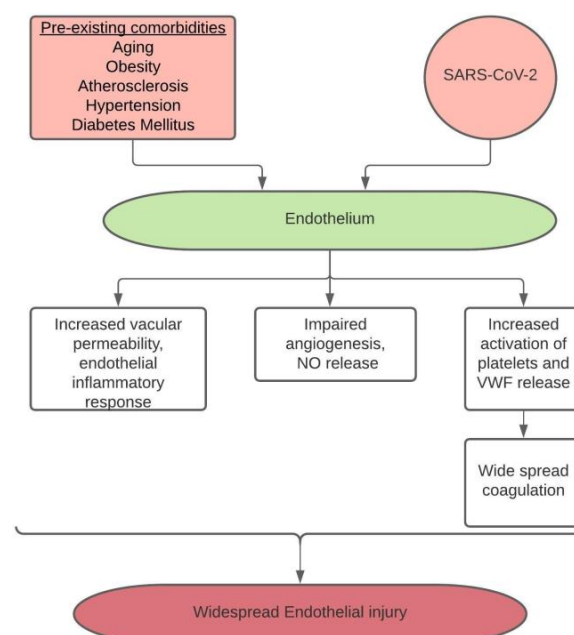


Figure 1: Endothelial injury.

ratio, low lung weight and low recruitability. The H phenotype meanwhile encompasses a lung with high elastance, high right-to-left shunt, high lung weight and high recruitability. Gattinoni et al. say that once there is an established viral infection, there is a reasonable amount of oedema that is seen in areas of the elastic lung. The viral infection seems to affect this elastic property of a normal lung. This contributes to high compliance of the lungs. The Italian scientists also suspect a dysfunctional hypoxic vasoconstriction mechanism in SARS-CoV-2 infections. Hypoxic vasoconstriction is a physiological phenomenon where the pulmonary vessels constrict in response to hypoxemia in order to allow blood flow only to the aerated lung tissue.[27] Reasons for this could be the ensuing endothelial damage that seems to be occurring.[28]

According to figure 1, pre-existing conditions such as ageing, obesity, atherosclerosis, hypertension and diabetes mellitus play a role in endothelial dysfunction. Similarly, the endothelium is also damaged with the entry of SARS-CoV-2 virus.[28] Tang et al. have reported that 71.4% of COVID-19 non-survivors are patients with DIC (Disseminated Intravascular Coagulation).[29] Studies have shown disrupted junctions, endothelial cell swelling as well as disruption of contact between the basement membrane and the endothelium. These findings are further corroborated by the detection of SARS-CoV-2 virus in the endothelial cells itself: an ominous sign of endothelial damage ensuing dysfunction.[30]

Now, the normal response to hypoxemia is increased respiratory drive, i.e. there is an increase in tidal volume, which again is a consequence of an increase in the negative intrathoracic pressure, further increasing compliance. This gives a picture of a proportional increase in both negative intrathoracic pressure and ventilation, maintaining near-normal compliance. This explains why a happy hypoxic could present without any dyspnea as the patient is inhaling the volume of air that is expected.[27]



Effect of various strains of SARS-CoV-2 on Happy Hypoxia

There is evolving literature on the genomic diversity of SARS-CoV-2. There is a paucity of data in this aspect. However, a British physician has proposed that the severity of COVID-19 hangs more on the host's response than a variation in genome diversity.[31]

Co-morbidities and Happy hypoxia

Although this is an evolving topic, there has been a fairly comprehensive study from France that has delineated data on the relationship between comorbidities, age, gender with happy hypoxia.

Patients as they age and diabetics tend to have a respiratory centre which may be desensitised to changes in gaseous elements. Silent hypoxia or happy hypoxia is more likely to have a poor outcome in those who are aged, male and those with chronic diseases.[32]

Virus-induced C-dysfunction & hypoxia

The peripheral afferent fibres present in respiratory tract respond to relevant stimuli and drive responses such as cough, tachypnea and dyspnea. These fibres are pulmonary C-fibres. Local changes in viral pneumonia could stimulate C-pulmonary fibres. The cytokine storm syndrome, a phenomenon touted to be characteristic of SARS-CoV-2 infection has the potential to damage these fibres and can be incriminated in a total or partial loss of their function. However, this hypothesis does collide in that some viral respiratory pathogens can induce upregulation of these fibres.[18,33] Virus-induced C fibres dysfunction could contribute to the absence of dyspnea in SARS-CoV-2 pneumonia.[18,33]

Role of RAS and Bradykinin in SARS-CoV-2

What is Renin Angiotensin System?

The RAS (Renin-Angiotensin System) maintains an equilibrium between blood volume and pressure with several products of the peptide angiotensin and its receptors. Figure 2 depicts the actions of ACE (Angiotensin Converting Enzyme) and ACE2. AT1 (Angiotensin receptor 1) allows vasoconstriction and sodium retention. The AT2 (Angiotensin receptor 2) receptor allows vasodilation and natriuresis. AngII (Angiotensin II) is an agonist at the AT1 receptor. The MAS1 receptor allows for vasodilation, anti-inflammatory and anti-fibrotic processes. Ang1-7 (Angiotensin 1-7) is an agonist at the MAS1 receptor and the AT2 receptor. Ang1-9 (Angiotensin 1-9) also is an agonist at the AT2 receptor. All these must be viewed as an interlinked web.[34]

Vitamin D is a RAS regulatory molecule. Renin expression can be suppressed by Vitamin D. This invariably increases AngII levels and with it, enhances its deleterious effects. ARDS has been implicated in those with vitamin D deficiency.[35]

What is Bradykinin?

BK (Bradykinin) is a product formed via the kinin-kallikrein pathway. In conjunction with the B2R (Bradykinin receptor 2) receptor, bradykinin's actions include vasodilation, natriuresis, and plasma exudative behaviour, increased vascular permeability. It perpetuates chronic inflammation with the B1R (Bradykinin receptor 1) receptor. It is responsible for a cough reflex, bronchoconstriction, and increases airways resistance.[35]

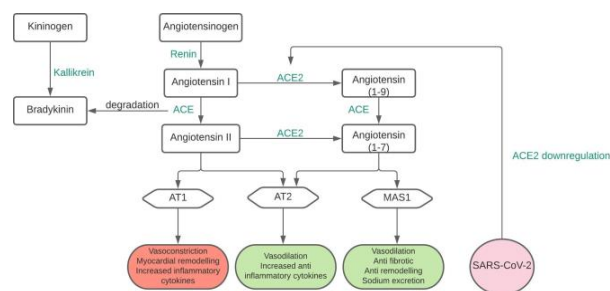


Figure 2: Renin Angiotensin System.

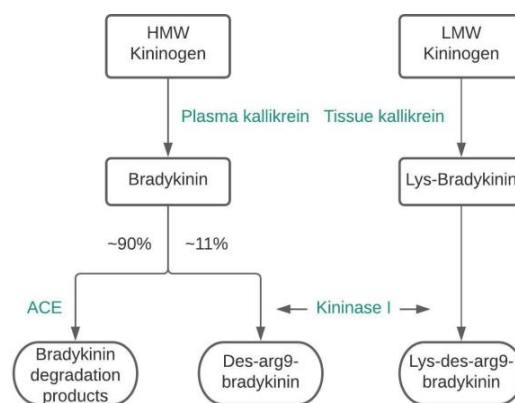


Figure 3: Kinin Kallikrein pathway.

Bradykinin regulation

The kinin-kallikrein system on activation produces kinins. BK binds to its receptors on endothelial cells to increase vascular permeability and cause capillary leakage.

As pictured, BK is generated by proteolysis of kallikrein on kininogens. Kallikreins are serine proteases and can be divided into plasma kallikreins and tissue kallikreins.[35,36,37] In order to regulate these BKs, there are measures in place to degrade these molecules in a timely fashion.

Kinins are broken down to inactive molecules by kininases I and II. Plasma carboxypeptidase M/N is another name for kininase I. It acts on BK or Lys-Bradykinin to yield des-arg9-bradykinin or Lys-des-arg9-bradykinin, respectively, which are ligands for B1R. B1R is a bradykinin receptor on endothelial cells that are up-regulated under pro-inflammatory conditions. Cytokine storm is one of the hypotheses suggested for SARS-CoV-2 and inflammatory mediators like IL-1 and TNF- α as part of this syndrome can up-regulate B1R. Kininase II is identical to ACE. Bradykinin and Lys-bradykinin are the ligands that stimulate the constitutively produced B2R receptors on endothelial cells.[36,37]

RAS and Kinin-Kallikrein pathways

About 90% of bradykinin is degraded by ACE. This keeps bradykinin localised and keeps its varied effects in check. About 11% of bradykinin, however, is converted into des-Arg9-bradykinin by kininase I. ACE2 which strongly prefers to cleave des-Arg9-bradykinin is dysfunctional in SARS-CoV-2. This allows an unchecked increase in AngII, which can potentiate

its vasoconstrictor role just as increased des-Arg9- bradykinin can potentiate its damaging role in vasculature via B1R activation.[36,37]

From this discussion, we can infer that ACE and ACE2 are important for keeping excessive kinins in check and its supposed dysfunction by the SARS-CoV-2 virus could lead to lung injury and more importantly severe outcomes like ARDS. Upregulation of ADAM-17 and subsequent activation of inflammatory mediators further suppress ACE2 expression. This, in turn, up-regulates RAS and AngII, pronouncing its effects. In part, due to the inflammation of respiratory tissue, programmed death of ACE2 producing cells occurs, i.e. Clara cells and type II pneumocytes die, further reducing ACE2.[38]

These pathogenic developments could be damaging to mechanisms of dyspnea, leading to the lack of it or increasing the severity of it in later stages of the disease course.[36,37] So, it wouldn't be odd to deduce that SARS-CoV-2 interaction with ACE2 down-regulates the function and expression of ACE2. To summarise, the kinin-kallikrein system is affected by SARS-CoV-2 patients. Studies have detected BK precursor kininogen, and kallikrein zymogens in SARS-CoV-2 patient samples and bradykinin degradative enzymes have been noted to be down-regulated. B1R is normally expressed at basal levels. However, in the case of SARS-CoV-2, both BK receptors are expressed in great amounts. SERPING1 gene that codes for the C1-Inhibitor that inhibits FXII, the starting point for the extrinsic pathway of coagulation is highly down-regulated, which further increases BK.[38] This leads to the discussion of Bradykinin Storm.

Hyaluronic acid synthesis and degradation

Before we begin to explain bradykinin storm, we must understand another component of it which is hyaluronic acid (HA). HA is a complex carbohydrate polymer found in connective tissues. HA is known to be able to trap about 1000 times its weight in water, and when in conjunction with water, it results in a hydrogel. One could compare it to 'jello'. Hyaluronan synthase is an enzyme that is coded by the HAS1, 2, and 3 genes. It is the enzyme responsible for HA production. HA is degraded by hyaluronidases, and they are encoded by the HYAL1 and HYAL2 genes. Both of these genes interact with CD44 (an HA receptor) for their activity.[38]

In SARS-CoV-2, studies have suggested that HA synthases are up-regulated and hyaluronidases down-regulated. CD44 gene codes for the HA receptor required for its degradation. As a result, there is increased amounts of HA in the lung tissues, which along with increased kinins could form hydrogel material of thick consistency, negatively impacting gas exchange or diffusion.[38] Additionally, it has been suggested that Ang II up-regulates CD44 expression.

Elevated kinins can induce IL-2, which has been found in high concentrations, via CD44, causing vascular hyperpermeability. Interestingly, CD44 knockout models do not show hyperpermeability features.[38] This involvement of HA in association with RAS and BK pathways strengthen the hypotheses that there is in fact, the involvement of all these pathways in the pathogenesis of SARS-CoV-2.

Build up of such 'jello' material, and further development of ARDS would definitely lead to diffusion defects in the pulmonary alveoli, thereby hypoxemia and an increase in the A-a gradient all of which will finally materialise as respiratory symptoms of breathlessness, air hunger. It also implies that apart from the cytokine storm, which has been cited as one of the damaging

factors of SARS-CoV-2, there are other pathways too in play.

Bradykinin storm

Increased production of HA, dysfunctional RAS and bradykinin pathways all culminate to affect the gas exchange. The viscous 'jello' accumulating in the bronchoalveolar spaces is incriminated for this phenomenon. HA has long been associated with the development of ground-glass opacities, and rightly so, hyaline membranes correlating to ground glass radiographic appearance have been seen in SARS-CoV-2 patients. The hydrogel is also responsible for somewhat heavy lungs that are seen in severe SARS-CoV-2 patients as discovered by a study which states SARS-CoV-2 lungs are 4.6 heavier than healthy ones. Although this hydrogel formation seen in ARDS patients represents a late-stage event in severe cases of SARS-CoV-2 infections, if the cause is indeed an overproduction of HA, it could be a point of valuable intervention as the condition can be easily identified, and treated.[29]

Greatly increased kinins can cause electrolyte derangements like hypokalemia which is a known arrhythmogenic and can cause sudden cardiac death. A recent report on this matter corroborates that hypokalemia occurs in severe SARS-CoV-2 infections. Symptomatic SARS-CoV-2 patients may also present with features like myalgia, fatigue, nausea, vomiting, diarrhoea, anorexia, headaches, all of which are seen in conditions of increased kinins. Keeping these pieces of evidence and theories in mind, it could be postulated that the pathology of SARS-CoV-2 could likely be the result of a predominant bradykinin storm than a cytokine storm, although, given the induction of IL-2 by BK, the two may be intricately linked.[38]

Coagulation cascade and SARS-CoV-2

Venous thromboembolism, acute limb ischemia, pulmonary embolism are some of the features of hypercoagulability. These have been reported in many SARS-CoV-2 patients. However, these seem to be a feature of severe COVID-19 disease. In light of inflammation, these thrombotic complications are being known as thromboinflammation or COVID-19-associated coagulopathy.[39] After entering the body, SARS-CoV-2 is recognised by the PAMP (Pathogen Associated Molecular Pattern) in the body to activate the immune system to clear the virus. However, excessive activation can cause a cytokine storm, damage the microvascular system, activate the coagulation system, inhibit fibrinolysis and the anticoagulant system. The resulting extensive thrombosis in microvessels could lead to DIC, microcirculation disorders and even MODS (Multiple Organ Dysfunction Syndrome).[40]

Thromboinflammation

Once a viral pathogen enters the realm of the immune system, it triggers the cascading coagulation reactions. These reactions are capable of now influence the inflammatory response. The action of both inflammation and coagulation together is called thromboinflammation.[39] TNF- α , IL-6, and IL-1 β are inflammatory mediators and are produced in excess in thromboinflammation. These mediators in excess cause a cytokine storm. In particular, IL-6 encourages the expression of tissue factor to activate thrombin. IL-6 has been seen in increased amounts in COVID-19 patients.[39]

Tissue factor is also the trigger that switches on the extrinsic coagulation cascade.[41] The intrinsic pathway is also activated



in the presence of inflammatory mediators because of their action on vascular endothelium. The enormous cytokine explosion, in conjunction with viral inflammation, leads to increased vascular permeability, multi-organ failure, and even death if high cytokine concentrations persist.[39]

These thrombotic features can be seen even in pulmonary vasculature foci of bleeding and microthrombi and can cause impaired gas exchange leading to hypoxemic conditions.[39] In this environment of inflammation and widespread thrombosis, there is increasing hypoxemia. This further starves the endothelial cells of oxygen, allowing more damage to it and circling back to increase coagulation. This set up is a vicious cycle of thromboinflammation.[39]

Alternative explanations for procoagulant blood with SARS-CoV-2 infections have also been suggested. Anticardiolipin, anti-B2 glycoprotein antibodies have been detected in SARS-CoV-2 patients. These are components seen in antiphospholipid syndrome and are known for their hypercoagulable activities.[42]

IL-6 Hypoxia and Protein S

Another aspect of hypoxia and the IL-6 induced cytokine storm is that both factors down-regulate a key anticoagulant, Protein S. It has been shown that in a population of stroke patients, IL-6 was up-regulated, and it caused downregulation of Protein S that resulted in venous thrombosis. It has also been demonstrated that hypoxia down-regulates Protein S expression. Protein S supplementation in experimental setups alleviated some symptoms of the infection. A substantial number of cases of severe infection with SARS-CoV-2 manifest both hypoxia and prothrombotic complications. As both hypoxia and IL-6-induced inflammation depress Protein S abundance, it may be reasonable to consider administration of Protein S in severe SARS-CoV-2 patients.[39]

Cytokines and SARS-CoV-2

Immune dysregulation in SARS-CoV-2

ACE2 is dysfunctional upon interaction with SARS-CoV-2. This signals changes in the RAS with AngII inciting pro-inflammatory cytokines. Epidermal growth factor receptor and TNF- α are produced by way of AngII activating NF- κ B and ADAM17. sIL-6R α , the soluble form of IL-6R α is formed under the influence of ADAM17. sIL-6R α allows the activation of STAT3. With both STAT3 and NF- κ B turned on, IL-6, the main mediator of inflammation is amplified and ready to exude a state of hyperinflammation.[42]

Few studies have shown that the development of cytokine storm syndrome could be due to the imbalance between proinflammatory and anti-inflammatory mechanisms, resulting in immune regulation disorder, presenting as an array of clinical features.[42]

ACE2 is ubiquitously found in the body. In SARS-CoV-2 patients, ACE2 was found on immune cells in the spleen and lymph nodes, suggesting that cells with ACE2 expression may also be infected with SARS-CoV-2. Another interesting phenomenon is the expression of activated monocytes in the peripheral circulation of infected COVID-19 patients. The activated monocytes can be identified easily as they express various clusters of differentiation subsets on their surface and are capable of producing inflammatory cytokines. Disease severity is high in those detected with activated monocytes.CD163, which is one of the subsets of CD expressed on the monocyte surface has been linked to hemophagocytic lymphohistiocytosis. This disease is

known to produce excessive inflammatory cytokines. All these mechanisms seem to be playing an active role in raging a cytokine storm and allowing deterioration in patient's health.[43]

Complement system contribution to Cytokine storm

The complement is an arm of the innate immune system which includes components that play a key role in defence against microorganisms including viruses. The viral inactivation by the complement cascade involves virus uptake, clearance by phagocytic cells, opsonising viruses, virus lysis and destruction of its membrane by membrane attack complex formation (C5b-9). This viral-induced complement activation promotes inflammatory processes. The strongest inflammatory peptide in the complement cascade is a complement factor 5a (C5a). It allows the secretion of pro-inflammatory cytokines along with C3a. Monocyte chemoattractant protein-1, activator protein-1, and NF- κ B under the influence of C5b-9 induce the release of IL-6 from vascular smooth muscle cells. [43,44]

Studies have shown that mice models deficient in C3 loads had milder SARS-CoV induced pathologic features like better respiratory function, reduced pathologic findings in the respiratory system, and lower circulatory and tissue cytokines and chemokines. This shows that activation of the complement system in the lungs of SARS-CoV infected mice leads to immune-mediated damages in the lungs.[44] Recent studies reported the involvement of excessive complement activation in SARS-CoV-2 via viral nucleocapsid N protein-mediated MBL (mannose-binding lectin) pathway Accelerated inflammatory behaviour, and lung damage is seen with MASP-2, a protease in the lectin pathway that induces downstream complement cascade.[44] There is enough evidence that goes to show the involvement of complement and its role in immune-mediated damage in SARS-CoV-2 patients.

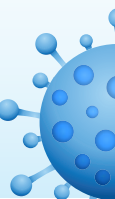
Treatment protocols

Hypoxia and its subtype, happy hypoxia can be identified fairly easily with the help of pulse oximetry and ABG (Arterial Blood Gas) analysis. When identified early, it can influence management strategies and avoid inadvertent iatrogenic errors.

In the initial days of the pandemic, the worst-hit nations faced before them cases of severe hypoxia. In the absence of clear cut protocols and the fear of aerosolisation of viral particles upon NIV (Non-Invasive Ventilation) and HFNC (High Flow Nasal Cannula), intubation became the primary management tool.[45]

Usually, hypoxia irrespective of symptoms is treated, but in a stepwise manner which includes high flow nasal cannula and non-invasive ventilation. This step-wise manner for various reasons was not employed in the treatment of COVID-19. [45,46]. There was excessive dependence on invasive ventilation for the treatment of COVID-19 patients. This resulted in a high mortality rate.[45]

The L phenotype, as discussed allows an increase in negative intrathoracic pressure and this over time may lead to a state of P-SILI (Patient Self Inflicted Lung Injury) in the backdrop of increasing inflammation to combat the virus. This ongoing situation increases oedema, thereby adding extra pressure. When this process reaches the threshold, the quantities of gas and the tidal volumes reduce. This can cause atelectasis. At this point, there could be a transit from L type to H type. The H type is prototypical for severe ARDS criteria which includes severe hypoxemia, bilateral infiltrates, high lung weight, decreased compliance and high recruitability.[27,47]



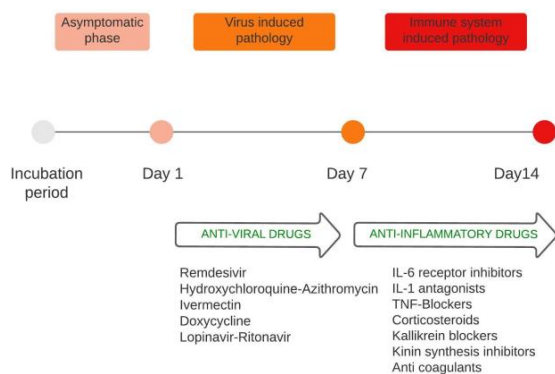


Figure 4: Timeline of SARS-CoV-2 infection.

The L-type deals with a dysfunctional hypoxic vasoconstriction mechanism and a V/Q mismatch leading to hypoxia. It would be useful, therefore to first provide FiO₂ to which these patients respond well. [27,47]

Prone positioning is another way to allow better oxygen delivery. It is a simple, effective, cost and personnel saving measure. Half an hour to two hours each in prone left lateral decubitus and right lateral decubitus have been helpful.

It could even be escalated to the use of non-invasive methods of oxygen delivery, i.e. HFNC, continuous positive airway pressure (CPAP) and NIV. [45]

If the respiratory drive is still uncontrolled, this would mean there is still a strong inspiratory effort which could further worsen P-SILI.[27,47]

Such patients may do well with early intubation. Type L patients with their increased compliance can tolerate high tidal volumes better than a Type H patient. Such patients require ventilator settings with reasonably high tidal volumes (7-9 mL/kg) and a low positive end-expiratory pressure(PEEP) of about 8-10cms of H₂O.

In type H, use of higher PEEP (>10 cms of H₂O) and lower tidal volumes (5-7 mL/kg) could be beneficial.[27,47]In conclusion, identifying and differentiating these 2 types of presentations may not only help with management but also drastically bring down mortality rates. Apart from treating hypoxia, there are several other target points in this disease which if identified, can help in recovery.

As depicted in figure 4, there may be a vague demarcation in the phases of this infection.[49]Accordingly, one must be able to identify and stratify the patients so that they are treated in a timely fashion and accurately.[49] In the first week of the infection, the viral load is high. It is high enough to cause pathology.[49]Drugs have been instituted to uniquely affect the life cycle of SARS-CoV-2 in vivo. Frantic measures such as repurposing of drugs have also come to the forefront in the form of ivermectin, Hydroxychloroquine, doxycycline, to name a few.[49] After being tested in a variety of clinical trials, there have been polarising results on remdesivir's beneficial effects.[41,47] Hydroxychloroquine, lopinavir-ritonavir have been shown to have no beneficial effects on COVID-19 mortality rate, hospitalisation duration or even initiation of ventilation according to the landmark Solidarity trial.[47]

Soon enough, the host immune system is triggered to fight

the invading pathogen as seen around day 7.[48]Unfortunately, it has been observed that the immune system is activated too little and too late.[48]

Since cytokines are being incriminated in the pathogenesis of SARS-CoV-2, blocking these cytokines may be beneficial. Antagonising NF- α B translocation, TNF- α , IL-1 will down-regulate their actions at the B1R. Anakinra is a well-known drug with a remarkable safety profile and blocks both alpha and beta components of IL-1.[35]

Tocilizumab, an IL-6 receptor blocker, is being tried to combat inflammatory actions of IL-6.[50]TNF blockers is a therapeutic intervention.[35]One must, however be aware of their well documented adverse effects. Since severe SARS-CoV-2 patients have a long drawn out disease, and there are many inflammatory characteristics in this disease, anti inflammatory drugs in the form of corticosteroids may be used.[34] Another approach would be the modulation of Renin levels via Vitamin D supplementation.[34]

Blocking kallikreins will result in less kinins and decreases both B2R and B1R ligands at the site of infection and subsequently less leakage via B1R and B2R. The drugs namely are aprotinin/ecallantide .[35,36]Mechanism of action of aprotinin is that it is a nonspecific serine protease inhibitor and preferentially works against plasmin and kallikrein. Aprotinin inhibits factor XII and prevents the activation of the extrinsic coagulation pathway. It also has a role to play in inhibition of the intrinsic pathway of coagulation, fibrinolysis, and attenuation of the pro-inflammatory response.[51]There has also been supportive date to support the anti-inflammatory actions of Aprotinin.[51,52]

Lanadelumab is a monoclonal antibody against the plasma kallikrein. Lanadelumab has been used for the treatment of angio oedema. The rationale to suggest lanadelumab is that this mAb can block the upstream axis that leads to kinin formation, avoiding the inflammatory and coagulation storm besides the complement system in SARS-CoV-2 infected patients, likely preventing the exacerbation of COVID-19.[53]

Blocking B1R and B2R signaling is another target for therapy. A B2R antagonist drug by the name of Icatibant has been approved for the treatment of hereditary angio oedema. A B1R antagonist drug is not yet available. Antagonism at the receptor level would be a good way to contain the virus severity.[35,36] Zinc could be of valuable mention here. Zinc is known to inactivate the serine proteases that the kallikreins are. This could explain the rationale behind zinc supplementations that have been suggested by authorities in the prevention and treatment of SARS-CoV-2 infections.[36]

Since coagulopathy has become a common observation in severe COVID-19 patients, it has become a norm to check on patients' coagulation parameters. Moreover, these parameters are also helping predict the progression of this disease. D-Dimer is one such parameter. Deranged parameters of coagulation warrants LMW heparin as a prophylactic.This therapy has become commonplace in the treatment of SARS-CoV-2.[54,55]

Conclusion

Asymptomatic hypoxia must be identified and addressed early in order to institute prompt care. In general, clinicians must have a low threshold for suspecting breathing troubles. Tachypnea and decreasing SpO₂ must raise the alarm for an impending respiratory failure. Frequency of respiration, chest retractions and use of accessory muscles must be accounted for when examining a patient. A high minute volume is must be looked into, and the clinician must identify the possible compensation



happening because of deranged gas exchange. Such patients likely require admission and radiographic studies can be used to aid in the diagnosis and management of this patient. Meanwhile, more studies to establish neurotropic causes for this silent hypoxia should be determined in order better to understand the management of patients with SARS-CoV-2 infection. The role of bradykinin in the pathogenesis of the SARS-CoV-2 infection must be further elucidated in studies in order to allow better treatment protocols and early recovery for patients. The RAS, bradykinin system, coagulation cascade, complement system and the cytokines are all in place to aid the body in destroying pathogens, and they work hand in hand. These interactions are complex and need more elucidation. Therapeutic agents, be it repurposed drugs or tailor-made drugs need more backing in terms of safety profile and efficacy. A clear picture of the pathogenesis of SARS-CoV-2 virus still seems to be evolving. As this evolves, so does our understanding of symptoms and signs such as breathlessness and dyspnea and so also, the management protocols.

Abbreviation

- COVID-19: Corona Virus Disease 2019
- SARS-CoV-2: Severe Acute Respiratory Syndrome Corona Virus 2
- RNA: Ribonucleic acid
- SARS-CoV: Severe Acute Respiratory Syndrome Corona Virus
- MERS-CoV: Middle Eastern Respiratory Syndrome Corona Virus
- ACE2: Angiotensin Converting Enzyme 2
- TMPRSS2: TransMembrane Serine Protease 2
- Respiratory centre: RC
- PaO₂: Partial gas pressure of dissolved oxygen in the blood
- PaCO₂: Partial gas pressure of dissolved carbon dioxide in the blood
- NTS: Nucleus Tractus Solitarius
- ARDS: Acute Respiratory Distress Syndrome
- PAO₂: Partial gas pressure of oxygen at the alveoli
- RSV: Respiratory Syncytial Virus
- ODC: oxygen dissociation curve
- SaO₂: Oxygen saturation in the blood
- Hb: Haemoglobin
- SpO₂: Oxygen saturation measured by pulse oximetry
- βCoVs: Beta Corona Viruses
- HIV: Human Immunodeficiency Virus
- DIC: Disseminated Intravascular Coagulation
- RAS: Renin-Angiotensin System
- ACE: Angiotensin-Converting Enzyme
- AT1: Angiotensin receptor 1
- AT2: Angiotensin receptor 2
- Ang II: Angiotensin II
- Ang 1-7: Angiotensin 1-7
- Ang 1-9: Angiotensin 1-9
- BK: Bradykinin
- B2R: Bradykinin receptor 2
- B1R: Bradykinin receptor 1
- HA: Hyaluronic acid
- PAMP: Pathogen Associated Molecular Pattern
- MODS: Multiple Organ Dysfunction Syndrome
- MBL: Mannose-Binding Lectin
- ABG: Arterial Blood Gas
- NIV: Non-Invasive Ventilation

- HFNC: High Flow Nasal Cannula
- P-SILI: Patient Self Inflicted Lung Injury

Funding

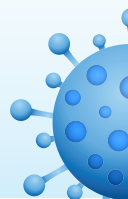
This study received no fund.

Conflict of interest

There are no conflicts of interest to declare by any of the authors of this study

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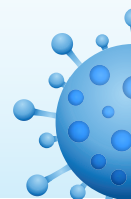
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Review article

Antiviral and immunomodulatory activity of curcumin: A case for prophylactic therapy for COVID-19

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ABSTRACT

Coronavirus disease-19 (COVID-19), a devastating respiratory illness caused by SARS-associated coronavirus-2 (SARS-CoV-2), has already affected over 64 million people and caused 1.48 million deaths, just 12 months from the first diagnosis. COVID-19 patients develop serious complications, including severe pneumonia, acute respiratory distress syndrome (ARDS), and or multiorgan failure due to exaggerated host immune response following infection. Currently, drugs that were effective against SARS-CoV are being repurposed for SARS-CoV-2. During this public health emergency, food nutraceuticals could be promising prophylactic therapeutics for COVID-19. Curcumin, a bioactive compound in turmeric, exerts diverse pharmacological activities and is widely used in foods and traditional medicines. This review presents several lines of evidence, which suggest curcumin as a promising prophylactic, therapeutic candidate for COVID-19. First, curcumin exerts antiviral activity against many types of enveloped viruses, including SARS-CoV-2, by multiple mechanisms: direct interaction with viral membrane proteins; disruption of the viral envelope; inhibition of viral proteases; induce host antiviral responses. Second, curcumin protects from lethal pneumonia and ARDS via targeting NF- κ B, inflammasome, IL-6 trans signal, and HMGB1 pathways. Third, curcumin is safe and well-tolerated in both healthy and diseased human subjects. In conclusion, accumulated evidence indicates that curcumin may be a potential prophylactic therapeutic for COVID-19 in the clinic and public health settings.

1. Introduction

Coronavirus disease-19 (COVID-19) is a dreadful respiratory illness caused by a newly discovered coronaviruses (CoV) strain known as SARS-CoV-2. SARS-CoV-2 much resembles SARS-associated coronavirus (SARS-CoV) that caused the SARS pandemic in 2003. It was first detected in Wuhan city, Hubei province, China, in December 2019, and as of Dec 02, 2020, over 64 million people are diagnosed with COVID-19, with around 1.48 deaths reported across the world (*Source: Johns Hopkins University*). WHO has declared COVID-19 as a global pandemic, and the prediction is that the number of deaths due to COVID-19 will further worsen in the coming months (Abais et al., 2015; Wu et al., 2020b). In most cases, COVID-19 patients exhibit fever, dry cough, dyspnoea,

fatigue, and myalgia (Chen et al., 2020c; Huang et al., 2020; Wu et al., 2020a). However, in severe cases, COVID-19 patients develop fatal complications such as severe pneumonia, acute respiratory distress syndrome (ARDS), septic shock, arrhythmia, and acute cardiac injury (Wang et al., 2020). Other than the management with ventilator support and other supportive care, there are no effective treatments available for COVID-19. Therefore, there is an urgent need for the discovery and development of therapeutics for COVID-19.

The discovery and development of an effective therapeutic agent against SARS-CoV-2 is a time-consuming process. Alternatively, repurposing of already-licensed pharmaceuticals may provide a faster path for developing effective therapeutics for COVID-19. First, effective drugs against SARS-CoV were tested against SARS-CoV-2 in the laboratory and

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clinical settings, and the results were very encouraging. These studies prompted WHO to initiate a large global mega trial called 'SOLIDARITY' for testing four therapeutics for COVID-19: i) remdesivir, an inhibitor of RNA-dependent RNA Polymerase; ii) antimalarial drugs chloroquine and hydroxychloroquine; iii) anti-retroviral drugs, lopinavir-ritonavir that are HIV protease inhibitors; and iv) immunomodulatory agent, interferon-beta. Additionally, vaccine trials (Amanat and Krammer, 2020) and convalescent plasma therapy (Bloch et al., 2020; Shen et al., 2020) for SARS-CoV-2 are also under investigation; the outcomes are very promising. So far, some vaccination trials for COVID-19 have shown to be safe and effective in inducing robust humoral and cellular responses in the participants (Jackson et al., 2020; Ramasamy et al., 2020; Walsh et al., 2020). Although it is good news, it is likely to take many months to vaccinate the entire global population.

Along with repurposing approved drugs, scientists are also actively seeking safe, natural products with antiviral pharmacological activity as potential prophylactic therapeutics for COVID-19. Turmeric (*Curcuma longa*) is a perennial herbaceous, rhizomatous plant of the ginger family Zingiberaceae. It is widely used in Ayurveda, Siddha, and traditional Chinese medicines for its medicinal properties such as antiviral, analgesic, antimicrobial, antiproliferative, and anti-inflammatory activity (Aggarwal and Sung, 2009; Karimi et al., 2019; Padmanaban and Rangarajan, 2016; Patel et al., 2020). Turmeric is also the most popular spice across the globe, especially in India. Turmeric's medicinal properties are primarily attributed to three main curcuminoids—curcumin, demethoxycurcumin, and bisdemethoxycurcumin. Curcumin (diferuloylmethane) is the most abundant bioactive curcuminoid in turmeric. It elicits diverse pharmacological activities, including antioxidant, anti-inflammatory, antibacterial, antiviral, and immunomodulatory activity (Aggarwal and Sung, 2009; Karimi et al., 2019; Padmanaban and Rangarajan, 2016; Patel et al., 2020). Curcumin has been an effective antiviral agent against many enveloped viruses, including respiratory viruses such as influenza A virus and Respiratory Syncytial Virus (Praditya et al., 2019). More importantly, curcumin is also reported to be effective against SARS-CoV in in vitro studies (Wen et al., 2007). Additionally, findings from animal models suggest that curcumin supplementation intervenes in several respiratory diseases, in particular, acute respiratory distress syndrome (ARDS), acute lung injury, pneumonia, pulmonary fibrosis, and sepsis by modulating inflammation and oxidative stress (Lelli et al., 2017; Venkatesan et al., 2007). US Food and Drug Administration (FDA) has approved curcuminoids as "Generally Recognized As Safe" (GRAS). Several clinical studies have documented the tolerability and safety profile of curcumin both in healthy subjects and patients. In the present review, we have discussed i) broad-spectrum antiviral activity of curcumin against enveloped viruses including SARS-CoV-2; ii) immunomodulatory activity of curcumin against infectious ARDS; iii) safety profile. Because curcumin as a food component is consumed widely, we provide a strong case for testing curcumin as a promising prophylactic, therapeutic candidate for the treatment of COVID-19 in clinical and/or public health settings.

2. Pathophysiology of COVID-19

COVID-19 is caused by beta-coronavirus, and its genome sequence is 79% similar to SARS-associated coronavirus (SARS-CoV) (Lu et al., 2020); therefore, it was named SARS-CoV-2. SARS-CoV-2 is an enveloped virus with positive sense, single-strand RNA genome of size ~30 kb. Like other coronaviruses, the SARS-CoV-2 genome encodes for four major structural proteins—spike (S) protein, membrane protein, envelope protein, and nucleocapsid protein (Fehr and Perlman, 2015). The membrane protein is the predominant structural protein that helps in the virion assembly by interacting with other structural proteins and maintains the viral shape. Nucleocapsid protein interacts with the viral genome and regulates the replication process. Envelope protein is the smallest structural protein, which helps in viral maturation, and budding. The spike protein protrudes from the surface of the SARS-CoV-2 and attaches to

angiotensin-converting enzyme 2 (ACE2) protein expressed by target lower airway cells (ciliated epithelial cells and type II pneumocytes) and mediates the entry of the virus into the cell (Hoffmann et al., 2020; Walls et al., 2020). The Spike protein is a homotrimer, and each monomer of spike protein consists of S1 and S2 subunit. The S1 subunit consists of the receptor-binding domain that interacts with ACE2 (Tai et al., 2020). The SARS-CoV-2 spike protein binding affinity for ACE2 correlates well with the rate of transmissibility and severity of the diseases (Hoffmann et al., 2020; Walls et al., 2020; Zhou et al., 2020).

The pathogenesis of COVID-19 is yet to be completely understood; however, to a great extent, it resembles to severe acute respiratory syndrome (SARS) pandemic. Common symptoms associated with COVID-19 patients were fever, dry cough, myalgia, fatigue, and dyspnoea. The average time period from onset of symptoms to hospital admission was 7 days, and all patients with COVID-19 were associated with mild-to-severe pneumonia (Huang et al., 2020). The systemic inflammation, as indicated by plasma levels of multiple interleukins including IL2, IL7, IL6, IL10, GCSF, IP10, MCP1, MIP1A, and TNF α , was elevated in COVID-19 patients as compared to healthy subjects, which further increased in ICU admitted patients (Chen et al., 2020a; Huang et al., 2020). Also, ICU admitted COVID-19 patients showed an immunosuppressive phenotype characterized by severe lymphopenia and lower IFN-gamma levels (Chen et al., 2020a). Few COVID-19 patients in ICU also developed secondary infections. Histopathological analysis showed typical ARDS features, including an influx of mononuclear cells, including monocytes and lymphocytes, into air spaces, bilateral diffuse alveolar damage, and desquamation of alveolar epithelial cells, and hyaline membrane formation (Xu et al., 2020). The mortality was mainly due to respiratory failure caused by ARDS and multiorgan failure (Du et al., 2020; Huang et al., 2020).

3. Antiviral effects of curcumin against enveloped viruses including SARS-CoV-2

A large body of evidence has documented curcumin's direct antiviral activity against several enveloped viruses (Praditya et al., 2019), including SARS-CoV (Table 1). Wen et al. (2007) used cytopathic effects of SARS-CoV in Vero 6 cells as a cell-based assay to screen phytochemicals against SARS-CoV. They reported that curcumin (at 20 μ M and 40 μ M) showed significant anti-SARS-CoV activity. The same study reported that curcumin inhibits SARS-CoV 3CL protease activity, which is vital for viral replication. Few studies have utilized computational modelling tools and predicted that curcumin interacts with S protein and ACE2 protein and potentially intervenes in viral entry into lung cells (Pandey et al., 2020). Based on these pleiotropic effects of curcumin, it is postulated that curcumin may directly intervene SARS-CoV-2 entry and/or replication and prevent infection (Soni et al., 2020). 4-octyl-itaconate, a pharmacological agonist of transcription factor NRF2 was reported to repress SARS-CoV-2 replication in lung cells by an independent interferon mechanism (Olagnier et al., 2020). Furthermore, the same study revealed that the activation of the NRF2 pathway by another structurally dissimilar agonist dimethyl fumarate inhibited SARS-CoV-2 replication, suggesting that NRF2 agonists are potential drug candidates for repressing SARS-CoV-2 replication (Olagnier et al., 2020). We (Pandey et al., 2011; Thimmulappa et al., 2008) and others (Fattori et al., 2015; Jiménez-Osorio et al., 2016; Li et al., 2016) have previously reported that curcumin is a promising NRF2 agonist, and administration of curcumin activates NRF2 pathway in lungs of mice (Garg et al., 2008; Shen et al., 2015; Thimmulappa et al., 2008). So, it is conceivable that curcumin may also exert antiviral activity against SARS-CoV-2 by activating the NRF2 pathway.

A recent study employed genome-wide screening using CRISPR-Cas9 and discovered HMGB1 as an important pro-viral host factor in determining SARS-CoV-2 infection (Wei et al., 2020). HMGB1 is a non-histone nuclear protein that binds with DNA and regulates transcription (Harris et al., 2012). However, under stress conditions such as viral infection, the



Table 1. Antiviral effects of curcumin against enveloped viruses, which causes human diseases.

Sl. No.	Viruses Name	Conc. & Duration (Hours)	Human Disease	Mechanism	Reference
1	SARS-CoV	In vitro Study (20 & 40 μ M)	Severe acute respiratory syndrome	Inhibit SARS-CoV 3CL protease	(Wen et al., 2007)
2	Influenza A virus	In vitro Study (30 μ M)	Respiratory illness	Disrupts virus envelope; Inhibits haemagglutinin activity; Abrogates NF- κ B signaling	(Chen et al., 2013; Dai et al., 2018; Ou et al., 2013)
3	Respiratory syncytial virus	In vitro Study (10 μ g/ml)	Respiratory illness	Inhibits viral replication and budding	(Obata et al., 2013)
4	Herpes simplex virus type 1	In vitro Study (30 μ g/ml)	Cold sores	Not Reported	(Zandi et al., 2010)
5	Japanese encephalitis virus	In vitro Study (30 μ M)	Encephalitis	Disrupts of viral envelope	(Chen et al., 2013)
6	HIV	In vitro Study (30 & 40 μ g/ml)	AIDS	Inhibit HIV proteases & HIV-integrase	(Mazumder et al., 1995; Sui et al., 1993; Vajragupta et al., 2005)
7	Hepatitis B & C virus	In vitro Study (40 μ M) In vitro Study (20 μ M)	Liver disease	Downregulates PGC-1 α ; Inhibit RNA replication & viral assembly	(Anggakusuma et al., 2014; Rechtman et al., 2010)
8	Zika	In vitro study (5 μ M)	Zika Fever	Inhibit virus binding to host cell	(Mounce et al., 2017)
9	Chikungunya virus	In vitro study (5 μ M)	Chikungunya fever	Inhibit virus binding to host cell	(Mounce et al., 2017)
10	Dengue virus	In vitro study (52.97 μ g/ml)	Dengue fever	Disrupt viral envelope	(Chen et al., 2013; Nabila et al., 2020)

intracellular expression of HMGB1 is markedly elevated, and it is also secreted into the extracellular milieu (Harris et al., 2012). The extracellular HMGB1 function as a danger-associated molecular pattern further augments inflammatory responses by binding to Toll-like receptors and or activating inflammasome complex (Harris et al., 2012). Wei et al. (2020) observed that SARS-CoV-2 infection in Vero-E6 cells increased intracellular and extracellular levels of HMGB1. Furthermore, the authors found that genetic disruption of HMGB1 repressed SARS-CoV-2 replication in Vero cells. Mechanistic studies revealed that HMGB1 down-regulates transcriptional expression of ACE2 epigenetically, and the study concluded that HMGB1 antagonist might be a potential drug candidate for protecting from SARS-CoV-2 susceptibility (Wei et al., 2020). Several studies have demonstrated that curcumin pre-treatment represses HMGB1 expression (Da et al., 2019; Gu et al., 2015) and dampens HMGB1 mediated proinflammatory responses (Cheng et al., 2018; Wang et al., 2012). Therefore, curcumin supplementation may potentially protect from SARS-CoV-2 infection by down-regulating ACE2 expression.

Curcumin was also effective against the respiratory virus, influenza A virus (IAV), and respiratory syncytial virus (RSV), which are the common causal agents of acute respiratory infections in the community (Chen et al., 2013; Dai et al., 2018; Ou et al., 2013). Curcumin inhibits IAV hemagglutinin's binding, a homotrimeric membrane glycoprotein, with host cell receptors (Ou et al., 2013). Curcumin also impairs the replication and budding of RSV in human nasal epithelial cells by inhibiting NF- κ B and cyclooxygenase 2 signaling, implicated in RSV replication and budding (Obata et al., 2013). Mounce et al. (2017), reported antiviral effects of curcumin against the Zika and Chikungunya virus. The investigators demonstrated that curcumin or its derivatives attenuated the Zika and Chikungunya virus's infectivity by modifying its surface proteins, which resulted in blockage of its binding and entry into the host cells (Mounce et al., 2017). Curcumin and its analogs were also effective in inhibiting HIV replication by targeting HIV protease (Sui et al., 1993), HIV integrase (Mazumder et al., 1995; Vajragupta et al., 2005), and HIV tat protein (Ali and Banerjee, 2016). Anggakusuma et al. (Anggakusuma et al., 2014) studied the antiviral effects of curcumin against the hepatitis C virus. They observed that curcumin impaired virus binding and fusion with cell membranes by affecting the viral envelope's fluidity. Zen et al. (Chen et al., 2013) assessed whether curcumin's broad-spectrum antiviral activity is mediated by disruption of the enveloped virus's membrane structure. To address this, the authors evaluated the antiviral activity of curcumin against IAV, and other RNA enveloped virus (New castle disease virus, Dengue virus, Japanese encephalitis virus), and DNA enveloped (PRV swine herpes virus, vaccinia virus) in Vero cells. The authors observed that the curcumin effectively inhibited plaque formation when the virus was in-direct contact with the agent (during pre-and co-treatment experimental regimen); however, its antiviral activity was lost when Vero cells were treated post-infection. Furthermore, curcumin was ineffective against the non-enveloped virus, enterovirus 71. The authors concluded that curcumin's intrinsic ability to disrupt the membrane integrity of enveloped viruses was the common mechanism for inhibiting the viral infectivity (Chen et al., 2013).

Emerging evidence suggests that antiretroviral drug lopinavir-ritonavir, a protease inhibitor exerts antiviral activity against SARS-CoV-2 (Choy et al., 2020). Unfortunately, combination lopinavir-ritonavir in COVID-19 patients showed no clinical benefits (Cao et al., 2020); however, the results of other on-going trials with lopinavir-ritonavir awaited. Hoffmann et al. (2020) reported that camostat mesylate, an inhibitor of serine protease TMPRSS2, effectively blocked the entry of SARS-CoV-2. Lopinavir/ritonavir (Chu et al., 2004; Yao et al., 2020) and camostat mesylate were also effective against SARS-associated coronavirus (Zhou et al., 2015). In vitro studies have demonstrated the potency of curcumin to function as an HIV protease inhibitor (Sui et al., 1993).

In summary, curcumin exerts antiviral activity against the enveloped virus by multiple mechanisms such as direct interaction with viral

membrane proteins, disruption of the viral envelope, inhibition of viral proteases, and modulating host factors NF- κ B, NRF2 and or HMGB1 pathways. Given that in vitro studies have confirmed the antiviral activity of curcumin against SARS-CoV, it is tempting to speculate that curcumin may also attenuate SARS-CoV-2 infectivity by mechanisms as summarized above.

4. Immunomodulatory activity of curcumin suppress cytokine release syndrome and mitigates progression to ARDS

The death of severely ill COVID-19 patients is associated with respiratory failure and/or multiorgan failure caused by ARDS and septic shock. ARDS and/or sepsis's pathogenesis involves an early hyperactivated inflammatory response characterized by a "cytokine storm" (Chen et al., 2020a, 2020c). A positive association between cytokine release syndrome (CRS) and the severity of illness and mortality among COVID-19 patients is reported by many studies (Tang et al., 2020). Immunomodulatory drugs are likely to effectively mitigate ARDS progression or sepsis by dampening early inflammatory response following infectious insults (Tang et al., 2020; Yadav et al., 2017). A recently concluded clinical trial found that dexamethasone, a widely used immunomodulatory drug, effectively improved the survival of severely ill hospitalized COVID-19 patients compared to placebo (Horby et al., 2020; Tomazini et al., 2020). This finding has renewed the interest in finding safer and more effective immunomodulatory therapeutics to treat COVID-19. Analysis of lung transcriptome and the circulatory inflammatory cytokines profiles of COVID-19 patients indicated that NF- κ B, inflammasome, IL-6 trans-signaling, and HMGB1 signaling may be driving the CRS (El-Hachem et al., 2020; Lee et al., 2020). We present several lines of evidence to illustrate how pleiotropic effects of curcumin could dampen CRS and mitigate the progression to ARDS and/or sepsis in COVID-19 patients.

Curcumin administration via oral route alleviated reovirus 1/L-induced-ARDS in mice that recapitulate the clinical features of ARDS (Avasarala et al., 2013). The same study reported that curcumin lowered interleukins levels such as IL6, MCP1, and IFN gamma by abrogating NF- κ B activation in the lungs (Avasarala et al., 2013). In most cases, the clinical course of respiratory viral infection is exacerbated by secondary bacterial infections. Curcumin also effectively protects against lethal bacterial pneumonia (Zhang et al., 2019). Direct delivery of water-soluble curcumin into the lungs of mice infected with *Klebsiella pneumoniae* dramatically improved the survival and reduced lung and blood bacteremia compared to the vehicle-treated group. The improved survival of the infected mice treated with curcumin was associated with significantly reduced levels of inflammatory mediators (IL1 β , TNF α , IL6, KC) in bronchoalveolar lavage fluid, lung tissue, and serum as well as diminished oxidative tissue injury as compared to vehicle treatment (Zhang et al., 2019). Most studies have revealed that curcumin alleviates viral-induced pulmonary inflammation by abrogating the activation of NF- κ B signalling (Zhang et al., 2019) potentially by inhibiting upstream IKK β kinase activity (Jobin et al., 1999; Kim et al., 2011; Xu and Liu, 2017).

Cytokines, especially IL1 β and IL6, were markedly elevated in severely ill COVID patients admitted to intensive care units compared to stable COVID-19 patients (Conti et al., 2020; McElvaney et al., 2020). These observations have implicated inflammasome activation in driving CRS (Cauchois et al., 2020; Lee et al., 2020). Several studies have found the potency of curcumin to block inflammasome activation through Nod-like receptor family, pyrin domain-containing 3 (NLRP3), and inhibit secretion of mature IL-1 β (Yin et al., 2018)) and abrogate pulmonary inflammation (Liu et al., 2018; Zhang et al., 2019).

A growing body of evidence suggests that a higher circulatory IL6 level is predictive of severity of illness and mortality in COVID-19 patients (Nasonov and Samsonov, 2020), and abrogating IL6 signalling by JAK inhibitors is advocated to be an additional way to mitigate the progression to ARDS in COVID-19 patients (Nasonov and Samsonov, 2020). Although the direct role of IL6 per se in acute lung injury is

conflicting, IL6 is implicated in hyperactivation of immune responses; vascular dysfunction leading to multiorgan failure; fibrotic responses by trans signalling mechanisms in which the complex of IL6 with soluble IL6 receptor (SIL-6R) promote pro-inflammatory cytokine expression in T helper (Th)1 cells, monocytes and stromal cells (fibroblasts and endothelial cells) via activation of downstream JAK/STAT3 signaling (Barkhausen et al., 2011; Scheller et al., 2014). Selective blockade of IL6 trans-signaling pathway in macrophages dampened inflammatory cytokine secretion and protected from polymicrobial sepsis in mouse models (Barkhausen et al., 2011). CRS also mediates endothelial injury and increases the risk for coagulopathy in COVID-19 patients, further worsening the prognosis. Hospitalized COVID-19 patients are associated with elevated levels of plasminogen activator inhibitor-1 (PAI-1). Kang et al. (2020), reported that IL-6 trans-signaling plays a crucial role in endothelial dysfunction during microbial infection resulting in secretion of PAI-1, promoting thrombosis. The same researchers showed blockade of IL-6 trans-signaling by Tocilizumab decreased endothelial dysfunction and circulatory levels of PAI-1 in COVID-19 patients. Curcumin effectively blocked IL6 trans-signaling (Bharti et al., 2003; Hahn et al., 2018; Weissenberger et al., 2010) and inhibited the progression of inflammatory diseases (Zhao et al., 2016; Zhu et al., 2017). Curcumin is also reported to exert anticoagulant activity by reducing TNF alpha-induced endothelial tissue factor (Pendurthi et al., 1997)) and by directly inhibiting thrombin activity (Kim et al., 2012). Chen et al. reported that curcumin administration significantly reduced plasma fibrinogen and fibrin deposition in kidney in rat model of LPS-induced endotoxemia (Bierhaus et al., 1997).

Circulatory levels of HMGB1 positively correlate with severe illness in COVID-19 patients (Chen et al., 2020b). Extracellular HMGB1 functions as an inflammatory cytokine and plays a crucial role in the pathogenesis of acute lung injury and/ARDS (Andersson et al., 2020) by upregulating inflammation. In mouse models, curcumin administration down-regulated HMGB1 expression and attenuated LPS-induced acute lung injury (Cheng et al., 2018). Moreover, curcumin supplementation also protected from HMGB1 mediated vascular injury and hepatitis (Wang et al., 2012) in mouse models.

Besides inhibiting proinflammatory signals, curcumin also upregulates anti-inflammatory responses. Curcumin administration alleviated acute lung injury induced in cecal ligation and puncture-induced sepsis model, and it was accompanied by elevated numbers of regulatory T cells (FOXP3 β T-reg) and M2 Macrophages (Chai et al., 2020). T-reg and M2 macrophages suppress activated immune cells (CD4 β , CD8 β T cells) via TGF- β and IL-10 secretion and facilitate inflammation resolution (Chai et al., 2020). In vitro studies revealed that curcumin enhanced the differentiation of T-reg cells and the polarization of M2 macrophages (Chai et al., 2020). These findings suggest that curcumin treatment may improve the resolution of pulmonary inflammation and tissue repair by increasing T-reg and M2 macrophages. In the later stages of COVID-19, some severely ill patients develop myelosuppression characterized by a lower number of blood neutrophils and monocytes, which increases the risk for secondary infections (Liao et al., 2020). Curcumin has been shown to potentiate myelopoiesis in mouse models, although the underlying mechanisms are not clear (Vishvakarma et al., 2012). Few studies have also revealed that curcumin mediates immunomodulatory activity by affecting other molecular targets such as NADPH oxidase, and NRF2. Besides direct antioxidant activity, curcumin dampens reactive oxygen species (ROS) generation by inhibiting NADPH oxidase activity (Derocette et al., 2013; Huang et al., 2015). ROS generated by NADPH oxidase activity is implicated in over-activation of the innate immune response, inflammation, tissue injury, and death during sepsis (Bernard et al., 2014; Kong et al., 2010). Curcumin also activates transcription factor NRF2, a master regulator of cellular antioxidant defenses, including heme oxygenase-1 and GSH-biosynthesizing enzymes (Dai et al., 2018; Pandey et al., 2011). Activation of the NRF2 pathway in shown to mitigate oxidative tissue injury in the lungs (Rangasamy et al., 2004; Thimmulappa et al., 2006a), inhibits pulmonary inflammation



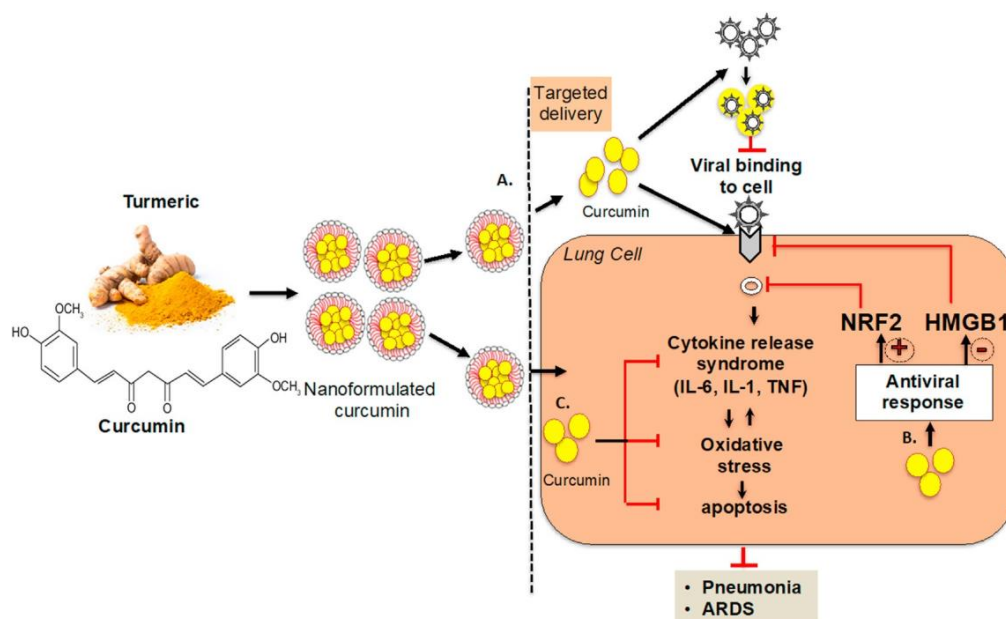


Figure 1. The schematics representing the potential mechanisms by which curcumin may be effective against COVID-19 (A) Antiviral activity of curcumin against SARS-CoV-2 mediated by disrupting the viral envelope, S protein and or ACE2, which prevents the entry of the virus into the cells. B. Curcumin induces antiviral responses by positively regulating NRF2 and repressing ACE2 expression by negatively regulating HMGB1. C. Curcumin mediates immunomodulatory responses by inhibiting cytokine response syndrome and oxidative stress and thus mitigating the progression to pneumonia and or ARDS following SARS-CoV-2 infection.

(Harvey et al., 2011), protects from an acute lung injury, ARDS, and or sepsis (Cuadrado et al., 2019; Kong et al., 2011; Thimmulappa et al., 2006a, 2006b, 2007; Yamamoto et al., 2018).

As illustrated in Figure 1, a large body of evidence provides a strong rationale that curcumin supplementation could alleviate cytokine release syndrome, oxidative stress, apoptosis, and ensuing tissue injury following viral infection; thus, it could be a promising therapeutic for COVID-19.

5. Safety profile, bioavailability, and clinical efficacy of curcumin

In ayurvedic medicine, turmeric has been employed to cure a broad spectrum of common ailments, and similar usage has been noted in Chinese traditional medicine. Clinical trial in asthmatics using turmeric extract was associated with better disease control than placebo (Manarin et al., 2019). Because of its diverse pharmacological activities and FDA approval as "Generally Recognized As Safe," curcumin has been evaluated to treat various human diseases in over 100 clinical trials (www.clinicaltrial.gov). We have summarized the selected clinical trials conducted in the last 10 yr in Table 2, and these human trials were conducted both in healthy subjects and diseased patients. Almost all the clinical trials have revealed that curcumin supplementation is safe and well-tolerated even at doses as high as 8 g/day. There is significant accumulated evidence suggesting curcumin or curcumin containing nutraceuticals mitigate various human diseases by exerting anti-oxidant and anti-inflammatory actions. Randomized clinical trials (RCT) have shown that curcumin, when supplemented as adjunctive therapy maintained and or induced remission in ulcerative colitis patients (Coelho et al., 2020). Hanai et al. (2006) reported that curcumin supplementation (two doses of 1g/day) for six months as an adjunct therapy in patients with stable ulcerative colitis was well tolerated and significantly protected from remission and improved the quality of life as compared to placebo. Lang et al. (2015) conducted a multicentre RCT in patients with mild to moderate ulcerative colitis. They observed that patients receiving curcumin (3g/day) and mesalamine showed significant clinical remission compared to the placebo plus mesalamine group. In an RCT, Campbell et al. (2019) reported

beneficial effects of curcumin in young adults with high-risk for cardiovascular diseases (body mass index >30). Curcumin supplementation (500 mg/day) for 12 weeks significantly reduced serum levels of homocysteine and concomitantly increased HDL-cholesterol (HDL-C) levels, however, there was no improvement in blood pressure as compared to placebo (Campbell et al., 2019). Panahi et al. (2015) compared lipid profiles in patients with metabolic syndrome at baseline and eight weeks after curcuminoids supplementation (1g/day). When compared to baseline, curcuminoid supplementation for eight weeks significantly increased HDL-C as well as reduced serum levels of LDL-C, total cholesterol, triglycerides, and lipoprotein(a) (Panahi et al., 2014). Nanoformulation of curcumin was also evaluated in patients with rheumatoid arthritis. Administration of curcumin nanomicelle (40mg, 3 times/day) to rheumatoid arthritis patients for 12 weeks reduced the clinical disease score (tender joint count and swollen joint count) compared to baseline. In another RCT, Amalraj et al. (2017) also reported that supplementation of highly bioavailable curcumin formulation reduced the clinical symptoms in patients with rheumatoid arthritis as compared to placebo. Furthermore, supplementation of curcumin at high doses showed clinical improvement in gastrointestinal disorders, namely in gall-bladder, gastric ulceration, irritable bowel disease, tropical pancreatitis, and biliary motility (reviewed in (Gupta et al., 2013).

Except for a few trials demonstrating clinical benefits, most curcumin trials showed no significant clinical benefits (White et al., 2019). Inadequate clinical efficacy of curcumin is attributed to poor bioavailability at the target site due to low absorption, instability at physiological pH, rapid hepatic metabolism, and systemic clearance (Liu et al., 2016). Upon oral consumption, a large portion of the ingested curcumin is excreted in feces, and the intestines absorb a relatively smaller amount. The absorbed curcumin is rapidly metabolized by the liver yielding an aqueous-soluble moiety eliminated by the kidney (Pan et al., 1999) and therefore, plasma levels of curcumin remains below detection limits. In contrast, the plasma levels of curcumin metabolite, curcumin-O-glucuronide were detected by 30 min after curcumin intake by healthy human subjects and reached to a maximum concentration of 29 ng/ml by 2.57h (Cheng et al., 2019). Although curcumin levels of



Table 2. Completed clinical trials of curcumin in healthy and diseased subjects with various disorders.

Sl. No	Disease condition	Dose	Sample size; Study design; study Duration	Study Outcome	Reference
1	Rheumatoid arthritis	1.2 g/day	N ¼ 18; double blind, cross over study; 15 days	Significant improvement in pain and physical function scores	S. D. Deodhar et al., Preliminary study on antirheumatic activity of curcumin (diferuloyl methane). <i>Indian J Med Res</i> 71, 632–634 (1980).
2	Osteoarthritis (Knee)	1.5 g/day	N ¼ 367; Randomized, multicenter study; 30 days	No significant Changes	V. Kuptiratsakul et al., Efficacy and safety of Curcuma domestica extracts compared with ibuprofen in patients with knee osteoarthritis: a multicenter study. <i>Clin Interv Aging</i> 9, 451–458 (2014).
3	Osteoarthritis (Knee)	0.5 g twice per day	N ¼ 120; Randomized, Single blind, multicenter study; 42 days	Significant improvement in pain and physical function scores	K. Madhu et al., Safety and efficacy of Curcuma longa extract in the treatment of painful knee osteoarthritis: a randomized placebo-controlled trial. <i>Inflammopharmacology</i> 21, 129–136 (2013).
4	Osteoarthritis (Knee)	0.5 g twice per day	N ¼ 40; Randomized, double-blind placebo-controlled parallel trial; 42 days	Significant improvement in pain and physical function scores	Y. Panahi et al., Curcuminoid treatment for knee osteoarthritis: a randomized double-blind placebo-controlled trial. <i>Phytother Res</i> 28, 1625–1631 (2014).
5	Metabolic disorders	0.5 g twice per day	N ¼ 117; Randomized controlled trial; 56 days	Significant decrease in inflammatory cytokines (MCP-1, TGF- β , IL-6 and TNF- α)	Y. Panahi et al., Antioxidant and anti-inflammatory effects of curcuminoid-piperine combination in subjects with metabolic syndrome: A randomized controlled trial and an updated meta-analysis. <i>Clin Nutr</i> 34, 1101–1108 (2015).
6	Psoriasis	2g/day	N ¼ 63; Randomized, double-blind, placebo-controlled; 84 days	Reduction in PASI Score (erythema, scaling and induration of lesions) and serum IL-22 tier	E. Antigo et al., Oral Curcumin (Meriva) Is Effective as an Adjuvant Treatment and Is Able to Reduce IL-22 Serum Levels in Patients with Psoriasis Vulgaris. <i>Biomed Res Int</i> 2015, 283634 (2015).
7	Scalp Psoriasis	Turmeric tonic, twice per day	N ¼ 40; Randomized, <1–Soft-enter Run-on–> double-blind, placebo-controlled; 63 days	Reduction in PASI Score (erythema, scaling and induration of lesions) and improvement	P. Baharini et al., Turmeric tonic as a treatment in scalp psoriasis: A randomized placebo-control clinical trial. <i>J Cosmet Dermatol</i> 17, 461–466 (2018)
8	Radiation dermatitis	6g/day	N ¼ 30; Randomized, double-blind, placebo-controlled; Until completion of radiotherapy	Reduction of Radiation dermatitis severity scores	J. L. Ryan et al., Curcumin for radiation dermatitis: a randomized, double-blind, placebo-controlled clinical trial of thirty breast cancer patients. <i>Radiat Res</i> 180, 34–43 (2013).
9	Healthy (Aged adults)	1.5g/day BCM-95®CG (Biocurcuma™)	N ¼ 160; Randomized, double-blind, placebo-controlled trial; 365 days	No significant differences in clinical parameters and cognitive measures	S. R. Rainey-Smith et al., Curcumin and cognition: a randomised, placebo-controlled double-blind study of community-dwelling older adults. <i>Br J Nutr</i> 115, 2106–2113 (2016).
10	Healthy (Aged adults)	Longida® Optimized Curcumin, in 1 month dose of 400 mg	N ¼ 60; Randomized, double-blind, placebo-controlled Phase 3/4 trial; 30 days	Improvisation of alertness and <1–Soft-enter Run-on–> contentedness; as well as decreases levels of LDL cholesterol	K. H. Cox et al., Investigation of the effects of solid lipid curcumin on cognition and mood in a healthy older population. <i>J Psychopharmacol</i> 29, 642–651 (2015).
11	Alzheimer Disease	0.09 g curcumin in theracurmin; twice per day	N ¼ 46; Randomized, double-blind, Two groups; 540 days	Improvement in Buschke selective reminding test, visual memory and attention.	G. W. Small et al., Memory and Brain Amyloid and Tau Effects of a Bioavailable Form of Curcumin in Non-Demented Adults: A Double-Blind, Placebo-Controlled 18-Month Trial. <i>Am J Geriatr Psychiatry</i> 26, 266–277 (2018).
12	Anxiety and depression	1g/day	N ¼ 50; Randomized, double-blind, placebo-controlled study; 56 days	Significant decrease Inventory of Depressive Symptomatology score	A. L. Lopresti et al., Curcumin and major depression: a randomised, double-blind, placebo-controlled trial investigating the potential of peripheral biomarkers to predict treatment response and antidepressant mechanisms of change. <i>Eur Neuropsychopharmacol</i> 25, 38–50 (2015).
13	Anxiety and depression	1g/day	N ¼ 56; Randomized, double-blind, placebo-controlled study; 56 days	Significant decrease Inventory of Depressive Symptomatology score	A. L. Lopresti et al., Curcumin for the treatment of major depression: a randomised, double-blind, placebo controlled study. <i>J Affect Disord</i> 167, 368–375 (2014).

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Table 2 (continued)

Sl. No	Disease condition	Dose	Sample size; Study design; study Duration	Study Outcome	Reference
14	Anxiety and depression	1g/day	N ¼ 108; Randomized, double-blind, placebo-controlled study; 42 days	Significant decrease in antidepressant behavioral response, along with decrease in inflammatory cytokines in the plasma	J.J. Yu et al., <i>Chronic Supplementation of Curcumin Enhances the Efficacy of Antidepressants in Major Depressive Disorder: A Randomized, Double-Blind, Placebo-Controlled Pilot Study</i> . <i>J Clin Psychopharmacol</i> 35, 406–410 (2015).
15	Anxiety and depression	1g/day (C3 Complex formula)	N ¼ 30; Double blind, cross over trial; 30 days	Significant decrease Beck Anxiety Inventory scale	H. Esmaily et al., <i>An investigation of the effects of curcumin on anxiety and depression in obese individuals: A randomized controlled trial</i> . <i>Chin J Integr Med</i> 21, 332–338 (2015).
16	Anxiety and depression	0.5 g/day	N ¼ 40; Randomized, double-blind, placebo-controlled study; 35 days	Reduction in rapid depressive symptoms reduction	J. Bergman et al., <i>Curcumin as an add-on to antidepressant treatment: a randomized, double-blind, placebo-controlled, pilot clinical study</i> . <i>Clin Neuropharmacol</i> 36, 73–77 (2013).
17	Anxiety and depression	1 g/day	N ¼ 60; Randomized controlled trial; 42 days	Reduction in Hamilton depression rating scale	J. Sanmukhani et al., <i>Efficacy and safety of curcumin in major depressive disorder: a randomized controlled trial</i> . <i>Phytother Res</i> 28, 579–585 (2014).
18	Cardiovascular disorder (Hypercholesterolemic)	0.2 g/day	N ¼ 70; Randomized, double-blind, placebo-controlled study; 28 days	Reduction in total cholesterol	J. J. A. Ferguson et al., <i>Curcumin potentiates cholesterol-lowering effects of phytosterols in hypercholesterolemic individuals: A randomised controlled trial</i> . <i>Metabolism</i> 82, 22–35 (2018).
19	Cardiovascular disorder (Obese)	0.5 g/day (C3 complex capsules)	N ¼ 30; Randomized, double-blind, cross over study; 30 days	Reduction in pro-oxidant-anti-oxidant balance and serum Triglycerol	A. Sahabkar et al., <i>Curcuminoids modulate pro-oxidant-antioxidant balance but not the immune response to heat shock protein 27 and oxidized LDL in obese individuals</i> . <i>Phytother Res</i> 27, 1883–1888 (2013).
20	Metabolic syndrome	1.89 g/day	N ¼ 65; Randomized, double-blind study; 84 days	Reduction in low density lipoprotein cholesterol and triglycerol and triglycerol/high density lipoprotein cholesterol ratio	Y. S. Yang et al., <i>Lipid-lowering effects of curcumin in patients with metabolic syndrome: a randomized, double-blind, placebo-controlled trial</i> . <i>Phytother Res</i> 28, 1770–1777 (2014).
21	Metabolic syndrome	2.4 g/day and 1.5 g/day	N ¼ 250; Randomized, double-blind, placebo-controlled study; 56 days	Improved Body Mass Index, body fat and waste circumference	F. Amin et al., <i>Clinical efficacy of the co-administration of Turmeric and Black seeds (Kalonji) in metabolic syndrome - a double blind randomized controlled trial - TAK-MeS trial</i> . <i>Complement Ther Med</i> 23, 165–174 (2015).
22	Inflammatory Bowel Disease (mild to moderate active ulcerities colities)	3 g/day	N ¼ 50; Randomized, double-blind, placebo-controlled study; 30 days	Improvement in clinical symptoms	A. Lang et al., <i>Curcumin in Combination With Mesalazine Induces Remission in Patients With Mild-to-Moderate Ulcerative Colitis in a Randomized Controlled Trial</i> . <i>Clin Gastroenterol Hepatol</i> 13, 1444–1449.e1441 (2015).
23	Hepatoprotective effects	0.237 g/day	N ¼ 60; Randomized, double-blind, placebo-controlled study; 84 days	Reduction in alanine aminotransferase, Aspartate amino-transferase levels	S. W. Kim et al., <i>The effectiveness of fermented turmeric powder in subjects with elevated alanine transaminase levels: a randomised controlled study</i> . <i>BMC Complement Altern Med</i> 13, 58 (2013).
24	non-alcoholic fatty liver disease	0.07 g/day	N ¼ 80; Randomized, double-blind, placebo-controlled study; 56 days	Reduction in weight and body mass index and improvement liver ultrasonographic findings	S. Rahmani et al., <i>Treatment of Non-alcoholic Fatty Liver Disease with Curcumin: A Randomized Placebo-controlled Trial</i> . <i>Phytother Res</i> 30, 1540–1548 (2016).
25	Chronic kidney disorder	0.32 g/day	N ¼ 101; Randomized, double-blind, placebo-controlled study; 56 days	Reduction in lipid peroxidation and increase in antioxidant activity	A. S. Jiménez-Osorio et al., <i>The Effect of Dietary Supplementation With Curcumin on Redox Status and Nrf2 Activation in Patients With Nondiabetic or Diabetic Proteinuric Chronic Kidney Disease: A Pilot Study</i> . <i>J Ren Nutr</i> 26, 237–244 (2016).

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Table 2 (continued)

Sl. No	Disease condition	Dose	Sample size; Study design; study Duration	Study Outcome	Reference
26	Chronic prostatitis/Chronic pelvic pain syndrome	0.2 g	N ¼ 60; Randomized, single-blind, placebo-controlled study, Phase II; 30 days	Improvement in chronic Chronic Prostatitis Symptom Index	G. Morgia et al., A phase II, randomized, single-blind, placebo-controlled clinical trial on the efficacy of Curcuma and Calendula suppositories for the treatment of patients with chronic prostatitis/chronic pelvic pain syndrome type III. Arch Ital Urol Androl 89, 110–113 (2017).
27	Type II Diabetes Mellitus	0.3 g/day	N ¼ 100; Randomized double-blind, placebo-controlled study; 84 days	Reduction in fasting blood glucose and free fatty acid levels	L. X. Ma et al., Curcuminoids exert glucose-lowering effect in type 2 diabetes by decreasing serum free fatty acids: a double-blind, placebo-controlled trial. Mol Nutr Food Res 57, 1569–1577 (2013).
28	Type II Diabetes Mellitus	2 g/day	N ¼ 60, Open label randomized clinical study; 28 days	Decrease in fasting blood glucose, low density lipoprotein cholesterol and anti-inflammatory molecule hs C-reactive protein	N. Mathilil et al., Efficacy of Turmeric as Adjuvant Therapy in Type 2 Diabetic Patients. Indian J Clin Biochem 30, 180–186 (2015).
29	Type II Diabetes Mellitus	0.08 g/day (nano-formulation)	N ¼ 70, Randomized double blind, placebo control add-on clinical study; 90 days	Reduction in fast blood glucose, triglycerol, glycated hemoglobin a1c, and body mass index	H. R. Rahimi et al., The effect of nano-curcumin on HbA1c, fasting blood glucose, and lipid profile in diabetic subjects: a randomized clinical trial. Avicenna J Phytochem 6, 567–577 (2016).
30	Type II Diabetes Mellitus	0.45 g/day	N ¼ 8, Open-label, randomized control study; 11 days	Decrease in glucose, low density lipoprotein cholesterol, very low density lipoprotein cholesterol and triglycerol	P. Neerati et al., Evaluation of the effect of curcumin capsules on glyburide therapy in patients with type-2 diabetes mellitus. Phytother Res 28, 1796–1800 (2014).
31	Obesity (female)	2.8 g/day	N ¼ 62, Randomized, double-blind, placebo-controlled, crossover study; 70 days	No significant changes in clinical parameters	F. Di Piero et al., Potential role of bioavailable curcumin in weight loss and omental adipose tissue decrease: preliminary data of a randomized, controlled trial in overweight people with metabolic syndrome. Preliminary study. Eur Rev Med Pharmacol Sci 19, 4195–4202 (2015).
32	Obesity	1 g/day	N ¼ 30, Randomized, double-blind, cross over study; 28 days	Reduction in inflammatory cytokines, and vascular endothelial growth factor	S. Ganjali et al., Investigation of the effects of curcumin on serum cytokines in obese individuals: a randomized controlled trial. ScientificWorldJournal 2014, 898361 (2014).
33	Beta-thalassemia	0.5 g/day	60	Reduction in oxidative stress, iron levels and increase in hemoglobin concentration and antioxidant level.	O. U. Yanpanitch et al., Treatment of β -Thalassemia/Hemoglobin E with Antioxidant Cocktails Results in Decreased Oxidative Stress. Increased Hemoglobin Concentration, and Improvement of the Hypercoagulable State. Oxid Med Cell Longev 2015, 537954 (2015).
34	Beta-thalassemia	1 g/day	N ¼ 68, Randomized, double-blind, controlled clinical study; 84 days	Reduction in total & direct bilirubin content. Increase in antioxidant activity, hemoglobin, ferritin, iron, and catalase activity.	E. Mohammadi et al., An investigation of the effects of curcumin on iron overload, hepcidin level, and liver function in β -thalassemia major patients: A double-blind randomized controlled clinical trial. Phytother Res 32, 1828–1835 (2018).
35	Breast Cancer (metastatic)	0.5–8 g/day	N ¼ 14, open-label, Phase I clinical trial; 7 days	Reduction in carcinoembryonic antigen tumor marker; Vascular endothelial growth factor showing anti-angiogenic effect	M. Bayet-Robert et al., Phase I dose escalation trial of docetaxel plus curcumin in patients with advanced and metastatic breast cancer. Cancer Biol Ther 9, 8–14 (2010).
36	Pancreatic cancer	0.2–0.4 g/day	N ¼ 16, Phase I clinical trial	Improved fatigue- and association with quality of life scores	M. Kanai et al., A phase I study investigating the safety and pharmacokinetics of highly bioavailable curcumin (Theracurmin) in cancer patients. Cancer Chemother Pharmacol 71, 1521–1530 (2013).



were undetectable, plasma PK levels of curcumin-O-glucuronide corresponded with pharmacodynamic (PD) responses of curcumin such as increase in NRF2 regulated antioxidant gene expression and suppression of histone deacetylase (HDAC) 1, HDAC2, HDAC3 and HDAC4 in blood cells. The study underscored the potential role of curcumin metabolite in mediating the PD responses of curcumin. Intense research is being underway to improve curcumin's bioavailability by developing a formulation to increase its solubility, stability, and absorption (Jyoti et al., 2019; Liu et al., 2016). The formulations such as water-soluble curcumin, curcumin nanomicelle, and curcumin plus piperine have increased the bioavailability of curcumin and improved the clinical efficacy of curcumin.

6. Nanoformulation of curcumin for pulmonary delivery: an alternative delivery approach

Broad-spectrum antiviral activity and immunomodulatory activity provides a strong rationale for testing curcumin for COVID-19 treatment. However, low bioavailability is the major obstacle in attaining the therapeutic potential of oral curcumin. In contrast, pulmonary delivery of curcumin will overcome this limitation and offers several advantages: direct delivery of high concentration of curcumin to the site of infection; direct contact of curcumin with the virus SARS-CoV-2; direct deposition into lower airways and alveolar region; larger surface area for deposition and absorption; lower intra- and extracellular detoxification enzymatic activity in the pulmonary system (Borghardt et al., 2018). The nanotechnology-based formulation has dramatically eased drug delivery to the pulmonary system (Selvaraj et al., 2018; Smola et al., 2008). Scientists have developed curcumin encapsulated nano-carriers such as liposomes (De Leo et al., 2018), niosomes (Obeid et al., 2019), lipid complexation (Gupta and Dixit, 2011), micro/nano-emulsions (Sood et al., 2014; Yu and Huang, 2012) and polymeric nanoparticles (Umerska et al., 2018). This nanoformulated curcumin could be delivered in dry powder, nebulizer, solution, nasal spray or gel (Sood et al., 2014). Curcumin at physiological pH of 7.4 is unstable with a shelf life of 10 min, and the pH of the respiratory tract ranges from 7.2 to 7.4. The nanoformulation of curcumin would be protected from exposure to alkaline pH and thereby improve curcumin's stability at the target site. Furthermore, nanoformulations of curcumin could also be engineered for longer retention, sustained release, and penetration across the mucus barrier (Sung et al., 2007). Clinical studies of liposomal curcumin, microparticle curcumin, and micelle curcumin by oral delivery have been found to be safe (Yallapu et al., 2015) and shown to be effective in reducing markers of oxidative stress (Helli et al., 2021). Animal studies have shown that inhalable curcumin effectively mitigates lethal bacterial pneumonia (Zhang et al., 2019). FDA has already approved inhalable powder of antibiotic tobramycin, and the nebulized liposomal formulation of ciprofloxacin was found to be effective in reducing *Pseudomonas aeruginosa* infection in a phase III clinical trials for non-CF bronchiectasis (Haworth et al., 2019).

In summary, accumulated evidence suggests that the pulmonary delivery of nanoformulated curcumin such as liposomal curcumin would help in deposition of curcumin in the lower airways at a higher concentration, which may inhibit SARS-CoV-2 infectivity and concomitantly mitigate pulmonary inflammation and the progression to ARDS.

7. Conclusions

There is an urgent need for therapeutics against COVID-19 outbreak. Besides vaccine trials, few therapeutics such as remdesivir and or interferon-beta based on prior knowledge of antiviral activity against SARS-CoV, are in clinical practice for the treatment of COVID-19. Recognizing the public health emergency, perhaps it is imperative to evaluate phytochemical curcumin for management or treatment of COVID-19 in a randomized clinical trial because i) it is relatively safe; ii) it shows broad-spectrum antiviral activity against enveloped viruses; iii)

it may suppress SARS-CoV-2 infection by directly modifying spike protein and or ACE2 and inducing host antiviral responses by targeting NRF2 and HMGB1; iv) it exerts immunomodulatory activity by blocking NF- κ B, inflammasome, HMGB1, and IL-6 driven inflammatory responses; v) it dampens ROS production by inhibiting NADPH oxidase and alleviates oxidative tissue injury by increasing antioxidant defenses by modulating NRF2.

Declarations

Author contribution statement

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No data was used for the research described in the article.

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The authors declare no conflict of interest.

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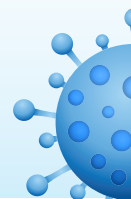
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Management of Leprosy in the Context of COVID- 19 Pandemic: Recommendations by SIG Leprosy (IADVL Academy)

Background

Rising numbers of COVID-19 cases in India: The world is facing an unprecedented pandemic of coronavirus (SARS-CoV-2)/COVID-19 with rising numbers being detected in India. The Indian Association of Dermatologists Venereologists and Leprologists (IADVL) Special Interest Group (SIG) on leprosy, with guidance from *IADVL academy of Dermatology*, has come out with recommendations on the management of leprosy patients in the current context.

- **General risk factors for Covid-19 relevant to India:** People of all ages can be infected by the new coronavirus (COVID-19). The risk of becoming severely ill with COVID-19 appears to increase in individuals aged >60 years and in those with pre-existing morbidities like cardiovascular disease (e.g., hypertension, persons who have had, or are at risk of heart disease or stroke), chronic respiratory disease (e.g., chronic obstructive pulmonary disease), diabetes, cancer, smoking, and immunosuppression. Certain laboratory alterations such as neutrophilia and elevated levels of lactate dehydrogenase (LDH) are also associated with a greater risk for the development of severe forms of COVID-19^[1-3]

Possibility of leprosy-Covid-19 co-infection: More than 200,000 leprosy cases per year have been recorded globally^[4] since 2008 with India contributing around 60% of these cases every year. Studies published so far on COVID-19 from other parts of the world, including one with >1000 cases, have not yet detected leprosy patients co-infected with COVID-19,^[5] nonetheless we should be alert to the possibility of such an occurrence in India.

Challenges specific to leprosy patients: It is too early to understand the dynamics of such a co-infection. However, this document discusses in brief the potential challenges faced in such a situation.

- **Patients on corticosteroids for treatment of leprosy reactions and nerve function impairment:** Prednisolone is immunosuppressive in a dosage ≥ 10 mg per day or a total cumulative dose ≥ 700 mg. Consequently, considering that most patients in leprosy reactions require long periods of treatment with varying doses of prednisolone, they should be considered immunosuppressed and, therefore, more vulnerable to any infection.^[6] The current interim guidance from world health organization (WHO) on clinical management of severe acute respiratory infection when COVID-19 infection is suspected advises against the use of corticosteroids, unless indicated for another reason^[3]

- **Patients with other laboratory alterations:** Patients with mid-borderline, borderline-lepromatous or lepromatous leprosy may have high levels of *LDH and can develop neutrophilia* during type 2 leprosy reaction (erythema nodosum leprosum), and hence theoretically are at a *higher risk* for severe COVID-19 infection^[7]
- **Limited availability of multidrug therapy (MDT) and Clofazimine:** Shut downs and social distancing advocated in the country are likely to constrain and limit the access to MDT and other key leprosy services. There is already a nation-wide shortage of clofazimine in India for over last 6 months
- **Poverty and overcrowding:** Majority of people suffering from leprosy belong to the lower socioeconomic group and are at a high risk due to overcrowding and poor living conditions. The social distancing to prevent spread of COVID-19 infection is difficult to practise in such situations
- **Increasing stigma and discrimination:** As evident from the initial reports, COVID-19 patients put under quarantine are at risk of discrimination and social stigma.^[8] Furthermore with centuries old discrimination and stigma towards leprosy, those patients with co-infection could be more vulnerable. They may also be apprehensive to come forward for evaluation or testing for the fear of getting quarantined and losing their income.

Suggested Recommendations

1. IADVL and SIG leprosy will play a key role in advocacy on behalf of leprosy affected individuals and their families during the COVID-19 epidemic
2. Patients of leprosy registered for treatment should be advised to continue MDT and practice all suggested guidelines and precautions to prevent COVID-19 as applicable to general population and report immediately to the COVID-19 nodal point in case of symptoms of fever, cough and breathlessness. The use of telephone, social media, and Whats App are being used to communicate key messages to the patients. An alternative could be that ASHA workers or other healthcare workers in each region can send SMS in local languages to the patients regarding collection and continuation of the MDT. The Leprosy Mission Trust has started their tele-counselling services for leprosy patients in English, Hindi, Tamil, and Malayalam
3. Health units should consider the possibility of providing A-MDT (accompanied MDT) drugs for all registered leprosy patients^[9] for 3/6 months, avoiding monthly return of stable patients



4. Ministry of health should be requested to inform state and district health centres to make provision for extra quantity of MDT blister packs and medicines to provide for three months of A-MDT for all registered patients, old and new
5. To maintain compliance and adherence to MDT by registered patients, health centres should be advised to dispense MDT blister packs and other treatments to all leprosy patients who approach them, even if they are registered with other centres or the private sector,^[9] till such a time the travel restrictions are in place
6. Leprosy patients who develop acute signs and symptoms of lepra reaction/new nerve function impairment/neuritis during the course of regular treatment or any drug allergy or adverse effects should report immediately to the closest functioning leprosy treatment facility/general health centre for assessment and treatment. As an alternative the use of telemedicine consultation/using social media like Whats App/SMS should be explored and encouraged. Caution should be exercised on the use and dosage of corticosteroids, which are immunosuppressants
7. Please note that the leprosy patients who are **on corticosteroids are at higher risk** of developing complications from COVID-19.^[6,10] In addition patients with factors/comorbidities such as age >60, diabetes mellitus, ischemic heart disease, hypertension, and renal disease the risk is much higher. Hence all such patients should follow strict confinement to their homes and all other social distancing norms during this period of pandemic, more than normal population or other leprosy patients
8. In leprosy patients already on corticosteroids, their dose should be reduced as permissible in a given case to a minimum dose which controls the reaction, preferably to prednisolone 20 mg/day and tapered 5 mg every 2 weeks while evaluating the patient using telemedicine consultation/WhatsApp. However, patients on chronic glucocorticoid therapy (>3 months) are at increased risk of adrenal suppression or failure and in these cases steroid dose may be reduced more cautiously and we should keep in mind that few patients with chronic ENL generally require corticosteroids for a longer period hence the benefit from continuing steroids may outweigh the small increase in the risk of acquiring COVID-19.
9. The use of other immune suppressants like azathioprine, methotrexate, cyclosporine which produce severe immunosuppression should be avoided
10. Chloroquine is historically known to be useful in the management of type 2 lepra reactions.^[11,12] Hydroxychloroquine has also been shown to play a role in the prevention and treatment of COVID-19 pneumonia.^[13,14] We advocate the use of hydroxychloroquine in the management of type 2 lepra reactions as a steroid sparing agent as per recent Govt. of India/ICMR guidelines for management of COVID-19 infection.^[15] A detailed history of heart disease for structural heart disease, previous history of ventricular arrhythmia or syncope, implanted heart rhythm devices and co-administration of other QT prolonging drugs should be taken along with baseline electrocardiography (ECG) to estimate the QTc interval should be done prior to starting treatment and the drug avoided in such patients^[16]
11. Colchicine has been found to be beneficial in the treatment of mild and moderate ENL^[12] through its ability to inhibit the release of proinflammatory cytokines and chemokines. Patients with severe COVID-19 were also noted to have higher serum levels of pro-inflammatory cytokines (TNF- α , IL-1, and IL-6) and chemokines (IL-8). Colchicine at present is under clinical trial as a potential drug to prevent severe COVID disease^[17]
12. Similarly, Thalidomide is very effective in treating severe and recurrent ENL through its anti TNF α action and could potentially benefit patients of leprosy with COVID-19 co-infection. However, its availability for Hansen patients is generally a concern in the health centres in the country and health authorities should pay attention to this at present scenario. Thalidomide has anti-inflammatory, anti-fibrotic, anti-angiogenesis, and immune regulation effects, however in view of its teratogenic effect it should be used with caution. Patients on Thalidomide should be continued at the minimum dose permissible which controls the ENL
13. Minocycline due to its antimicrobial and anti-inflammatory action,^[18,19] pentoxifylline, and NSAID's can also be considered as steroid sparing agents in the management of mild to moderate type 2 lepra reaction
14. In the present context of non-availability of clofazimine/nonavailability of MDT blister pack, the recommended alternative regimen for MB disease^[20,21] is as follows: Rifampicin 600 mg + Dapsone 100 mg + Ofloxacin 400 mg (or Minocycline 100 mg) once a month; followed by Dapsone 100 mg + Ofloxacin 400 mg (or Minocycline 100 mg) daily till the time patient is in a position to contact original treatment facility registered for MDT treatment
15. Apart from the above, hand washing, personal hygiene, use of protective face masks and social distancing to prevent COVID-19, and taking care of nutrition, infections and infestation is important to maintain immunity
16. Elective re-constructive surgeries should be rescheduled to a later date. Acute surgical interventions like nerve abscess decompression to relieve nerve pain and restore nerve function can be scheduled as indicated and as per the availability of a functioning surgical facility
17. Enhanced emphasis should be placed on self-care techniques. Patients should be educated on active and



passive home-based physiotherapy and wound care and prevention of disability services including the use of splints and supports

18. Keeping in mind that a significant proportion of patients are from a lower socioeconomic stratum, we recommend the use of social media platforms to make them aware of the food security and socioeconomic measures initiated by the central and local Governments. They may also be utilized to provide psycho-social counselling for needy patients facing increased stigma, discrimination and depression from job loss or isolation due to social distancing/quarantine, including mobilizing community to support leprosy affected individuals and their families.

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Conflicts of interest

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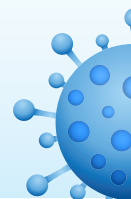
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Perceptions, Experiences, and Challenges of Physicians Involved in Dementia Care During the COVID-19 Lockdown in India: A Qualitative Study

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Introduction: With 5.3 million people living with dementia in India and the pandemic wreaking havoc, dementia care has faced unique challenges during the outbreak, with reduced healthcare access, travel restriction, long-term lockdown and fear of hospitalization. We explored the experiences and barriers faced by the physicians involved in dementia care during the lockdown period.

Methods: A qualitative approach was used with purposive sampling. After an initial pilot, 148 physicians were included in the study. They were virtually interviewed in-depth based on a pre-designed semi-structured questionnaire, in areas related to tele-consultations, attributes related to dementia care, challenges faced and way forward. Interviews were recorded, transcribed and thematically analyzed using Nvivo-10 software. Triangulation, peer debriefing and respondent validation were used to ensure rigor.

Results: The overarching categories that emerged were “Tele-medicine as the future of dementia care in India,” “people living with dementia being uniquely susceptible to the pandemic with a triple burden of: *age, ageism and lack of autonomy*” and “markedly reduced healthcare access in this population with significant mental health burden of caregivers.” The experiences of the physicians were categorized into their challenges during the lockdown period and perceptions related to specific facets of dementia care during the crisis. The general physicians expressed special “unmet needs” of dementia-specific training and specialist collaboration. Most of the participants perceived ambiguity related to the newly released telepsychiatry guidelines.

Conclusion: Resource constraints and pandemic burden are currently high. This study looks at the “voices” of those actively providing dementia care during the ongoing crisis and to the best of our knowledge, is the first one from India to do so. Concurring with their experiences, PwD and their families are exposed to multiple vulnerabilities during COVID-19, need tailored care, especially at the primary healthcare level which includes general physicians. These relevant “voices” are discussed in light of the new tele-psychiatry guidelines and further optimization of dementia care in an aging India.

Keywords: dementia care, COVID-19, lockdown, healthcare workers, experiences, India



INTRODUCTION

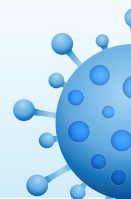
Older adults have been one of the most vulnerable populations during the Coronavirus 2019 (COVID-19) pandemic. Besides being exposed to the physiological risks of infection and increased fatality, it is further compounded by frailty, medical comorbidities, polypharmacy and pre-existing pulmonary complications (1). Furthermore, they are also prone to the persistent psychosocial offshoots of the pandemic including grief, isolation, loneliness, depression, anxiety and sleep disturbances (2). Among the elderly, people living with dementia (PwD) have been especially affected during the pandemic and consequent lockdown, with a multitude of factors contributing to the same. Lack of cognitive stimulation, mobility restriction, isolation, worsening of behavioral and psychological symptoms of dementia (BPSD), enhanced confusional states, increased chances of delirium, reduced adherence to precautionary measures, increased risks of abuse and institutionalization are some of the many factors contributing to the worsening of their overall health and cognitive status, and thus the consequent frailty (3, 4). The world is aging fast and it is projected that 1 in 5 people from the low and middle-income countries (LMIC) are going to be above 60 years of age. With an increase in older adults, there would be a proportionate increase in dementia prevalence, with a 5–7% projected rise in India and China. The absolute number of PwD is estimated to double by 2030, and treble by 2050, especially in the sub-continent (5). With a present 5.3 million dementia cases in the country, huge mental health gap (mhGAP), inadequate penetration of telepsychiatry and prolonged lockdown and economic downfall due to COVID-19, India has been facing unique challenges with dementia care. Marginalization, human rights deprivation, reduced healthcare access, increased symptoms of BPSD, social segregation and abuse have been reported sporadically among PwD in India during the last 6 months (6, 7). Systematic research in this area is still lacking. With a paradigm shift of mental healthcare delivery to virtual platforms, it is vital to understand the experiences and challenges faced by the nation's physicians while providing dementia care.

In general, physicians and other healthcare workers have faced unique plight during the pandemic. Studies have shown increase in stress, burnout, absenteeism, and stigma especially among the frontline workers (8, 9). Increased rates of depression, anxiety, sleep disturbances and post-traumatic stress have been reported among the physicians in a recent systematic review, especially in the developing countries with limited resources and increased COVID-19 burden (10). India is one of the low and middle-income countries (LMIC) that has one physician per 1,456 people as compared to the 1:1,000 ratio recommended by the World Health Organization (WHO) (11). It is also one of the countries with highest pandemic case load and due to the heterogeneity of the population, physicians in all specialties have faced significant challenges in delivery of adequate healthcare services during these crisis times. Even though differences have existed between the Indian Medical Association (IMA) and the Indian Government related to the COVID-19 policies for physicians, the administration has attempted several constructive steps in

this regard (12). Healthcare resource building, ensuring medical safety for the physicians, staffing guidelines and timely payments, training in tele-consultations and round-the-clock psychological support are some of these measures. The Ministry of Health and Family Welfare (MoHFW), Government of India has mentioned about training guides for all level of healthcare workers, salary insurance, specific protocols for management of COVID-19 cases, testing and rational use of Personal Protective Equipment (PPE) in its officially released “measures” to ensure safety of healthcare workers (13). Nevertheless, systematic assessment of their daily challenges, taking into account their perspectives while policymaking and evaluating their psychosocial distress are sub-optimal that affect the implementation of the above-mentioned measures. The rise in violence, stigma, discrimination and dissatisfaction among the medical fraternity and prevalent misinformation in the media resonate the same (12). Gauging the situation, the WHO has collaborated with the Indian Government in training health workers and paramilitary forces in pandemic-specific measures using training of trainers (ToT) approach. The covered areas are epidemiology of COVID-19, bio-medical waste management, triage, mock drills, management of cases and peer-support for emotional well-being (14). While dealing with neurocognitive disorders itself is a challenging task during the pandemic, physicians in geriatric care face this “dual burden” of personal career-related adversities as well as the difficulties in caring for PwD during the pandemic-crisis. With this in the background, this study attempted to explore the “voices” of health care workers (HCW) at multiple sites in India with relation to consultations and care for PwD and their families.

METHODS

The study adopted a qualitative design with a constructivist approach and was approved by the JSSAHER Institutional Ethics Committee (JSSAHER University, Mysore) in March 2020. A “constructivist” paradigm as opposed to a positivist approach enables the researcher to stay “hypothesis-free” and conduct the work with the possibility of “multiple truths.” This is especially important in studying public perceptions as they cannot be statistically scaled or quantified and hence an *a-priori* hypothesis will be redundant in this case. It also helps in building an empathetic and collaborative relationship with the study participants, which is vital in qualitative methodology (15). A semi-structured interview guide was designed comprising of open-ended questions based on detailed discussion among the researchers, their clinical experiences related to the ongoing challenges of dementia care and existing literature on the challenges of HCW. It was piloted on eight participants initially and subsequently refined. Using professional connections and the directory available from the Indian Psychiatric Society (IPS), the physicians were contacted through email. Both snowballing and purposive sampling were used. The initial email asked if the particular physician was involved in consulting PwD during the lockdown period and were providing virtual consultations as well. These two conditions were necessary for inclusion in



the study. Also, the mail explained the objectives and purpose of their study and sought their electronic informed consent. All participants provided explicit consent for participation in the study. The researchers ensured that the participation is well-distributed among the specialties (psychiatrists, neurologists, general physicians) who are involved in dementia care, the area and set-up of practice, age, gender and years of experience. This was again obtained through purposive and representative sampling. Physicians involved in long-term dementia care facilities were excluded as the patient profile, consultation patterns and physician engagement would have a totally different profile in that case and could potentially dilute the overall study results.

Though initially aimed at a multi-site Indian study, this particular paper looks at participants from various states of Southern India. The study was conducted between April–June 2020 when India was undergoing complete lockdown due to COVID-19. The actual interview was held virtually over Zoom/Google Meet over 1–3 sessions after obtaining consent. The first author, who was trained and certified in qualitative research methodology, conducted the interviews in Hindi and English. Each session lasted for an average of 102 ± 10.5 min. The semi-structured interview guide was used with open-ended probes, prompts and regular memo writing which would be later used for analysis (**Box 1**). The questions were aimed to explore their experiences, perceptions, and challenges related to dementia care consultations, with special emphasis on virtual service delivery. The interviews were recorded with consent and the responses transcribed and translated verbatim with back-translation with a researcher with bi-linguistic proficiency.

Analysis

Charmaz's applied thematic analysis was used for the study (16). Data from the participants was generated through the above-mentioned semi-structured interview guide. Each interview was read word-by-word and coded (initial codes followed by clustering of codes to form "focused codes" and finally the mutual relationship between codes called axial coding). The coding was done by two independent researchers (first and fourth authors), who are trained in qualitative research. This was accompanied by a process of memo analysis and constant comparison back-and-forth with the coded data and the original transcripts for the rigor. The responses were analyzed in context and framework and the final hierarchy of themes and categories were reached only after rigorous discussion and brainstorming by all the researchers. Considering the voluminous amount of qualitative data, NVivo 10 software was used to organize and aid the analysis. However, each dataset was still manually coded for "immersion in data" and context which are important factors in such analysis. Nvivo 10 necessarily helps in storage, codification, organization and categorization of the qualitative data. It also facilitates the analysis, but the steps and process of coding and constant comparison have to be manual and can only be assisted by the software. Thematic saturation was achieved with 138 participants, however, 10 more were interviewed for super-saturation. After the initial invitation, 45 physicians hadn't responded and 23 did not consent for the study. Among the latter, majority mentioned lack of time while some others did

BOX 1 | Semi-structured interview guide used for the study.

- How has dementia care been different from you during the COVID-19 related lockdown?
- How do you feel about tele-consultation for people living with dementia and their caregivers?
- Please describe the facilitators and barriers related to virtual consultations for dementia care.
- How were the challenges in dementia consultations different from the pre-COVID times?
- What were the concerns expressed by people with dementia and their caregivers during your consultations? How did you manage them during the lockdown times?
- How has clinical and psychosocial concerns in dementia changed during the ongoing crisis?
- How has your role as a physician involved in dementia care changed due to the pandemic situations?
- What have your personal challenges been? (*not included in the study*)
- Considering the uncertainties of the pandemic, how do you foresee dementia care in the post-pandemic aftermath: please describe.

For the general physicians

- What were the challenges in "primary dementia care" that you have faced and what were your perceived "unmet needs"?
- How has primary dementia care been different during COVID-19 times?
- How do you think your consultations for people living with dementia were different from specialist consultations?

not provide a reason for unwillingness to participate. Rigor was enhanced by triangulation in analysis, peer debriefing and respondent validation (where the initial results after the first round of analysis were presented to 50% of the sample and their inputs were sought about whether the results represented their "voices") (17). The entire process of analysis was completed in about 2 months.

RESULTS

The terms physicians, general physicians (GPs) and HCW have been used interchangeably. The socio-demographics of the participants and their responses toward the interview are presented in **Table 1**. The mean age of the participants was 39.2 ± 5.3 years and the mean years of experience was 10.2 ± 2.4 . The main categories and themes are summarized in **Table 2**. The results are divided mainly into the challenges faced related to dementia-case consultations during the lockdown, their experiences about various attributes of dementia care during that period, specific perceptions related to virtual (tele/video) service delivery and finally the specific themes that emerged related to the GPs. The authors agree that the GPs form a heterogeneous population and are bound to have different requirements and challenges with regards to dementia care, irrespective of the pandemic. However, considering the scarcity of specialist services in a developing country like India, GPs form the backbone of health care attending to most first consultations of neuropsychiatric disorders. Hence, the authors included them in the study which wanted to explore the experiences of any physicians dealing with PwD. Nevertheless, the detailed results



TABLE 1 | Socio-demographics of the study participants ($n = 148$).

Attribute	Types	No. (%)
States	Karnataka	68 (45.9)
	Tamil Nadu	31 (20.9)
	Andhra Pradesh	20 (13.5)
	Kerala	29 (19.5)
Specialty	Psychiatrists	66 (41.9)
	Neurologists	32 (21.6)
	General Physicians	50 (33.7)
Age (years)	25–35	49 (33.1)
	35–45	56 (37.8)
	45–55	25 (16.9)
	> 55	18 (12.2)
Gender	Male	80 (54.0)
	Female	68 (46.0)
Area of practice	Urban	72 (48.6)
	Semi-urban	30 (20.3)
	Rural	46 (31.1)
Set-up of practice	Government	53 (35.8)
	Private (solo)	75 (50.7)
	Private (organization)	20 (13.5)
Experience (years)	0–5	23 (15.5)
	5–10	52 (35.1)
	> 10 years	73 (49.3)
Modes of consultation during the lockdown	Only telephonic	7 (4.7)
	Only video	21 (14.1)
	Both telephonic and video	80 (54.1)
	Virtual and in-person	40 (27.0)
Opinion about the study interview	Useful	115 (77.7)
	Not useful	10 (6.7)
	Neutral	15 (10.1)
	Preferred not to say	8 (5.4)

related to the experiences of the GPs, their challenges and unmet needs will be presented in a separate paper. The overarching themes across all three specialties and irrespective of any other attributes included the recognition of PwD to have a “dual” vulnerability during the COVID-19 related crisis, concerns about their reduced access to care and perceived utility of “tele-medicine” as a promising platform for dementia care even in the post-pandemic aftermath. Most of the participant physicians shared their own “stress” as well during the lockdown crisis (though that was not a part of the study), welcomed the interview and felt that sharing their experiences especially related to dementia care was cathartic for them as well.

The verbatim excerpts supporting the generated themes are presented below (Table 2). Due to space constraints, only the pertinent ones are included in the manuscript. The detailed responses from the study are available from the authors on request.

DISCUSSION

Tele-Medicine for Dementia Care: Pros and Caveats

Telemedicine aims at providing health care at distance to vouchsafe the interest of advancing the health of individuals

and their communities (18). In a socio-culturally diverse and populated nation like India, virtual consultations can go a long way in reducing stigma, travel costs and enhancing healthcare access. This is in sync with the increased internet coverage in rural areas over the last decade and tripled smartphone usage during the pandemic (19). As highlighted in this study, physicians found themselves at a critical crossroads with tele-dementia care during the lockdown. This assumes a renewed importance for maintenance treatment in PwD, monitoring, management of BPSD and caregiver education, especially with the increased risk of complications and infection following hospitalization during the pandemic. Soares et al. (20) while discussing telecare for BPSD during COVID-19, describe it as a “viable tool” for monitoring clinical stability, however, cautions about cost, resistance to change, age of the patient, and technical challenges. Implementing remote memory clinics has also been recommended to help screening, digital cognitive training, pragmatic benefits of which can outlast the pandemic (21). HCP in this study rather admitted technical ease in consultations but were worried about the virtual assessments. The PwD may be technologically challenged, not comfortable with screen usage, compromised cognition may be further deteriorated due to the above. Vision and hearing impairment may compound the above leading to errors in assessment and compliance with instructions. Challenges in the cognitive assessment in general in the Indian population get more challenging virtually due to the multitude of cultural practices and vernacular languages, which predilect faulty assessment due to the dearth of language-sensitive assessment scales (22). Further, BPSD made cross-sectional assessments and monitoring for symptomatic severity problematic according to the physicians, leading to inadequate titration of psychotropic dosages.

Along similar lines, the assessment of physical health status was mentioned by many as a hurdle, especially in non-AD and those with medical co-morbidities. This increased the frequency of adverse effects due to psychotropic use in patients with dementia. The problem of patient's autonomy was a major “highlight” based on the current rights-based model and person-centered approach. According to our study, physicians were concerned about tele-care vicariously promoting proxy consultations, which mostly the patient's voices staying “unheard.” This can have a significant impact on dementia care during an already existing biopsychosocial crisis.

The newly released telemedicine and telepsychiatry guidelines 2020 (23), though helpful standards are still a long way from translating into actual clinical practice. The lack of awareness thereof and legal implications consequent to violation of the same is a harsh reality, as reflected by the “perceptions” in our study. Most anti-dementia drugs and anti-psychotics come in the “list B” of these guidelines and can only be given on follow-ups, which leads to difficulty in decision-making during the first consults (23). In the guidelines, a tele follow-up consultation is defined as “*patient consulting with the same psychiatrist within 6 months of his/her previous in-person consultation*” and the present consultation is for the continuation of care of the same clinical condition. Pragmatically, this is not always possible due to the



TABLE 2 | Categories and themes from the analysis ($n = 148$).

Categories	Themes (% response)	Verbal excerpts of participants
Challenges	<ul style="list-style-type: none"> Virtual cognitive assessment in PwD (91%) Worsening of behavioral and cognitive problems (90%) Fear and stigma about in-person care (62%) Availability of medications (43%) Lack of patient advocacy: the establishment of therapeutic rapport (95%) 	<ul style="list-style-type: none"> "It was indeed very difficult to apply scales over phone/video. The connection kept breaking and the patient could hardly comprehend what is being asked for" "Most patients felt "locked inside" their rooms in absence of any stimulation and their agitation increased as well as memory disturbances" "In most districts memantine and psychotropics were not available. Even though unmanageable at home, the family was scared of getting her admitted" "I rarely spoke to the patient. Most virtual consults were on a proxy. It made engaging the patient all the more difficult"
Experiences of dementia care during lockdown period	<ul style="list-style-type: none"> Overuse of psychotropics to control BPSD (72%) Reduction of autonomy and self-report (88%) Perceived abuse from the patients (overt and covert) (69%) Loneliness and isolation: contributing to behavioral worsening (96%) Lack of basic amenities and Caregiver burnout/stress (85%) 	<ul style="list-style-type: none"> "I found myself in a helpless situation. It was difficult to explain behavioral management to the family. I had to hike up the dose of risperidone multiple times" "She complained of being locked in her room for the fear of getting infected and infecting others. Almost always she was tearful..." "Most of my dementia patients are having increased depression, anxiety and sleep disturbances due to the prolonged loneliness and having no one to interact with" "The husband was more concerned about the helper. The paid caregiver was off during the lockdown and he was even afraid to go to the market for daily necessities"
Perceptions related to the online consultation	<ul style="list-style-type: none"> Ambiguity related to the Telemedicine guidelines and legal implications (67%) Ease of online consultation by the patients and reduced need for hospital visits (52%) Enhanced access to healthcare for the patient population (69%) Better maintenance treatment (47%) Better cross-referral and discussion of other medical conditions (42%) Ease of delivering basic psychoeducation involving multiple caregivers (62%) Use of AI for cognitive stimulation (27%) 	<ul style="list-style-type: none"> "We know about the guidelines being released. But its being hardly followed. I am not really aware of the legal responsibilities" "Patients keep requesting for physical examination. It's so essential in neuropsychiatry. How will I prescribe without being sure..." "It was easier to discuss with the cardiologist virtually, sometimes on the same platform. The need for physical referrals often delays it" "For those who are doing well, they were quite satisfied with the tele-consultations" "I didn't expect my rural clients to be so comfortable with video consults. They were quite tech-savvy, it surprised me. This is going to be the new norm" "Demonstrating Lumosity/Brainwave/Cogmap was much easier. It was hands-on and certain families could implement it"
Specific perceptions of the general physicians	<ul style="list-style-type: none"> Challenges in assessment and screening of dementia (84%) Overuse of medications (67%) Lack of perceived satisfaction with the care delivery (52%) Better expert referrals and discussion (42%) Better learning: the need for virtual training (80%) 	<ul style="list-style-type: none"> "Dementia has always been a challenge to us, especially early identification and conveying the diagnosis. The COVID times have made it even more difficult" "Virtual consults are easy, but I often don't feel we are doing enough for the clients apart from prescribing the same meds" "It is easier to virtually reach out for the district psychiatrist regularly. It helps a lot in understanding the cases. I hope it stays that way" "Tele-medicine needs to specifically focus on training us in dementia care"
**Overarching themes	<ul style="list-style-type: none"> PwD considered as "especially vulnerable population": Triple burden of "age, ageism and autonomy" (95%) Decreased access to care (91%) The perceived benefit of telemedicine as a "way of future" for dementia care (90%) 	<ul style="list-style-type: none"> "I keep hearing about "vulnerable" populations during the pandemic. Well, these individuals share the burden of age, stigma and memory issues." "People living with dementia are in an impoverished state. They are most deprived of care among all the other psychiatric illnesses" "At least others can express their need, they are sadly not able to "convey" that and are often neglected in this crisis, lonely and isolated..." "It might have its limitations, but the way forward with limited manpower is telemedicine. It's the way to go, especially in developing countries." "Dementia care has a huge potential to be digitalized. Policies, guidelines and training need to be tailored accordingly"



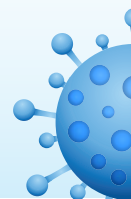
individual preferences of the patients and professional availability of the physicians. Hence, prescribing medications for dementia patients over telephonic follow-ups was an “ambiguous” area for most psychiatrists. More than half of the neurologists and two-thirds of general physicians in our sample were not aware of the newly released guidelines. One of the possible reasons could have been that the guidelines were released during the time of the present study and were not yet popularized when the interviews were being conducted. Besides, there was also confusion about the applicability of the “same condition for continuation of care” as the initial visit necessary for telephonic follow-up. For example, many patients with dementia opted for review consultations to deal with the associated medical comorbidities or familial issues, which were not directly linked to the cognitive disorder *per se*, for which they had initially consulted. Another important concern raised by our participants was related to the consent of the patients and advanced directives. These tend to emerge as vital issues in dementia care, especially in areas of palliative care, end-of-life management and physician-assisted suicide (24). Though the Telepsychiatry guidelines explicitly discuss about documenting patient’s consent, comfort to speak about his/her issues in the presence of family members and following the advanced directives as laid down by the patient: more than 90% of all our participants were not clear about the exact provisions to be followed. However, neither these guidelines nor the Indian Mental Healthcare Act (MHCA), 2017 specifically address the end-of-life concerns and related medico-legal issues in dementia care. The need for multiple online consultations for prescription along with the unavailability of medications during the lockdown in rural pockets, delayed the initiation of treatment. Though some doctors mentioned the use of AI for home-based cognitive exercises, they were limited to the urban areas and were themselves trained in the same. Most of our participants mentioned resistance to the use of “digital interventions” by the caregivers apart from basic consultation. The advocacy of online or digitally-assisted cognitive training and rehabilitation for dementia patients was 67, 31, and 15% in the psychiatrists, neurologists and general physicians in our study, respectively.

In a yin-yang world, the advantages of telemedicine are also many which were resonated in our study. In India, respite centers for PwD are their own homes with primary caregivers usually being family members. Thus, with the advent of tele-medicine the synchronous sensitization and education of the patient along with multiple caregivers including paid attenders, has not only becoming easier but also economical. The community approach of facilitating availability, affordability, accessibility, acceptability, continuity is further enshrined on tele-consultations (25). Tirthalli et al. (26) have rightly pointed out the difficulty in in-person consultations with face-masks, as a mental status examination is much more about “non-verbal cues” rather than clinical interviewing. This need for “unmasking of mind” becomes all the important in dementia care, where the expressive and comprehensive deficits tend to be further compromised “behind the mask.” Hence, the scope of tele-consultations. Multiple caregivers could be involved in the “behavioral assessment and analysis” in our study, which helps the treatment of BPSD. This is in line with our participants

looking up to telemedicine as the “future of integrated dementia care” that involves easy cross-specialty referral. With a rapidly aging sub-continent with increased dementia-burden and limited, localized specialized resources, tele-care has been viewed by the physicians as a “dual-edged” path.

Dementia Care During the Ongoing Pandemic

The ongoing pandemic has a bidirectional effect on dementia. The chances of cognitive impairment including delirium are higher in patients with COVID-19 who are already having dementia (3). Besides, the lack of understanding, comprehension, following social distancing protocols and hand hygiene predisposes PwD to the outbreak. The social isolation and loneliness perceived by our HCW can potentially worsen both the cognitive symptoms and BPSD (27). Added to that, was the “perceived abuse and prejudice” that was reported by the care-providers and they felt the “virtual medium” as a barrier for appropriate psychosocial interventions in this regard. Abuse and ageism related to dementia have been reported to be on the rise in developing countries, which can further impair the quality of life in PwD (1, 7). During the lockdown restrictions, the loss of autonomy and “coercive care” were also reported by our participants which was often relayed by the caregivers themselves. Similar “helplessness and benevolent restrictive” measures were reported by the caregivers in another qualitative study from India during the COVID-19 situation (28). These can hamper the dyadic relationship between PwD and their caregivers, consequently increasing the vicious cycle of elder abuse (29). Especially, in the Indian context where family members have the onus of caregiving and dementia is considered to be a part of normal aging. The above “red flags” were mentioned as reasons for a delay in diagnosis and help-seeking during the lockdown, with the need to use an inadvertent dose of psychotropics for “immediate relief” of both patients and caregivers, however increasing the risk of adverse effects and potentially against the “first-line” non-pharmacological management guidelines for BPSD (30). “The start low go slow” approach was reported as “better said than done” by our physicians, as medicines with sedative properties were self-titrated by the caregivers. The necessary need for the caregivers to identify signs of deterioration, adverse effects, medical complications were also hampered by the time and bandwidth-limited digital consultations during the lockdown. Due to the rising COVID caseload in India and predominant deaths in the older age-group (31), even patients needing hospitalizations were requested to be managed online, which was a major perceived challenge by the HCW. Significant caregiver burden emerged, mostly due to BPSD, uncertainty, socio-economic issues, and lack of paid caregivers, which have also been reported in studies from other developing countries (32). They could be better dealt with tele-consultations, as per the physicians involved in dementia care. Expectedly, caregiver interventions have the potential to improve the overall health of PwD as well.



Another important factor is the fear of COVID-19 that reduces healthcare access in older adults and their families, as well as builds up stigma for hospital visits. Both these factors can impair dementia care together with the imbalanced healthcare resource allocation in many countries. The physicians in our study reported difficulty in maintaining in-person appointments with significantly reduced compliance even when the out-patient services were running. Similar findings have been reported from Italy by Spalletta et al. (33) where 66.7 and 77.4% of patients had missed out on their first and follow-up visits, respectively, during the first wave of the pandemic, mainly due to the administrative restrictive measures imposed to curb the viral spread. The authors highlighted enhanced access of healthcare by PwD and their caregivers as a “compelling priority” to prevent burden of the gradually re-opening healthcare clinics. Van Jaarsveld (34) mentions about the “digital divide” that has impacted the elderly population and their healthcare system the most and focuses on digital literacy as an important facilitating tool for optimal utilization of tele-medicine services. The same was resonated by most of our physicians supporting digital-training of all stakeholders involved in dementia care (patients, caregivers, healthcare workers, and administrators) and highlighting the importance of digital health-education to improve public awareness. Service delivery and resource allocation for dementia care were also concerns raised by the participants. Decreased community support, primary healthcare facilities and social networking were reported among Spanish older adults in a recent study (35). Triage during pandemic care, especially critical care beds and ventilators, tend to be vital, more so in settings with limited resources. This assumes paramount importance in older adults, who are more susceptible to both mortality and morbidity due to COVID-19. A cross-sectional online survey done in Canadian physicians reported “presence of dementia” and likelihood of survival as two important factors in deciding healthcare resource allocation during the pandemic (36). The participants of the study were unsure about the required social support to organize and implement the necessary resource allocation. This has been replicated in Indian studies as well where the physicians have felt underprepared to make appropriate health-triage decisions especially in older adults, and perceived lack of emotional support (37). In our study, the general physicians reported this concern much more, especially those working in primary and sub-urban healthcare settings with limited resources. In many cases, patients affected with COVID-19 with comorbid dementia were considered to be the “last priority” due to therapeutic nihilism. This would affect both the course of dementia as well as the infection, impairing the overall quality of life. The neurologists in our study preferred psychiatric referrals for psychosocial interventions and focused more on pharmacotherapy for the control of BPSD.

The “Triple Burden” During COVID-19: Age, Ageism, and Autonomy

There is a complex and dynamic interaction between an individual with dementia who has high dependency needs, living with various psychosocial adversities including the risk

of abuse that is further complicated by the challenges posed by COVID-19 pandemic. This tetrad of “age, ageism, autonomy and COVID-19” expressed in our study seems to act synergistically in increasing the burden of PwD. Aging inherently poses several challenges and the risk of severe illness from COVID-19 increases with age. Eighty percent of the COVID-19 deaths in developed countries and 50% of the COVID-19 deaths in India have been adults more than 60 years of age (38). COVID-19 has posed special needs of social distancing and self-isolation. In this highly dependable population requiring a physical form of care, this could lead to neglect, prejudice of ageism and also physical abuse which might go unnoticed by the physician over tele-consultations or go unreported. This is concerning with an already rising rate of elder abuse in India during the lockdown (39).

While the need for dependency and care is acknowledged, our participants felt it essential to balance it by preserving the autonomy of the PwD. While autonomy is an ethical construct that demands the highest advocacy, studies have reported that autonomy restriction can further increase the behavioral problems related to dementia (40). Some of the important factors leading to abuse according to our study could be poor knowledge about managing BPSD among the caregivers, caregiver burden, restriction of autonomy, and limitations of virtual consultations. Various studies have reported the successful use of patient-tailored, home-based psycho-educational interventions delivered *via* user-friendly online platforms to handle behavioral disturbances in PwD and reduce mood as well as anxiety symptoms among their caregivers which have resulted in an improved quality of life of the dyad (41).

Barriers for the General Physicians in India

India has 0.75 psychiatrists per 100,000 population compared to six psychiatrists per 100,000 population in high-income countries (42). Also, there is only one neurologist catering to a population of one million in India. Dementia care is majorly dealt with by primary care set-ups in communities (43). Studies have reported that primary care physicians face challenges in diagnosis, and a majority of the PwD go unrecognized (43). The existing treatment gap for dementia in India is estimated to be around 90% with scarce specialist resources (44). Previous studies have identified barriers such as lack of support for patients, caregivers, and physicians, time and financial constraints, stigma, diagnostic uncertainty, and concerns around disclosure of the illness in the diagnosis and management of PwD among the primary care physicians (45). Another study among primary care physicians identified challenges such as lack of confidence in neurocognitive evaluation, implementation of screening, interpretation of standard diagnostic procedures, and prognostication. Unique needs such as managing medical comorbidities, polypharmacy, behavioral and psychological symptoms further complicate the care of the PwD (46). This study highlights several of these challenges similarly faced by physicians as the previous studies that have been conducted worldwide and additionally identifies certain COVID-19 related unique concerns. While on one hand, some of the challenges faced by the primary care physicians have further accentuated during COVID-19, several areas are



identified which appear to hold a promise. The physicians in this study have identified telemedicine as a potential tool to assist management of PwD including facilitation of cross-referral. They have however expressed dissatisfaction due to the perceived lack of training in terms of holistic management of a PwD and need to use “more sedative medications” to manage BPSD during COVID-19.

The recently released telepsychiatry guidelines also mention about the collaborative consultation between any healthcare workers and the psychiatrist, especially in community and custodial settings (23). These include primary care physicians, nurses and other allied healthcare professionals. It provides for such cross-consultations in custodial, correctional, community areas, and rehabilitation centers as well as during home-visits, medical camps, and primary healthcare establishments. While such provisions were welcome for dementia-care and psychiatric training by the general physicians, the challenges conveyed by our participants were excessive workload, lack of digital resources and good connections in primary healthcare centers, poor collaboration with the specialists and time-constraints. More than half of the general physicians in our sample reported time being a crucial component in the dementia-care as the “need for quick improvement in behavioral symptoms” and “waiting for specialist referral” often led to losing the patient to follow-up. This often led to self-perceived “threat to their competence,” reduced confidence for dementia care and increased use of psychotropics in our participants. They revealed the need for “better guidance” and cross-collaboration with psychiatrists and neurologists to manage patients with dementia and their families, but most were unaware of the newly released guidelines that could facilitate the same. Given the dearth of trained health professionals who manage dementia, alternative options of capacity building, task shifting, training, and the use of digital mental health intervention are highly recommended. The recently launched ECHO project by the National Institute of Mental Health and Neurosciences (NIMHANS) in Dementia Care is one such promising step (47). Further exploration of the “unmet needs” of general physicians involved in primary dementia care will help address policies and programs. Adequate tele-training of primary HCW, cross-collaboration and specialist guidance might be more pragmatic in the “digital future of dementia care” as mentioned by the physicians in our study.

The present study being qualitative has its inherent limitations, one of which is limited generalizability. However, qualitative studies in general are not intended to have widely generalizable findings, as the perceptions of individuals are contextual from a constructivist vantage point of research, where even a “single voice” matters. Also, our sample size is relatively larger for a qualitative study and we have tried our best to have a representative sample from various regions, area of practice, and age-groups through purposive sampling. The physicians were however only from South India, and cannot be considered to be a pan-Indian sample. The other possible limitation is the researchers’ bias while coding the data, themselves being physicians and facing similar challenges. We tried to deal with this by “constant comparison” of the analyzed results with the verbatim excerpts from the participants. Also, at each level of

coding, there was rigorous discussion among the researchers with independent coding by two researchers. Lastly, the study was conducted during the period of COVID-19 related lockdown and the associated psychosocial challenges could have colored the opinion of the physicians; however, that was one of the objectives of the study. Besides, we haven’t categorized the results based on age, years of experience and speciality but we also didn’t find any major differences in the perceptions/experiences based on these attributes. There were certain nuanced variations in the themes among the groups which are highlighted in the discussion. To summarize, even with these pragmatic limitations, the study was rigorous in design and analysis with the results being grounded in the “voices” of the participants.

CONCLUSION

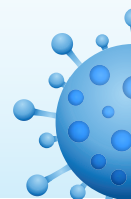
The pandemic has been an unprecedented crisis for vulnerable populations. The Indian Ministry of Health and Family Welfare (MoHFW) in its “Health Advisory for Elderly Population during COVID-19” has stressed the special needs of older people with cognitive impairment, their healthcare access and preservation of rights and autonomy (48). The newly released telemedicine guidelines will serve as an effective anchor for implementing virtual “dementia care,” provided the physicians are well-versed with it. Most of the 5.3 million PwD are in the semi-urban and rural areas of India, and tele-health even with its pragmatic “caveats” can reduce travel costs, enhance access to care, decrease infection risks during a pandemic and improve specialist consultations. This study looks at the “voices” of those actively providing this healthcare and to the best of our knowledge, is the first one from India to do so. Concurring with their experiences, PwD and their families are exposed to multiple vulnerabilities during COVID-19, need tailored care, especially at the primary healthcare level which includes general physicians. Addressing the unmet needs of the physicians involved in dementia care during this time, improvisation of virtual cognitive assessments and cognitive rehabilitation, and further research into the systematization of digital platforms for such purposes can shape practice and policies even in the post-pandemic aftermath and during such futuristic crises. The newly released telepsychiatry guidelines have the potential to form an effective anchor for the same, and subsequent research into dementia care in India needs to explore the understanding, implementation and feedback related to the same.

DATA AVAILABILITY STATEMENT

The original contributions generated for the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by JSS Academy of Higher Education and Research.



The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

DB, PV, and BV were involved in data collection, curation, organization, and drafted the manuscript. DB and TR were independently involved in analysis, and also responsible for editing and supervising. All authors have read and

approved the final version of the manuscript, and involved in the study conceptualization, intellectual content, and design.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Commentary

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COVID-19 infection: The prospects of pharmacotherapy

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Abstract:

The disastrous outbreak of coronavirus disease 2019 (COVID-19) has triggered the investigation of several therapeutic options following the redundancy of specific drugs against it. The virus possesses advanced molecular mechanisms to effectively invade the host cell compared to its counterparts. It results in a seamless and coherent infection and transmission, attributing to its enhanced pathogenicity. The drugs that are currently being employed against COVID-19 inhibit the viral load in different stages of infection, including host cell-virus interaction, viral entry into the host cell, and viral replication inside the host including genome replication and polypeptide chain production. This commentary emphasizes the pharmacotherapeutic options available from the perspective of viral life cycle and pathogenicity.

Keywords:

Coronavirus disease 2019, diagnosis, SARS-CoV-2, therapeutics, transmission

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The ongoing detrimental effects of the coronavirus disease 2019 (COVID-19) have stipulated the investigation of numerous therapeutics in the absence of specific treatment.^[1,2] Unlike MERS-CoV and SARS-CoV-1, the other two viruses of the family, COVID-19 or SARS-CoV-2 has been a global pandemic and it is reported by the WHO as such.^[3,4] The pandemic has spread over 208 countries, with China reporting more than 90% of the cases and deaths, being the central hub.^[5] Although the disease shows symptoms associated with pneumonia, its genetic constitution and structural features have been attributed to its extensive pathogenicity and infection across the globe.^[5,6] Herein, we report the various pharmacotherapeutics used against COVID-19 in brief, so that it can facilitate health-care providers with foundational knowledge on pharmacotherapeutics that are both currently being used and under clinical investigation at the molecular level. The mechanisms of the drugs targeting the

virus have been discussed alongside with original indication, possible COVID-19 indication, dosage information, and side effects.

Most of the drugs that are currently being used to treat COVID-19 were once used against both MERS-CoV and SARS-CoV-1, as the SARS-CoV-2 possesses >80% similar genome to that of SARS-CoV-1.^[6,7] Along with these, antiviral, antimalarial, antiparasitic, and anti-protozoans are also being used.^[8] Although a majority of drugs are designed to interfere with the viral genome replication,^[9] they also display an array of mechanisms such as inhibiting host cell-virus interaction. For example, hemagglutinin, a viral glycoprotein that mediates the adsorption of viral particles to host cell membrane, can be targeted by nitazoxanide, an antiprotozoal drug which was used against diarrhea.^[10] A metabolite of the drug known as tizoxanide binds to hemagglutinin to deactivate it. Doses recommended are based on age groups; 1-3-year-olds were recommended with

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Commentary

100 mg, 4–11 years with 200 mg, and above 12 years with 300 mg for 5 days, orally. Adverse effects of nitazoxanide include nausea, headache, and abdominal cramps. Patients may also come across discoloration of urine and eyes, dizziness, and skin rash.^[10] Another drug known as arbidol hydrochloride or umifenovir also works in the same mechanism. It was originally designed to treat influenza and arbovirus.^[8,9] Since it is under clinical investigations, the doses and side effects are yet to be revealed.

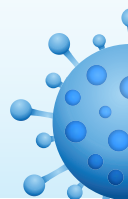
In case of successful adsorption, SARS-CoV-2 tends to enter the host cell using ACE2 protein as a gateway.^[10] In this stage, few drugs try to inhibit the virus from entering the host cell. Chloroquine and hydroxychloroquine impair the glycosylation of ACE2, by disrupting viral S protein, thereby preventing the entry of SARS-CoV-2 into the host cell. Both were used to treat malaria, HIV-1, and autoimmune diseases due to their anti-inflammatory and immunomodulatory effects.^[8,11] Apart from impairing ACE2, they also increase intracellular pH in host cells, thus inhibiting RNA synthesis. Being weak bases, they impair acid vesicles and inhibit the activity of viral enzymes, ultimately inhibiting the viral entry to the cell in case of pH-dependent endocytosis.^[12] Chloroquine is consumed as 500 mg twice for 5 days and hydroxychloroquine as 400 mg on the 1st day, followed by 200 mg twice a day for 4 days, orally.^[10] Adverse effects of these drugs include nausea, vomiting, abdominal cramps, and a metallic taste, whereas acute toxicity may pose in the development of neuropathy, retinopathy, and cardiopathy.^[10] In addition to these drugs, two more drugs known as emodin and promazine also inhibit ACE2 by the same mechanism. However, their dosage and adverse effects are not reported because they are yet to clear the clinical trials.^[8]

Owing to the modified genome structure and advanced structural features, SARS-CoV-2 is more lethal than its counterparts.^[6] It can invade the host cell despite maximal efforts from the innate immune system. In such cases, the impairment of its replication proves to be an efficient objective. Drugs designed to interfere with the viral replication exert a mechanism known as molecular mimicry. This phenomenon occurs when a non-functional molecule mimics the action of the actual biomolecule thereby inhibiting the actual process from occurring. For example, an antiviral drug known as remdesivir, which was used against Ebola and MERS-CoV viruses, mimics guanosine nucleoside, and its incorporation into the RNA replication impairs the process finally halting the viral replication and growth.^[11,12] The same mechanism is being used by ribavirin, which was formulated to treat hepatitis viruses and SARS-CoV-1.^[13] Both the drugs

are now been used to treat COVID-19.^[9,13] Remdesivir is taken as 200 mg on the 1st day, followed by 100 mg for up to 10 days intravenously, and ribavirin as 400 mg for 14 days, twice a day. Remdesivir has been associated with adverse effects such as nausea, vomiting, and rectal bleeding, whereas ribavirin results in hemolytic anemia, hypocalcemia, hypomagnesemia, and embryonic toxicity in pregnant women.^[10] The other two drugs, favipiravir and sofosbuvir, with the same molecular mechanism are under clinical investigation with their dosage and side effects yet to be revealed.^[8]

In addition to the binding to RNA as a nucleoside analog, few drugs act as inhibitors of aspartic acid protease inhibitors. These proteases are needed for the production and maturation of viral genomes.^[10] The combination of lopinavir and ritonavir is one of the most practiced therapies against COVID-19. Known for their antiviral effects against HIV-1, they are used to treat SARS-CoV-2 by inhibiting the protease enzyme.^[8,9] It is recommended that 100–200 mg of the drug should be given for 14 days for patients with symptoms of COVID-19. However, these drugs can cause intolerable gastrointestinal toxic effects such as diarrhea, fatal pancreatitis, and hepatic maladies.^[10] Alongside lopinavir/ritonavir, several other drugs are present that are potent enzyme inhibitors. For example, nelfinavir is another protease inhibitor, which is reported to have similar properties like that of lopinavir/ritonavir. It prevents proteolytic cleavage of the viral polyprotein precursors into individual functional proteins. Ivermectin is an antiviral drug once used to treat HIV-1 and dengue, which is now employed against SARS-CoV-2.^[11] It can dissociate the preformed IMP α / β 1 heterodimer, which aids in the viral protein displacement. As the protein displacement is essential for maintenance of viral replication, targeting this displacement across the host cell would be a feasible option to inhibit the viral life cycle.^[11] Yet another serine protease inhibitor, nafamostat, is said to inhibit transmembrane protease serine 2 associated with the fusion process that facilitates the entry of SARS-CoV-2. In addition to this, two more antiviral drugs used to treat influenza known as oseltamivir and zanamivir are reported to inhibit neuraminidase enzyme that may prevent the entry of the virus into host cells.^[8] These drugs also reported to aid in the reduction of viral load by reducing the shedding. These drugs, i.e., nelfinavir, ivermectin, nafamostat, oseltamivir, and zanamivir, have not cleared the clinical tests; hence, their dosage level for treating COVID-19 remains unknown.^[8]

Among the different types of drugs used against SARS-CoV-2, we comment on only one drug with



Commentary

original antibacterial indication. Azithromycin possesses the ability to prevent secondary bacterial infection.^[14] Originally designed for treating bacterial infections, it is also reported to have antiviral activity. Although precise mechanisms remain unknown, potential mechanisms have been proposed for the putative antiviral properties. One of the first mechanisms is similar to chloroquine and hydroxychloroquine, by increasing the intracellular pH level to dismantle the viral replication process, thereby leading to inhibition of viral growth.^[11] The second mechanism proposed is mediated by the amplification of interferon (IFN) pathway of the host cell. Clinical data suggest that the viral load reduction is attributed to the ability of azithromycin to induce pattern recognition receptors (IFNs and IFN-stimulated genes). In addition to this, it acts directly on bronchial epithelial cells to regulate their normal function by reducing mucus secretion.^[11] The recommended dosage of azithromycin is 500 mg on the 1st day, followed by 250 mg for 4 days.^[8]

In conclusion, owing to the pharmacotherapeutic options currently available, we highlight the fact that the pandemic can be controlled with effective treatment, along with the maintenance of social distancing and quarantine. This is supported by many studies that have been conducted and reported on the significance of stringent lockdown regulations in reducing the viral escalation. Apart from this nonpharmacological management, some of the drugs are now being used, which have already cleared the clinical trials. We also emphasize that, with the absence of specifically designed drug as well as a potential vaccine, a combination of drugs with different and effective doses is the only solution to bring out the optimal management of the disease.

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Conflicts of interest

There are no conflicts of interest.

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Review Article

Proposed drug interventions for SARS CoV 2 infection

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ABSTRACT

As the pandemic has already taken lots of lives across the globe, there's an urgent need for finding treatment options that might help in protection of infected people by either slowing or preventing the progression of the disease. It's important to understand the structure of virus, the mechanism by which it enters the host cell, replicates and infects other cells causing progression of the disease. This article focuses on use of already available and approved drugs for treatment of corona virus based on their mechanism of action and the structure and the life cycle of the virus.

Keywords: Corona virus treatment, Covid 19 drug intervention, Covid 19 treatment

INTRODUCTION

As the pandemic has already taken lots of lives across the globe, there's an urgent need for finding treatment options that might help in protection of infected people by either slowing or preventing the progression of the disease. It's important to understand the structure of virus, the mechanism by which it enters the host cell, replicates and infects other cells causing progression of the disease.

It has been noticed that the SARS CoV 2 virus has 82% nucleotide identity to the SARS CoV 1 virus and 89% to the bat SARS-like-CoVZXC21.¹

STRUCTURE

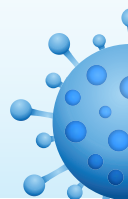
It is an encapsulated virus with non segmented positive sense single strand RNA.

Similar to the SARS CoV 1 virus it appears to be a part of beta group of sub family coronaviridae belonging to coronavirinae family of viruses which belongs to the Nidovirales order.²

Structurally corona viruses contains S protein, M proteins, E protein and N protein. S protein or the spike protein (s1 and s2), is a trimeric Class 1 fusion protein plays a role in attachment of virus to host cell, uses its N terminal for the same.^{3,4} M protein the membrane protein, it is the most abundant protein, has a large C terminal and a small N terminal and is responsible for providing shape to the virus.^{5,6} E protein is thought to be a transmembranous protein responsible for release of new formed viruses, in SARS CoV it is supposed to play an important role in pathogenicity.^{7,8}

N protein is present in Nucleocapsid and has two separate domains, the N terminal and C terminal domain (NTD and CTD), both of these bind to RNA and are important in tethering the RNA to the RTC (replication-transcription complex) and for packaging the genome into the new capsids.⁹⁻¹²

Apart from the mentioned ones, another protein called the HE (hemagglutinin esterase) might also be present in some, it binds to sialic acid on host cell surface glycoproteins and can show acetyl esterase activity, may help S protein in attaching to the cell.¹³



GENETIC STRUCTURE AND GENOMIC REPLICATION

The RNA has 5' cap structure and 3' poly A tail that enables it to act as messenger RNA and it can be used to translate proteins. It contains sequences which code for nsp (non-structural proteins) which are located in the replicase gene and occupies the majority of the genome. It also has some regions which remain untranslated called as UTR (untranslated regions), and these are located on both 5' and 3' ends. TRS (transcriptional regulatory sequences) are present in the initial part of all structural and accessory genes are important for the expression of the same.

RNA can directly translate polyprotein 1a and 1b (pp1a/pp1ab), which encodes nsps forming RTC (replication-transcription complex) in vesicles produced by ERGIC (endoplasmic reticulum golgi intermediate compartment).¹

IMPORTANT PHASIS IN VIRAL CYCLE

1. Attachment and entry into the cells
2. Replicase protein expression
3. Genome replication and transcription
4. Assembly of constituent proteins and genome to form virus
5. Release of viruses to ECF or directly to other cells

Authors will now focus only on important aspects where drugs might act and help in preventing spread or progression of disease in all of the above mentioned phases (Figure 1).

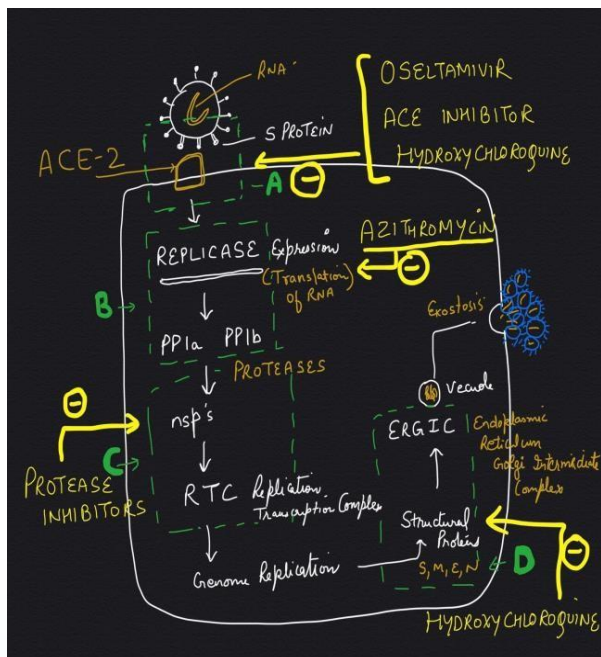


Figure 1: Life cycle of virus and possible drug interactions.

Attachment and entry into the cells

Corona viruses attachment starts with interaction of the S protein with the surface receptors, the receptor binding domains (RBD) are located on S1 and fusion sequence on S2. There are different receptors like DPP4, ACE2, CEACAM1, APN which are used by different corona viruses. SARS CoV 2 uses ACE 2 receptor. However, entry can occur in absence of the enzymatic domain of these receptors.^{3,14-16}

Proposed intervention point A

For attaching to cells, HE protein also helps, it binds to sialic acid on host cell surface, which is a part of glycoproteins. Sialic acid for being available for HE needs to be cleaved from glycoproteins which is carried out by neuroaminidases.

Proposed intervention point B

After binding the virus needs to access the cytoplasm of the host cell. The S protein is cleaved twice, first cleavage is done between S1 and S2, separating both and is carried out by proteases like CATHEPSIN leading to fusion of the membranes. Second occurs within S2, exposing the fusion peptide. This fusion peptide inserts into the membrane followed by joining of 2 heptad repeats forming a anti parallel 6 helical bundle/bridge through which the cytosol, its contents and the viral genome enters the host cell.^{3,14}

Important

The first cleavage is carried by acid dependant protease - cathepsin, the second cleavage of S2 occurs within Acidified lysosomes.

Proposed intervention point C

Replicase protein expression

The RNA genome translates to produce pp1a and pp1b by using frame shift mechanism aided by pseudoknot blocks. Once translation is over, the resultant polyprotein needs to be cleaved into its constituents. It is done by proteases like P1pro and Mpro. The cleavage and production of individual nsps are responsible for decrease and altered innate immune response.¹⁷⁻²⁰ The P1pro can alter and decrease Ub-dependent cellular responses to viral infection.²¹

Proposed intervention point D

Genome replication and transcription

RNA replication starts following the translation, it produces both genomic and sub genomic (negative sense RNA) fragments. The RNA polymerase recognises leader sequences of TRS (TRS L) and starts replication however

it stops at at particular TRS B (body), and starts synthesising the sub genomic negative sense RNA fragments as well.^{22,23} The N protein tightly binds the RNA in a bead on string pattern, two specific substrates have been identified on RNA for N protein, these are TRSs and genomic packaging signal.^{24,25}

Proposed intervention point E

Assembly of constituent proteins and genome to form virus

After replication of genome is completed, structural proteins are translated, S, E, M and are incorporated into the Endoplasmic reitculum (ER) from where they pass along the ERGIC (endoplasmic reticulum golgi intermediate compartment).^{26,27} N protein which is covering the genome is bud into the membrane of vesicles containing structural proteins.²⁸ M and E proteins function together to form envelope, E protein also plays a role in release of viruses by altering host secretory pathways.^{29,30} (Figure 5).

Release of viruses to ECF or directly to other cells

Once the virions are ready they are transported within the vesicles to the cell membrane and by exostosis it allows the newly formed viruses to spread to extra cellular space, where it can be detected and can also infect other cells.

Important

The glycosylation in golgi apparatus and transport requires acidic environment and be altered due to presence of basic substances.³¹

Proposed intervention point F

However in some cases the S protein can directly attach to adjacent cell forming a cytoplasmic connection which can be used for direct transfer of encapsulated virion to neighbouring cells without being spilled in extra cellular space and without being detected.

Proposed intervention point G

Possible drug interventions

Already few drugs have been used in various parts of the world with uncertainty, here try to provide list of drugs and their mechanism by which they may prevent the progression of disease.

Oseltamavir

It is a viral neuraminidase inhibitor, used in viral infections where viruses use neuroaminidase to bind to glycoproteins of host cell membrane for splitting sailic

acid and releasing the new viral progeny into extracellular space.

In corona virus, the main effect could be at the binding site. Oseltamavir may prevent formation of sailic acid on surface which is required by HE protein for helping S protien in attaching to host cell.

At intervention point B

Hydroxychloroquine / chloroquine

It is a 4-Aminoquinoline, used as anti malarial drug. It gets accumulated in lysosomal vecuoles of parasite causing altered heme polymerisation leading to accumulation of toxic heme and death.

In corona virus - The affinity of drug to accumulate in higher concentration in LUNGS (100 folds), specifically lysosomes and endosomes can be used.

It is basic and can alter the pH of the endosomes where the splitting of fusion protein in S2 of corona virus takes place and can prevent further fusion of virus and host cell membranes.

At intervention point C

It can also be accumulated in vecuoles formed by golgi apparatus and alter the pH, golgi apparatus requires acidic pH for glylosylation and transport and hence the viral products once formed can be prevented form being assembled and transported to other cells (Figure 2) (Figure 4).

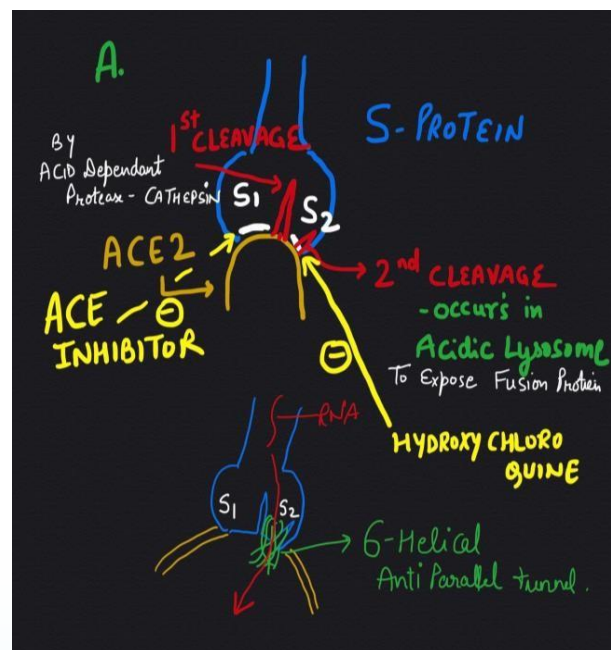


Figure 2: Attachment of S protein and cleavage of S1 and S2.

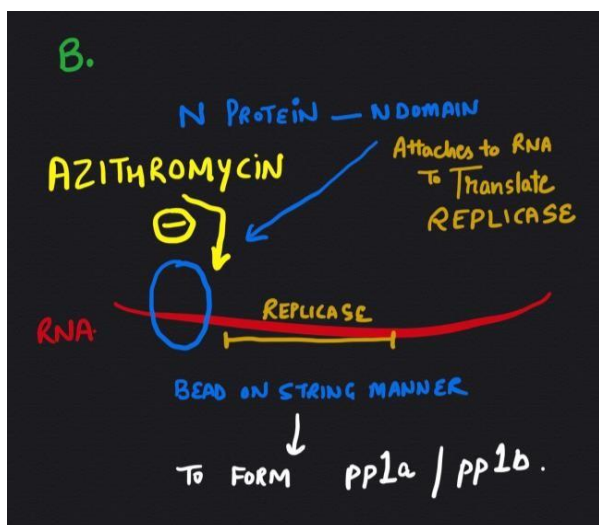


Figure 3: Expression of replicase gene.

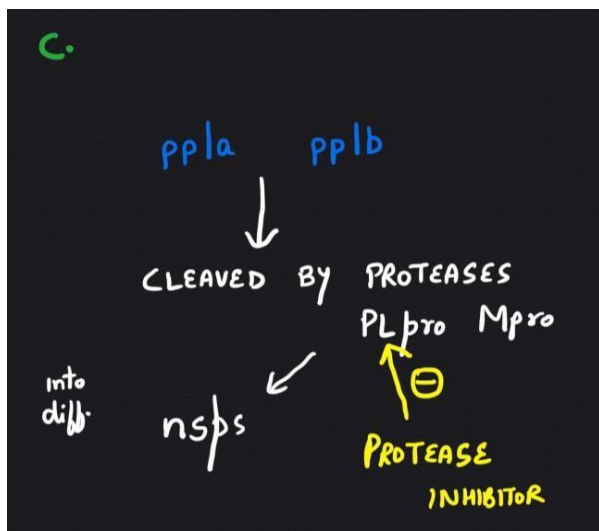


Figure 4: Splitting of Polyprotein 1a and 1b by protease.

At intervention point F

Protease inhibitor

Anti viral drugs used to treat HIV infections, they bind to the proteases that help in splitting of polyproteins in the vacuoles of ERGIC.^{32,33}

In corona virus - The similarity of HIV 1 aspartic proteases and Candida albicans Sap2 has already been demonstrated based on one or more substrate site similarity and hence the HIV protease inhibitors are known to act against other enzymes as well.³⁴

Response in patients with corona points the need for mapping the structural similarity between substrate sites

and exposed sites of Plpro protease and Mpro of corona virus and HIV 1 aspartic protease (Figure 3).

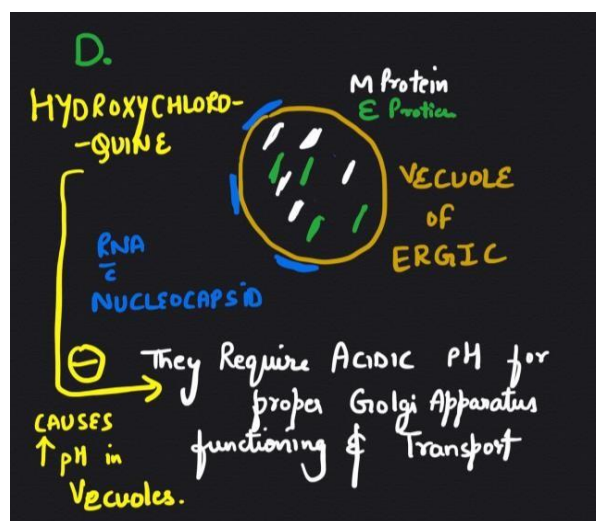


Figure 5: Assembly of virus proteins into virion inside ERGIC.

At intervention point D

Azithromycin (macrolides)

It is a macrolide that binds to 50s subunit of bacterial ribosome and interferes with translation. The macrolide binding site is composed primarily of RNA. Two segments of 23S rRNA, the central loop of domain V and the loop of hairpin 35 from domain II, are believed to be the major components of the drug binding site on the ribosome.³⁵ 50s sub unit also has highest number of positively charged basic residues of arginine and lysine which might play a role in binding of macrolides.³⁶

In corona virus - The binding of N protein to RNA via its N terminal has shown to be linked with high amount of Lysine and Arginine residues that binds to the RNA of the virus. Inside the N Terminal Domain of N protein of SARS-CoV, positively charged lysine and arginine residues have been proposed that bind a 32 nucleotide stem-loop structure located at the 3' end of the SARS-CoV RNA genome.^{37,38}

So Azithromycin can bind to the binding site rich in lysine and arginine on the N terminal domain of N protein of corona virus preventing it to bind to RNA and preventing the expression of replicase gene (Figure 2).

At intervention point D

ACE inhibitors

Bind to angiotensin converting enzymes in circulation as well as tissue proteins. Highly lipophilic variants like moexipril, ramipril show more affinity for tissue proteins.



In corona virus - They can work by 2 mechanisms, ace inhibitors will bind to ACE 2 receptors that reduces less number of ACE 2 proteins available for identification by virus.

The inhibition however will later lead to up regulation of ACE 2 expression, which will be helpful in patients in ARDS, it will prevent further progression of ARDS towards fibrosis by inhibiting of signaling pathways involved in tissue fibrosis and will also have additional benefits like cardioprotective and nephroprotective affect.^{39,40} (Figure 1).

At intervention point A

NaHCO₃ Nebulisation (in ARDS cases)

NaHCO₃ (sodium bicarbonate) - The airway acidifies in a variety of inflammatory lung diseases, airway alkalization improves absorption of cationic bronchodilators, such as albuterol and tiotropium, both in airway epithelia and smooth muscle cells.⁴¹

In corona virus - In cases of ARDS, pulmonary as well as lactic acid acidosis can occur, nebulisation even in absence of acidosis might be helpful by creating basic pH in the airway which hampers ACID dependant protease (cathepsin) to cleave S1 protein for attachment.

At intervention point A

Metabolisation of various drugs

1. Oseltamivir is activated in liver but excreted via urine.⁴²
2. Hydroxychloroquine is metabolised in liver by cytochrome P450 isoenzyme CYP2D6.⁴³
3. Lopinavir is metabolised exclusively by cytochrome P450 isoenzyme CYP3A and ritonavir inhibits the same and hence is used with lopinavir.⁴⁴
4. Ramipril is metabolised by liver and urine both to glucuronate conjugate in liver and diketopiperazine derivative in kidneys and mostly is excreted by urine.⁴⁵
5. Azithromycin is metabolised by liver but does not induce or affect any other medication.⁴⁶

A combination drug therapy based on multiple target sites might prove to be helpful in preventing further damage by suppressing the disease progression.

A combination of some of the drugs mentioned above might prove helpful severe patients whereas in mild cases drugs like azithromycin and hydroxychloroquine, either alone or in combination may prevent development of complications. Tab Azithromycin might also prove to be helpful as a prophylactic drug in patients with contact or infected patients without symptoms as it will prevent expression of replicase gene.

CONCLUSION

This article focuses on use of already available and approved drugs for treatment of corona virus based on their mechanism of action and the structure and the life cycle of the virus. Further research needs to be done for developing drugs with specific action against the novel corona virus, which could be targeted either to S protein receptor binding site, or against Plpro protease inhibitor of the virus.

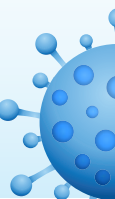
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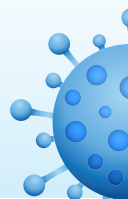


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Pharmacotherapy of COVID-19: A Perspective of Pathogenicity and Life Cycle

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The world has witnessed COVID-19 or SARS-CoV-2 as one of the most hazardous viral outbreak in the history of mankind. Since its emergence in December 2019, it has been affecting the global health with no reported pharmacotherapeutic agent that can neutralize its substantial pathogenicity and escalation around the world. This is attributed to its remarkable molecular pathways followed in course of its life cycle, which is completed in and around the host cell. With the usage of these evolved mechanisms, the virus can effectively invade and replicate in the host cell. The complete analysis of life cycle has resulted in reporting of some molecular targets, which can be neutralised with the usage of pharmacotherapeutic agents. These agents tend to bind to their targets to inactivate them. This review focusses on those targets as well as the potent drugs that currently have been employed to reduce the viral load, in the perspective of its life cycle and pathogenicity. Alongside the drugs that are currently being used, we also report potent drugs that are yet to clear the clinical investigation.

Keywords: COVID-19, SARS-CoV-2, life cycle, pathogenicity, molecular targets, pharmacotherapeutics.

The emergence of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) from an animal market in Wuhan city, Hubei province of China in the December of 2019 has created a global health, social and economic crisis, which the world had not witnessed for over a century.

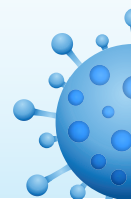
It was originally designated as the 2019 novel coronavirus or 2019-nCoV, later as SARS-CoV-2 by the International Committee on Taxonomy of Viruses (ICTV). Subsequently, it was named as coronavirus-19 or COVID-19 by the world health organisation.^{1,2} To this date, the contagion has

spread over 212 countries, resulting in 40,88,848 cases and 2,83,153 deaths, and been officially declared as pandemic by the WHO, owing to its extensive and widespread pathogenicity and enhanced mode of infection compared to its counterparts.³ This has resulted in the world lockdown condition, where international and domestic trades and travels have been called off to avoid further infection and transmission of the disease.⁴ As a result, financial losses have triggered the economic crisis, with possible fall of 13.0-32.0% global trades and reducing global GDP by 2.0%.⁵ The literature depicts that symptoms of this virus are like that of pneumonia, including headache, fever, dyspnea, non-productive cough and fatigue. However, patients may also develop acute respiratory distress and hypoxia, which needs timely ventilation.^{4,5} Transmission of the virus occurs between infected and healthy human individual through inhaling aerosols that are produced by coughing, sneezing and direct close contact.⁶ Possible animal to human transmissions including bat, snake and pangolin animals are under investigation as the virus is expected to have emerged from the animal market.⁷ It is supported by the emergence of other two viruses of the same family, middle east respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV-1, which were originated from bats using camels and civet cats as intermediate hosts, respectively.^{6,7} Thus far, treating the patients is said to be a stressful task as the virus is highly contagious and can affect even the medical personnel. However, timely and efficient supply of personal protective equipment (PPE), detection kits, drugs along with careful treatment can result in the quicker recovery of the patients.⁸ As the healthcare services largely depend on the supply of PPE and drugs, it becomes essential for the pharmaceutical industries to supply the same. Along with PPE, the important role in controlling the pandemic is played by pharmacotherapeutics.^{9,10,11} Though vaccines are not yet discovered, it is reported that few of the drugs that are being used for other viruses from the same family have been tested effective and some more are yet to clear the clinical trials against SARS-CoV-2.¹² The drugs which were used once to treat MERS-CoV and SARS-CoV-1 are now being employed against SARS-CoV-2, as the latter shares about 80% similar genome with the SARS-CoV-

1.⁶ Many of these drugs possess anti-viral properties and were used to treat viral infections like HIV-1, influenza, Ebola, hepatitis-B and C, and malaria. These are either used individually or in combination based on the response from the patient. Many of these drugs are reported to be used originally as anti-bacterial and antiprotozoal agents, which are also known to possess antiviral properties.^{9,12} In this review, we report the different drugs used against COVID-19, along with their chemical properties, mode of action, original indication, dosage recommendations, and adverse effects. Apart from drugs being used we also report drugs that are yet to clear their clinical trials. We aim to provide this information to facilitate healthcare providers and people with foundational knowledge on pharmacotherapeutics that are both currently being used and under clinical investigation.

Notable features of covid-19 pathogenicity

The pathogenicity of COVID-19 is attributed to its structural and functional modifications compared to its counterparts, MERS-CoV and SARS-CoV-1. The SARS-CoV-2 belongs to the genus β -coronavirus, family *Coronaviridae* and order *Nidovirales*.^{6,13} Though several human coronaviruses including HCoV-NL63, HCoV-OC43, HCoV-HKU, and HCoV-229E were reported to circulate in humans for centuries, they were only linked with mild respiratory diseases.^{14,15} The most lethal variants SARS-CoV-1, MERS-CoV and SARS-CoV-2 have zoonotically been transmitted from other mammals in the recent years.^{7,16} The most lethal of them, SARS-CoV-2 possesses a large, single-stranded, positive-sense RNA as its genome of approximately 27-32 kb length.^{17,18} It comprises of 6-10 genes with first gene encoding for replication and transcription. The rest of the genes are structural genes that codes for structural proteins including the spike (S), membrane (M), envelope (E) and nucleocapsid (N) [Figure 1]. Here, membrane constitutes the viral coat and nucleocapsid packages the viral genome. Some of these are transformed into glycoproteins after undergoing glycosylation in the Golgi apparatus.¹⁹ The spike (S) is a surface glycoprotein reported to play an important role in binding of the virus to the host cell. The glycoprotein is primed by 2 proteases, Angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2). With ACE2 being responsible for



posing as a receptor, SARS-CoV-2 binds to the host cell. Thus, it proves a gateway for the entry of the virus into the human cell.^{19,20}

In 2003, the Guangdong province of China reported the outbreak of SARS-CoV-1, leading to acute respiratory distress syndrome (ARDS). Later, the outbreak spread to rest of the world, resulting in 8000 infections and 776 deaths.^{21,22} Nearly a decade later, Saudi Arabia reported another coronavirus infection in 2012, which was named as MERS-CoV. In this virus, infection begins from a mild respiratory injury leading to severe respiratory disease, and alike SARS-CoV-1, patients witness ARDS and renal failure. This outbreak resulted in more than 2400 infections and 838 deaths.^{23,24} In December 2019, the SARS-CoV-2 outbreak was witnessed in China, which has reported 90% of the cases till date. These viruses use different animals as their reservoirs with a common origin, bat.^{25,26} SARS-CoV-2 is also reported to be originated from bats, later believed to be transmitted through pangolin. This is supported by a study, where it was found that a coronavirus isolated from Malayan pangolin possess 99% similarity with SARS-CoV-2; with infected pangolins displaying similar symptoms like that of humans infected with COVID-19.^{26,27} After all, there is a significant difference in transmission patterns between these viruses. Viral shedding is one of the notable factors where the progeny is released into external environment after completing the reproduction. In case of MERS-CoV and SARS-CoV-1, it occurs only after the onset of symptoms, hence transmission occurs after the medical help.² However, considering its predominant human-human transmission especially in communities and families, it was reported to spread even far before the occurrence of symptoms and possess similar half-lives (1.1-1.2 hrs) in aerosols.²⁸ Another study reported its extensive transmission, where two proven COVID-19 recovered patients showed positive in tests conducted few days later.²⁹ Meanwhile, the incubation time is also high compared to SARS-CoV-1.^{30,31} Thus, it takes a great amount of time to show the symptoms before which the infected might spread the disease to several others.^{32,33} The virus remains viable on solid surfaces like plastic and steel for a considerable amount of time.⁷ In the perspective of detection and diagnosis, SARS-

CoV-2 cannot be detected effectively by RT-PCR, loop-mediated isothermal amplification (LAMP), or chest CT, where SARS-CoV-1 was efficiently diagnosed with RT-PCR alone.³⁴ Owing to these factors, the disease can be declared as more contagious than the other two viruses.

Pharmacotherapeutics used against COVID-19

To this date, many of the drugs have been used by medical professionals to treat COVID-19, either individually or in combination, according to their national healthcare guidelines, though there is no specific drug available to treat the contagion.^{1,2} However, these drugs are employed due to their proven efficacy against other coronaviruses. Most of them are anti-virals used against diseases like hepatitis, Ebola, influenza, and HIV-1. Some of the drugs with original indications including anti-inflammatory, anti-bacterial, immunomodulatory functions are also used.^{9,12} These drugs inhibit the viral load at different intervals including host-pathogen interaction, viral entry into the host cell, replication of viral genome and viral polypeptide production [Table 1]. Herein we discuss the effects of these drugs and their mode of action on molecular targets with respect to the viral life cycle.

Drugs inhibiting the viral adsorption

The mode of infection of COVID-19 chiefly begins with inhaling aerosols from infected person, which then enters the respiratory system like that of pneumonia and tuberculosis.⁴ These aerosols comprising of viable viral particles enter the alveolar cavity and unload the virus thus letting the virus gain entry into the alveolar cells. Apart from alveolar cells, the virus is reported to affect heart cells, as the respiratory system interact with the heart directly. This is supported by the higher amount of secretion of ACE2, which aids in the binding of virus to the host cell. As the heart is said to be the principle organ for circulation, the virus spreads throughout the body resulting in the damage of digestive system. The occurrence of nausea, vomiting and diarrhea supports this hypothesis. Further, the virus is reported to damage kidney and liver, which is supported by the symptoms showing renal failure and bile duct, respectively.³⁵ It is worth mentioning about spike (S) protein, which facilitates the entry of the virus. It is primed by the host cell protease and recognized by the cellular receptor. In case of humans, a serine protease receptor known as TMPRSS2 is



responsible for the priming the spike protein and ACE2 is employed as a receptor.^{20,36} In other words, the surface glycoprotein plays the role of a key to open the door and facilitate the viral entry into the host cell. It is also reported to show high binding affinity with ACE2, compared to SARS-CoV-1. Based on the cryo-EM structure, it is evident that out of several functional domains the receptor binding protein (RBD), fusion domain (FD) and the S2 cleavage prove to be potential targets for drug development.^{37,38}

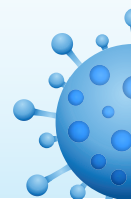
Chloroquine: Chloroquine and its analogues have been used to control malaria since early 1900s.³⁹ The multimodal properties of chloroquine analogues and their minimal toxicity profile has initiated clinical investigation to prove their effect on virus-induced illnesses such as HIV-associated immune reconstitution inflammatory syndrome.⁴⁰ Chloroquine is reported to impair the glycosylation process of ACE2, thus impairing its interaction with spike protein, subsequently the host cell-virus interaction.³⁹ These analogues also increase the pH level and thus inhibit activities like protein biosynthesis and dysfunction of enzymes. These mechanisms of chloroquine-mediated pH alteration are been applied to disintegrate viral replication. Since the mechanism proves to be potent to treat COVID-19, it has been used alongside the other drugs.⁴⁰ For treating COVID-19, 500mg of the drug is given twice a day for 10 days.⁴² In February 2020, a study reported the inhibitory activity of chloroquine against SARS-CoV-2 with an EC_{50} at 48 hours of 1.13 μ M in Vero E6 cells.⁴³ These findings have upheld the clinical usage of chloroquine in China at the time of outbreak.⁴⁴ Results from trials revealed that chloroquine inhibits the exacerbation of COVID-19. However, high doses of chloroquine may result in the development of retinopathy, though it is well tolerated with some common adverse effects like nausea, vomiting, abdominal cramps, and metallic taste.⁴⁵

Hydroxychloroquine: Hydroxychloroquine also belongs to the analogues of chloroquine and has been treated as one of the most effective therapeutic option for the management of COVID-19.⁴⁶ Both chloroquine and hydroxychloroquine prevent clathrin complex formation during endocytosis. Besides, hydroxychloroquine uses the same mechanism of chloroquine; increasing

the intracellular pH level to disintegrate the cellular activities of the virus [Figure 2]. In addition to this, hydroxychloroquine is also reported to impair the glycosylation of ACE2 protein, thus inhibiting the host cell-virus adsorption through impairing the interaction of spike protein.³⁹

Hydroxychloroquine was assessed using pharmacology based pharmacokinetic (PBPK) modelling on Vero cells against SARS-CoV-2 along with chloroquine. This study revealed that potency of hydroxychloroquine (EC_{50} of 0.72 μ M) was greater than that of chloroquine (EC_{50} of 5.47 μ M).⁴⁶ In addition to this, a similar open-labelled, non-randomized study conducted in France showed positive effect against COVID-19 in combination with azithromycin.⁴⁷ In the wake of this evidence, U.S. FDA cleared this drug for emergency uses across USA.⁴⁸ Though dosing recommendations are not yet deduced, current pharmacokinetic models suggest 400 mg of the drug twice on the first day, followed by 200 mg twice a day for four days, orally.⁴⁶ It has been reported that hydroxychloroquine possesses superior cytotoxic effects compared to chloroquine.⁴⁹ These include dermatologic adverse effects like lichenoid reactions, photosensitivity, and acute generalized exanthematous pustulosis can occur with hydroxychloroquine. It has also been reported that persons with history of diabetes showed hypoglycemic symptoms and loss of consciousness upon consumption.⁵⁰ In addition to chloroquine and hydroxychloroquine, there are two more drugs that work using the same mechanism of impairing ACE2 function, known as emodin and promazine. The original indication of emodin was found to be under investigation against the polycystic kidney disease. It is yet to clear the clinical trials as it is still being investigated for its anti-viral effects. Promazine is a discontinued drug used for treating psychomotor conditions. It is possible COVID-19 is off-label use anti-viral response. The dosage information and adverse effects on COVID-19 patients of these two drugs is not yet revealed, as they are still being investigated.¹²

Like ACE2, another enzyme known as TMPRSS2 also facilitates the viral entry to the cell. When the COVID-19 virus tends to enter the host cell, it becomes essential for the spike protein to get cleaved and activated to facilitate



the viral entry to the cell.⁵¹ Therefore, inhibition of the TMPRSS2 protease would become a potential target for anti-viral drug development. Recently three drugs known as camostat mesylate, nafamostat and K11777 have shown to possess potent effects against COVID-19. Camostat mesylate was originally designed to treat chronic pancreatitis.¹² Whereas, K11777 was used as an anti-parasitic agent, to treat toxoplasmosis.⁵² Nafamostat was originally used as an anti-microbial and anti-coagulant agent.^{53,54} Though all three drugs are potent to inhibit TMPRSS2, their clinical evaluation is yet to be completed. Hence, their dosage recommendations and adverse effects are not revealed yet.

Hemagglutinin esterases are the group of viral envelope glycoproteins that facilitate the surface adsorption of virus and the host cell membrane.³⁶ According to a study conducted by Zeng et al, the CoV-hemagglutinin (CoV-HE) complex underwent considerable modifications to facilitate the optimal binding of the virus into the host cell. It is also reported that, the plasticity of CoV-HE is attributed to the functional redundancy between spike protein and hemagglutinin component.⁵⁵ Thus, it becomes evident that hemagglutinin also play an important role in the binding of the virus to the host cell, as well as provide another potential site for drug development. Aiming the exploitation of this mechanism, few drugs have been employed to treat COVID-19.

Nitazoxanide: Nitazoxanide is a U.S FDA approved benzamide drug, which is used to treat diarrhea caused by *Giardia* spp.⁴² It is known for its anti-protozoal activity and has also been used against various Gram-positive and Gram-negative bacteria.^{56,57} Another reported study of nitazoxanide reveals it also shows anti-viral activity, against influenza.⁵⁸ After ingestion, it gets converted into its active state metabolite, known as tizoxanide. It inhibits the hemagglutinin formation and protein implantation in plasma membrane.^{59,60} It may facilitate IFN-1 production to inhibit hemagglutinin, thus showing its anti-viral effects.⁶¹ The pharmacological effects of nitazoxanide proved to be effective against SARS-CoV-2 with EC₅₀ value of 2.12 μ M in Vero E6 cells at 48 hours of incubation.⁶² But in case of human trials, a study conducted on 5 positive patients

proved its inefficiency. Sub-group analysis of these patients showed no difference even after days of hospitalization. Doses recommended for SARS were based on age groups; 1-3-year olds were recommended with 100 mg, 4-11 years with 200 mg, above 12 years with 300 mg for 5 days, orally. The side effects of nitazoxanide include, abdominal cramps, nausea, headache along with discoloration of urine, diarrhea, dizziness and urticaria.⁶³ In addition to nitazoxanide, another potent entry inhibitor known as arbidol hydrochloride or umifenovir also works using the same mechanism. The drug has been approved by China and Russia. Arbidol is reported to prevent the fusion of the viral envelope with endosome after endocytosis. The recommended dosage for COVID-19 and adverse effects on patients are not yet revealed as the drug is yet to clear the trials.^{12,64}

Drugs inhibiting the viral genome replication

After the successful entry of the virus into the host cell, the virus replicates its genome irrespective of its nature. In case of COVID-19, as the genome is RNA, the replication is done using both continuous and discontinuous mechanisms at cytoplasmic membranes. The replication process is reported to be mediated by 20-kb length replicase gene. The replicase complex is composed of 16-subunits and cellular proteins. Apart from RNA-dependent RNA polymerase and RNA helicase, COVID-19 is believed to possess different RNA processing enzymes including endoribonuclease, ADP ribose 1'-phosphatase, and 2'-O-ribose methyltransferase. These proteins are present at cell membrane and aid in the production of mature RNA in the cytoplasmic membrane.⁶⁵ The impairment of replication can prove a potential target for few drugs to inhibit the viral replication.

Remdesivir: Remdesivir is an anti-viral drug that was originally developed to treat Ebola hemorrhagic fever with ongoing trials. It is an investigational monophosphoramidate of an adenosine analog developed by Gilead Sciences, Inc.^{66,67} Though it has not been approved for usage globally, remdesivir is being used to treat COVID-19 with phase 3 clinical trials on the run.⁶⁸ Both *in vitro* and *in vivo* studies were conducted and revealed that remdesivir has the antiviral activity against *filoviridae*, *paramyxoviridae* and the *coronaviridae* including MERS-CoV, SARS-CoV-1 and SARS-CoV-2.^{69,70} It has been reported



that remdesivir has shown an EC_{50} at 48 hours of 0.77 μ M in Vero E6 cells.⁴³ Being a pro-drug, remdesivir gets metabolized in cells and tissues to become an active nucleoside triphosphate that interferes with RNA polymerase activity of the virus [Figure 3]. Other potential mechanisms like lethal mutations and chain termination may also pose beneficial to use it as an anti-viral drug.⁷¹ It

is reported that once remdesivir was used to treat Ebola patients.⁶⁷ Another study conducted by Sheahan *et al.*, revealed its efficiency against MERS-CoV and SARS-CoV-1 activity.⁶⁹ However, the dose under clinical investigation is 200 mg on first day, followed by 100 mg for up to 10 days intravenously.⁶² The first report of treating COVID-19 patient came in US, where a patient

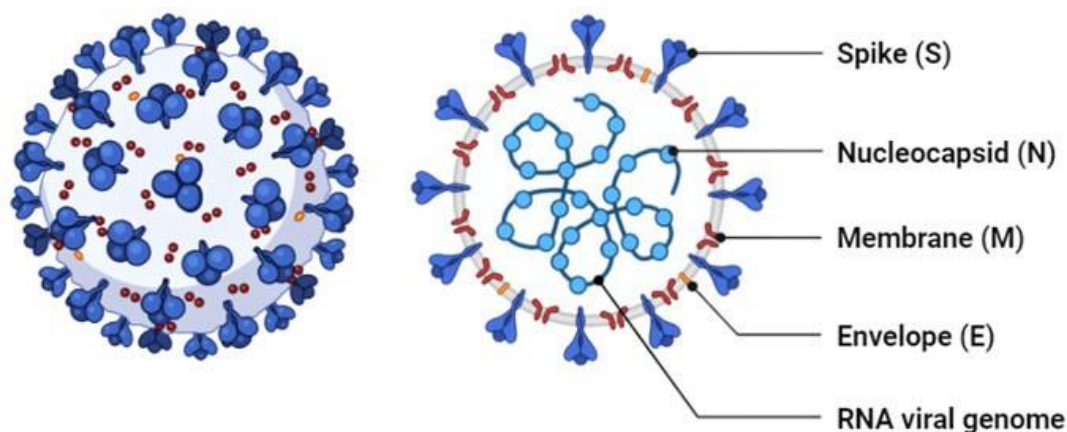


Fig. 1. Structure of SARS-CoV-2

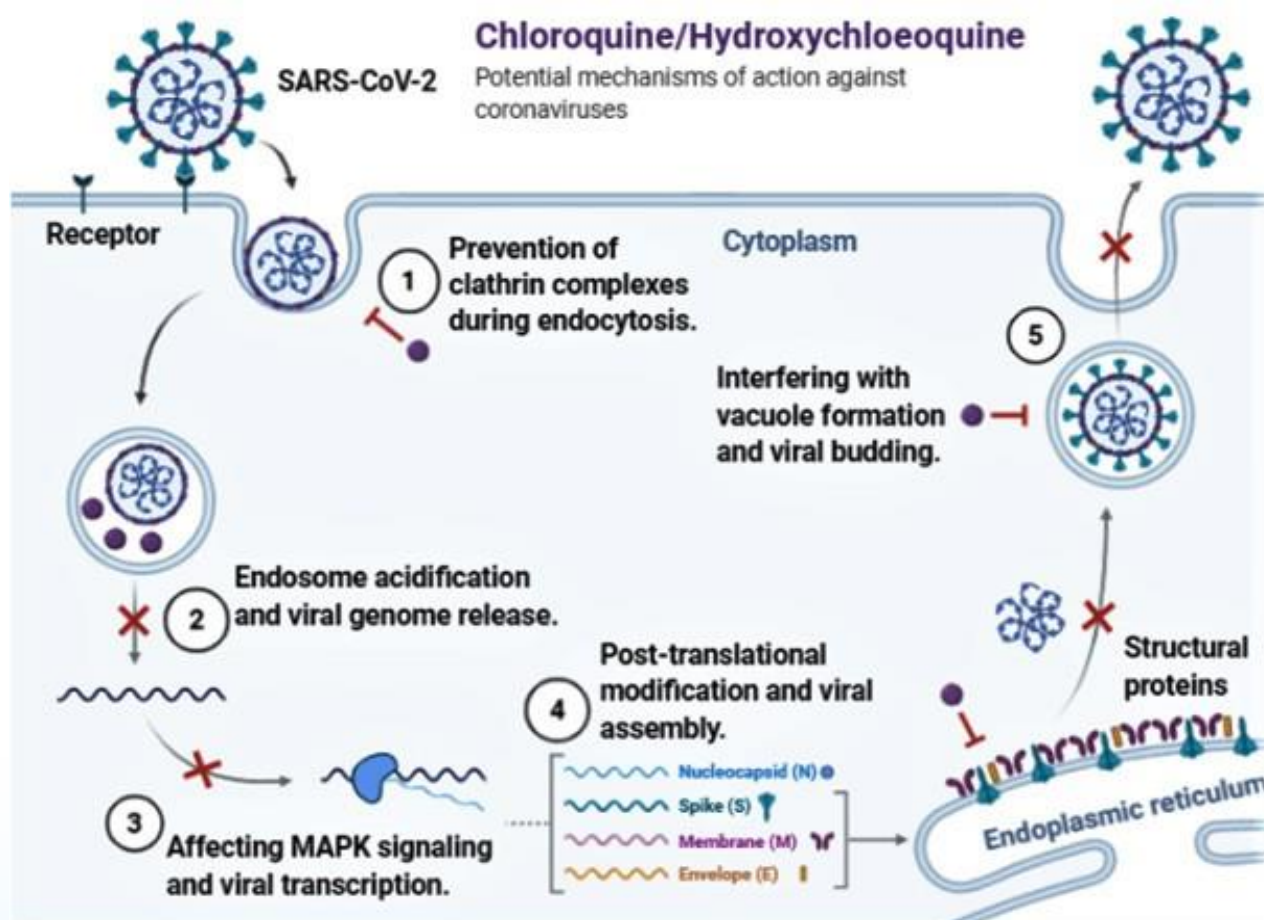
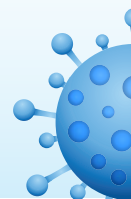


Fig. 2. Working mechanism of chloroquine and hydroxychloroquine



received the treatment with remdesivir for 7 days and found to have shown clinical improvement, though nasopharyngeal swab was positive.⁷² This study reported no side effects but, few cases revealed minor adverse effects like nausea, vomiting and rectal bleeding.⁶²

Ribavirin: Ribavirin affects the viral RNA synthesis, thus disintegrates the viral life cycle as it belongs to the class of purine nucleoside analog. Being a prodrug, it gets modified in liver upon consumption, where its metabolic structure starts mimicking with guanosine. This enables its incorporation into viral RNA, ultimately resulting in the RNA synthesis inhibition.⁷³ As the molecular mimicry can occur in many viruses with the presence of RNA, Ribavirin can be found effective against an array of viruses including hepatitis-B, hepatitis-C, and respiratory syncytial virus. This stipulated the investigation for anti-viral activity of the drug against SARS and MERS outbreaks.⁷⁴ During the SARS outbreak, 70% of hemolysis and 49% of anemia cases were reported out of 126 treated with ribavirin.^{75,76} US

had to restrict the use of ribavirin due to lack of *in vitro* susceptibility and high toxicity levels. With respect to SARS-CoV-2, Wang et al., assessed it is *in vitro* activity and found an EC₅₀ of 109.5 μ M, which is nearly 100 times less potent compared to remdesivir.⁷⁶ These findings initiated the usage of ribavirin on COVID-19 and it is now recommended that oral ribavirin should be given as 400 mg for 14 days, twice a day. However, adverse effects may arise in few patients including hemolytic anemia, hypomagnesemia and hypocalcemia. Pregnant women are advised not to use ribavirin because of its embryonic toxicity.⁷⁴

Favipiravir: Favipiravir was developed by a Japanese firm known as Toyoma Chemicals. It acts as an RNA polymerase inhibitor by the mechanism of molecular mimicry. It structurally resembles guanine, and through competitive inhibition, reduces the efficacy of viral replication like remdesivir.⁷⁷ Though reports state its pharmacological potency against SARS-CoV-2, and better pharmacological activity than arbidol hydrochloride¹, favipiravir has got less

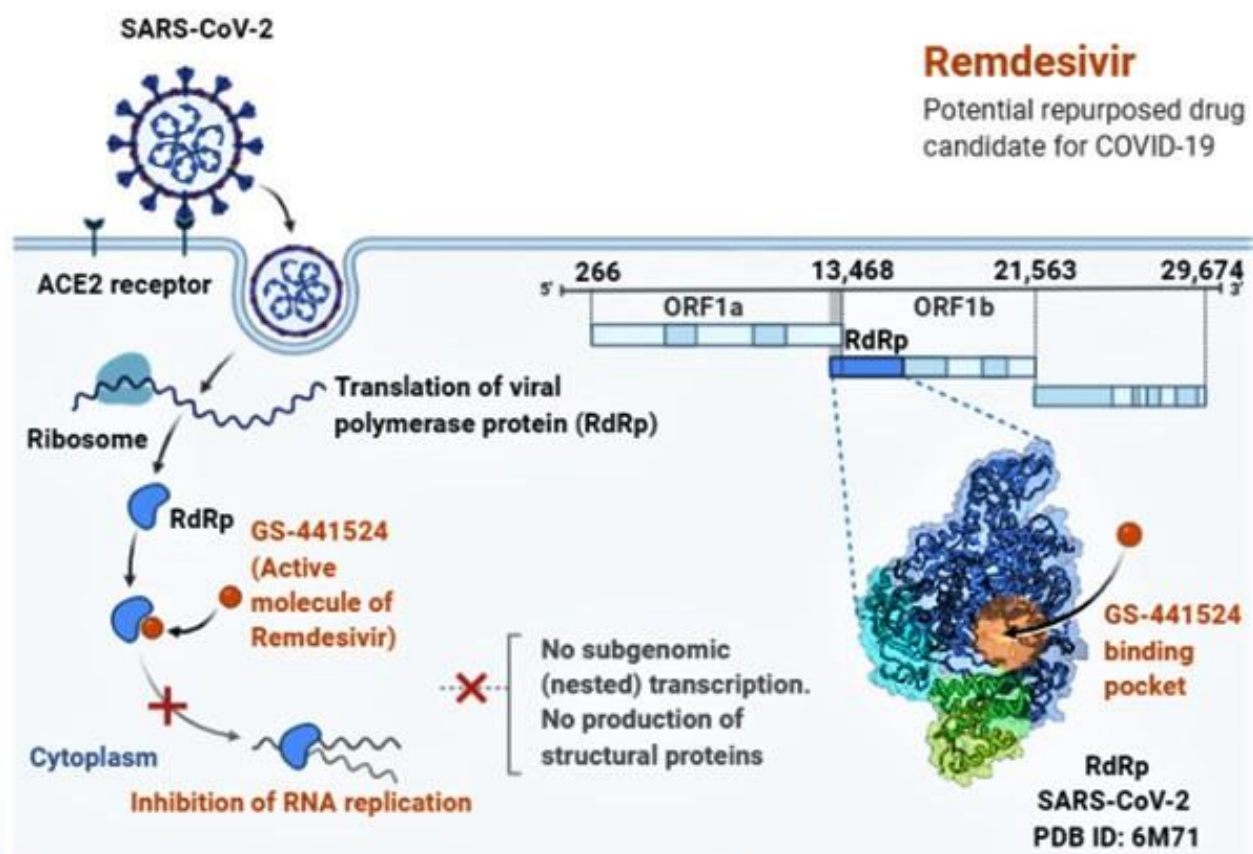


Fig. 3. Working mechanism of remdesivir



preclinical support.^{11,42} However, it can be used against influenza, the disease it was formulated to treat. Clinical studies have been on the run, where favipiravir is used in combination with IFN- α to assess viral inhibition and immune system enhancement. National Medical Products Administration of China approved favipiravir as the first anti-COVID-19 drug in China, as it successfully cleared the clinical tests with minimal side effects.⁹ Sofosbuvir, which was used against hepatitis-c infection, uses the same molecular mechanism to impair viral genome replication. Its dosage and side effects are not yet deciphered as the drug is still under clinical investigation.¹²

Ivermectin: Ivermectin is an anti-parasitic drug approved by U.S FDA which has got the potency to show anti-viral properties. It has been used to treat HIV-1 and dengue viruses. The mechanism of ivermectin reveals that it can dissociate the preformed IMP α . β 1 heterodimer, which aids in the protein displacement.⁷⁸ As

the protein displacement is essential for the maintenance of viral replication, targeting the protein displacement across the host cell would be a feasible option to inhibit viral life cycle. A recently conducted study reported that ivermectin reduced the viral RNA up to 5000-fold after infection with SARS-CoV-2 for 48 hours.^{9,79,80} With the proven results for anti-parasitic activity, ivermectin is under clinical trials to prove its potency against COVID-19.

Drugs inhibiting the viral protein synthesis

Once the replication of genome becomes complete, the translation starts in the cytoplasm. Polyproteins and structural proteins are produced because of translation. Two polypeptides known as ppla and pplab are processed by either a chymotrypsin-like protease (3CLpro) or main protease (Mpro) and one or two papain-like proteases into 16 nsps. sgRNA's of virus get translated into produce all the structural and accessory proteins. Here, it becomes worthwhile to

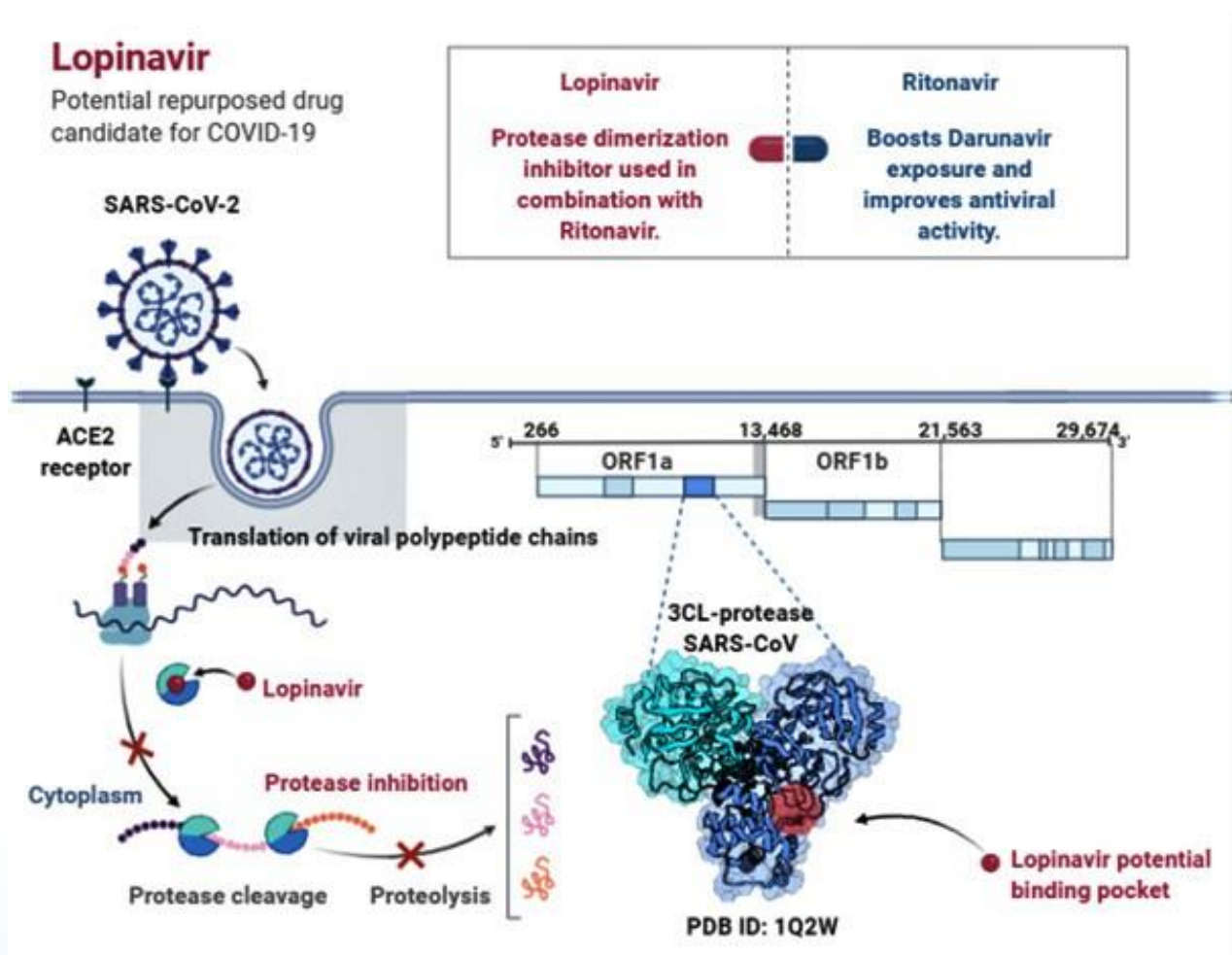


Fig. 4. Working mechanism of lopinavir/ritonavir

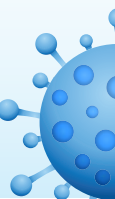


Table 1. Pharmacotherapeutic agents used against COVID-19 [11,12,42]

Acting Stage	Classification	Name of the Drug	Chemical Formula	Original Indication	Possible COVID-19 Indication	Dosage
Viral Entry Inhibitors	Viral S protein Inhibitors	Chloroquine	$C_{18}H_{26}ClN_3$	Malaria, HIV, Autoimmune Diseases	Off-label use for anti-viral treatment	500 mg twice for 5 days, orally
		Hydroxychloroquine	$C_{17}H_{26}ClN_3O$	Malaria, HIV, Autoimmune Diseases	Off-label use for anti-viral treatment	400 mg on first day followed by 200 mg for four days, twice, orally
	TMPRSS2 Inhibitors	Emodin	$C_{15}H_{10}O_5$	Polycystic kidney disease	Anti-viral drug under investigation	Unknown
		Promazine	$C_{17}H_{26}N_2S$	Treating psychomotor conditions	Anti-viral drug under investigation	Unknown
		Camostat mesylate	$C_{21}H_{26}N_4O_8S$	Chronic pancreatitis	Off-label use for anti-viral response	Unknown
Hemagglutinin Inhibitors	Hemagglutinin Inhibitors	K11777	$C_{32}H_{38}N_4O_4S$	Anti-parasitic	Anti-viral drug under investigation	Unknown
		<i>Nafamosta</i> It	$C_{19}H_{17}N_5O_2$	Pancreatitis	Off-label use for anti-viral response	Unknown
		Nitazoxanide	$C_{12}H_{19}N_3O_5S$	Diarrhea	Off-label use for anti-protozoal treatment	Doses for SARS were based on age groups; 1-3-year olds were recommended with 100 mg, 4-11 years with 200 mg, above 12 years with 300 mg for 5 days, orally
RNA	Arbidol Hydrochloride Nucleoside	$C_{22}H_{36}BrClN_2O_3S$	Unknown	Anti-viral drug under investigation	Unknown	
		Remdesivir	$C_{27}H_{35}N_6O_8P$	Ebola virus, MERS-CoV	Off-label use for anti-viral treatment	200 mg on first day, followed by 100 mg for up to 10 days intravenously
Replication Inhibitors	Analogues	Ribavirin	$C_8H_{12}N_4O_5$	Hepatitis-A, Hepatitis-B, SARS	Off-label use for anti-viral treatment	400 mg for 14 days, twice a day
		Favipiravir	$C_8H_8FN_3O_2$	Influenza	Off-label use for anti-viral treatment	Unknown
		Ivermectin	$C_{38}H_{74}O_{14}$	Unknown	Off-label use for HIV-1 and anti-viral treatment	Unknown
Protein	Protease	Sofosbuvir	$C_{22}H_{28}FN_4O_9P$	Hepatitis C virus infection	Off-label use for anti-viral treatment	Unknown
		Lopinavir and Ritonavir	$C_{74}H_{96}N_{10}O_{10}S_2$	HIV-1	Off-label use for HIV-1 treatment	200 mg -100 mg for 14 days through oral consumption
		Nelfinavir	$C_{33}H_{49}N_3O_7S_2$	HIV-1	Off-label use for HIV-1 and anti-viral treatment	Unknown
Synthesis Inhibitors	Neuraminidase Inhibitors	Oseltamivir	$C_{16}H_{28}N_2O_4$	Influenza	Off-label use for anti-viral treatment	Unknown
		Zanamivir	$C_{12}H_{18}N_4O_7$	Influenza	Off-label use for anti-viral treatment	Unknown
Unknown	Bactericidal	Azithromycin	$C_{38}H_{72}N_2O_{12}$	Bacterial Infections	Antibiotic	Unknown

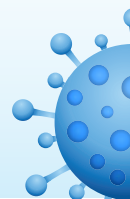
mention the production all the four main structural proteins, including spike protein.⁶⁵ Thus, the protein production can be targeted to inhibit the viral growth, as it involves a set of enzymes posing as potential targets.

Lopinavir and Ritonavir: Lopinavir is reported to be an aspartic acid protease inhibitor developed to treat human immunodeficiency virus-1 (HIV-1) [Figure 4]. It is administered along with ritonavir in a fixed-dose combination.⁸¹ Ritonavir is a CYP3A4 and CYP450 inhibitor that enhances the concentration, half-life as well as the pharmacokinetic activity of lopinavir. It has been revealed that the combination of lopinavir and ritonavir provides potent and sustained reduction of viral activities in HIV-1 patients.^{82,83} This has prompted interest in the assessment of the efficacy of the drug of other viruses including COVID-19. Studies have revealed its efficacy on both SARS and MERS viruses.⁸⁴ In addition to this, Chu *et al.*, reported that 4mg/mL of lopinavir and 50 mg/mL of ribavirin inhibited SARS-CoV-1 after 48 hours incubation.⁸² Similarly, another study conducted by de Wilde *et al.*, revealed that lopinavir inhibited SARS-CoV-1 with EC_{50} 17.1 ± 1 in Vero cells.⁸³ They reported that combination of lopinavir and ritonavir possessed better anti-viral activity than lopinavir alone. Thus, the results became a pavement for the treatment of SARS-CoV-1. In case of COVID-19, it proves to be efficient in case of mild and moderate infections.¹² But another clinical study found no benefits of lopinavir and ritonavir in case of severe infections. Lopinavir/ritonavir is formulated as a single tablet and a dose 200 mg -100 mg for 14 days through oral consumption is advised.⁸¹ Adverse effects of lopinavir include diarrhea, fatal pancreatitis, and hepatic decomposition.⁸⁵

Nelfinavir: Nelfinavir was originally developed for treating HIV-1 in combination with other anti-virals. It acts as a HIV-1 protease inhibitor, inhibiting the life cycle viral life cycle. It was used with other drugs via alternate mechanisms. But with the development of newer drugs for HIV, nelfinavir was excluded from the list. It is reported that the drug binds to the active site of HIV-1 protease enzyme and inhibits the cleavage of precursors of Gag-Pol polyprotein chain that are essential for the survival of HIV-1 inside the host. The residues left after the molecular

process are no longer infectious. Nelfinavir was proved a potent drug against SARS during the 2002 outbreak, with *in vitro* approaches.⁸⁶ In this study, it successfully inhibited the SARS-CoV-1 in Vero cells. Again, it was used against SARS-CoV-2 because of the >80% similar sequence with SARS-CoV-1.²¹ Out of the 20 drugs assessed, nelfinavir proved the most efficient drug. As all these studies were conducted on cell lines, human dose for COVID-19 is still unknown. However, for patients with hepatic maladies, nelfinavir is not recommended.^{87,88} Major side effects of nelfinavir include nausea, flatulence and diarrhea.⁸⁹

Neuraminidase determines the transmissibility of the influenza virus by interacting with sialic acid to cleave it, which in turn helps the virus replication and shedding. In fact, it facilitates the viral breakout from the host cell after the completion of viral genome replication, translation, and assembly of the viral particles.⁹⁰ Oseltamivir and zanamivir are the two more drugs reported to have their effects on viral genome translation. Both these drugs were used against influenza, by targeting a surface glycoprotein known as neuraminidase. These neuraminidase inhibitors are yet to clear the clinical trials. Therefore, the details on dosage and adverse effects are currently not revealed.¹² Apart from drugs with anti-viral indication, azithromycin is the only drug reported to have anti-bacterial effects as its original indication, though employed against COVID-19. It is reported that, azithromycin was originally designed for the prevention of secondary bacterial infection and it also possesses anti-viral activity.^{12,91} Damle *et al.*, have reported the 3 possible mechanisms shown by azithromycin to bring out the reduction in viral load. The first mechanism is like chloroquine and hydroxychloroquine, increasing the intracellular pH level of the cell to dismantle the viral replication process to halt the replication. The second mechanism suggests that the viral load reduction is attributed to the ability of azithromycin to induce pattern recognition receptors (IFNs, and IFN-stimulated genes). In addition to these, it is reported to act directly on the bronchial epithelial cells to regulate their normal function by reducing mucus secretion.⁹¹ The dosage recommendations of azithromycin are 500 mg on first day, followed by 250 mg 4 days.¹²



Challenges in drug and development

To this date, there is no reported drug that completely inhibits the viral activity in case of COVID-19. In the drug development, it becomes essential to have animal models to test and reveal the mechanisms underlying COVID-19 pathogenicity.⁸⁵ Though cell cultures prove to be efficient animal, models give better results in case of physiological analysis.⁹² As most of the research has been conducted with the COVID-19 potent therapeutics is linked with Vero cells,¹¹ the results may vary in case of human beings. In a study, various animal models tested for SARS-CoV replication, showed significant infection.⁹³ Tests against MERS-CoV, they were not vulnerable to the infection due to the absence of DPP4 receptor.⁹⁴ But in case of SARS-CoV-1 they showed up with severe disease symptom.⁹⁵ Therefore, development of suitable animal models to conduct pharmacotherapeutic studies in order to understand the behaviour of potential targets.

Apart from the requirement of animal models, clinical dosage of the drugs also plays an important role in the COVID-19 therapy. To this date, no drug has been available with international recommendations.⁹⁶ All the above reported drug dosages are given either under national healthcare guidelines or are still under clinical investigation. Besides, due to their variety of original indications, these drugs cannot be used directly against COVID-19.^{9,12} Furthermore, physiological changes must be considered, which arise because of the drug action. Cytotoxicity is one of the major assays performed in case of drug development as it determines the viability of cells against the developed drug. Being popular drugs used to treat COVID-19, both chloroquine and hydroxychloroquine are reported to cause ventricular dysrhythmias, hyperkalemia and systemic lupus erythematosus (SLE) respectively, in case of abnormal dosages.⁴⁹ In addition to this, many of the drugs have not cleared QT analysis, which is essential for the normal functioning of the ECG, including hydroxychloroquine. Considering these factors, the need to identify a potential drug attribute has been the need of the hour.^{97,98}

Alongside the dosage aspects, treating COVID-19 patients with non-COVID-19 diseases/disorders becomes hectic due to the drug-drug reaction between COVID-19 and non-COVID-19

therapeutic agents. As a result, patients who can be successfully tested for drug dosage against COVID-19 cannot be tested any longer for other drug because of the effect of other non-COVID-19 therapeutic agent.⁹⁹ For example, if a COVID-19 positive patient with additional rare genetic disease or diabetes may witness adverse effects due to the administration of both type of drugs.¹⁰⁰ Therefore, it becomes difficult to analyse accurately the pharmacological effect of the COVID-19 drug in the presence of non-COVID-19 drug. Thus, patients may also hamper the R&D activities associated with pharmacotherapy. Despite the reduction in the spreading of the disease, the quarantine and lockdown conditions have also resulted in handicapping the R&D activities like clinical data investigation including case studies, patient visits, data on pharmacokinetic, pharmacodynamic, efficacy limits, cytotoxicity limits and evidences.¹⁰¹ Though clinicians have effectively handled these issues with the help of technology and taken umpteen care towards collection and handling of samples from remote areas, careful interaction with patients, effective usage of digital media to cover data collection, assessment and presentation there exists several gaps owing to which the containment of the disease has not been achieved. Quantitative analysis has been reduced due to altered schedules of pharmacokinetic and pharmacodynamic data collections, and other model-based analysis. This has significantly affected the vaccine production, from which the COVID-19 would have been controlled at a notable.^{101,102}

CONCLUSION

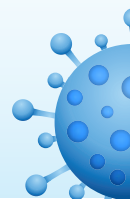
The outbreak of COVID-19 has raised unprecedented challenges before the world relating to healthcare and drug development. Pharmaceutical industry has responded to the situation with maximal efforts and still it is being employed to it. Through much of the research has been conducted out on the life cycle and pathogenesis, most of the potential targets to tackle have been revealed. These targets exist at different stages of life cycle of the virus and can be effectively neutralised with accurate and adequate dose of specific drugs. As the review highlights about the different drugs that are being



employed to treat the COVID-19, it specifically denotes the mechanisms of both the virus and the drug, their point of contact, and the pathogenicity at molecular level. Though many of the drugs are being used against the pandemic, their universal dosage levels and other pharmacological details are not revealed as they are still given under national healthcare guidelines of respective countries. To this date, WHO has not recommended any of the above reported drug although a few of them have received approval by the FDA. Thus, it becomes evident that advanced research on the drugs is to be done. It is worthwhile to highlight about using animal models to observe effective results. With the animal models, the complete pathophysiology of the disease as well as the effect of the drug can be understood. Also, more potent drugs should be tried with clinical investigations to report their efficacy against the COVID-19; along with the combination of drugs with different dosages against induced COVID-19 models. The best results can be obtained with the pharmaceutical industry employing 'One Health' approach where comprehensive efforts from different sectors sharing the data to effectively control the pandemic.

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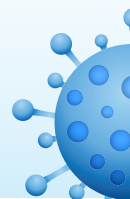
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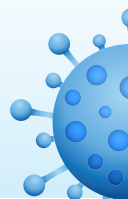
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Implementation and Evaluation of Virtual Anticoagulation Clinic Care to Provide Incessant Care During COVID-19 Times in an Indian Tertiary Care Teaching Hospital

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Background: COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-II) has become a global pandemic disrupting public health services. Telemedicine has emerged as an important tool to deliver care during these situations. Patients receiving Vitamin K antagonists (VKA) require structured monitoring which has posed a challenge during this pandemic. We aimed to evaluate the impact of Virtual anticoagulation clinic (VAC), a Telehealth model on the quality of anticoagulation, adverse events, and patient satisfaction vis-a-vis standard Anticoagulation clinic (ACC) care.

Materials and methods: A bidirectional cohort study was conducted in the Department of Cardiology, JSS Hospital, Mysore. Two hundred and twenty-eight patients in the VAC and 274 patients in the ACC fulfilling inclusion criteria were the subjects of the study. Telehealth tools like WhatsApp and telephone were used. Time in therapeutic range (TTR), Percentage of International normalized ratio in range (PINRR), and adverse events were analyzed and compared between the VAC group and the ACC group, between pre-COVID and COVID ACC groups, and between the VAC group and the same pre-COVID cohort. Patient satisfaction was assessed by a questionnaire at the end of 8 months. Descriptive statistics were used for the patient characteristics and inferential statistics for the comparisons between pre-VAC and VAC care.

Results: The mean TTR was $75.4 \pm 8.9\%$ and $71.2 \pm 13.4\%$ in the VAC group and ACC group, respectively ($p < 0.001$). The mean PINRR was $66.7 \pm 9.4\%$ and $62.4 \pm 10.9\%$ in the VAC group and ACC group respectively, ($p < 0.001$). There was no significant difference in TTR between the VAC group and the same pre-COVID cohort. The TTR differential between the pre-COVID and COVID ACC groups was significant. In either group, no major adverse events were seen. The most common tools used for data exchange were WhatsApp (83%) and SMS (17%). Seventy-four percent of patients were extremely satisfied with the overall VAC care.



Conclusions: Virtual anticoagulation clinic, a telehealth model can be used as an alternative option to deliver uninterrupted anticoagulation care during pandemic times.

Keywords: anticoagulation clinic, vitamin K antagonist, time in therapeutic range, percentage of international normalized ratio in range, telehealth

INTRODUCTION

COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-II) has become a global pandemic disrupting public health services (1). In these time frames, effective clinical care for patients with various chronic cardiovascular and other disorders has gained considerable attention from various stakeholders (2). In this predicament, Telehealth a virtual platform for the care provider and seeker has great potential in providing cardiovascular care which is evidently quite ideal (3). Its utility for patients on oral anticoagulants is one domain that needs to be addressed. Of the anticoagulants, vitamin K antagonists (VKAs) have a narrow therapeutic index with variable dose-response and diet/drug interactions (4). Patients taking VKAs require International normalized ratio (INR) monitoring and dose titration to achieve therapeutic INR for optimal outcomes (5). Patients taking VKAs may have multiple comorbidities like advanced age, hypertension, diabetes mellitus, and others. Studies have shown that patients with these risk factors are susceptible to severe COVID-19 infection necessitating a strategy to mitigate exposure of such patients (6, 7).

Telehealth services help to provide patients with the necessary care while minimizing the risk of transmitting SARS-CoV-II to healthcare workers and patients (8). The notion of telemedicine was incorporated in the Anticoagulation clinic to provide uninterrupted virtual care to patients taking VKAs. This study was conducted to evaluate the impact of Virtual anticoagulation clinic care (VAC) on the quality of anticoagulation, adverse events, and patient satisfaction vis-a-vis standard ACC care.

MATERIALS AND METHODS

Study Design and Participants

A bidirectional observational cohort study was conducted on patients enrolled in the VAC and ACC at the Department of Cardiology, JSS Hospital, Mysore from March to November 2020. Institutional ethical committee approval was taken. A total of 521 patients were registered in ACC till March 2020. Among these, 234 patients opted for VAC care and 287 patients opted for ACC care. For calculation of TTR, patients who had more than 3 months of ACC care before March 2020 with at least 3 INR values in both groups were included in the study. Newly enrolled patients in the ACC and those patients who had less than 3 months of ACC care before March 2020 were excluded from the study. A total of 228 patients in the VAC care group and 274 patients in the standard ACC care group were eligible for analysis. The patient enrolment process is depicted in **Figure 1**.

Anticoagulation Quality Assessment Tools

The anticoagulation related quality measures like Percentage Time in Therapeutic Range (%TTR) (9), Percentage of INR within Range (PINRR) (10), extreme INRs, and adverse events were analyzed. Patient satisfaction toward VAC care was assessed by administering five items self-developed questionnaire with scores 0 to 4 from extremely satisfied to not at all satisfied at the end of 8 months.

Anticoagulation Clinic (ACC)

JSS Hospital, Mysore has an established ACC since February 2017 comprising a multidisciplinary team comprising a Senior cardiologist, Junior cardiologist, Clinical Pharmacist, Clinical Pharmacy interns, and trained nursing staff. Key issues such as patient education (VKA risks/benefits, potential diet/drug interactions), ordering relevant laboratory tests (once a month INR testing), titrating the dose of VKAs to meet the INR target, facilitating procedures requiring interruption of VKAs, and adverse effects associated with VKAs were addressed.

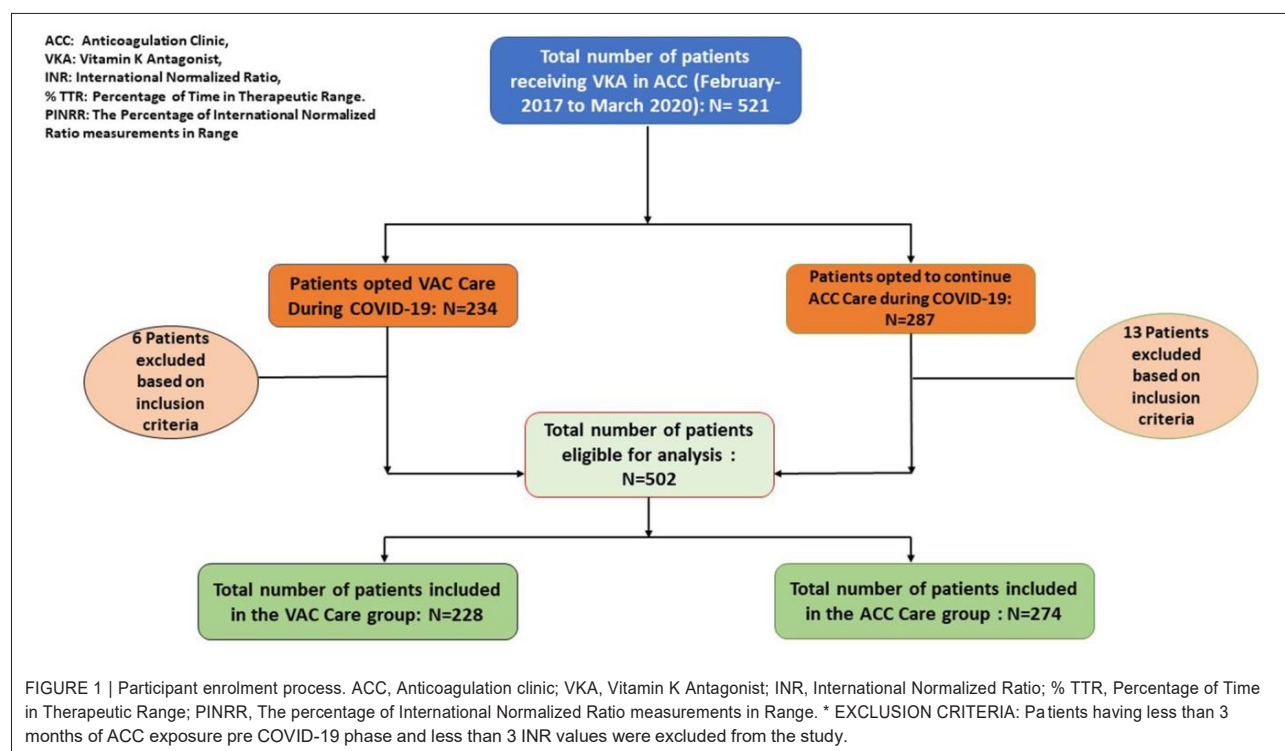
Virtual Anticoagulation Clinic (VAC)

VAC was initiated in March 2020 to provide sustained care to patients taking VKAs registered in ACC during the COVID-19 pandemic. Telehealth tools like WhatsApp and telephone were used as per Telemedicine practice guidelines (11). WhatsApp and SMS were used for the asynchronous exchange of the data. Patients were supposed to undergo INR testing once a month and communicate the INR report and if any symptoms related to bleeding, Transient Ischemic Attack (TIA), or stroke by any of the tools quoting their ACC identification number. Based on the INR value, dose titration was done and advice regarding the next INR testing was given. Patients with INR <1.5 and INR >5.0, major bleeding, and systemic embolic events were advised for the hospital visit. TTR and PINRR were calculated by Rosendaal linear interpolation technique for each patient. Calculations were performed with the assistance of a template made available by INR Pro (12). Major bleeding was defined by the International Society on Thrombosis and Haemostasis criteria (13). Stroke/Systemic embolic events were defined as the combined endpoints of ischaemic stroke, TIA, and systemic embolic events.

Statistical Analysis

Data was entered in MS Office Excel 2019 and analyzed by using IBM SPSS Statistics Version 25. Continuous variables were expressed as mean \pm standard deviation (SD). Categorical variables were expressed as absolute numbers and percentages. Descriptive statistics were





used for patient characteristics. *T*-test and chi-square tests (χ^2) were used for comparisons between groups. All tests were two-tailed, $p < 0.05$ was considered to be statistically significant.

RESULTS

The mean age of the patients in the VAC group and ACC group was 55.62 ± 13.77 years and 53.72 ± 11.8 years, respectively. The majority of the patients in the VAC group were from rural areas (57%). On the contrary, only 30% of the patients were from rural areas in the ACC group. Patients characteristics are depicted in **Table 1**. Atrial fibrillation was the most common indication for VKA therapy in both groups. Acenocoumarol was the most common VKA prescribed. Mean TTR in VAC group and ACC group was $75.4 \pm 8.9\%$ and $71.2 \pm 13.4\%$, respectively (p -value = 0.001). Mean PINRR in the VAC group and ACC group was $66.7 \pm 9.4\%$ and $62.4 \pm 10.9\%$, respectively (p -value = 0.0002). Patients in the VAC group underwent more frequent INR testing when compared to those in the ACC group. Two patients had a minor lower gastrointestinal bleed in the VAC group. None of the patients had major adverse events in either group. Three patients were scheduled for an in-person visit in the VAC group. Anticoagulation related parameters in the VAC group and ACC group are depicted in **Table 2**. There was no significant difference

in TTR between the VAC group and the same group during pre-COVID ACC care. There was a significant difference in TTR and PINRR between the pre-COVID and COVID-ACC groups ($p < 0.0001$). The number of INR tests performed per patient was less in the ACC group during the COVID pandemic. Anticoagulation related parameters between the groups are depicted in **Table 3**.

WhatsApp 189 (83%), followed by SMS 39 (17%) were the most common tools used for the exchange of data. One hundred and sixty-nine (74%) of patients were extremely satisfied with overall VAC care and 187 (82%) of patients were extremely satisfied to continue virtual care as assessed by a 5-item questionnaire. The patient satisfaction score and questionnaire are depicted in **Figure 2** and **Table 4**.

DISCUSSION

In our study, the principal findings were (1) Patients in the VAC group had greater control of anticoagulation in the form of more time spent in the therapeutic range compared to ACC during the COVID pandemic (75.4 and 71.2%, respectively). (2) There was no significant difference in TTR between the VAC group and the same patients in the Pre-COVID ACC care (3). There was a significant difference in TTR between the pre-COVID and COVID ACC groups.



TABLE 1 | Patient characteristics and anticoagulation related parameters.

Variables	VAC (N = 228)	ACC (N = 274)	p-value
Age (years)			
<60	118 (51.6)	156 (57.07)	0.9077
>61	110 (48.4)	118 (42.93)	0.2208
Gender			
Men	129 (57)	167 (60.84)	0.3841
Women	99 (43)	107 (39.16)	
Comorbidities			
Type 2 Diabetes Mellitus	53 (23.4)	89 (32.54)	0.0239
Hypertension	73 (32)	90 (33.01)	0.8102
Congestive heart failure	18 (7.8)	36.1 (13.20)	0.0520
Vascular disease [#]	29 (12.5)	31 (11.32)	0.6842
Educational status			
Literate	162 (71.1)	247 (90.09)	<0.0001 ^{††}
Illiterate	66 (28.9)	27 (9.9)	<0.0001 ^{††}
Location of residence			
Urban	98 (43)	194 (70.82)	<0.0001 ^{††}
Rural	130 (57)	80 (29.18)	<0.0001 ^{††}
HASBLED score			
≥3	69 (30.4)	57 (20.75)	0.0132 ^{††}
<3	158 (69.5)	217 (79.25)	0.0123 ^{††}
Vitamin K Antagonist			
Warfarin	16 (7)	6 (2.36)	0.0121 ^{††}
Acenocoumarol	212 (93)	268 (97.64)	0.0123 ^{††}
Indications for VKA*			
Atrial fibrillation	137 (60)	192 (70.28)	0.0159 ^{††}
Mechanical Valve replacement	8 (3.4)	44 (16.03)	<0.0001 ^{††}
Deep vein thrombosis / Pulmonary embolism	80 (35.1)	38 (13.69)	<0.0001 ^{††}
Cortical venous thrombosis	3 (1.5)	0	–

[#] Vascular disease: Coronary artery disease, Peripheral arterial disease; *VKA: Vitamin K antagonist.

^{††} statistically significant p-value has been obtained by performing chi-squared test.

Due to the COVID pandemic, healthcare was inaccessible to the majority of the patients. Telehealth-based VAC initiated during that period could deliver uninterrupted care to the patients on chronic VKA therapy. Patients in the virtual care group could maintain their mean TTR similar to that of ACC care during the pre-COVID state. Wherein patients in the ACC care group were unable to maintain the mean TTR because of less frequent INR testing and in-person visits. Similar telehealth-based studies conducted on patients with chronic warfarin therapy have reported mean TTRs ranging from 66 to 74% (14–16).

Several meta-analyses of randomized and real-world trials have found that TTRs and PINRRs are generally equal to or below 60% (10, 17, 18). The European consensus document recommends a TTR of >70% for optimal outcomes (19). NICE guidelines recommend a TTR of > 65% for patients with

TABLE 2 | Anticoagulation related Quality Parameters.

Variables	VAC (N = 228)	ACC (N = 274)	p-value
Number of INR [†] draws (1,544)	1,324	1,019	–
Average number of INR [†] draws/ Patient	5.8	3.72	–
Mean TTR% ^{††}	75.4 ± 8.91	71.2 ± 13.4	0.0018 [†]
Mean PINRR %**	66.7 ± 9.4 %	62.4 ± 10.9%	0.0002 [†]
Tests Over Range	129 (9.7%)	113 (11.11%)	0.2660
Tests Below range	151 (11.7%)	142 (13.9%)	0.1124
Extreme INRs			
INR >5.0	14 (1.06)	15 (1.51)	0.3323
INR < 1.5	30 (2.26)	75 (7.32)	<0.0001
Adverse events			
Major	0 (0%)	0	–
Minor bleeding	2 (0.8%)	0	

[†]INR: International Normalized Ratio; **PINRR: Percentage of International Normalized Ratio in the Therapeutic Range; ^{††} TTR: Time in Therapeutic Range.

^{††} statistically significant p-value has been obtained by performing chi-squared test.

[†] statistically significant p-value has been obtained by performing t-test.

AF on VKA therapy (20). In our study, achieved TTRs in both groups were above the proposed benchmark of >65–70%. One of the main reasons to achieve mean TTR > 70% in our study was because our cohort of patients were those registered in the ACC managed by a multidisciplinary team. Even randomized controlled trials and studies related to Anticoagulation clinics have documented better control of INR compared to community settings that were possible due to frequent monitoring, organized care, and improvement in adherence to VKAs (10, 17).

Other important and desirable points to note were that these patients had multiple comorbidities and could be treated with the reduced risk of exposure to COVID-19 infection during transit to the hospital, cost savings for travel, and no major adverse events. The majority of the patients were satisfied with overall virtual care and opted for virtual care even in the post-COVID state.

The tenable reasons for the patients to continue to benefit from following up in VAC are several. Patients were educated during their initial visits to the regular anticoagulation clinic about the importance of regular follow-up with PT/INR testing, risks of discontinuation, clinical benefits of continuous and uninterrupted use of VKAs. Also, the ease of contacting the care provider through dedicated service like a 24/7 contactable phone number could have helped the patients. Prior consultation on a one-to-one basis with the care provider may also have increased the confidence as it is reflected in the data on the satisfactory questionnaire. In our study, the majority of the patients (74%) were satisfied with overall virtual care. Eighty-two percent of the patients were extremely satisfied in continuing virtual care even in the post-COVID scenario.

In our study, 57% of the patients who availed virtual care were from rural areas. WhatsApp was the most common chat platform used. A recent study by the Internet & Mobile Association of India (IAMAI) and



research by Neilsen, reported that there are 227 million active internet users in rural areas in India as of November 2019 (21). This digital penetration can transform the delivery of virtual care to patients with chronic diseases in remote locations.

Preferably, patients who require VKAs, must visit in person initially and ideally should achieve at least two consecutive INRs in the therapeutic range before they could be transitioned

to virtual anticoagulation clinic care for optimal patient-centered outcomes.

This pilot study has paved a path of utilizing telehealth to manage patients on chronic VKA therapy during the COVID pandemic. Though short-term results are promising, more extensive and larger multi-centric studies with a longer duration of follow-up are required to assess the feasibility and efficacy of the virtual anticoagulation clinic.

TABLE 3 | Assessment of Anticoagulation parameters among Pre-VAC (pre COVID) and VAC care.

Anticoagulation parameters	VAC care (n = 228)	Pre-COVID care (n = 228)	p-value	ACC COVID-19 care (n = 274)	ACC pre-COVID care (n = 274)	p-value
Number of INR [†] draws	1,324	1,467		1,019	1,551	
Average number of INR [†] draws/ Patient	5.8	6.43	-	3.72	5.66	-
Mean TTR% [*]	75.4 ± 8.91	77.58 ± 8.85	0.0506 [#]	71.2 ± 13.4	79.12 ± 9.3	<0.0001 [#]
Mean PINRR % ^{**}	66.7 ± 9.4 %	69.68 ± 11.50	0.0241 [#]	62.4 ± 10.9%	67.8 ± 10.4	<0.0001 [#]
Tests Over Range	129 (9.7)	118 (8.1)	0.1375	113 (11.11)	96 (6.2)	<0.0001 ^{††}
Tests Below range	151 (11.7)	106 (7.26)	0.0001 ^{††}	142 (13.9)	129 (8.3)	<0.0001 ^{††}
Extreme INRs						
INR >5.0	14 (1.06)	0	-	15 (1.51)	10 (0.66)	0.0339 ^{††}
INR < 1.5	30 (2.26)	11 (0.75)	0.0009 ^{††}	75 (7.32)	8 (0.5)	< 0.0001 ^{††}
Adverse events						
Major	0 (0%)	0	-	0	0	-
Minor bleeding	2 (0.8%)	0		0	0	

[†]INR: International Normalized Ratio; ^{**}PINRR: Percentage of International Normalized Ratio in the Therapeutic Range ^{*}TTR: Time in Therapeutic Range.

^{††} statistically significant p-value has been obtained by performing chi-squared test.

[#] statistically significant p-value has been obtained by performing t-test.

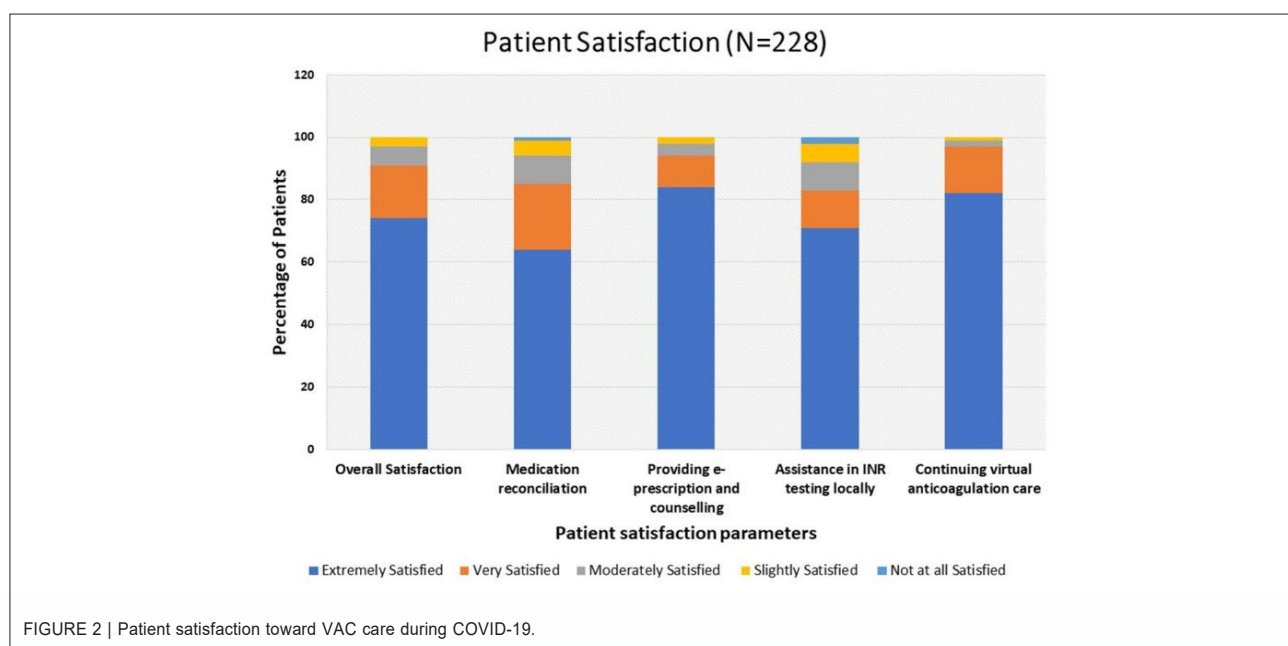


FIGURE 2 | Patient satisfaction toward VAC care during COVID-19.



TABLE 4 | Patient satisfaction toward virtual anticoagulation care (VAC) during COVID-19 pandemic (N = 228).

S. No	Parameter*	Response** n (%)
1.	Overall satisfaction of patients on VAC care during COVID 19	Extremely satisfied (4)
		Very satisfied (3)
		Moderately satisfied (2)
		Slightly satisfied (1)
		Not at all satisfied (0)
2.	Medication reconciliation	Extremely satisfied (4)
		Very satisfied (3)
		Moderately satisfied (2)
		Slightly satisfied (1)
		Not at all satisfied (0)
3.	Providing e-prescription and education reinforcement (counseling)	Extremely satisfied (4)
		Very satisfied (3)
		Moderately satisfied (2)
		Slightly satisfied (1)
		Not at all satisfied (0)
4.	Assistance in INR monitoring locally despite lockdown during COVID 19	Extremely satisfied (4)
		Very satisfied (3)
		Moderately satisfied (2)
		Slightly satisfied (1)
		Not at all satisfied (0)
5.	Continuing virtual anticoagulation care	Extremely satisfied (4)
		Very satisfied (3)
		Moderately satisfied (2)
		Slightly satisfied (1)
		Not at all satisfied (0)

*Feedbacks for Q1 – Q7 were obtained through a 5-point Likert scale with scoring 0 – 4, 0 = Not at all Satisfied, 1 = Slightly Satisfied, 2 = Moderately Satisfied, 3 = Very Satisfied, 4 = Extremely Satisfied. **Data represented as frequency and proportion.

STRENGTHS AND LIMITATIONS

The virtual anticoagulation clinic, a telehealth model that was developed during the onset of the COVID-19 pandemic to facilitate uninterrupted anticoagulation care, which could help maintain the quality of anticoagulation and minimize the risk

of exposure to COVID-19. Our study has limitations such as single-center, lack of randomization, small patient population, and shorter duration of follow-up.

CONCLUSIONS

This preliminary study showed that a virtual anticoagulation clinic can serve as a feasible alternate care model to provide uninterrupted anticoagulation care for patients on chronic Vitamin K antagonist therapy during the COVID-19 pandemic.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by JSS Medical College and Hospital, JSS AHER. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work. SKS, SPSB, and OJG designed and formulated the hypothesis. RV and OJG performed data collection. SKS and OJG prepared manuscript. ND and RM reviewed the manuscript. MB, OJG, and SKS performed statistical planning and analysis. All the authors approved the manuscript for publication.

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Assessment of Clinical Pharmacists' Assistance for Patients With Established Cardiovascular Diseases During the COVID-19 Pandemic: Insights From Southern India

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Objectives: We aimed to assess the clinical pharmacist-initiated telephone-based patient education and self-management support for patients with cardiovascular disease during the nationwide lockdown during COVID-19 pandemic.

Methods: A prospective single-center telephone-based cross-sectional study was conducted among patients at the Cardiology Department and its speciality clinic at a 1,800-bed tertiary care hospital in Southern India. A validated 8-item clinical pharmacist aided on-call questionnaire with two Domains was administered during and after lockdown (15 March and 8 June 2020). Clinical pharmacist-provided educational assistance on self-management practices were in accordance with the guidelines of Indian Council of Medical Research (ICMR) and World Health Organization. Comparisons was performed using sign test and association of responses were analyzed using the Goodman and Kruskal's gamma test. All the tests were two-tailed, $p < 0.05$ was considered to be statistically significant.

Results: Of the 1,080 patients, 907 consented with a response rate of (83.9%) and 574 (96.36%) patients were analyzed post-intervention. Majority of the patients were male (54.7%) and had Acute Coronary Syndrome [NSTEMI (42.10%), STEMI (33.92%) and Unstable Angina (9.86)]. The majority of subjects had at least two co-morbid conditions [(Type II Diabetes (48.33%), Hypertension (50.11%)] and were rural population (82.5%) as self-employed (43.1%) with a middle-class economy (31.6%). In the Domain-1 of checklist the awareness toward complications caused by COVID-19 in cardiovascular diseases ($Z = -19.698$, $p = 0.000$) and the importance of universal safety precautions enhanced after clinical pharmacist assistance [$(Z = -8.603$, $p = 0.000)$ and ($Z = -21.795$, $p = 0.000$)]. In Domain-II of checklist there was a significant improvement in patients awareness toward fatal complications caused by COVID-19 ($Z = -20.543$, $p = 0.000$), maintenance of self-hygiene ($Z = -19.287$, $p = 0.000$), practice of universal safety precautions ($Z = -16.912$, $p = 0.000$) and self-isolation ($Z = -19.545$, $p = 0.000$). The results of our study population varied from baseline evaluation (41.7%, $n = 907$) to post-intervention (95%, $n = 574$) based on Literacy, employment status and economic status.



Conclusions: The proactive role of clinical pharmacists in providing instructional services in collaboration with cardiologist during the pandemic circumstances increased patients understanding and mitigated infection exposure among patients, health care professionals and also assuring the continuity of care in patients with established cardiovascular diseases.

Keywords: COVID-19, cardiovascular diseases, clinical pharmacist, SARS-CoV- 2, corona virus 19

INTRODUCTION

In the last two decades, clustering and incidence of severe acute respiratory infections are one of the major threats to public health. Coronavirus disease (COVID-19) was first recorded in Wuhan, China, by the end of December 2019. Since then, COVID-19 has rapidly spread around the world. The COVID-19 was declared as a global pandemic on 11th March 2020 by the World Health Organization. COVID-19 has a major impact on public health and has a direct or indirect impact on social and economic activities. The exponential increase in the number of patients with COVID-19 in the past 6 months has overwhelmed health-care systems across the world. This is due to an inadequate understanding of the dynamic interplay of shifting epidemiology, publicity, pandemic prevention strategies, risk identification, and public health behavior (1). Cardiovascular disease is common comorbidity observed in patients infected with SARS or MERS (10 and 30% prevalence, respectively) (2). Currently, there is no promising evidence from randomized clinical trials (RCTs) that any potential therapy improves outcomes in patients with either suspected or confirmed COVID-19. Neither clinical trial data is supporting any prophylactic therapy.

The pre-existing cardiovascular disease seems to be linked with worse outcomes and increased risk of death in patients with COVID-19. Patients requiring intensive treatment had a significantly higher prevalence of chronic health conditions such as diabetes, cardiovascular and cerebrovascular disease (3). Moreover, COVID-19 itself can cause induce myocardial injury, arrhythmia, acute coronary syndrome and venous thromboembolism (4). Providing clinical care for patients with chronic cardiovascular disease and other comorbidities during pandemic times is challenging. Telehealth is an ideal platform to deliver clinical care during disasters and pandemics. Telemedicine negated the risk of COVID-19 exposure or transmission (5). In India, providing healthcare is a challenge, telemedicine ensures the safety of patients and health workers, especially when there is a risk of infection (6). India's digital health policy advocates the use of digital tools and focuses significantly on the use of telemedicine services, particularly at the grassroots level in the health and wellness Centers, where a mid-level provider/health worker can connect patients to doctors through technology platforms to provide timely and best possible care (7).

Citizens can make informed choices, defend themselves and comply with prescribed practices by focusing on what can be done during COVID-19 and when adequate resources are accessible, easily understood and communicated via reliable

and accessible networks (8). Therefore, through collaboration between clinical pharmacist and cardiologist, we aimed to provide educational assistance regarding self-management practices in patients with existing cardiovascular diseases to mitigate exposure to COVID-19 infection.

METHODS

Study Design and Participants

A prospective single-center telephone-based cross-sectional study was conducted among patients at the Cardiology Department and its speciality clinic at a 1,800-bed tertiary care hospital in Southern India serving 37 specialities. A validated 8-item clinical pharmacist aided on-call questionnaire with two Domains (**Table 1**) was administered during and after lockdown (15 March and 8 June 2020). Majority of the participants with acute coronary syndrome were the subset population of an ongoing clinical study and are currently being followed up. Clinical pharmacist-provided educational assistance on self-management practices was in accordance with the guidelines of Indian Council of Medical Research (ICMR) and World Health Organization.

Reliability and Validity of the Questionnaire

Initially, the questionnaire was validated by selected faculty and research team using facial and content validation methods to ensure readability. To assess overall reliability, the internal consistency of individual items in each questionnaire domain was examined by the researchers. The questionnaire consists of two domains and eight questions pertaining to awareness and knowledge of subjects toward COVID-19. Each question consists of two responses which was scored as Yes is 1 and No is 2. The score for the questionnaire range between 8 and 16, for the purpose of identifying the status of awareness and knowledge, participants are divided into high knowledge (8–12) and low knowledge (13–16) categories that has been derived by cumulative score. Finally, the survey questionnaire was administered to patients by a clinical pharmacist to facilitate better understanding. Higher score (>12) for the questionnaire indicates that patients have lack of awareness and knowledge which indicates the need for educational assistance. This telemedicine questionnaire of clinical pharmacists to assess awareness and knowledge regarding COVID-19 for patients with established cardiovascular diseases was self-developed with scoring, there are no references identified to cite this conjecture.



TABLE 1 | 8-item telemedicine questionnaire checklist of clinical pharmacists to assess awareness and knowledge regarding COVID-19 for patients with established cardiovascular diseases.

S no	Questions	Response	Score
Domain-I: Assessment of awareness			
1	Are you aware of the spread and impact of Novel corona virus 2019?	YES	1
		NO	2
2	Are you aware of the complications caused by Novel corona virus among patients with cardiovascular diseases?	YES	1
		NO	2
3	Are you aware of your present and past medical history	YES	1
		NO	2
4	Are you aware of the importance of universal safety precautions to prevent getting infected from Novel corona virus?	YES	1
		NO	2
Domain-II: Assessment of knowledge			
5	Do u know that Novel corona virus cause (SARS-nCoV-19) life threatening fatal complications among patients with cardiovascular complications and other co-morbid conditions?	YES	1
		NO	2
6	Do you know that self-isolation and maintenance of hygiene can aid in preventing infection from Novel corona virus cause (SARS-CoV-2)?	YES	1
		NO	2
7	Do you know how to follow universal safety precautions to prevent getting infected from Novel corona virus?	YES	1
		NO	2
8	Do you know that self-quarantine is a procedure followed by people who are at risk during epidemic?	YES	1
		NO	2

The following questions in the domain-I and II are related to assess awareness and knowledge toward COVID-19 or SARS nCov-II infection in patients with established cardiovascular diseases by a clinical pharmacist through telephone.

This questionnaire is copyrighted and can be used as a tool for patients with established cardiovascular diseases without any changes and other clinical groups (can be modified accordingly) to assess awareness and knowledge about COVID-19 or SARS nCov-II infection.

The score for this questionnaire range between 8 and 16, participants are divided into high knowledge (8–12 score) and low knowledge (9–12) categories that has been derived by cumulative scores. Higher score (> 12) for this questionnaire indicates that patients have lack of Awareness and Knowledge which indicates the need for educational assistance.

Sampling Method

This study followed a non-probability sampling method among the target population (subjects with established cardiovascular diseases at a tertiary care hospital).

Outcome

The primary outcome of the study is to identify the impact of the clinical pharmacist-initiated educational guidance on COVID-19 pandemic among patients with established cardiovascular disease. The secondary outcome is to ensure continuity of care and compliance with the prescribed drugs.

Statistical Analysis

Data were entered in MS Office Excel 2019 and analyzed using the IBM SPSS Statistics Version 25. Continuous variables were presented as mean \pm standard deviation (SD). Categorical variables were presented as absolute numbers and percentages. Comparisons between baseline and post assistance scores among the individuals were performed using sign test, Association of Responses with socio-demographic variables were analyzed using the Goodman and Kruskal's gamma test. All tests were two-tailed, $p < 0.05$ was considered to be statistically significant.

RESULTS

Of the 1,080 patients contacted by telephone, the response rate at the baseline was 907 (83.9%) and 574 (63.28%) post-intervention. The majority (54.7%) of the study population were male and had at least two co-morbid conditions (44.56%) in the age group (61–80 years) (Table 2). The patients in the study had Acute Coronary Syndrome [NSTEMI (42.10%), STEMI (33.92%) and UA (9.86%)] followed by associated comorbidities as described in Table 3. The questionnaire developed was administered during and after nationwide lockdown. In the Domain-1 the patients were aware of the spread of COVID-19 ($p = 0.000$) and their current condition ($p = 0.000$). However, majority of them were not aware of the complications caused by COVID-19 among patients with cardiovascular diseases ($Z = -19.698$, $p = 0.000$) and the importance of universal safety precautions, their awareness enhanced after clinical pharmacist assistance [(Yes = 85.01 vs. 98.08%, No = 14.99 vs. 1.92%, $Z = -8.603$, $p = 0.000$) and (Yes = 11.84 vs. 94.94%, No = 88.15 vs. 5.05%, $Z = -21.795$, $p = 0.000$)]. In Domain-II regarding knowledge aspect majority of the patient's knowledge improved regarding fatal complications caused by COVID 19 (Yes = 22.12 vs. 95.98%, No = 77.87 vs. 4.01%, $Z = -20.543$, $p = 0.000$), the process of self-isolation, maintenance of self-hygiene (Yes



TABLE 2 | Descriptive Summary of Demographics (*N* = 574).

S. no.	Parameter	Summary [#]
		(<i>N</i> = 574)
1.	Age (in years)	21–40 30 (5.32%)
	41–60	254 (44.34%)
	61–80	257 (44.56%)
	81–100	33 (5.76%)
2.	Gender	Male 314 (54.7%)
	Female	260 (45.23%)
3.	Literacy	Below high school 206 (36%)
	High school & above	287 (50%)
	Graduate & above	81 (14%)
4.	Economic status	Lower class 62 (10.7%)
	Upper-low class	254 (44.1%)
	Middle class	181 (31.6%)
	Upper class	77 (13.6%)
5.	Employment status	Salaried 111 (19.4%)
	Self-employed	248 (43.1%)
	Homemaker	215 (37.5%)
6.	Marital status	Married 530 (92.2%)
	Divorced/Widowed	51 (8.8%)
7.	Location	Urban 100 (17.5%)
	Rural	473 (82.5%)
8.	Smoking habit	Smokers 123 (21.5%)
	Non-smokers	450 (78.5%)
9.	Alcoholism	Occasional 153 (26.7%)
	Chronic	78 (13.5%)
	Non-alcoholics	401 (69.8%)
10.	Time spent on call per patient	22.54 ± 11.23 min ^a

[#] Data represented as number (proportion), ^adata represented as Mean ± SD, SD: Standard Deviation.

= 33.97 vs. 99.12%, No = 66.02 vs. 0.88%, $Z = -19.287$, $p = 0.000$), the importance of universal safety precaution (Yes = 44.94 vs. 94.94%, No = 55.06 vs. 5.06%, $Z = -16.912$, $p = 0.000$) and regarding self-quarantine (Yes = 25.08 vs. 91.98%, No = 74.91 vs. 8.02%, $Z = -19.545$, $p = 0.000$) depicted in **Table 4**. The individual responses of the patients for every question at baseline was evaluated to correlate the association of sociodemographic variables with awareness and knowledge which demonstrated that the responses of the patients varied based on Literacy, employment status and economic status as represented in **Table 5**.

DISCUSSION

Pandemics and epidemics are a widespread problem then and now as COVID-19. During such periods, people in the community face several challenges. Lack of awareness and consciousness often leads to an uneasy attitude which could adversely affect the patients with established cardiovascular complications. Different stakeholders in their respective countries are working together to “flatten the curve” by joint

TABLE 3 | Clinical parameters.

S. no.	Parameter	Summary [#]
		(<i>N</i> = 574)
1.	Acute coronary syndrome (ACS)	UA 57 (9.86%)
		NSTEMI 242 (42.10%)
		STEMI 195 (33.92%)
2.	Venous thromboembolism (VTE)	DVT 48 (8.4%)
		PE 33 (5.8%)
3.	T2DM	277 (48.33%)
4.	HTN	288 (50.11%)
5.	Kidney disease	72 (12.56%)
6.	T2DM + HTN	292 (50.86%)
7.	COPD	211 (36.73%)
8.	Depression	22 (3.8%)
9.	Atrial fibrillation	17 (2.9%)

T2DM, Type 2 Diabetes Mellitus; HTN, Hypertension; COPD, Chronic obstructive pulmonary disease; UA, Unstable angina; NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST-Elevation Myocardial Infarction.

[#] Data represented as number (proportion).

prevention initiatives led by the WHO. With a practically sufficient global lockdown, Pharmacists appear to be the first contact point for meeting the health requirements of the public (8).

We studied the role of clinical pharmacists' assistance for patients with established cardiovascular diseases during the COVID-19. The principal findings in our study at initial assessment were (1) Most of the patients were aware of their medical condition (CVD and comorbidities), (2) Most of the patients were aware of SARS-CoV-2 (COVID-19) infection, (3) majority of the patients were unaware of fatal complications caused by COVID-19 and association of COVID severity with CVD and comorbidities, (4) most of them were unaware of the importance of universal safety precautions, (5) majority of them don't know that self-quarantine is a procedure followed by people who are at risk during the epidemic.

Pharmacists continue to play their role in promoting continuity of pharmaceutical care, as well as supporting governments for disseminating information on precautions related to COVID-19 spread (13). Pharmacists are an integral part of health care performing exceptional roles in past pandemics and health crises, with some, such as Ebola and Zika, posing global health security risks (9). In this study after assessing the awareness and knowledge we provided educational assistance which helped our patients to gain (1) knowledge regarding fatal complications caused by COVID 19, (2) the process of self-isolation, (3) maintenance of self-hygiene, (4) the importance of universal safety precaution and (5) regarding self-quarantine practice. The Chinese Centre for Disease Control and Prevention recently published the largest COVID-19 case series in mainland China; the overall fatality rate was 2.3% (1,023 deaths among 44,672 confirmed cases), but the mortality rate in



TABLE 4 | Comparison of on call checklist responses before and after the clinical pharmacist assistance/intervention.

S No	Questions	Baseline responses	Post assistance/intervention responses			Z-value	P-value
			Yes	No	Total		
Domain-I:							
Q1	Are you aware of the spread and impact of Novel corona virus 2019?	Yes	487	0	487	−8.603	0.000*
		No	76	11	87		
		Total	563	11	574		
Q2	Are you aware of the complications caused by Novel corona virus among patients with cardiovascular diseases?	Yes	109	0	109	−19.698	0.000*
		No	390	75	465		
		Total	499	75	574		
Q3	Are you aware of your present and past medical history?	Yes	563	0	563	−	1.000
		No	0	11	11		
		Total	563	11	574		
Q4	Are you aware of the importance of universal safety precautions to prevent getting infected from Novel corona virus?	Yes	68	0	68	−21.795	0.000*
		No	477	29	506		
		Total	545	29	574		
Domain-II:							
Q5	Are you aware of the importance of universal safety precautions to prevent getting infected from Novel corona virus?	Yes	127	0	127	−20.543	0.000*
		No	424	23	447		
		Total	551	23	574		
Q6	Do u know that Novel corona virus cause (SARS-nCoV-19) life threatening fatal complications among patients with cardiovascular complications and other co-morbid conditions?	Yes	195	0	195	−19.287	0.000*
		No	374	5	379		
		Total	569	5	574		
Q7	Do you know how to follow universal safety precautions to prevent getting infected from Novel corona virus?	Yes	257	0	257	−16.912	0.000*
		No	288	29	317		
		Total	545	29	574		
Q8	Do you know that self-quarantine is a procedure followed by people who are at risk during epidemic?	Yes	144	0	144	−19.545	0.000*
		No	384	46	430		
		Total	528	46	574		

*Statistically significant p-value (2-tailed, < 0.05) has been obtained by performing Sign test.

patients with underlying CVD reached 10.5% (10). However, these results emphasize the potential risk of fatality in our patients with established cardiovascular disease and provide evidence regarding the need for intensive treatment on the infection (11).

The other measure which has been mentioned a lot in recent weeks is hand hygiene. The World Health Organization (WHO) regards handwashing with soap and water and friction with hydroalcoholic gel as the most effective measures for the prevention of infections and antimicrobial resistance (12). Research in major public universities following the H1N1 influenza pandemic reported inadequate compliance with preventive measures, such as residence at home when the virus is ill to prevent transmission in 2009 linked to the results of this study (14). Researchers can work with public agencies/health departments to set up information and awareness centers through participatory groups that may have significant population effects. Our

study helped to implement preventive measures, such as isolation, quarantine and community confinement, early identification of cases, social assistance and the provision of patient-specific instructions.

As a consequence of COVID-19, the need for social distancing forced us to use all the resources in our toolbox, and telehealth is one of them that accelerated its adoption globally (15). Telehealth strategies should be encouraged with a view to increasing access and providing care to the patients with chronic diseases to promote continuity of their care which made us adapt the new normal practices. We need to make a conscious effort to avoid any possible worsening of the digital divide, and the government needs to take that responsibility in this case (16).

What was wonderful about it was during this pandemic when our patients are generally considered to be at greater risk of having more severe COVID-19 disease and when they have been asked to stay at home, through virtual



TABLE 5 | Association of baseline responses with socio-demographic variables among study participants.

Question	Response	Literacy			Employment status			Economic status				p-value					
		1	2	3	Gamma	p-value	1	2	3	4	Gamma						
Q1	Yes	138	270	79	-0.776	0.000*	83	230	177	55	223	153	56	0.008*			
	No	68	17	2			28	18	38	7	31	28	21				
Q2	Yes	13	70	26	-0.532	0.000*	20	49	40	0.000	0.999	35	208	157	66	-0.329	0.000*
	No	193	217	55			91	199	175	27	46	24	11				
Q3	Yes	198	285	80	-0.556	0.055*	99	233	197	-0.042	0.761	46	246	175	70	-0.310	0.047*
	No	8	2	1			12	15	18	16	8	6	7				
Q4	Yes	4	32	32	-0.767	0.000*	26	20	22	0.266	0.021*	38	227	171	70	-0.465	0.000*
	No	202	255	49			85	228	193	24	27	10	7				
Q5	Yes	21	70	36	-0.520	0.000*	32	41	54	-0.008	0.925	44	38	26	19	0.336	0.000*
	No	185	217	45			79	207	161	18	216	155	58				
Q6	Yes	51	102	42	-0.323	0.000*	24	74	97	-0.337	0.000*	29	101	106	41	-0.196	0.003*
	No	155	185	39			87	174	118	33	153	75	36				
Q7	Yes	67	175	15	-0.076	0.275	47	113	97	-0.025	0.720	26	77	102	52	-0.379	0.000*
	No	137	113	67			64	135	118	36	177	79	25				
Q8	Yes	48	82	14	0.014	0.864	22	63	59	-0.114	0.157	19	53	54	7	0.094	0.222
	No	158	205	67			89	185	156	43	201	127	70				

*Statistically significant p-value has been derived from application of Goodman and Kruskal's gamma test

Literacy: 1: Below high school, 2: High school & above, 3: Graduate & above. Employment: 1: Salaries, 2: Self-employed, 3: Homemaker. Economic status: 1: Lower class, 2: Upper-Low class, 3: Middle class, 4: Upper class.



visits, we are still able to maintain their continuity of care, evaluate their COVID-19 awareness and knowledge, and provide instructional assistance and mitigate their exposure to infection. Overall, the results reflect what might develop into a new standard of future health care, particularly during contagious outbreaks (17). In this difficult time, hopelessness is the mother of acceptance, virtual practices have become a new normal. But hopefully, as we emerge from this pandemic, the telemedicine infrastructure will remain and benefit those in need.

Strengths and Limitations

During the times of stretched clinical resources due to COVID-19, our research results helped to add new ways to reduce COVID-19 spread in patients with established cardiovascular diseases. Although our study is a single-center study involving a clinical pharmacist, despite its limitations, the results in our study suggest that the extended role of the clinical pharmacist may also be beneficial to other clinical groups. In addition, more awareness amongst the study patients could also be attributed to govt initiated awareness programmes on COVID-19 (18). The results of this study may not be generalizable beyond India due to differences in clinical pharmacist practice worldwide.

CONCLUSIONS

The clinical pharmacist may, however, play a pro-active role in promoting patient-specific treatment decisions by serving as a resource for physicians and other health care professionals to mitigate adverse events caused by SARS nCoV-2 infection in

patients with established cardiovascular disease. The enhanced role of clinical pharmacists in providing instructional services should mitigate infection transmission during the COVID-19 pandemic.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary materials, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The institutional ethics committee has approved this study and participants have been informed of the purpose of the study before participating and voluntary consent is obtained virtually. All procedures performed in this study involving human participants were consistent with the Declaration of Helsinki 1964 and its subsequent amendments or comparable ethical standards.

AUTHOR CONTRIBUTIONS

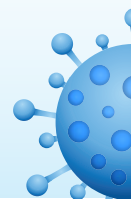
All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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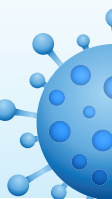


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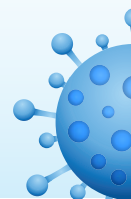


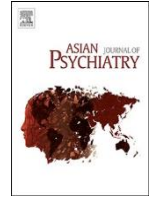


9. Social Impact of Lockdown

SI No	Title	SDG IMPACT
68	Revisiting 'The Plague' by Camus: Shaping the 'social absurdity' of the COVID-19 Pandemic, Banerjee D., Rao T.S.S., Kallivayalil R.A., Javed A., Asian Journal of Psychiatry, 54, 1876-2018	Goal 3: Good health and wellbeing
69	Role of Social Support in Women facing Domestic Violence during Lockdown of Covid- 19 while Co-habiting with the Abusers: Analysis of Cases Registered with the Family Counseling Centre, Alwar, India, Sudhir Pratap Singh., Meerambika Mahapatro., Moksh M Prasad Journal of Family Issues, 0192-513X	Goal 5: Gender equity Goal 3: Good health and wellbeing
70	Women's mental health and domestic violence in India during COVID-19 pandemic, Bhavika Mansharamani., Dr Kishor M., International Journal of Health & Allied Sciences, 10, 92-94, 2278-4292	Goal 5: Gender equity Goal 3: Good health and wellbeing
71	Biopsychosocial intersections of social/affective touch and psychiatry: Implications of 'touch hunger' during COVID-19, Debanjan Banerjee., Velmarini Vasquez., Marisin Pecchio ., Muralidhar L Hegde., Rao Ks Jagannatha., Dr Sathyanarayana Rao T.S., International Journal of Social Psychiatry, 0020-7640	Goal 5: Gender equity Goal 3: Good health and wellbeing
72	"The Graying Minority": Lived Experiences and Psychosocial Challenges of Older Transgender Adults During the COVID-19 Pandemic in India, A Qualitative Exploration, Banerjee D., Rao T.S.S., Frontiers in Psychiatry, 11, 1664-0640	Goal 5: Gender equity Goal 3: Good health and wellbeing
73	The 'othering' in pandemics: Prejudice and orientalism in COVID-19, Debanjan Banerjee., Roy Abraham Kallivayalil., Dr Sathyanarayana Rao T.S. Indian, Journal of Social Psychiatry, 36, 102-106, 0971-9962	Goal 10: Reduced inequalities Goal 3: Good health and wellbeing
74	"Unheard voices of the pandemic": Psychosocial vulnerabilities of the Indian migrant population during COVID-19 crisis, Debanjan Banerjee., Dr Sathyanarayana Rao T.S., Indian Journal of Social Psychiatry, 36, 84-86, 0971-9962	Goal 10: Reduced inequalities Goal 3: Good health and wellbeing
75	Covid-19 and Namaste, PRASHANTH KULKARNI., SHRUTHI KODAD., Dr Manjappa M., Influenza Other Respi Viruses, 1-2	Goal 3: Good health and wellbeing

76	The Silent victims of the Pandemic: Children and adolescents during the COVID-19 crisis, Vyjayanthi N V., Debanjan Banerjee., Dr Sathyanarayana Rao T.S., Journal of Indian Association for Child and Adolescent Mental Health, 16, 17-31, 0973-1342	Goal 10: Reduced inequalities Goal 3: Good health and wellbeing
77	The “Untold” Side of COVID-19: Social Stigma and Its Consequences in India, Prama Bhattacharya, Prama Bhattacharya, Sathyanarayana Rao T S, Indian Journal of Psychological Medicine, 42, 382-386	Goal 10: Reduced inequalities Goal 3: Good health and wellbeing
78	Psychology of misinformation and the media: Insights from the COVID-19 pandemic, Debanjan Banerjee, T. S. Sathyanarayana Rao ¹ , July 18, 2021, IP: 117.248.84.244], 0 Indian Journal of Social Psychiatry	Goal 3: Good health and wellbeing
79	The Role of “Attributions” in Social Psychology and their Relevance in Psychosocial Health: A Narrative Review, The Role of “Attributions” in Social Psychology and their Relevance in Psychosocial Health: A Narrative Review, Indian Journal of Psychiatry, January 22, 2021, IP: 103.2.232.	Goal 3: Good health and wellbeing Goal 10: Reduced inequalities
80	“Too Far or Too Close...”: The changing scenes of sexuality during the pandemic 1 2 Debanjan Banerjee , TS Sathyanarayana Rao, Indian Journal of Health, Sexuality & Culture Volume (6), Issue (2), December 2020	Goal 3: Good health and wellbeing Goal 10: Reduced inequalities
81	Psychosocial Framework of Resilience: Navigating Needs and Adversities During the Pandemic, A Qualitative Exploration in the Indian Frontline Physician, Debanjan Banerjee, T. S. Sathyanarayana Rao, Roy Abraham Kallivayalil and Afzal Javed, Front. Psychol. https://doi.org/10.3389/fpsyg.2021.622132	Goal 3: Good health and wellbeing Goal 10: Reduced inequalities
82	Sexual functioning during the lockdown period in India: An online survey Sandeep Grover, Mrugesh Vaishnav ¹ , Adarsh Tripathi ² , T. S. S. Rao ³ , Ajit Avasthi ⁴ , P. K. Dalal ² , Aseem Mehra, 1 Indian Journal of Psychiatry, Volume 63, Issue 2, March-April 2021	Goal 3: Good health and wellbeing Goal 10: Reduced inequalities
83	Uncertainty, Sex and Sexuality during the Pandemic: Impact on Psychosocial Resilience Debanjan Banerjee, Sanchari Mukhopadhyay, Abhinav Tandon and T.S. Sathyanarayana Rao	Goal 3: Good health and wellbeing Goal 10: Reduced inequalities





Short communication

Revisiting 'The Plague' by Camus: Shaping the 'social absurdity' of the COVID-19 Pandemic

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ABSTRACT

COVID-19 has emerged as a global health threat. The catastrophic reaction to a pandemic in spite of knowing the deadly outcomes, has been referred to as the 'social absurdity'. Such reaction creates a negativistic outlook with regard to the infection, thus contributing to chaos and preventing containment. In this article, the current pandemic of COVID-19 is revisited through the lens of Camus' 'La Peste, 1947'. The philosophical roots of social 'absurdity' during a pandemic are critically discussed in the context of death anxiety. Subsequently, ways of reshaping it are highlighted, borrowing from the theories of existentialism and positive psychology.

1. Prologue

When the world welcomed 2020 like any other new year, we knew little of what awaited us in the next few months. Originating in the Hunan province of China towards the end of last year, the novel coronavirus (SARS-CoV-2) causing Coronavirus disease 2019 (COVID-19) has already gripped human life by its reigns during the first few months. The COVID-19 pandemic has affected more than ten million globally, claiming the lives of almost five lakhs so far (World Health Organization Situation Report 163, as on 1st July, 2020), the numbers rising as we speak. Besides public health infrastructure, the virus has ripped through global economy, travel, national and international policies. Starting from various cities locking down their borders to small-scale set-ups crashing and thousands losing their livelihood, agitation has been soaring over need for testing and treatment. Masks and sanitizers have become the rarest commodities and various fake products are on the rise. Besides the infection, people are also falling prey to faulty treatments, false assurances and plethora of misinformation (Garrett, 2020). The chaos that has befallen the pandemic reflects history, when the 'pestilences' (bubonic plague) and the Spanish Flu had rampaged the world. The WHO mentioned COVID-19 as one of the largest outbreaks that the modern world has ever seen. In the pursuit of biological cures and vaccines against the virus, the socio-political infrastructure of the human ecosystem has been sadly neglected. Added to

that is the plethora of misinformation that has led to stigma, xenophobia and panic in interpersonal, social and political domains. COVID-19 in that sense is a 'digital pandemic' in which the 'tension and chaos' spread faster than the virus itself. Beyond just public health, psychosocial discourse related to the outbreak is on rise. Keeping the same in background, the authors were encouraged by the personal reflections of the Editor of this journal where he calls for a global action on mental health during the ongoing pandemic (Tandon, 2020a, 2020b). Furthermore in the subsequent editorial, he stresses on "opportunity amidst tragedy and uncertainty" highlighting the need to understand the ongoing pandemic in varied socio-cultural contexts (Tandon, 2020b). Hence, the authors attempt to glance at COVID-19 through a different lens. This article will glance at the 'social absurdity' that the world faces during this pandemic, drawing parallels with a classic drafted years back about a fictional illness that plagued the world.

2. Revisiting 'The Plague': through the lens of Camus

While world's scientific forum is racing towards vaccine and anti-viral development to find a definitive cure, have we really developed a practical and rational psychological reaction to COVID-19? In his classic of 1947, the Plague (La Peste), Camus speaks about an infection that destroys more than half of a town's population. Referring to the classical 'black death' or the Bubonic plague, he aptly mentions that

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"pestilences" keep repeating themselves, but the world still reacts to them with surprise. The inevitability of human sufferings through illnesses often comes as a 'sudden' realization provoking panic and fear among the masses. Considered to be one of the greatest of its times, 'The Plague' back in those days sets the human behavioural pattern at times of a pandemic. It mentions that "habits tend to get lost initially and they start returning when the infection ceases" (Camus, 1947). In psycho-analytic terms it might be considered to be the inevitable 'Thanatos instinct' that disturbs the 'normative obvious' while existentialism points towards the 'eternal truth of death' transforming the habitual life into that of absurdity. In both cases, it is the susceptibility of a civilization to sudden extermination just as many species in the past have met their detrimental fate (Felman, 2013). This intense 'fear of end' while knowing the very obvious has been the basis of human absurdity during the time of pandemics. Existentialism further proposes this absurdity to rise out of the conflict between constant search for meaning in life versus the apparent 'nothingness' of the universe (Thompson, 1995). Like reaction to grief, the reaction to such a biological disaster is also individualized, leading to various forms of denial, anger, frustration, dissociation, somatization and sublimation. In fact, the altruistic records mentioned in the Decameron written about the times of bubonic plague, have later been interpreted as healthier forms of defence during such 'pestilences' (Marafioti, 2005). While it can be argued that Camus might have drafted 'The Plague' through the screens of colonialism, as a rebellious attempt against the prevalent political ideologies of those times: several aspects of the 'social distancing', the vulnerabilities of the health care workers, the plight of the population and the prevalent chaos, all seem to resonate with the current situation. Globally indeed we are "plagued and sapped" as the people of the town in the novel.

Zooming out of the philosophical underpinnings, the threat is indeed true: we do have an illness that has affected the whole of world! Stress is but the norm at the times of pandemics but the world has an exaggerated response of 'mass-hysteria', fear of uncertainty and isolation as billions are locked down in an attempt to contain the outbreak. This is the 'storm of absurdity' which COVID-19 has taken the world into. In the midst of statistics about the number of cases, fatalities and recoveries, this important 'psychosocial' construct is largely neglected, as it subtly affects the society at a large, deeply impacting our quality of life and thoughts for months to come. Historians have inferred from past such infections, that they almost always unfold as 'social dramas'. The response pattern described by epidemiologists has been repetitive: denial and ignorance, recognition of the crisis, attempts to blame and explain, and finally the loss and resolution (Phillips, 2004). Camus in 'The Plague' wisely draws similar connotations saying that knowledge, beliefs and memories are the true offshoots that one wins after the war between plague and life is fought. In simpler terms, the obvious chaos attempts to stabilize the society which has been alternatively termed as 'Creation's theory of conservation' according to some philosophers (Hanson, 2020). While the human civilization is scattered and isolated due to the virus, many rare species of birds and animals are again seen to surface, plants living longer and air becoming clearer. This has been termed as 'reverse chaos' in one of the recent articles in the Guardian (The Guardian, Comments, as on 8 April 2020). In that way, 'The Plague' is not a tale of despair, but that of rejuvenation and lessons learnt for 'redemption' through the 'obvious' sufferings.

3. Analysing the 'Absurdity': role of death anxiety in social response

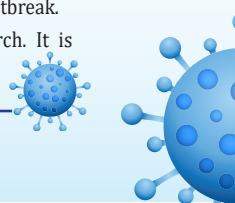
Can a thematic analysis of this psychosocial behaviour be then attempted: using an anthropological point of view? Besides denial, chaos, blame, stigmatization, loneliness and depression the other prevalent theme is the 'over-the-edge' fear of contamination, that is much beyond the usual precautionary measures of social distancing, hand and respiratory hygiene. This leads to significant hoarding of protective

medical devices, toilet paper, soaps and sanitizers. The 'socio-cultural lines' also tend to get marked as the mental health needs range from the luxury of 'loneliness in isolation' for the socially affluent individuals to basic living amenities and self-dignity for the homeless and migrant workers. The higher socio-economic class continues to have higher 'acute death anxiety', knowing well that COVID-19 is not a fatal infection. As mentioned in disaster management literature, 'mortality salience' is inversely proportional to the social class structure (Västfjäll et al., 2014). This 'survival of the fittest' often leads to public chaos, violence, increase in poverty and unemployment and eventually increase in criminality and aggression that can impact public health much more than the virus itself. To reiterate, in the words of Hongchen (2006), the human species has not yet obtained a rational response to its 'impending mortality'. Finally, going back to Camus, humans bury this 'social drama of the plague' deep in their unconscious as a response to resolution of each pandemic. This social drama during pandemics or epidemics gives rise to the panic-laden psychosocial reactions at a large, referred to as the 'absurdity of the plague' (Hongchen, 2006). This 'absurdity' has been reflected in the international 'blame game', the interpersonal xenophobia, the chaotic spread of misinformation and the rat-race for 'statistical' coverage of the pandemic numbers. The long lost virtues of 'solitude' and emotional bonding through time spent with loved ones (rather than virtual world) have resurfaced into 'realization' converting 'loneliness' into a significant offshoot of the pandemic.

The most ominous threat for an unknown infection that is extremely contagious, is its uncertainty till an effective medication develops. Especially so, when it spreads so fast across the world. It serves as a pervasive reminder of our 'end', which can be disturbing. This often leads to 'death-denying' behaviours that influence the global scenario. These can be competition for health-care, discrimination, 'othering' and mutual blaming which can strain international and inter-racial relations. Likewise COVID-19 has given rise to conspiracy theories against certain countries related to the origin of the virus, with the debate ongoing. Similar behaviours have been noticed in the past too. Anti-Jew sentiments during the Bubonic Plague of 14th century, the 'Spanish Flu' being a misnomer even though the virus did not originate in Spain, anti-Asian remarks during the SARS pandemic and racial discrimination during the Ebola outbreak in Africa: all are examples of desperate needs for 'scapegoating' to explain the uncertainty (Hays, 2005). Similarly during COVID-19 blame against China was rampant, WHO was accused of being 'lacklustre' and in various South-East Asian and European countries stigma is prevalent against people with 'Mongoloid' features irrespective of their origins (Jones, 2020). As the current pandemic spreads out its claws globally, these panic-inducing reports have become all the more viral.

The Novel coronavirus has ironically hijacked our daily life and communication, more than the respiratory system. It becomes difficult and confusing for the general public to be bombarded with plethora of data being updated every day. Similarly discordant messages are prevalent about the lifespan of the virus, the presumed duration of the pandemic, routes of infection, safety precautions, dietary habits and the necessary period of lockdown. Not one day has passed in last two months, on which every source of media has not debated or argued about one or more of these aspects, ultimately with an ambiguous solution in the end. 'Learned helplessness' to these effects of media, has driven billions in their living rooms to consume the loads of data-feeds about the virus and its fatalities throughout the day for months altogether. The penetration of this effect is now even more as social media is the primary 'consumption' of people stranded at homes. This confusion and a 'constant threat of mortality' increases the 'absurdity' during a pandemic and hence panic-stricken behaviour (Ingram, 2016). The mutual blame will eventually further divide us socio-politically only to be affected by another wave of infection or a new pandemic some days later. Stigma and marginalization will increase the pre-existing ageism, social stratification and hate that will proceed beyond this outbreak.

This 'death anxiety' has been a topic of extensive research. It is



defined as an innate driving force behind the human motives in life, that influences various aspects of behaviour and interaction (Neimeyer and Van Brunt, 1995). Based on the Terror Management Theory (TMT) by Greenberg et al. (1997), increased death terror during global threats shape society and acculturate the world. Examples of such 'death reminders' are fundamentalist beliefs and terrorism, substance abuse, attachment security threats, economic competition, aggression for dominance and wars. With the prevalent instability during COVID-19, it might seem that the 'death threat' is higher this time, hence contributing to the increased chaos and adverse effects on social health.

4. The way to change: borrowing from positive psychology

To borrow a quote from the movie Contagion (Shamberg et al., 2011, 0:45:20), directed by Steven Soderbergh,

"We tend to admire more during the times of such crisis, only to evolve beyond it..."

Human resilience is remarkable and history is the greatest proof of it. Many psychological theories talk about making peace with the 'inevitable death', a technique hard to master. The 'absurd behaviour' can be modified into a rational one in the face of stress, loss, suffering and death (Tomer, 1992). The 'death threat' need not always be perceived as morbid. Resilience and acceptance can help convert our behaviour towards positivism, flexibility and personal growth. New interpretations of the crisis can improve functioning and quality of life at times of such adversities. Based on disaster management research, lessons are always learnt after each crisis and the resultant optimism needs to be incorporated both into the psyche and at a broader level, the policy making. Sadly this is often not implemented (Vernberg et al., 2016). It needs another large-scale threat to make the world realize that its vulnerable and bring back the primal fear, that stays concealed in the vague delusion of invulnerability. Even in the face of COVID-19, if the mandates of global health agencies, precautionary measures of distancing are followed and behavioural responses organized, situations will start to improve. Self-care can foster care for others, exercise can promote health and mindfulness can help us reflect on our own selves. Social adherence helps taking care of the marginalized population, fosters growth and prevents stigma (Murphy et al., 1987). Based on positive psychology research, 'death threat' during a disaster can also lead to new avenues and goals like creativity, generativity, solving existential questions (purpose of life), higher standards and personal growth oriented behaviour (Wong and Tomer, 2011): all of which are for the 'healthier change'.

Difficult times also tend to increase our harmony with the nature. Practically not idealistically, there is a need to 'share' the Earth with other species instead of usurping their space. Expanded understandings of our existence can help build new opportunities at such times. A conscious attempt to accept the stress, live through the uncertainty, refrain from indulgence in social media and prevent unhealthy behaviours like hoarding, blaming or stigmatizing can lead the way forward. There needs to be a fine but firm balance between 'unrealistic optimism' and 'panic-driven fear of extermination'. That helps buffer the 'death anxiety' for an 'inclusive social growth'. In the words of Furer and Walker (2008), this anxiety can serve to modify the cognitions more towards self-sustenance and self-consciousness. The possible negative outcomes of this crisis can be used to find 'positive paths' ahead. Ultimately COVID-19 has stranded us all together, with more time for our families and ourselves, time that was long due. People can engage in lost hobbies, revise forgotten skills and nurture strained relationships. The social extravaganza of any celebration can be converted into true enjoyment and bonds can be mended. Even the nature has modified itself to be cleaner and purer in just few months as unnecessary human movement has got restricted. All these might have seemed idealistic last year, but a microscopic virus was all that was needed to turn these into a reality. Critics might well argue that in the face of an imminent

biological threat gripping the world, this discussion is philosophical at best. The authors however choose to consider 'social and humanistic realizations'

5. Epilogue

The renowned sculptor Bernini once said, "Where there is death, there is a new meaning." Many of his great arts depict fragility yet rejuvenation of life (Perlove, 1995). This reminds us of yet another landmark existential work to understand and appreciate the 'sense and purpose of life' through adversities. Sublimating our death fears through a new meaning has been the basis of logotherapy, when Frankl details his ordeal and survival at the Nazi concentration camps as means to discover "meaning in life" (Frankl, 2004). The solution to the 'absurdity' at the face of COVID-19 is to achieve creativity and personal meaning, eventually decreasing the pan-panic and implement better coping and growth. This will help interpersonal as well as international connections. Hardships and struggle for survival have formed the face of human civilization for decades; 'pandemic outbreaks' are just reminders of the same. The philosophy of Camus can once again be revisited to develop a non-judgemental approach to counter the innate fear, anxiety and despair for the eventual joy and gratitude, that human resilience has always been capable of. The biopsychosocial damage done by COVID-19 cannot be undone. However, like 'The Plague', let this also be a 'tale of redemption and survival' and not that of gloom and despair.

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Debanjan Banerjee: Conceptualizing, Writing - review & editing, Writing - original draft, Data curation, Visualization. T.S. Sathyanarayana Rao: Conceptualizing, Supervision, Writing - review & editing, Validation. Roy Abraham Kallivayalil: Conceptualizing, Supervision, Writing - review & editing, Validation. Afzal Javed: Conceptualizing, Supervision, Writing - review & editing, Validation.

Declaration of Competing Interest

None.

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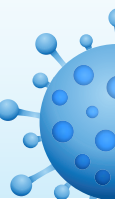
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Role of Social Support in Women facing Domestic Violence during Lockdown of Covid-19 while Cohabiting with the Abusers: Analysis of Cases Registered with the Family Counseling Centre, Alwar, India

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Abstract

The present study aims to analyze the role of social support in the lives of women survivors of domestic violence who filed a complaint with the Mahila Salah and Suraksha Kendra (MSSK) Alwar, India, while residing with the abusive husband and his family during the lockdown period of COVID-19. The study explores the role of MSSK with extended vulnerability of women during the lockdown period at large. This study adopts an exploratory qualitative method. A total of 36 married women who had filed a complaint with MSSK before and during the lockdown were included. Interviews with

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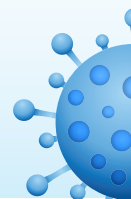
the women were held through telephonic conversations on vulnerability, coping mechanism and extent and forms of social support. Thematic content analysis was done in a stepwise manner. Results show that degeneration of social support model is time -bound and the accuracy of applying this model wane under extended condition of vulnerability caused due to COVID-19. MSSK can expand support by creating and integrating virtual community networks to detect and deter violence during the lockdown. The study suggests that the government can ensure and empower bystanders with skills of modern communication. The existing physical institutional delivery mechanism need to evolve strategies that are resilient to emerging threats from the vulnerable ecosystem.

Keywords

domestic violence, COVID-19, India, social support, coping, mental health, family counseling center

Introduction

The current pandemic of COVID-19 has led the world into a frenzy. Practicing safe hygiene, social distancing, and travel restrictions have become common sights throughout the globe. Effects of COVID-19 include a spike in domestic violence (DV) and is presumed to be seen continually across the globe as stress continues to mount (Peterman et al., 2020; Weitzman & Behrman, 2016). Many victims of DV are still trapped with the perpetrators, with no means to report it. International studies have shown that women are more likely to face violence when confined with little or no support of law enforcement agencies due to the lockdown (Campbell et al., 2017; UN News, 2020). The Government of India announced a nationwide lockdown from March 25 to May 17, 2020, to contain the spread of the disease. This unprecedented crisis has led to rapidly increasing stress, sudden shifts in daily routines, unemployment, alcohol abuse, and a rapid onset of scarcity in the availability of essential commodities alongside limited access to social support systems. All of these have been identified as risk factors of DV globally (Devries et al., 2013; Zahran et al., 2009). Learning from past pandemics, the risk of serious psychological consequences increases with the increase in the duration of quarantine (Brooks et al., 2020). Additionally, the accumulation of stressful events poses a risk of significant physical and/or emotional harm (Campbell et al., 2017; Catalá-Miñana et al., 2017). These adverse effects may extend for long periods due to continued abuse, ongoing psychological effects of abuse, or fear of the abuser (Stewart & Vigod, 2017). It is a frequently reported



behavior in abusers to try to isolate and control their victims so as they may not report violence (Mahapatro, 2018). As the mobility of the victim is restricted and the perpetrator can easily control access to social media and other means of possible reportage, it is next to impossible for the victim to reach out for help. Places of worship and communal places of congregation that were used for finding emotional reprieve are inaccessible during current times (Gelder et al., 2020). As a consequence of controlling behavior by the abusers, mental distress increases and may range from heightened stress, frustration, and anger to severe depression and post-traumatic stress disorder (Fulu et al., 2013). Suicide has been reported following the imposition of quarantine in previous outbreaks (Barbisch et al., 2015). The situation is forcing people to remain confined to their homes with limited access to essential services and minimized social support options. Current situations further enable the abuser to easily hush the victim.

Social support has been found to both mediate (Beeble et al., 2009) and/or moderate (Kaslow et al., 1998) the relationship between intimate partner violence (IPV) and mental health. Social support can be interpreted as social capital (Putman, 1995). It is an important intervention during stressful events in the family and the individual's life (Cooke et al., 1998). Under undue stress, social support is key in relieving the victim's distress. Research has identified the beneficial effects of social support on women's overall mental health (Ferrari et al., 2016; Harandi, 2017). Having stronger family support increases the strength to deal with psychological distress as well as with the abuse. A woman staying with an abusive husband and his family is twice more likely to develop psychological distress compared to a woman having the support of her parents (Mahapatro & Singh, 2019). Adequate social support decreases the risk of violence in a relationship and its negative impacts if present (Cohen et al., 2000; Katerndahl et al., 2013). The perception that one has access to informational, emotional, psychological, financial, and/or instrumental aid has been associated with positive health outcomes (Lindsay & Yates, 2004). Emotional support by friends and family prevents deterioration of mental health (Bosch & Bergen, 2006; Coker et al., 2002) by them acting as a buffer or moderator to provide a positive impact regardless of the severity of abuse (Cohen et al., 2000; Meadows et al., 2005;). The interactions and dynamics of social support are complex, but they always show a positive correlation with the quality of life and negative correlation with the extent of depression in the victims (Beeble et al., 2009).

Longitudinal studies carried out among the abused women in an Australian shelter have shown that social support in the lives of women causes a substantial reduction in posttraumatic stress disorder, depression, and anxiety (Martin & Mohr, 2001), whereas ongoing abuse and the absence of social

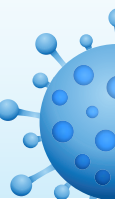


support contributes to psychological distress. Another longitudinal study by Sullivan and colleagues found that higher social support was related to decreased abuse and higher quality of life at multiple points in time of the study (Bybee & Sullivan, 2002). Abused women who receive emotional, tangible, and institutional support are less vulnerable to psychologically damaging effects of violence and their physical safety is also maintained (Panaghi et al., 2013). Social support influences coping strategies and provides greater perceived options that contribute to increasing the feasibility of a battered woman's ability to deal with abusers. Earlier studies have reported that social support works in both ways, directly promoting recovery from stressful experiences and crises experienced in the family as well as the protective role of a buffer against the effects of life stressors (House 1981). A study conducted by Mahapatro and Singh (2019) revealed that women who were supported by their parental family moved on to engage in active coping. It was also reported that they needed more social support, particularly from their parental family. They said that an institution could only provide temporary relief from fear and anxiety, but support from the parental family was permanent. In India, the concept of a woman seeking formal support and institutional help is not welcomed by the community. Therefore, the government-designed and implemented institutional programs have often not been utilized optimally. It is only the natal family that extends support to the abused women.

The Context and the Problem

In the Indian context, after getting married, when women move to the husband's family, it is seen as a detachment and social isolation from her kinship and natal family. In a situation such as this, where her support system has considerably narrowed (Turner & Marino, 1994), she is expected to forgo her established social capital and strive to adjust in every circumstance with her limited social support. In Indian cultures, women are seen as more of a collective unit of society, and social support is conceptualized as an interdependent culture and a transaction of sorts in which one person seeks help from another (Taylor et al., 2004).

At the time of crisis, when the women are in distress due to DV, they are left with meager social support to cope with violence they are subjected to (Mahapatro & Singh, 2019). Therefore, the investigation of social support is a prerequisite for social and mental resilience during family violence. In India, DV is recognized by the law, predominantly experienced by women, and characterized by "physical, sexual, or psychological harm by the husband or his family members in a domestic sphere" (*The Gazette of India*, 2005). The DV Act of 2005 recognizes the legal rights of women and has



established a decentralized model of Family Counseling Centers (FCCs) in every district of India. The FCC is implemented in collaboration with the police, judiciary, NGOs, and other departments throughout the country (Singh & Mahapatro, 2018). Alwar district headquarters has a Mahila Salah and Suraksha Kendra (MSSK), an FCC that addresses different elements of awareness and women empowerment. The centre, with its women-centric and culture-sensitive approach, has improved the utilization of legal remedies and providing psychological assistance in an integrated approach for better coping. In the absence of social support, these interventional programs are the only remaining instruments to create a positive impact by translating the abuse experienced by individual women into a cumulative human-rights discourse. In these processes of intervention, the victims are actively engaged and made empowered in order to utilize different methods of coping (Mahapatro & Singh, 2019). The institutional support to women survivors of DV is an important policy instrument for improving the survivors' well-being, especially in an unsupportive social context. The abused women register their complaint with these centers while residing with the abusive husband and their family, and they need not to move out of the home.

During COVID-19, coping strategies utilized by battered women registered with MSSK and residing with the abuser allowed several inferences to be made. Previous studies have reported that every year, about 200 DV cases are registered with the MSSK of Alwar district (Singh & Mahapatro, 2018). The MSSK was closed during the lockdown and started operating again on April 20, 2020, under orders of the government. Due to limited mobility during the lockdown, the MSSK could operate solely through mobile phones. However, the country-wide use of this intervention provided a unique opportunity to further investigate the situation during the lockdown period. The present study aims to analyze the situation regarding the role of social support to women survivors who filed a complaint with the MSSK Alwar, India, while residing with the abusive husband and his family members during the COVID-19. Further, the study explores the role of MSSK during the period of lockdown.

Methods

Study Design: The study adopted an exploratory qualitative method. Ethical approval for the study was obtained from SAPNA, the NGO running the FCC at Alwar.

Study area/setting: The MSSK, one of the FCCs serving women who have suffered domestic violence located in Alwar, Rajasthan, was selected for this study.

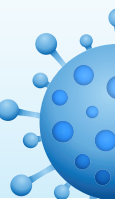


Study population and sample size: The study participants were composed of married women facing abuse who had filed a complaint with the MSSK, and who were staying with the abusive husband and his family and wished to continue the marriage. Those women who had filed for divorce were excluded because they had not been staying with the husband or his family. With the help of the register and records maintained by the counselors at MSSK, the women participants were selected. A total of 36 women who had registered with MSSK from January to April 2020 were considered; while 6 new cases (March 23–April 15, 2020) during the first lock down, and 33 earlier registered cases (January to March 22, 2020) were followed up. Only three women were excluded as they were not able to be reached, one of those interviewed had terminated the marriage or registered under divorce. MSSK was open to physical visits and registering complaints after April 15, 2020. The interviews were conducted in the month of April 2020 telephonically.

Data Collection

The interview schedule was open-ended in nature and structured to examine four key determinants: incidence of DV, role of MSSK, social support available to them, and the coping mechanisms provided to them, in order to deal with their traumatic experiences. The qualitative nature of these interviews helped to glean critical insights into the interviewees' perception. Moreover, each woman respondent's attitude and sensitivity to dealing with everyday situations at home was also assessed.

Interviews with women were held only after obtaining their verbal consent. The women were approached by the female counselors of MSSK over the phone. They had to be telephoned several times before they could be reached. A few limitations that were encountered in virtual communication included fear of a lack of privacy and confidentiality. In many cases, women were reluctant to answer questions about violence that they deemed unimportant in comparison to their immediate concerns regarding food, money, health, and the prevailing situation. Some women refused to answer questions over the phone and wanted to talk through a physical confrontation in MSSK only. However, measures were taken to minimize the risk of this non-response bias by allowing respondents to choose a suitable date and time. Thereafter, the counselor tried several times to contact the women when they could respond without the fear of their conversation being interrupted or eavesdropped. This was essential to guarantee their safety, apart from preserving the ethics and protocols of research so that respondents were comfortable enough to respond freely. Additionally, as per the government guidelines, follow-up measures were taken by the counselors and they were



expected to call each survivor and understand their situation, extend support, and ensure their safety. During the COVID crises, women were not in a mood to talk to the counselors of MSSK. However, the telephonic conversation could not be continued for more than a certain period, with the time of conversation varying between 10 and 20 minutes. Access to information over messaging platforms was limited due to the vulnerability of privacy.

Data Analysis

Interview data was analyzed using content analysis. In all the cases, individuals were assessed to see whether the social support changes in terms of its form and nature during the lockdown period compared to the usual phenomena. The criteria were determined as previously outlined in the theoretical model of social support (House, 1981). The description of incidental details was recorded in a narrative form. This allowed the perception of women's experiences of DV in a situational context and helped in examining how the shifting of subjectivity assisted in changing their social support and coping strategies.

Definitions Used

1. Definition of DV: The study used the definitions of DV as defined in the Domestic Violence Act 2005, India (*The Gazette of India*, 2005), and analyzed under physical, sexual, psychological, or economic violence.
2. Coping: Coping is a process through life where women are capable of combating and using different skills and resources. The term coping was used to mean the processes by which survivors engaged to seek support, redress, and transform some form or forms of damage they had suffered.
3. Social Support: Four types of social support have been studied as per the definition given by House (1981): (a) emotional support (providing empathy, listening, love, trust, and care); (b) instrumental support (providing aid in terms of cash or kind); (c) informational support (providing advice, suggestions, and information related to better coping); and (d) appraisal support (providing affirmation, feedback, social comparison, and self-evaluation).

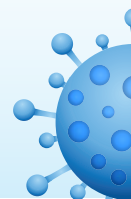
Results

Social support and coping with violence during the lockdown



Social support has been studied with the following four factors as given by House (1981). In the current context, some of the situations seen are as follows:

1. **Emotional support:** During the first few months of marriage, the family acts as a source of emotional support. The mother of the woman listens to her empathetically. Yet it is not a permanent solution. One of the women raised a question, “How many times will they listen to the same story? It doesn’t help much after a few months if the violence continues in the same manner.” During the lockdown, an alteration in the form of violence was also seen as physical abuse moderated. Although psychological violence persisted, it did not affect the women as deeply as before because the tension associated with the lockdown overshadowed their personal conflicts. The major factor influencing abuse was the consumption of liquor. As due to the lockdown liquor was unavailable, the severity of violence decreased greatly. Some respondents reported that the husbands were fearing COVID-19 and turned into god-fearing men. Other survivors reconcile their condition as “my individual suffering is not of such a huge amount that I talk about what’s happening in my home, when the whole world is suffering due to corona.” Some respondents reported that they were not getting time with their husbands to discuss issues or to introspect because they would return in the evening in a state of inebriation and exhibit violent behavior. In the absence of alcohol, as they could spend more time together, communication improved, and they got time to introspect and discuss issues with their husbands. Even if their husbands gave them a little time to voice themselves and talk about issues, they felt elated.
2. **Instrumental support:** Generally, while getting married, the natal family offers monetary support to their daughter in the form of a part of their property or money. But in many cases, as the parents of the woman themselves belong to middle and low-income families, they can’t provide much to support their daughters. Some respondents reported that their parents support a divorce so that they can have a better life with the alimony as compared to their unbearable present condition. However, they find it difficult to make any final decision that does not have a detrimental effect on their children’s future.
3. **Informational support:** Parents try to advise and guide their daughter, but it doesn’t help much because of a marked variation in the context and situation vary. Mostly women said that since it was an unprecedented crisis with limited options and information asymmetry, a sense



of fear regarding the family's well-being had developed in the abusers, which made them spiritually inclined and helped them cope better.

4. **Appraisal support:** The natal family keeps trying to soothe things to absorb the pain, tolerate the torture, and try to uphold the woman's morale. It does help get through the situation, but it does not change the situation. It is often the parents of the survivor who have helped them in reporting the case to the authorities. Additionally, it is not a common practice for bystanders or neighbors to report cases to the authority. As stated by a survivor, "when I am trapped in the house with my violent husband, it severely limits contact with my natal family and the outside world. With the scenario being the 'worst-case' possible where there is a threat to our lives, I am left with no option but to forgive and ignore as much as possible." Another survivor reported, "I keep things to myself as there are other things to think about such as how to run the household when it has become so difficult to get things during the lockdown."

These observations point out that the model is applicable over a relatively shorter duration of time. As the length of abuse extends for years, the rigidity in applying the model starts decreasing. In the present situation, as the woman is not economically independent and instrumental support is largely absent, social support stands for a relatively short duration after which due to long term abuse it falters. Regarding emotional and appraisal support, it is reported that the mother of the abused woman is the primary support giver. In the current time of lockdown, the woman is not able to contact her primary support giver, her mother, as the perpetrator is always around and has access to any and every means of communication, and the freedom to express herself is low. As the woman has no other option but to reside with the perpetrator, lodging a complaint with the institution remains the only form of assurance to the victim. Else, if the situation is not sufferable by the victim, she can choose to reside in the institution, an implication of which is publicly declaring her absence of any form of social support. In such a situation, the matter becomes publicly known and neighbors, friends, and family get word of it, but the victim is at least given a chance to thrive at the institution. A common concern for the women is coping during the lockdown with limited social capital available to them. It was inquired whether the victims shared their problems with their close friends and their natal families. They said that even if they did inform their friends and family, there is hardly anything they could do except worry. With the change in form, nature, and severity of DV during COVID-19, the role of social support and coping strategy hasn't changed to a great extent.



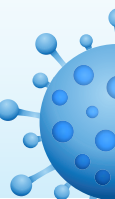
The women who approach MSSK learn about the other victims who have been suffering. It provides a means for social comparison and self-evaluation that acts as a form of appraisal support from the institution. It also gives them a sense of security seeing other women in a similar situation approaching the institution during their time of need. The institution then becomes an important place to find support and develop coping mechanisms as more than the institution itself the victims place their trust on the people representing the institution. Women reported that physical access to MSSK provided a higher degree of emotional satisfaction, yet the steps taken by the MSSK during the lockdown restrictions, had still provided them some form of social support to deal with their problems. For the women, even these subtle changes in the behavior of their husbands gave them a sense of positive well-being. However, during the current time of crises, the women are unable to approach the MSSK and are not able to see the standard for social comparison and are not able to evaluate themselves.

Role of MSSK during Lockdown

The lockdown has limited the MSSK to communicate with the women through mobile phones, which lacks compassionate and continuous counseling. With the constant presence of family members, and without face-to-face confidence-building interaction, mobile phones can only provide emergency services for women, especially for women reporting violence for the first time. Although the MSSK counselors appeal to the registered victims to check their well-being, they were unable to bring out refined personalized narratives due to paucity of time and the possibility of breach of privacy. As the husband is constantly at home, access to the phone is not easy. The women do not prefer messaging platforms because it leaves behind evidence. This has further decreased reportage. The counsellor reported that even if they wished to help the survivor, they could not do much as their details including phone numbers and files were in the office of the centre, the calls are received at the centre, and until the lockdown eased the staff did not have access to the records outside the centre.

Discussion

The pandemic has led to an imbalance in various factors and a new social equilibrium. Changes in certain perceptions and gross increase in risk factors is causing a surge in the number of cases pertaining to DV. The pandemic created social acceptance to psychological abuse, with an increased risk of developing anxiety and depression. Social support is a dynamic perception



that changes with the extent and gravity of the problem along with the support that a woman's natal family and friends can deliver at the time of crisis (Bosch & Bergen, 2006). In the initial days of conflict and abuse by the husband and his family members, support is offered by the natal family, particularly her mother who listens to her pain and provides emotional support. As the duration of the lockdown extends along with the risk of abuse, the natal family is still willing to provide support, but the victim's need for social support exceeds what is available to them, thus decreasing their ability to cope using the available social support. House's (1981) model of social support doesn't work to a great extent if the time period is lengthened substantially. If the situation is likely to continue, vulnerability due to the COVID-19 crisis increases and the model starts to lose its efficacy. Since the types of support available to the women readily are emotional, informational, and appraisal, without its instrumental form, the perceived support of the women makes them feel hopeless, suggesting higher dependency on institutional support as it is tangible. The mediation period was interminable and traumatic; the institutional support to women survivors of DV was an important policy instrument for improving survivors' well-being. Parson (2010) reported similar results in his study of battered women. With the change in nature of problem during COVID-19, degeneration of social support is a time-bound phenomenon in the absence of instrumental support, and its waning or buffering action isn't affected much.

In the women's point of view, majority of the coping strategies were based on problem focused approaches where the central cause of stress was the abusive partner or relation. By resolving various peripheral possible causes of conflict, the women used to deal with the stressor. A shift is being seen as the husband spends more time to reflect and retrospect with the woman, which leads to resolution of minute differences and decreases the risk of violence. When the husband spends even a little bit of time listening to the women's problems and matters of the home that they want to discuss with them, the women feel a sense of elation. This is supplemented by the gross reduction in alcohol consumption. Alcohol is a recurrent theme that largely contributes to violence due to the alterations in behavior that it causes (Mahapatro, 2018). Extended time spent at home helped partners to cope better under the lockdown. Spiritual inclination of the husband due to fear of the pandemic and other fears associated with the financial crisis eased day to day differences. Few of the women reported that "the extent of violence before the lockdown set in was so severe that the amount of abuse during lockdown doesn't feel as much because we can understand his situation." Some others reported that "the little time given by my husband during the lockdown, time he had not given me otherwise, felt very gratifying." The husbands tried to

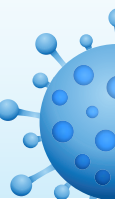


transform their outlook to reassure themselves in these trying times. This shift is helping decrease the peripheral burden of coping.

Women think that disengaging from the abusive husband or leaving the abusive husband are not the only solutions. Upon leaving abusive partners, women have to encounter a number of challenges including navigating through many transitions, which bring with them potential for increased tension or conflict. Such changes are not always welcome by society. In reality, the women don't have a buffet of avenues to cope; most of the times they choose to forgive the abuser to avoid confrontation and drown themselves in household chores to forget the instances of abuse. Another more favorable aspect of emotional coping for women is the formation of social networks. It's a positive step instead of justifying abuse and habituating it. Women who struggle in their current social networks in addition to coping with ongoing conflicts with the husband and his family, might not benefit from the usual interventions of social support. The reason may also be attributed to the fact that women have less social support and are neither well adept nor have the privacy to use information and communication technology to reach out for help.

Some limitations of the study are attributed to the telephonic conversations. As the time duration on the call is short, responses were short and interviews were concise. Some were using their husbands' phones and, due to the presence of other family members, a reporting bias may have crept in, making it difficult to draw conclusions on the state of mental distress and severity of violence suffered by the women during the lockdown.

The interventions from MSSK proved to be transformative for the survivors in the society as they spoke of this process as both the transformation of the self and giving rise to the embodiment of social transformation through social exchange. Similarly, other studies reported that online or telephonic support helps decrease anxiety, stress, and depression when the identity is not disclosed. It acts as a buffer to protect individuals from different aspects, particularly against certain life stressors. The paper highlights how traditional physical institutional arrangements have ceased due to the lockdown that has been imposed. An analysis of the need for a dynamic, virtual structure to adapt to the existing ecosystem is necessary. With the lockdown in place, both the victims and MSSK are struggling to find a channel for communication on both ends. Trying to reach out to them over the phone doesn't provide much of a solution as the perpetrators are constantly present; accessing the phone or even finding enough privacy to report the situation accurately, is difficult. During times like pandemics, people start developing a sense of unease towards the system. The physical presence of the counselor provides continuous counseling with compassion that builds confidence. The mobile



phone is only able to provide emergency services for women (Mahapatro & Singh, 2019). It is crucial to create a new instrument or device to access services from the MSSK.

On the whole, the study suggests that the psychological impacts of lockdown and being trapped with the abusers are wide-ranging, long-lasting, and unabating. The results suggest that the government should take the initiative to ensure their safety and well-being. This may be achieved by means of awareness campaigns and of dissemination of coping and stress management techniques to combat boredom, activation of social networks, and emotional help and counseling through telecommunication. MSSK should augment its infrastructure by integrating virtual community networks through emerging technology to monitor violence and follow up cases during the lockdown. Another concern is that of bystanders and neighbors. Instilling a sense of moral and social responsibility will improve reportage (Campbell, 2020). Frontline workers such as postal workers, garbage collectors, food delivery persons, and home appliances repair persons, and people who visit the family and discern DV, should come forward and report violence in the current times. The MSSK's interventions can further rebuild social networks of women to address the conflicts and reduce vulnerability with timely access of rights while seeking justice. The findings of the paper suggest that existing institutional arrangements need to evolve strategies that are resilient to emerging threats in the existing ecosystem.

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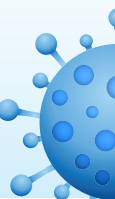
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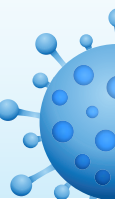
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Women's mental health and domestic violence in India during COVID-19 pandemic

Sir,

COVID-19 pandemic is an unprecedented humanitarian crisis in recent times, and it has affected people adversely. In any disaster, women are considered vulnerable because of many biopsychosocial factors. One of the important areas of concern is about the impact on mental health of women and increase in domestic violence against women (VAW), more so during the pandemic, which has been observed in many countries all over the world.

The United States Department of Justice Office on VAW has defined domestic violence as "a pattern of abusive behaviour in any relationship that is used by one partner to gain or maintain control over another intimate partner."^[1] According to the Protection of Women from Domestic Violence Act of India, 2005, it is defined as "any act of commission or omission or conduct resulting in physical, verbal, emotional, sexual and economic abuse."^[2] It includes insulting, controlling behavior, physical abuse, sexual abuse, psychological abuse, emotional abuse, threatening, stalking, cyberstalking, and economic abuse.

Globally, one-in-three women experience intimate partner violence. The economic costs of this violence range from 1% to 4% of global gross domestic product.^[3] Two-third of married women in India are victims of domestic violence.^[4] Multiple studies have found a relationship between natural disasters or any other extreme events with increase in the rates of interpersonal violence. Disasters appear to exacerbate preexisting social inequalities, disproportionately victimizing women, especially in developing nations, which can occur due to various reasons including stress due to physical confinement, economic disruption, possible unemployment, scarcity of basic provisions, and limited social support.^[5]

The COVID-19 pandemic caused by the novel coronavirus SARS-CoV-2 and the World Health Organization

recommended social isolation and containment measures. The Indian government announced a countrywide lockdown, starting at midnight on March

24, 2020, requiring that people stay at home and leave only for an essential reason. But home may not be always a safe place, in fact, it is often considered as the place where abuse occurs against women. This is because in largely patriarchal India society, power dynamics can be distorted by those who abuse, often without scrutiny from anyone from the outside. Unintentionally, "lockdown" and other restrictions may be granted more freedom to people who abuse "behind closed doors."^[6]

As social isolation requires families to remain in their homes, it increases interpersonal arguments and conflicts. The fear and uncertainty associated with the pandemic, along with unemployment and economical stressors, mainly in developing countries, can affect individuals and men may develop maladaptive behaviors to cope with the situation, which triggers domestic abuse.^[7] Men in India, because of sociocultural context, believe in dominance and blame the spouse; women thus are at the receiving end in all aspects including financial issues.^[7,8] There is also depletion of existing social support of friends and extended family and fewer opportunities for people living with family violence to call for help.^[7] These behaviors can significantly affect their mental health and well-being.

United Nations Women, a special wing of UN, has referred to the rise in VAW during the COVID-19 pandemic and accompanying lockdowns as the "Shadow Pandemic."^[9] A recent article reported on the pattern of the surge of domestic violence cases being repeated globally. It highlighted alarming figures, for example, a rise of reports of domestic violence by 40% or 50% in Brazil.^[10] In the UK, one of the leading domestic abuse organizations reported that calls to the UK Domestic Violence Helpline increased by 25% in the week following the announcement of tighter social distancing and lockdown measures by the government. During the same period, there was a 150% increase in visits to the support website.^[11]

India, with existing concern for gender-based violence (and ranked the fourth worst country for gender equality, according to public perception), is showing similar trends. After the announcement of nationwide lockdown, the number of domestic violence complaints received by the National Commission for Women (NCW) had increased significantly. Until early April 2020, there was a twofold increase in complaints related to VAW. As complaints surged, the NCW raised an urgent alert to announce mental health helplines for those witnessing any form of domestic violence, starting a WhatsApp number +917217735372 in addition to existing pan India helpline 181 and 1091. According to a report, Uttar Pradesh recorded the highest number of complaints among all states. About 86% of the women who experienced violence never sought help, and 77% of the victims did not even mention the incident to anyone.^[12] In a recent study, it was seen that districts in which a greater proportion of husbands reported that beating wives was justified, saw a greater increase in



domestic violence complaints in red zone districts relative to green zone districts.^[13]

Domestic violence can lead to long-term negative consequences to victims due to emotional and psychological distress ranging from low self-esteem, anxiety, depression, posttraumatic stress, and substance use to suicidality.^[14] A cross-sectional study from India showed the association between violence and self-reported gynecological complaints, low body mass index, depression, and attempted suicide.^[15]

Among all the issues around the COVID-19 pandemic, the crisis of increasing domestic VAW and mental health of women has received little attention. As the repercussions of this can be long term and damaging, not only for its victims but also for the entire country, it is necessary to take active measures in controlling VAW. Forming new support systems via online portals and reinforcing existing ones, speedy processing complaints, and awareness campaigns, can be a few measures. It is important that all health-care professionals in India are made aware of the women's mental health issues and trained to offer support and address the issues. Further research studies are required in this crucial area during the COVID-19 pandemic.

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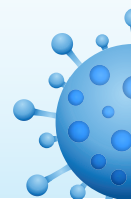


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Biopsychosocial intersections of social/affective touch and psychiatry: Implications of 'touch hunger' during COVID-19

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Abstract

Background: Humans are neurobiologically wired for touch receptivity. Social touch is a common and mutual way of expressing affection, care, and intimacy. From an evolutionary perspective, affiliative and affectionate touch are considered necessary for social and cognitive development throughout life-stages and across species. The emergence of the COVID-19 pandemic as a public health threat has mandated social distancing as a measure to contain the global outbreak. Travel restrictions, lockdown, and quarantine have led to separation and segregation, giving rise to social touch deprivation that might have adverse biopsychosocial consequences.

Methods: Affective touch has rarely been discussed within the purview of social psychiatry. We attempted to review the neurobiological, social, and behavioural correlates of social and sexual touch, as well as the neurophysiological models involved.

Results: The unmyelinated peripheral C-fibre afferents projecting to insular cortex and somatosensory areas form the prime pathway for affective touch. 'Top-down' modulation via the periaqueductal grey area, rostroventral medulla and sub-cortical structures, and 'Bottom-up' approach via the dorsal horn of the spine form the two theoretical models of 'social touch' system. The mu - opioid receptor (MOR) implicated in the Brain Opioid Theory of Social Attachment (BOTSA) and social neuropeptides like oxytocin and vasopressin are the primary neurochemical substrates involved. Sexual intimacy involves other neurotransmitters, with increased oxytocin activity in the limbic structures, Nucleus Accumbens, Anterior Cingulate, and Prefrontal Cortex. The discrimination and amalgamation of touch senses, their affiliative value and emotional valence in humans are based on a complex interplay between psychobiological, environmental, and personal factors.

Conclusion: The neurobehavioral and emotional effects of 'touch hunger' and strategies to mitigate it during COVID-19 are discussed in the context of psychoneuroimmunity and stress.

Keywords

COVID-19, pandemic, touch hunger, social touch, intimacy, neurobiology, immunity

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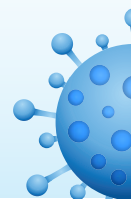
Introduction

The modern world has not seen a large-scale infectious disease outbreak like the Coronavirus disease 2019 (COVID-19). Caused by the novel coronavirus SARS-CoV-2, it has wreaked havoc in global health and economy over the last few months. According to the World Health Organization (WHO) COVID-19 Situation Report, as of February 2nd, 2021, 102,399,513 people have been infected by the virus, and more than a million succumbing to it, the numbers rising by the day (WHO, 2020). In the absence of a definitive biological cure or vaccine against the virus, social distancing has been considered the prime strategy to contain the outbreak. This has been imposed globally through the lockdown and quarantine measures (Singhal, 2020). While the medical symptoms and psychological stress of the pandemic fear have been primarily discussed, a vital aspect of wellbeing, the psychosocial impact of 'distancing' has not been sufficiently addressed. From the very anthropological origins, humanity has thrived on social formations and interpersonal bonds. The need to stay close to one another, meet, mate, or interact have been primal needs of the civilization, irrespective of the evolutionary phases (Thayer, 1986). One essential aspect of this interaction is 'social touch', which is fundamental in conveying care, affection, and love across species. This has evolved in the primates as shown by Harlow and other cognitive psychologists, as in how the sense of companionship, comfort, and care can be related through 'touch' or physical proximity (Thayer, 1986). This shapes development, attachment, social reward and salience systems, cognitive maturation, emotional regulation, and communication (Casco et al., 2019). Deprivation of this 'social touch' for prolonged duration can have a significant and long-lasting psychosocial impact on behavior and wellbeing. The COVID-19 pandemic crisis through social distancing has segregated people physically, preventing intimacy, and proximity like never before. The effect of 'touch deprivation' might seem easy to fathom but has far-fetched neurobiological and social implications. This article will review the neurobiological and psychosocial correlates of affective touch, its effect on coping and immunity, in the purview of the present pandemic, and discuss the relevance for psychological health. The terms 'social touch', 'affective touch', 'affiliative touch', 'sexual touch', 'intimacy', and 'touch hunger' were used for search in Pubmed, SCOPUS, PSYCHINFO, EMBASE, and Google Scholar. All articles related to the neurodevelopmental, neurophysiological, neurochemical, psychosocial, and psychosexual attributes of social touch were included in this narrative synthesis. The search was conducted between May, 2021 to August, 2021. To the best of our knowledge, there were no studies on the specific implications of social touch deprivation or 'touch hunger' during the ongoing pandemic. Hence, the discussion relevant

to COVID-19 and touch hunger in this paper is hypothetical, though it is based on the existing theoretical underpinnings of the review and provides important research directions for the future.

COVID-19 and social distancing: Emergence of 'touch hunger'

Human touch can bring about positivity and social bonding (Fredrickson, 2010). Be it the recommended kangaroo mother care in infancy, a tight embrace, a hand grasp, a pat on the shoulder, a gentle cuddle, the modern-day high-five or sexual intimacy, each has their own way of affecting the mind and wellbeing. How humans show their concerns toward their loved ones are neurobiologically wired to the areas in the brain, which are linked to social cognition (discussed in a later section). Common in daily lives, handshakes, hugs, and kisses are integral to social interactions. They tend to become like our daily habits, too mundane to be noticed. Only during pandemics such as this, when mandatory physical distancing needs to be followed worldwide, and gatherings or travel are restricted, the importance of 'touch' as a measure of communication comes to the forefront. Isolation has been the significant offshoot of separation and quarantine, as all forms of physical contact have become tabooed and fearful (Banerjee, 2020). This is more so for the frontline workers (health care professionals, police, delivery executives, other essential service providers, etc.), who are stigmatized and discriminated for the risk of increased exposure to infection (Montemurro, 2020). As the physical contact and intimacy have gradually decreased and abolished in some cases, 'touch starvation' or 'touch hunger' has risen, which can be psychologically distressing. Early in 1984, Renshaw (1984) had mentioned that humans starve for touch, just as they crave for food, and in both cases the longer the duration is, the more are the frustration and the distress. Even though initially 'touch hunger' was equated with sexual contact among couples (Field, 1994), later the same author in his book 'Touch' mentions about the multi-faceted aspects of 'touch sensitivity' in humans (Field, 2014). He discusses how touch is not only a valid form of emotional expression, conveying affection, and positive feedback to the brain, but also highlights the detrimental effects of 'touch deprivation' on the psyche. Touch starvation has shown to increase stress and compound trauma, disrupting psychological resilience and coping (Field, 2014). If chronic, this can increase the risk of depression, anxiety, grief, and complex post-traumatic stress disorders, especially in an already prevalent crisis (Field, 2014). 'Touch hunger' tends to be all the more distressing during the COVID-19 pandemic as the 'need for closeness' has to be balanced with the fear of this contagious infection. Beyond doubt, social distancing has proven to be an effective strategy in dealing with the outbreak. However, prolonged



deprivation of personal touch or sexual intimacy can worsen mood and anxiety states, making the person more withdrawn, thus generating a vicious cycle (Banerjee & Rai, 2020). The ‘fight-flight’ response to stress gets triggered in chronic touch deprivation, leading to adverse effects on stress management and immune reactions. It can affect digestive, cardiovascular, neurological, musculoskeletal, and respiratory systems of the body (Cascio et al., 2019). Considering the COVID-19 outbreak can often lead to immune system dysregulation and multi-organ dysfunction as causes of fatality (Cascella et al., 2020), ‘touch hunger’ can be theoretically hypothesized as a substantial risk for both the physiological as well as psychosocial effects of the virus. The outbreak has claimed several lives, prevented ceremonial funerals, social gatherings, and estranged families, all of which compound grief and bereavement. In absence of personal meetings due to the pandemic-related lockdown, this grief can be complicated due to ‘touch deprivation’ preventing effective expression of emotions (Field, 1994). Interpersonal support, face-to-face contact, and intimate bonds involving physical touch are protective factors for this problem, which can be absent during this pandemic (Qiu et al., 2020). A welcoming handshake or an encouraging pat on the back can convey messages more relevant than words, and this forms the backbone of mutual support in the global crisis of uncertainty. Attribution and interpersonal theories of social psychology state the necessity of reliance and proximity for reasoning out a problem (Försterling, 1988). Also, the interpersonal theories of suicide mention lack of perceived support and proximal connections as risk factors for hopelessness and self-harm (Van Orden et al., 2010).

Social distancing prescribed as a precautionary measure during the pandemics by the global health agencies, is one of the most effective ways of containing the infection (Singhal, 2020). Further, in the absence of a definitive treatment or a vaccine, distancing forms an important component of safety and promoting public health. However, the unprecedentedness and the chronicity of the ‘touch deprivation’ exacerbates the ‘touch hunger’. Hence, practically speaking, social distancing is a ‘dual-edged’ necessity and cannot be considered as a solely negative strategy. Also, even though physical proximity is desirable and can cause adverse consequences if withdrawn for long, there are certain flip sides to it. There have been increasing reports of intimate partner violence, marital discord, children and elderly abuse, as well as familial discord due to the prolonged entrapment of families and couples during the pandemic (Bradbury-Jones & Isham, 2020). For some, this are indeed the first times that they are ‘obliged’ to stay together, which can alter the interpersonal dynamics. Individuals who need their own comfort zone and ‘social space’ might be disturbed by over-stimulation with increased proximity, for example, those with autism spectrum disorders (ASD), Cluster

A personality disorders, and attention deficit hyperactive disorders (ADHD) (Brown et al., 2020). Even though distancing has been the ‘new norm’ for the last few months, cyberspace has brought about new avenues of social connectedness where both intimacy and relationships are digitalized. The need for ‘social or affective touch’ however might not be fully replaceable by technology. The truth is that with the advent of modern technologies and virtual links, we still cannot consider ourselves to be immune to ‘touch hunger’ at times of pandemics, as the personal ‘skin touch’ or physical intimacy have biopsychosocial correlates, which digitalization cannot possibly achieve. In that way, the COVID-19 pandemic is just another reminder for humanity to value the importance of social proximity and expression through ‘touch’. The understanding of physical intimacy with biopsychosocial correlates is opening newer understanding concept on Skin touch. Though ‘touch deprivation’ can affect any individual, certain societal, or personality patterns which necessitate more social connectedness, collectivism, and grouping might be at a greater risk. This is also applicable for people who are suddenly separated due to the pandemic after prolonged periods of co-habitation. Further, people who already have pre-existing attachment issues, maladaptive coping styles, psychiatric conditions, Cluster-B personality disorders, or those who are more socially comfortable within their communities like the minorities (due to age, gender, race, or ethnicity) might be more vulnerable to the effects of ‘touch hunger’ (Cascio et al., 2019). The neurobiological, psycho-behavioral, and immunological aspects of this ‘touch hunger’ will be discussed in the subsequent sections.

Social touch and affective regulation: Mechanisms involved

Skin covers the highest surface area of the body. The representation of lips, fingers, and toes in the sensory homunculus is also disproportionately larger compared to the other parts. Enhanced sensory processing for these areas has been evolutionarily linked to danger perception and mating (Longo et al., 2010). Subsequently, it has also been involved in the care and nurturing. At times of distress, both intimate and social touches can be portals of communicating anger, agitation, frustration, love, and grief. Repression of distress can trigger negative thoughts based on the diathesis-stress model (Monroe & Simons, 1991). Loneliness and self-absorption during prolonged quarantine can lead to lack of physical connection and existential crisis (Banerjee & Rai, 2020). Research has focused on the need for primates to cope or energize by the physical presence of others. In the early 1950s, Harlow conducted experiments with baby rhesus monkeys (Seay et al., 1964). They were separated from their mothers and put with artificial ‘mother figures’ made up of broken wire or soft



cuddly terrycloth. Food was kept alternately with both types of mother figures. It was found that irrespective of the quality, quantity, or presence of food, the baby monkeys preferred the 'cuddly mother', which they could hug with ease. The landmark studies by Harlow has later been replicated several times and formed the basis of mother-child attachment through proximity and touch (Champoux et al., 1992). When birds or animals peck or groom each other, it is not always cleaning but also a nurturing behavior, which has anthropological connotations of society formations and bonding (Washburn, 1978).

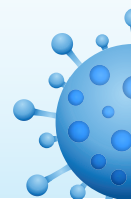
Touch is the earliest sensory modality to develop (Maurer & Maurer, 1988), which serves as a 'sensory anchor' on which the sense of self and physique extends (Bremner & Spence, 2017). Social touch has even been conceptualized prenatally. The exploration of the maternal uterine wall by the fetuses increases with the trimesters (Marx & Nagy, 2017). It has been interestingly proposed that the rhythmic stimulation of the lanugo hairs by the fetal movement in amniotic fluid, induces a social priming effect through oxytocin, the very first of the maternal-child bonding (Bremner & Spence, 2017; Washburn, 1978). Subsequently, throughout life, touch is used to convey reassurance, comfort, support, and empathy (Hertenstein et al., 2006). At the same time, whether the 'touch' is pleasurable or not is decided by the context, social appropriateness, identity of the toucher, and preferences of the one being touched. The physical characteristics of the tactile stimuli like gentleness, temperature, timings, and velocity are all important in deciding its perceived effects (Gazzola et al., 2012). After the peripheral reception of touch, several 'top-down' approaches operate before the subjective sensation is experienced. This involves sensory gating and awareness of contact, followed by the interpretation of these neural signals by the somatosensory cortex based on prior experiences or expectations and subsequently, the contextual cues (auditory, visual, olfactory, etc.) that determine the affectivity of the touch and the resultant sensation (pleasure or disgust) (Schmack et al., 2013; Taylor-Clarke et al., 2002). There are various neurobiological factors influencing the cue processing, cross-sensory relay, cognitive, and affective regulations of touch. A detailed discussion of the physiological mechanisms of mechano-receptive skin sensitivity and sensory pathways of touch sensation will be beyond the scope of the review. Here we will focus on the neurobiology governing the affective regulation of social touch.

Affective modulation of 'touch': Top-down versus bottom-up models

There has always been a debate with regards to when a touch can be considered social! The gentle caressing of a baby's body, or the playful cuddling between friends or the intimate foreplay in romantic relationships, the perceived 'pleasure' has been proposed to be regulated by the low-threshold

unmyelinated peripheral afferent fibers (C-touch or CT fibers). These nerve fibers are specifically sensitive to the stroking sensation and affective component of touch (Olausson et al., 2010). Like any other sensory stimuli, the fine-tuning of touch perception can both be explained by bottom-up and top-down models (Cascio et al., 2019).

Bottom-up approach. The CT afferents are essential to differentiate between affective and discriminative touches. They project to the posterior insular cortex, which deals with an emotionally relevant context for a sensory stimulus. This is in contrast to the discriminative touch relayed by the myelinated fibers to the primary somatosensory cortex (Olausson et al., 2002). Experimental models have also shown a significant relationship between the velocity of transmission (light touch versus sub-optimal touch) and the perceived pleasure, which has led to the concept of 'touch satiety' (Tricoli et al., 2014). Prosocial and intimate interactions involving caring or sexual touches (CT-mediated) release oxytocin, which promotes affective response. This complex interaction between touch and affective regulation is mediated by the Brain Opioid Theory of Social Attachment (BOTSA), which states oxytocin as a predominant neuropeptide in social interactions of mammals (MacHin & Dunbar, 2011). This process is all the more complicated in primates with the involvement of opioids in social reward and relationship salience (Henning et al., 2017). While the generic components of touch like shape, size, texture are not affect-laden, the CT fibers serve as a relay between the external stimulation and the internal affective content attached to it, which is seen in erotic or sensual touch (Jönsson et al., 2015). The bottom-up touch modulation through the CT fibers is also implicated in the 'social touch system', which explains the effect of personal significance on the touch. The posterolateral nuclei of thalamus form a vital area for sensory integration and then relaying it to the insular and somatosensory areas (Gazzola et al., 2012). Social neuropeptides can be released even when a person touches inanimate objects of interest (e.g. pen or diary for an author, guitar for a musician, brush for a painter, etc.). Similar affective arousal can occur when a person strokes his loved pet, or when one takes care of a sick person (McGlone et al., 2014). Certain areas are represented more in the brain for this 'affective valence' of touch like palms, lips, etc. (Longo et al., 2010). Quite understandably handshakes and handholding have widespread sociocultural acceptance for expressing greetings and care. Similarly, kissing is a universal connotation of intimacy. Studies have shown electroencephalogram mu wave suppression and increased heart-rate variability being associated with hedonic touch among couples and empathic touches in parent-child relationships (Peled-Avron et al., 2018). Understanding the affective component of touch solely based on the transmission by C-fibers appears to be an oversimplification, as it is a complex interplay of many emotional, social, and



physiological factors, which ultimately decides the perceptive value. There can also be blending of other sensations (tactile, thermal, etc.), which in synchronicity with the C-fiber transmission attaches emotional valence to the touch (Ackerley et al., 2012).

Top-down approach. Contextual factors play an essential role in this model. The identity, intent, and relationship with the person delivering the touch become important. Touch among strangers can be used for random greetings and communication, while in intimacy, it is vital for psychosexual wellbeing and bonding. Goldstein et al. (2018) showed romantic hand holding in partners to increase brain-brain coupling and decrease pain threshold. Though literature mentions the role of somatosensory cortex in top-down modulation, its role in affective regulation of touch is unclear. The familiarity and past experiences (topographical memories) play an important role. Hence fusiform gyrus, frontopolar cortex, and even the cerebellum has been implicated in the emotional processing of touch. Also, the subcortical regions of ventral striatum and amygdala (involved in the processing of affect, motivation, and fear) are involved in touch-processing (Perini et al., 2015). The entorhinal cortex (olfactory memories) and the medial temporal lobe (topographical memories) interact in determining the context of touch (Bonda et al., 1996). This multisensory input is understandable, as unpleasant odor or memories can often cause touch aversion; or as noted in post-traumatic stress disorder, a pleasant touch from a loved partner can be coupled with coercion or force used before. Similarly, fear of danger or death can reduce the affective content of touch due to increased threat perception (McGlone et al., 2014; Perini et al., 2015). To summarize, the cortical activation gives rise to the subjective experience of touch and the ascending nociceptive neurons in the dorsal horn are regulated by descending pathways from the brain (Woolf, 2011). The periaqueductal gray matter (PAG) in the midbrain forms a central control for the incoming nociceptive inputs from the rostroventral medulla (RVM) (Fields, 2004). The RVM further excites or inhibits the dorsal horn neurons. At a higher level, the valid affective value is assigned to a 'touch' by descending inputs from prefrontal cortex, hypothalamus, ventral striatum, which modulate the ascending sensory signals. These structures also have reciprocal connections with PAG to amplify or dampen the sensory threshold of affective touch (Fields, 2004; Urban & Gebhart, 1999). Studies using somatosensory evoked potentials have confirmed these top-down models of sensory processing and regulation of affect (Schubert, 2008).

Neurobiological correlates of social touch

Touch, as a measure of affection, can have widespread facets. Expectations, relationship dynamics, intimacy, care,

mood, and situational contexts are few of them. They can affect the sensory processing systems mentioned above in various ways (Caplan, 2014; Fabrizi et al., 2011). Neuroplasticity of the circuitry involved in touch processing has been well-studied in placebo responses, which are mediated through thalamus, insula, anterior cingulate cortex and the somatosensory areas (Amanzio et al., 2013; Martin et al., 2009). Expectations of touch and touch starvation have also been shown to affect nociceptive processing of sensory signals in the spinal dorsal horn (Geuter & Büchel, 2013). The other areas involved in hedonic processing, erotic tactile stimuli, and sexually intimate touches are dorsolateral prefrontal cortex (DLPFC), ventromedial cortex (vmPFC), hippocampal-amygdaloid complex, anterior insula, and midbrain (Esch & Stefano, 2005). These brain regions play an important role in affective processing of tactile stimuli, its association with emotions and integrating the available sensory inputs (Roy et al., 2012). On similar lines, Ellingsen et al. (2013) did a functional magnetic resonance imaging (fMRI) study to explore somatosensory processing of touch pleasantness. The effect of placebo (assurance and expectation) was studied on the perception of gentle touch and pain sensations. It was found that those who had strong placebo-induced touch pleasantness also showed increased activity in vmPFC, nucleus accumbens (NAc), amygdala, and brainstem regions. The coupling between vmPFC and PAG was also increased, indicating their importance in an emotional perception-touch relationship. Other imaging studies have shown the effect of visually appealing stimuli on increased affectivity of touch and emotional reasoning (McCabe & Castel, 2008), where ventral striatum, pregenual ACC and the parietal area were activated. Gender-based touch receptivity increased with oxytocin receptor agonist in a study by Scheele et al. (2014), which was associated with increased activities in the anterior insula, amygdala, precuneus, and brainstem. Overall, psychophysical correlates of touch involve dynamic integration of higher centers as well as the ascending pathways, along with emotions, memories, and environment. Top-down (controlling) and bottom-up (transmitting) systems, as discussed above, might give a better understanding of affective regulation involved in touch but proposed alone appear reductionist. It will be better to conceptualize this complex processing system as an integration of multiple homeostatic feedback circuits, which interact with abstract cognitive, psychosocial, and affective constructs (Fabrizi et al., 2011).

The neurochemical basis of touch: Emphasis on oxytocin

Most of the studies in this area are limited to neurochemistry of sexual touch. Substantial research have documented the role of several neurotransmitter systems and brain regions in sexual closeness and intimacy (Resnick, 2018). The processes are briefly summarized in Figure 1. Touch



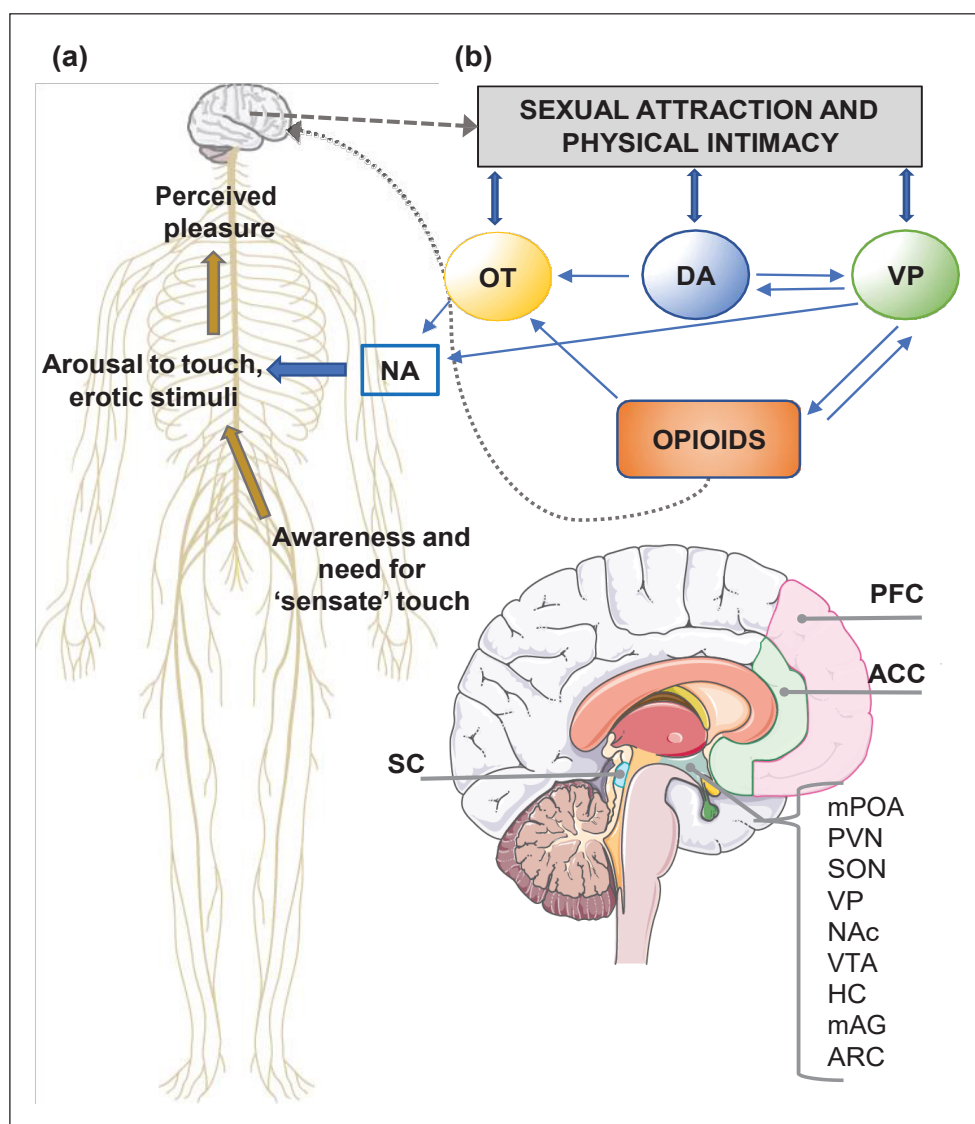


Figure 1. Neurotransmitter signaling and brain regions in sexual closeness and physical intimacy. (a) Awareness and need for 'sensate' touch lead to a response to erotic stimuli/arousal and sexual touch, which in turn results in the perceived pleasure. (b) The neurochemical and anatomical correlates involved in the process are depicted: NE: Noradrenaline, OT: Oxytocin, DA: Dopamine, VP: Vasopressin, PFC: Prefrontal cortex, ACC: Anterior Cingulate Cortex, SC: Superior Colliculus, mPOA: Medial Preoptic Area, PVN: Paraventricular Nucleus, SON: Supraoptic Nucleus, VP: Ventral Pallidum, NAc: Nucleus Accumbens, VTA: Ventral Tegmental Area, HC: Hippocampus, mAG: Medial amygdala, ARC: Arcuate nucleus.

having arousal role has a different neurochemical basis from nurturing or relaxing touch. The stimulus characteristics, appraisals behind the same and social expectancies modulate touch perception. A touch might be perceived as loving and sensual when from the partner, whereas might be aversive provoking disgust and negative emotions when from a stranger (Ackerley et al., 2014). The same stimuli evoking different types of emotional reactions can be postulated by two main neurotransmitter systems, the mu-opioid modulation (BOTSA, as discussed earlier) and

social neuropeptides like oxytocin and vasopressin. These two systems will be described further in details. Other chemicals like serotonin, dopamine, cannabinoids, etc. are also involved and briefly summarized in Table 1.

The Mu opioid system

The Mu opioid receptor (MOR) has been implicated in social reward, salience and modulation of affect (Chelnokova et al., 2014). It is also involved in hedonism,

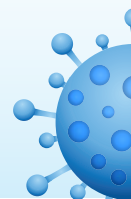


Table 1. Neurochemistry of social touch in animals and humans.

Neurochemical involved	Effect in animals	Effect in humans
Mu opioid receptor (MOR), brain opioid theory of social attachment (BOTSA) (Chelnokova et al., 2014; Dunbar, 2010; Loseth et al., 2014)	<ul style="list-style-type: none"> • Social grooming social play, huddling, pecking • Affiliative touch behaviours • Social relief in negative states 	<ul style="list-style-type: none"> • Hedonistic and sensual touches • Social bonding • Social relaxation (enables to interact) • Contact seeking, mating • Pain modulation through touch
Oxytocin, vasopressin (Social neuropeptides) (Bosch & Young, 2018; Campbell, 2008; Kemp et al., 2012; Macdonald, 2012)	<ul style="list-style-type: none"> • Social organization • Maternal-infant bonding • Leadership roles and bond formation • Social reward • Huddling and social rituals • Decreasing aggression 	<ul style="list-style-type: none"> • Maternal-child bonding and physical proximity • Enabling 'touch hunger' in social isolation • Monogamy • Need for physical contact in social interaction • Amplifying social identification • Sexual intimacy (hugging, kissing, caressing) • Social motivation and salience • Inhibiting social anxiety • The positive affect of affiliative touch
Serotonin (Cascio et al., 2019; McGlone et al., 2014; Perini et al., 2015)	<ul style="list-style-type: none"> • Tickling in rodents, pecking in bird couples • Social play 	<ul style="list-style-type: none"> • Social dependency • Pain modulation using touch (massage therapy)
Dopamine (Cascio et al., 2019; Dunbar, 2010; Esch & Stefano, 2005; Resnick, 2018)	<ul style="list-style-type: none"> • Mating • Partner selection and huddling • Sexual touches 	<ul style="list-style-type: none"> • Discrimination between affective and non-affective touches • Sexual intimacy and foreplay • Social 'craving'

motivation, and reward acceptance. Studies in various species have established the role of MOR in affective touch (social play, cuddling, pecking, and mating) (Dunbar, 2010). Loseth et al. (2014) had proposed the MOR modulation of Social Motivation (SM) model, which states the need of social integration and social support in rodents for survival and resilience. Especially when stressed or in adverse environmental conditions, the rodents attempted to relieve the negative emotion by social contact, which was modulated by the MOR. At the same time, during sexual intimacy and mating too, the MOR activity was increased in response to intimate touch and erotic stimuli. An extension of the BOTSA theory proposes that together with dopamine and serotonin, the MOR integrates the complex social relationships that humans can sustain for long periods (Pearce et al., 2017). The rewarding effects of social touch are mediated by endogenous opioids, which has been proven by naloxone's antagonistic effects on the same (Case et al., 2016).

Oxytocin: The Love-molecule of 'affective touch'

Oxytocin has been well-researched to have a primal role in attachment, social bonding, mother-child interaction, and

relationship commitments (Bosch & Young, 2018). A significant body of this research is in maternal bonding with infants and social affection in animals, which can be related to kangaroo mother care (physical proximity) (Olazábal & Young, 2006). Besides, oxytocin is central in socio-emotional processing, and the physiological (parasympathetic) correlates (Kemp et al., 2012). Similar to the BOTSA theory, oxytocin enables social closeness through positive reward feedback and decreases social anxiety (Campbell, 2008). Sexual intimacy, including caressing and fondling, has been involved with increased oxytocin receptors in the limbic system (Macdonald, 2012). Studies in macaque monkeys have shown oxytocin antagonists to decrease social grouping and mutual body picking behavior (Smith et al., 2010). Stress-related to social isolation leads to downregulation of oxytocin and vasopressin receptors in the ventral striatum, associated with subjective distress and touch starvation (Parker et al., 2005). Long term bonding in relationships and couple commitments have been related to oxytocin, especially in proximate relationships. Grooming and huddling behaviors are mediated by oxytocin release in the subcortical structures. Based on studies done on pet-owners, the dual-phase oxytocin release has been proposed: the first phase, when a



Table 2. Social touch and the functions served over the human lifespan.

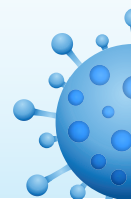
Life period	Expression of social touch	Social functions served
Pre and perinatal (Bystrova et al., 2009; Cascio et al., 2019)	<ul style="list-style-type: none"> • Rocking, bouncing, and swaying in the uterus • Temperature and movement of amniotic fluid 	<ul style="list-style-type: none"> • Tactile and proprioceptive learning • Social 'shaping' of the developing brain • Reinforcing maternal empathy and bonding preparedness
Infancy (Seidl et al., 2015; Stack & Muir, 1992)	<ul style="list-style-type: none"> • About 70% of mother-infant communication is through touch • Skin-skin contact (Kangaroo mother care) • Suckling • Self-stroking • Cuddling 	<ul style="list-style-type: none"> • Most important for social and cognitive development • Social communication • Attachment formation and security • Parent-infant emotional synchrony • Self-regulation • Vocabulary development • Cognitive shaping (executive functions)
Childhood (Dunbar, 2010; Jones & Brown, 1996)	<ul style="list-style-type: none"> • Postural repositioning • Object exploration • Expanding the repertoire of social touch (friends, school, strangers) • Physical play, tickling, huddling 	<ul style="list-style-type: none"> • Social touch has a central role in 'play' • Touch discrimination (good versus bad touch) • Social cognition • Development of a social reward system and trust • Continued cognitive maturation • Gender asymmetry in touch (males > females)
Adolescence, adulthood (Esch & Stefano, 2005; Hertenstein, 2011)	<ul style="list-style-type: none"> • Intimate touch, sensuality, foreplay • Friendly hugs, huddles • Handshakes 	<ul style="list-style-type: none"> • Further development of social cognition and reward • Sensuality and sensate exploration • Social bonds • Dependence • Social security • Preservation of autonomy • Existential issues (social coping against the fear of death) • Protection against psychological fear of falls
Old age (Hollinger, 1980)	<ul style="list-style-type: none"> • Caring strokes, hugs • Hand grasps 	

social approach is initiated, and subsequently if there is a social touch with positive affect, the second burst of oxytocin release helps in stress reduction (Uvnäs-Moberg et al., 2014). Intranasal use of oxytocin in humans promotes social touch and refines social identification of significant others (Ellingsen et al., 2013). The degree of oxytocin response is, however, dependent on the person's expectations and prior experiences. Direct touch of infants (hugging and stroking) by parents, sensual touch on the genitals in sexual practices and caring touch for the sick, all have led to increase in peripheral oxytocin levels (Moberg, 2003). Oxytocin thus probably plays a central role in integrating the social approach-avoidance, associating affection with social touch and building up 'touch hunger' in isolation (Harari-Dahan & Bernstein, 2014). Pharmacological intervention studies are, however, difficult in the absence of appropriate antagonists and further systematic studies are warranted to explore the role of oxytocin in affective and affiliative touch.

Psychosocial and behavioral aspects of touch

Touch can be a powerful way to communicate, and one of the earliest sensory facets to develop (Montagu, 2014). In the early years, touch helps in the formation of attachment and bonds (Harari-Dahan & Bernstein, 2014). The social touch from loved ones can help in reciprocating emotions and helps in developing social cognition. The consequent 'reward learning' benefits in the socialization of the brain (Clark-Elford et al., 2014). Subsequently, throughout life, it serves as an ongoing means of social growth, relationships, the formation of the self and social identity as well as appreciating the sociocultural norms. The various roles served by social touch over the lifespan are summarized in Table 2.

Numerous studies have shown touch to facilitate positive human behavior. It ranges from daily interaction in families to causal conversation among strangers and finally, behavioral



consumerism (Joule & Guéguen, 2007). In-person interaction helps psychotherapeutic rapport and has also been used as a principle of evidence-based sex therapies like sensate focus techniques, which has gained popularity among couples (Smith, 1998). Social touch not only includes the physical perception of touch per se, but also the personal proximity of interactions (Cascio et al., 2019). The very basis of massage therapies and acupuncture is based on touch mediated modulation of pain (as discussed earlier). Romantic relationships involving intimacy and physical proximity, has shown to increase the longevity of bonds and reduce stress (Ditzen & Heinrichs, 2014). Threat perception and balancing of touch and non-touch signals also play an essential part in the emotional processing of perceived pleasure, which needs to be wired and practiced when 'good touch/bad touch' is being explained to the children. The complex interaction between emotional and tactile stimuli eventually determines the reaction to it. In the study by Ellingsen et al. (2013) mentioned before, it was also shown that concomitant human touch helped in decreasing the negative affect to unfriendly and angry faces, which was further potentiated by oxytocin agonists. Sensory-social deficits are implicated in developmental disorders like autism and schizophrenia (Hertenstein, 2011).

In our daily lives, the role of touch in diminishing stress is paramount. A huddle during a football game, high-five after a winning shot in a doubles match, fist bump after a boundary in cricket or a handshake before the beginning of a contest originates from the sense of togetherness and greetings, that can be conveyed through this necessary yet straightforward gesture. On similar notes, shaking hands before a meeting or an interview has got popularized in an attempt to alleviate the stress levels. It can be argued that handshake is a westernized concept. Still, various other expressions of social touch like a hug, touching the feet of elders, cuddling the cheeks, patting on back, or placing an assuring hand over the shoulders are widely prevalent, irrespective of sociocultural differences. Additionally, certain tribes have their indigenous ways of social touch like the Gorkhas in North-East India (crossing their arms with that of others as an expression of goodbye) or the Bantus in Central Africa (tapping heads as a sign of greeting). Such examples are numerous across the world (Sin & Koole, 2013). Affective touch has also been shown to reduce hatred and aggression. Studies have shown that cultures and groups practicing more personal touch involving rituals have relatively lower rates of violence, hate-crimes, and agitation (Field, 1999).

In cases of social isolation like the present pandemic, all these above-mentioned measures provoke apprehension, stigma, and panic due to the fear of contracting the infection. The resultant 'touch-hunger' can increase the risk of depression, health anxiety, boredom, anger, insomnia, and exacerbate mental disorders like psychoses. It also gives rise to various forms of stigma, discrimination, and prejudice (Singh & Adhikari, 2020). People usually tend to

use inanimate objects like blankets, soft toys to cover themselves to soothe the 'skin hunger' for touch or engage in long bathes or massaging devices.

Sexuality and intimacy: The 'social touch' involved

Sexuality needs a special mention here. Sensual touch is the basis of eroticism and intimacy among couples. One of the significant reasons for erectile dysfunction, premature ejaculation and anorgasmia have been postulated as an inadequate understanding of the 'sensate' points of the body where a touch can lead to arousal (Sathyanarayana Rao et al., 2012). An essential component of sex education is to understand mutual sexual requirements in terms of closeness and time spent in physical proximity (Avasthi et al., 2017). This shifts the focus of pleasure and arousal from intercourse to foreplay in sexual practices (Avasthi et al., 2017). The emotional wellbeing of couples are directly related to the time they spend in each other's presence, casual touches (hugs, kisses, hand holding, etc.), or even the daily activities with some components of personal touch. This strengthens relationships and improves bonding (Hertenstein et al., 2006). Disharmony has been increasingly found in long-distance relationships, and partners with discordant shifts of work. Studies have also shown that the duration of foreplay is linked to sexual performance, the orgasmic pleasure, and perceived satisfaction, especially when the sexual foreplay includes mutually agreed sensual touches. The relational aspect of touch also makes a difference, whether it is playful, comforting, warning, or sexual, which determines the degree of perceived sexual pleasure (Laipson, 1996). Behavioral conditioning can happen in couples without variations in intimate touch, that can lead to sexual dysfunction and dissatisfaction (Hogben & Byrne, 1998). Psychosexual wellbeing is an important social component to deal with stress, especially during disasters and can have a direct relationship with immunity, which brings us to the next section related to affect-regulated touch and its impact on stress and immunity.

Social touch and affective content: Implications in stress and immunity

It is already well proven that the pathogenesis of COVID-19 is related to the immune response mounted against the virus, which in turn is associated with the case fatality. The subsequent discussion relates to the same. Qin et al. (2020) recruited 286 patients of severe COVID-19 infection and demonstrated that these patients had lower T-lymphocytes, increased neutrophil-lymphocyte ratio, decreased C-reactive protein (CRP), and peripheral anti-viral antibodies. Dysregulation of HLA-mediated immune system has been postulated as one of the significant causes of lung damage



leading to Severe Acute Respiratory Syndrome (SARS), a precursor of mortality (Shi et al., 2020). In line with this fact, the elderly and immunocompromised are at increased risk of infection. Any factor that alters the immune reaction can influence the pathogenesis of the COVID-19 infection. The Diathesis-Stress model mentions the release of sympathetic catecholamines that can affect the Hypothalamic-Pituitary-Adrenal Axis (HPA) and tamper with the normal immune responses (Zuckerman, 1999). Meta-analyses and reviews have shown stress to decrease the antibody proliferation to mitogens, Natural-Killer (NK) cell activity, and peripheral immunoglobulins. The Cytotoxic T cell activity was shown to be dysregulated with increased polymorphonuclear cells but decreased marginalization. Cytokine production was also inconsistent (Herbert & Cohen, 1993; Steptoe et al., 2007). Stress has been shown to increase psychological distress and risk for psychiatric disorders, which itself can have psycho-neuroimmunological implications. For example, the bi-directional relationship between depressive disorders and cell-mediated immunity (CMI) is well-established (Webster et al., 2002). Given the factors of the present COVID-19 crisis, the collective stress at physiological and psychosocial levels can impact the immunity and hence the course of illness. Studies have shown that people with chronic stress, sleeplessness, who are quarantined and deprived of social support, suffering from psychiatric disorders and the elderly with loneliness, to have a protracted course of illness and higher morbidity (Qiu et al., 2020).

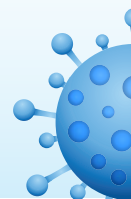
This is where the role of social touch comes into play. Firstly, sexual intimacy and emotional bonding among humans are considered to be useful measures of psychological resilience. People with 'touch starvation' are further exposed to stress if chronic and can increase the dual vulnerability to the pandemic. The brain acts in unison. The neurobiological mechanisms discussed before influences immunity through the same circuitry. The MOR has profound analgesic effects, aids emotional salience (Zubieta et al., 2001) and has an antagonistic impact on the HPA axis in response to environmental stress. Rodent experiments have shown opioids to help social stress coping and enhance social exploration (Van den Berg et al., 1999). The MOR activation provides relief from situational stress and intensifies contact seeking for personalization (Loseth et al., 2014). Oxytocin, on the other hand, has strong connections with the HPA axis as a stress buster. Wellings et al. (2019) in a large study involving three National Surveys of Sexual Attitudes and Lifestyles (NATSAL) reported increased coping with stress, better emotional wellbeing, and increased desire for intimacy in half of the women and two-thirds of the men in the sample. In humans, oxytocin decreases the release of adrenocorticotrophic hormone (ACTH) and cortisol in response to stressful stimuli (Chiodera & Coiro, 1987). In animal models, central blockade of oxytocin receptors increases the basal and stress-induced release of ACTH and corticosterone. Amygdala,

being a vital structure in fear processing, is involved in stress perception, which is mitigated by the oxytocin release through its direct and indirect connections with the paraventricular nucleus (Neumann et al., 2000). The effects of oxytocin both as an emotional bond and stress reliever, thus make it unique in the social relaxing and anxiolytic effects in primates, through the expression of social touch. Intranasal administration of oxytocin in monkeys has also shown to decrease peripheral levels of ACTH in response to social isolation (Parker et al., 2005). Finally, Holt-Lunstad et al. (2008) compared couples with controls, instructing them to practice mutual sensual touches for 3 days a week for 4 weeks, and the following biochemical changes were observed. Salivary oxytocin increased, as well as the stress makers like blood pressure, plasma cortisol, and alpha-amylase decreased. The baseline PMNs and lymphocytes were also stable.

Though affective regulation of social touch is an effective coping strategy at times of crisis, the direct biological effects on immunological markers are yet to be systematically studied. However, when the global crisis of the COVID-19 pandemic and physical distancing looms large, giving rise to 'touch hunger', the decreased resilience to this unprecedented situation can cause increased vulnerability. This concept is still a challenge and greater need to understand the above concept in the coming years. Further, in countries with higher infection rates, the consequent fear of infection, stigma, xenophobia, and panic might further compound social distancing leading to chronic physical separation, lack of social connectedness, and eventually 'touch deprivation' that can have biochemical and psychobiological implications (Montemurro, 2020). In summary, the biopsychosocial facets of 'touch hunger' and its effects on stress, immunity, and social bonding along with the vicious cycle of risks are depicted in Figures 2 and 3.

Strategies of mitigating the 'touch hunger': Ways forward

Today's world is digitalized with speedy connections through social media. Long-distance interactions and digital intimacy have evolved as replacements for personal proximity, which is far from close. With the best of virtual realities simulating auditory, visual, situational, and even somewhat tactile closeness, real interpersonal touch is still a long distance to go. Some emotional resonance through technology and virtual conferencing has been studied (Haans & Ijsselstein, 2006), but their applications are fraught with technical and sociocultural challenges. This introduces the ironic fact of whether artificial intelligence is prudent enough to gauge the 'touch hunger' when instead of personal warmth, one can only touch the inanimate damp screen of a digital device. Perhaps it will be much longer till we accept long-distance social touch, delivered through tweets, videos, memes, or messages as



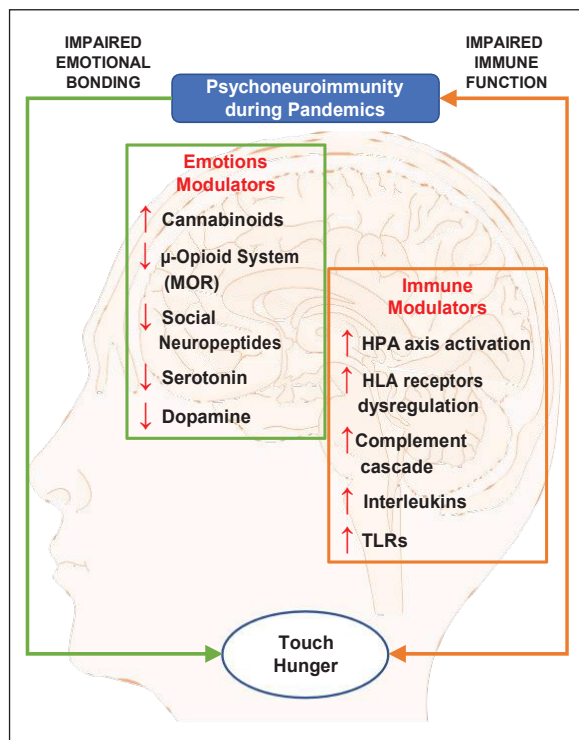


Figure 2. Neurobiological facets of 'Touch Hunger' and psychoneuroimmunity.

The lack of social touch can disrupt MOR signaling activation and reduces the levels of important emotional modulators such as serotonin and dopamine. The increase in endogenous stimulants like cannabinoids can increase to compensate for the comfort zone and relief that social touch provides. This also enhances the risk of substance abuse. Additionally, the reduction of social neuropeptides like oxytocin during stress and social distancing can fuel the activity of the stress-induced Hypothalamic-Pituitary-Adrenal Axis (HPA), which further tampers the immune system (dysregulated Complement cascade, HLA receptor activity, and raised Interleukin levels) thereby increasing the risk of infections during a pandemic. This perpetuates the vicious cycle of immunological risks and stress associated with impaired emotional and physical separation during infectious disease outbreaks like pandemics/epidemics.

HLA: Human Leucocyte Antigen; TLR: Toll-like Receptor; MOR: Mu Opioid Receptor.

the near equivalent of a hug, handshake, or kiss. Till then, it is crucial that in the face of the present COVID-19 crisis, social connectedness is attempted at its best even with physical distancing. The digital 'socialization' might emerge as the 'new norm' which might mitigate some of the adverse effects of 'social touch deprivation'. Families and couples locked down together can use this scope to spend more proximal time to strengthen their relationships. As mentioned before, for those who never had the chance to be in close proximity, this period can be a potential challenge and promote discord as well as interpersonal violence. Balancing relationship dynamics, perspective taking, improving communication, consensual sexual practices, and finally crisis interventions in case of alleged violence are some of the problem-solving strategies (Prime

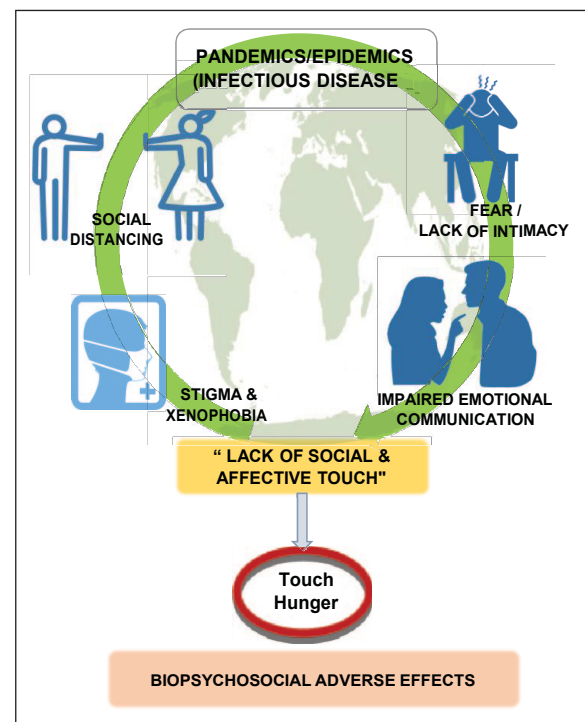


Figure 3. Affective touch deprivation during unusual pandemics/infectious disease outbreaks and consequent 'touch hunger'.

The lack of social and affective touch caused by social distancing to prevent infections, physical separation due to travel restrictions, stigma against infected patients, frontliners, and xenophobic attitudes against certain individuals/communities result in fear of infection, isolation, panic, and adverse mental health consequences. Fear of contracting the infectious disease also leads to impaired sexual closeness and physical intimacy. In turn, this may contribute to impaired emotional communication, chronic stress, and consequently a 'touch hunger' circularity.

et al., 2020). The authors would like to stress here that 'social touch' is a continuum and not a binary construct. Throughout the spectrum of its absence or presence, there can be various changes of human behavior and relationships, which need to be understood in a balanced rather than unidimensional way. As the virus is highly contagious and spreads through any form of contact, distancing and sanitation are vital. Still, beyond just the public health implications of the pandemic, billions are affected with a chronic 'touch hunger', which if neglected, can have chronic ill-effects on global health.

Understanding the implications of infectious disease outbreaks on social and affective touch is important, and that has been the intended goal of the review. Even though there has been plethora of quantitative and online surveys related to the psychosocial effects of the COVID-19 outbreak, they mainly deal with the categorical psychiatric disorders which only partly represent the emotional and social impact of the pandemic. 'Touch hunger' is often not appraised cognitively and thus not discussed during clinical interviews, though its chronic deprivation has been shown to affect mood, sleep,



relationships, anxiety, and physiological wellbeing (Field, 1994, 2014). Sensitivity is essential for clinicians and public health experts to individualize the strategies based on the vulnerable groups and the context of social touch deprivation. Finally, it is important to adopt a balanced perspective between the risks and benefits of social distancing in a given individual or family in the background of the ongoing outbreak. Healthy engagements between families, children, fostering social integration among the older adults, maintain sexual relationships within the purview of permissible safety and healthy use of cyberspace for social connectedness are the possible ways to mitigate 'touch hunger' during the pandemic. Phenomenological exploration of lived experiences in separate families/couples and comparative studies in those with or without physical proximity of their loved ones might prove to be fruitful to understand the biopsychosocial impact of COVID-19 on affective touch and intimacy.

Conclusion: Summarizing the perspectives

Human touch is essential for both short-term and long-term neuropsychological well-being and mental health. This is particularly critical during stress and period of elevated anxiety, as is happening because of the COVID-19 pandemic mandated social distancing. Human touch is also important for our ability to recover from illnesses. Throughout the article, we have opened avenues to understand the importance of social touch, its biopsychosocial underpinnings and 'touch deprivation' during the present COVID-19 pandemic scenario. Social distancing and lockdown have been effective strategies in combating the spread of infection and hence globally supported by the public health agencies. The authors do not intend to argue against these measures. The scope of this review is instead to highlight the concept of 'touch-hunger' during such unprecedented situations, that may have immense psychosocial consequences. Any form of physical separation, emotional and familial discord, custody loss of children, divorce, etc. can lead to touch hunger, the implications of which are beyond the scope of this review. It can also lead to an increase in psychiatric disorders, frustration, self-harm attempts, anger, and non-compliance to precautionary measures, all of which are additional burdens for public health. This review also glances at the mutual interaction between the neurobiological mechanisms of social touch, stress response and immunity. It highlights how physical proximity during such biological disasters is vital both for the physiological benefits of immunity (viral resistance and pathogenesis) and also for coping with the chronic stress of the pandemic. The somatosensory pathways (both bottom-up and top-down) help in deciding the discriminatory and hedonic value of touch, along with the contextual cues. Opioids and oxytocin are the two main chemicals involved, though it is more of a complex interplay among various other factors.

The pandemic has already widened its clutches. Systematic studies (both neurobiological and ethnographic) are necessary to understand the effects this 'touch deprivation' has or can have on human lives for months to come. Population-based studies will be necessary in people segregated from their families to understand the implications of 'touch hunger' on their biological functioning including sleep and quality of life. Lived experiences of couples who are entrapped for prolonged periods can be compared with those separated by large distances. On an ambitious scale, neurochemical and imaging parameters can be studied in people connecting virtually, to estimate how much they can compensate for the 'person touch'. The socio-cultural effects also need due consideration and the post-pandemic aftermath will be a good time for pre-post comparison in case of large anthropological surveys accounting for the effects of touch-hunger. Insights from this might help policy and health preparedness for such futuristic crises. The COVID-19 pandemic provides us with yet one more opportunity to explore this important but overlooked angle of the human psyche.

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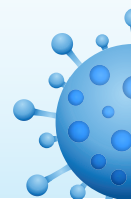
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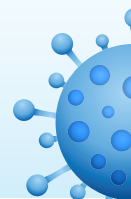
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“The Graying Minority”: Lived Experiences and Psychosocial Challenges of Older Transgender Adults During the COVID-19 Pandemic in India, A Qualitative Exploration

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Background: The Coronavirus disease 2019 (COVID-19) has emerged as a global health threat. Certain factors like age, an immunocompromised state, and social impoverishment, etc. can add to health vulnerabilities during this pandemic. One such group is older transgender adults, who often bear a combination of these risks. As the world is aging fast, their numbers have also been increasing. With this in mind, this study explores the lived experiences and psychosocial challenges of older transgender adults during the COVID-19 pandemic in India.

Methods: A qualitative approach was used. Ten individuals with “transgender” identity above the age of 60 were recruited with consent through purposive sampling. In-depth interviews were conducted on the telephone using a pre-designed interview schedule. They were recorded, translated, and transcribed verbatim. Hasse’s adaptation of Colaizzi’s phenomenological method was used for analysis. Independent coding and respondent validation were used to ensure the rigor of data.

Results: The super-arching categories (with themes) were marginalization (“second” priority, stigma, social disconnection), the dual burden of “age” and “gender” (ageism, othering, and psychosexual difficulties), and multi-faceted survival threats (physical, emotional, financial) during the pandemic. Social rituals, spirituality, hope, and acceptance of “gender dissonance” emerged as the main coping factors, whereas their unmet needs were social inclusion, awareness related to COVID-19, mental health care, and audience to their distress.

Conclusion: The elderly gender minorities are at increased emotional and social risks during the ongoing pandemic, and their voices are mostly unheard. The need for policy implementation and community awareness about their social welfare is vital to improving their health and well-being.

Keywords: COVID-19, coronavirus, pandemic, older adults, transgender, gender minorities, lived experiences, qualitative



INTRODUCTION

The last 8 months have seen the emergence of a new global health threat, the Coronavirus disease 2019 (COVID-19). After being declared a pandemic by the World Health Organization (WHO), it has affected more than 37 million, with nearly a million people succumbing to the infection (1). After a four-phased lockdown, India has faced a surge of cases and is presently among the countries with the highest case burden (1). Every section of the population has been facing unique challenges during the outbreak but certain minorities are at increased risk in terms of the direct effects of the virus, its psychosocial offshoots, and the lockdown and distancing measures that are used to attempt to contain it. Age and immunocompromised states have been documented to be the two most important factors in deciding the morbidity and fatality rate of COVID-19 (2). The elderly have a unique bio-psychosocial vulnerability. It includes increased pulmonary involvement due to the virus, risk of psychological disorders like depression, anxiety, sleep disturbances, and social factors like loss of autonomy, loneliness, and isolation (3). Certain minority sections have a combination of many such risk factors, one of them being the older transgender population (as a part of the Lesbian, Gay, Bisexual, Transgender, and Queer–LGBTQ community). They share the combined risks of all the issues mentioned above and are primarily neglected in disaster preparedness and management planning. Besides, victimization from the traditional social stereotyping, “third gender” based discrimination, and associated factors like poverty and administrative apathy, they also have increased dependency and segregation based on age. As a part of the Movement Advancement Project, a recent brief by the Centre for American Progress discussed that there are 2.7 and 1.1 million people of the LGBTQ community above the age of 50 and 65 years, respectively. Within this, 20 percent of them are “people of color,” which further worsens health disparities during COVID-19 (4). Data also showed that older transgender adults suffer from mistreatment at long-term facilities and that they have double the risk of poverty and social impoverishment (5). Many transgender individuals also remain on gender-affirming (hormonal or surgical) treatments that have been shown to improve their quality of life, especially in older adults (6), and access to and the availability of such treatments might be a challenge during disaster situations, leading to unforeseen physical and emotional consequences.

The World Professional Association for Transgender Health (WPATH), in association with the Sappho Good Practice Guide, India, has laid down consensus guidelines for diagnosis, hormone therapy, recommendations for sex reaffirmation surgeries, and subsequent follow-ups. The guidelines stress multi-disciplinary efforts, appropriate knowledge regarding the procedures, and adequate psychological support, both pre and post-treatments (7). However, prevalent misconceptions and misinformation in India have led to unscrupulous “conversion therapies” that are unfortunately recommended to “cure” transgender and homosexual individuals. Mostly practiced by faith-healers, preachers, shamans, and quacks, these “curative treatments” commonly involve unsupervised steroids and sex reassignment

surgeries (SRS) without consent and the understanding of the individuals involved, which can be psychologically devastating. Although there is no specific Indian law prohibiting “conversion therapy,” it has been proposed that it violates the Right to Privacy (Article 21 of the Indian Constitution) and has been widely regarded as “illegal and unethical” by the Indian Psychiatric Society (IPS) (8). A positive step in this regard has been the Transgender Person (Protection of Rights) Act, 2019, based on “equitable access to health” for this special population. Under this Act, the government provisions for accommodation and education for transgender persons and there is a mandate that at least one Government hospital in every state needs to provide SRS free of cost, with informed consent and counseling. The exact rules are expected to be further clarified and implemented soon, but whether it improves the “rights” of transgender individuals remains to be seen (9).

In India, transgender people are traditionally known as “Hijras.” They are often equated with “Kinnars” (mythological singers and dancers), as represented in the Kamasutra (ancient Hindu text of sexuality) and even in the epics like Mahabharata (in characters such as *Brihanalla* and *Shikhandi*) (10). For generations throughout history, they have undergone poverty, rejection, neglect, and separation from their own families due to their “identity.” Some even undergo rituals (Nirvaan) to remove their genitalia (11). Over time, their communities have become well-organized, claiming their rights. Irrespective of the widespread advocacy in popular media and literature, they have been subject to socio-economic neglect for decades and legal ambiguity about their sexual identity (12). Even though the Supreme Court in 2014 recognized the Hijras as the “third gender” and subsequently in 2018, decriminalized Section 377, which stated consensual sexual activity between adults of same-sex as a crime, the social acceptance of these legislations is far from reality, and the discrimination against these gender minorities continues (13). Literature related to their “own stories” is scarce, especially in the aged population.

METHODS

Study Design and Participants

The study followed a qualitative method, using a social constructivist paradigm. In contrast to the positivist paradigm, this paradigm permits the researcher to be open-minded and flexible in exploration, rather than intervening or analyzing based on pre-fixed notions. Furthermore, we chose the phenomenological approach as we wanted to understand the specific “experiences and challenges” of a particular population in the context of an ongoing crisis. Such paradigms have been used in previous studies for studying phenomena like experiences of motherhood, pain, and post-traumatic stress among women, war veterans, and disaster-survivors, respectively (14). Telephonic interviews were conducted with 10 elderly people (aged above 60 years) from the LGBTQ community, who identified their gender identity as “transgender.” We considered the age of “60” as a cut-off for the elderly in this population based on the United Nations/WHO age recommendations (15). However, a



range of people aged between 50 and 65 years has been taken in earlier studies on older LGBTQ adults. As access to this sector of the population is difficult, we used purposive sampling. The index participant was known to one of the researchers, who eventually introduced them to interested others. We tried to obtain detailed descriptions of their experiences and the challenges they have faced during the COVID-19 pandemic and the associated lockdowns. A phenomenological approach was used for analysis.

The Working Definition of “Transgender”

Though transgender or “trans” is commonly used as an umbrella term, for this study, we considered “transgender” as any person for whom their gender identity or expression is different from the sex assigned at birth (or that written in their birth certificate) (16).

We obtained appropriate ethical approval from the Institute board. The participants were initially contacted via telephone, informed about the objectives of the study, and we sought informed consent verbally. Interestingly, all 10 participants welcomed the study initiative and were willing to participate without hesitation. A General Health Questionnaire (GHQ)-12 and Hindi Mental Status Examination (HMSE) were used as screeners for any psychiatric and cognitive disorders. The cut-offs were 3 and 19, respectively (17, 18). We obtained thematic saturation with seven participants. However, we interviewed three more for super-saturation of the data. To ensure confidentiality, we assigned respective numbers (instead of names) to maintain anonymity in transcripts. All transcripts were audio-recorded with consent and then transcribed verbatim. Only the researchers had access to data, which was password protected. The study followed the Standards for Reporting Qualitative Research guidelines (19).

Procedures

The initial semi-structured interview schedule was designed based on a literature review, which was later modified based on the first two interviews. In that sense, they can be considered to be a pilot for this study. We recorded the socio-demographic details in a separate datasheet. The questions involved in the schedule were open-ended, facilitating rich data regarding their difficulties during the COVID-19 pandemic, their psychosocial needs, access to health care, perceived stigma and discrimination, and the effects of lockdown measures. The salient questions of the interview schedule are summarized in **Appendix**.

Probing questions like “*can you tell me more about it,*” “*how did that happen,*” “*please elaborate on the context,*” etc. were used to receive rich data on their lived experiences. The analysis was done simultaneously with data collection by both the researchers independently to add to the rigor.

Data Analysis

We used Haase’s adaptation of Colaizzi’s method for analysis (20, 21). It adopted a phenomenological model, which involves the exploration of the subjective experience under investigation. This approach was chosen as we wanted to know the “lived experiences” of the transgender population. The concept of “intersubjectivity” was used in the analysis to understand the

circumstances of “social suffering” from the viewpoint of these individuals. Colaizzi’s method essentially involves the following sequential steps:

- Familiarization (running through the transcript several times for a better understanding).
- Identification of significant statements and restating them in “general” terms.
- Formulating meanings relevant to the phenomenon of interest.
- Clustering “identified meanings” into categories, themes, and sub-themes.
- Rigorous discussion among researchers to develop an exhaustive description of the clustered themes.
- Developing a conceptual structure of the studied phenomenon.
- Respondent validation from the participants (seeking verification of the developed structure).

As mentioned, the verbatim transcripts were translated into English (with cross-translation to check for validity). The transcripts and memos were read several times through thematic coding until significant recurrent phrases emerged, and they were re-described in general terms to formulate contextual meanings and then organized and structured by discussion among the researchers. We clustered the super-arched topics into relevant categories and themes, along with verbatim data supporting each of them.

Ensuring Scientific Rigor

Trustworthiness and credibility are used to establish rigor in qualitative studies, which are different from the concepts of reliability and validity that underpin quantitative research (22). The researchers independently analyzed data using Colaizzi’s methods, as mentioned above, categorizing the themes based on the contextual factors affecting the participants, which were then discussed among the research team to reach a consensus on the structural organization of the results. After the first round of analysis, the researchers went back to the participants, five of whom were interviewed again as part of the process of “respondent validation.” Based on their inputs, the hierarchy of the data was modified and supplemented by this additional information. A data trail was maintained so that the steps of qualitative analysis could be traced back to the original interviews.

RESULTS

The sample consisted of 10 elderly people from the transgender community. Four participants identified as “third gender,” while two preferred “male” gender, one preferred female, and one did not want to disclose gender and orientation. Six participants resided with their families or friends, and four lived alone. Among the latter, one resided at an old-age care home and another in temporary shelters, frequently living on the streets. They belonged to various states of Karnataka, a mix of lower and middle socioeconomic status. Throughout the pandemic, eight of them resided in the same place, whereas two had changed



residence. One of these two included the homeless individual who kept changing temporary shelters for support. Only two participants received an old-age pension, as they had previously been employed in Government sector jobs. Six others were not aware of the senior citizen benefits of the country. Two were unemployed, whereas others did menial jobs for a living, apart from the homeless person, who at times begged at street signals. Four of them did not have a valid VOTER or AADHAR card (proof of identity in India). The mean age of the participants was 66.4 years. The mean GHQ-12 and HMSE scores were 1.7 and 25.2, respectively. The mean duration of the interviews was 45.20 min. We conducted the interviews in April and May 2020 when India underwent a four-phased lockdown to curtail the COVID-19 outbreak. The socio-demographic parameters for each of the elderly participants are mentioned in **Table 1**.

The experiences of participants during the pandemic were broadly categorized into feelings of marginalization (perceived stigma, discrimination, social exclusion, loss of dignity, and reduced access to health-care), vulnerability due to the “dual burden” of age and gender (prejudice of ageism, impaired sexual well-being, feelings of “othering”), as well as multiple physiological, psychosocial, and economic survival threats. Social rituals and festivities within their community, acceptance of their “gender dissonance,” and spirituality provided them hope and helped them cope with the adversities. Knowledge-attitude-practice (KAP) gap regarding the outbreak was a major concern among them, while the predominant “unmet needs” were social inclusion, emotional well-being, social benefits, and receiving an “outlet or audience” for their suffering.

The resultant super-arching categories and themes, along with the respective sub-themes, are summarized in **Table 2**. They are supported by the key verbal excerpts of the participants, which are mentioned in the table and contextualized in subsequent discussion.

DISCUSSION

Dual Burden of “Age” and “Gender”: Marginalization

Biological disasters like COVID-19 often hit the most vulnerable in the worst ways. Advanced age and belonging to a gender minority group are both crucial susceptibilities during the pandemic. They contribute to the “minority stress” of marginalized populations like the homeless, migrants, socially impoverished, and especially the Black,

Asian, and minority ethnic (BAME) communities, as already postulated during the ongoing outbreak. These include social insecurity, unemployment, experiences of racism, prejudice and xenophobia, lack of social welfare benefits, precarious work, increased risk of infection due to lack of precautionary measures and overcrowding, and most importantly, lack of knowledge and awareness related to the pandemic and its related issues (23, 24).

The study participants revealed a sense of increased “ageism” during the ongoing outbreak, which has also been raised as a potential concern in public health guidance measures for the “elderly” during COVID-19.

“Throughout our lives, we have been ‘observed’ differently, now it’s even more as we are old. We even get called names when we ask for help.”
(P6, on discussing information-seeking about the pandemic)

Such age-related prejudice and attitudes that consider the “elderly” as a “justified loss” for the sake of younger lives were also documented during the Severe Acute Respiratory Syndrome (SARS) and Ebola outbreaks (25, 26). Age itself becomes an essential factor for the “third gender” as many of the societal and sexually acceptable roles of transgender people tend to get to be affected by age.

In the Indian context, transgender people or *Hijras* take to baby showering ceremonies (*Badhaai*), which are an essential source of income, and during the pandemic have become scarce. Furthermore, the “sexual vitality” and “auspiciousness” of the *Hijras*, for which one welcomes them in ceremonies decreases with age, and hence older transgender adults often run out of income (27). Seven participants also looked at such social rituals as their source of coping and connectedness with society.

“We look forward to *Badhaais* and *Varanas* (rituals)! This is something we have been doing since we are young. Other people welcome us during these times. It has become our true festival! This disease has taken it away from us!”
(P4, on how she feels excluded from the society during the pandemic)

“In spite of all the ‘hate’ for us, society requires us for these ceremonies. Now, with the fear of infection, they don’t even allow us near people’s houses. Our livelihood and connections both are at risk!”
(P6, while describing the cessation of rituals during the ongoing crisis)

Most participants mentioned being the “second priority” for health and legal services, including access to medications, medical protective equipment, and testing.

“For [the] last three months, I have been so used to hearing: ‘people like you should come later, any way you are old, what’s the need. . . just go and stay with your people. . .’ It hurts you know, it feels we are ‘aliens’ in this world. This adds to my uncertainty. . .”
(P8, on help-seeking during COVID-19)

Indian society has been marked with discriminative social reactions toward transgender people, who are often the subject of ridicule and fun. Conforming to social acceptance, many of them reluctantly assume the “social roles” of sexually seductive behavior with the opposite sex, begging, or petty crimes. Talwar (28) in *The Third Sex and Human Rights* discusses the deprivation of human rights, poverty, and violence inflicted upon this community in India. Besides financial constraints and unemployment, many individuals from the *Hijra* community are forced to pursue a living through extortion, begging, exhibitionism, and sex work (an activity often socially stereotyped as associated with transgender individuals). The violence directed against transgender people has been widespread



TABLE 1 | The socio-demographics of participants.

Participant	Age	Age at transition	Socio-economic status	Sexual orientation	Living arrangement	Education	Job	Old-age pension
P1	64	18	Low	Bisexual	With son	Not formally educated	Unemployed	No
P2	60	22	Low	Gay	Alone	Class 10	Works in a shop	No
P3	67	Doesn't recall	Middle	Lesbian	Living with a partner	Graduate	Retired	Yes
P4	63	20	Low	Lesbian	With daughter	Class 4	Domestic help	No
P5	70	Doesn't recall	Middle	Queer	In old-age home	Class 6	Unemployed	No
P6	75	Doesn't recall	Low	Gay	With friends	Not formally educated	Vegetable vendor	No
P7	60	28	Middle	Bisexual	With partner	Class 12	Private company	No
P8	69	23	Low	Lesbian	Temporary shelters	Not formally educated	Begging	No
P9	65	Doesn't recall	Middle	Bisexual	Joint family	Graduate	Retired	Yes
P10	71	30	Low	Didn't disclose	Alone	Class 8	Manual labor	No

and often brutal, and is documented as taking place in their places of residence, prisons, police stations, and other public spaces (29). Boggs et al. (30), in their focus group discussions of 73 older LGBTQ participants, mentioned the intersection of “ageism” and “cisgenderism” as an under-recognized barrier to health, social and legal access. Trans PULSE, an Ontario-wide research study, showed a lack of sensitivity to health care and discrimination in health care access among the transgender population (31). This is more pronounced in a pandemic crisis, as amidst the vulnerability, these participants are also the victims of “othering” that classically forms the “we vs. they” dichotomy. “Othering” is a term used to denote expressions of prejudice based on a “group identity,” in this case the “third gender.” Social stereotypes help to maintaining and perpetuate this group-based inequality and marginalization, thus depriving a certain “group” of their rights and social privileges (32).

“See, here she has come again. . . I have heard this all my life! Now it has increased, and the moment I go to any shop, people start behaving weird and push away. It’s as if... I am the source of infection.”
(P2, when asked about social reactions during the pandemic)

“They were supplying free masks and soaps. I couldn’t stand in the queue due to the constant ridicule and mockery that I saw in people. At times I feel. . . getting the infection is better than facing such insult at this age!”
(P9, discussing the precautionary measures)

The resultant “minority” stress has been explained in terms of the Health, Stigma, and Discrimination model (33), where facilitators like disasters, societal apathy, and prejudice toward age-related and sexual minorities can eventually lead to detrimental psychosocial outcomes during crises (23).

Six participants reported self-stigma, a common finding in the LGBTQ community when they feel guilt about their “sexuality” and social notions that are against them, meaning they are further

segregated from the mainstream and adopt their “community customs and rituals” (34). Social attribution theories posit that a constant negative stereotype against a certain individual or group can lead to self-doubt, decreased self-esteem and self-stigma, when that individual or group starts internalizing those “faulty beliefs” and attributes them to their social status (35). This causes further social exclusion and decreased help-seeking, especially during crises, which worsens othering.

“I have always been seen as ‘seductive’ in personal and professional circles; I have no idea why! Now I have come to believe that probably my gender is responsible for this. . . age changes a lot in you. . . and there are certain ‘blames’ you cannot take any more at this age.”
(P10, on how she was blamed for being “provocative” in public)

“I feel that I am different. . . I have always felt that way. . . people passing sexual comments and ridiculing me. . . that’s how we, Hijras live. . . even in this situation, we need to go out for living. . . but get threatened by people and police telling we are on ‘business’! I get tired of my ‘appearance’ at times and wish it was different.”
(P4, when asked about livelihood challenges)

In the above excerpts, participants mentioned social stereotypes against their communities and how they have internalized these misrepresentations over time. While P10 started “believing” the blame attributed to her gender, P4 wished she could change her appearance for the “sake of society.” Other transgender individuals in our study also mentioned “reduced self-esteem” and developing a “hatred toward themselves” after constantly battling social injustice and prejudice. The self-stigma generated in an already marginalized community can be further detrimental to their ability to cope during the crisis.

Loneliness, social disconnectedness, and depression were reported by 8 out of 10 participants. Major factors that have influenced these feelings include restricted travel, physical distancing, and difficulties in using and accessing technology



TABLE 2 | Categories, themes, and verbal excerpts of the analysis.

Super-arching category	Subordinate themes	Verbal excerpts from participants
Marginalization	"Second priority" in health care	"Be it medicine shops or checkups at clinics, the moment they saw me they told me to wait or come later." (P2)
	Stigma & discrimination (including self-stigma)	"I have faced this throughout life. Now people look at me in a way as if I am responsible for the virus." "Masks help not only against the virus Saheb but also to protect my identity."
	Social disconnection from peers	"Amidst all these fears of infection, I wish we could meet and spent some time singing as we used to. But can't travel during the lockdown."
	Perceived loss of dignity	"People around have never really liked me. But now they ridicule me..." "Who likes to be treated as an object. I am simply dictated terms by the police on the road and my old-age home manager."
Dual burden of "Age and Gender"	Prominence of ageism	"I hear things like... you people won't change even when you are old! Why Saheb, what have we done!" "My family and neighbors don't want to come near me as I am old and probably have got more of the infection..."
	Deprived psychosexual needs	"Intimacy with my partner is a major comfort. But he goes for work. So, we don't feel comfortable making love..."
	"Cornered" in their communities	"I am mostly not able to join the group due to age. Now even when they discuss any health-related matters among themselves, I am left out."
Multi-faceted "Survival threats"	Physiological	"When they distributed masks, they did not give me. I already stay in an overcrowded room with three others." "I wanted to get tested, but they told me to get HIV testing!"
	Psychological	"I feel really lonely and sad. My partner is far away. And people don't talk to me over here."
	Financial	"I had a small job in a shop. That has been closed due to lockdown. No one wants to offer me any financial help. I don't want to resort to begging like others." "The Baadhaai (baby-showering) ceremonies are our main source of bread. We are not being allowed anywhere."
	Social rituals and pride celebrations	"I know about this place where all of us gather and celebrate. Someone told me it is this time of the year. I wish it could have happened." "I am looking forward to the online Pride festivals. It will give me a lot of support in this lockdown."
Coping	Acceptance of the discomfort of belonging to the "third gender"	"What the pandemic taught me was that the virus doesn't discriminate. I finally will at peace with my identity."
	Spirituality	"My prayers and faith in God kept me moving all these days, even when I had to beg for a living. Never knew it will be so helpful now!"
	Hope	"I have seen worst times, Saheb. I am hopeful this, too, shall pass!" "I believe in tomorrow. The rest of my days, I want to live with that belief. It helps in this uncertainty."
	Knowledge, attitude, practice (KAP) related to COVID-19	"I only know that old people are dying. Do I need to get tested? Some medicine is being recommended. Should I take it?" "Someone was explaining something in the local language in a meeting about COVID. They didn't let me in!"
Unmet needs	Social inclusion	"I stay alone. Every day with a fear that I will get the infection and die without treatment. I wish I could share this with others."
	Mental health care	"Every time I have gone to the doctor, people like you when they grow old, these things happen. Nobody asks or understands why I get sad and anxious!"
	The audience for their "voices"	"I don't know after how many days, someone asked this Budda (old man), about his difficulties!" "You really want to know how we feel, or it is just for your research?"



(in 5 participants). Even though digital connectivity and telemedicine have repeatedly been used during the pandemic, they can be real challenges in lower and middle-income (LAMI) countries like India, where technology still fails to reach the masses, especially in the rural areas and minorities. Furthermore, age, with its sensory and cognitive limitations and frailty, can impair the appropriate use of video-connections with loved ones, which can lead to further loneliness and social segregation. Berger (36), in his classic text “Gay and Gray,” describes cases of homosexual and transgender men whose narratives reveal loneliness, existential crisis, and “age” as an acceptance of the age-old discrimination that they face. The “discomfort with their gender” that some participants experienced during most of their lives due to their “transgender” identity seemed more acceptable during the pandemic, as they navigated these adversities. Some attributed these problems to age, others to wisdom, while others felt that “suffering” due to COVID-19 has made them more resilient.

“All throughout I wished I was like the ‘others’! My gender kept bothering me like a curse from birth. Living through so much of difficult times, it mattered little. . . Everyone was suffering and dying the same way. I don’t know when, but I had stopped wanting to be ‘different!’”
(P2, while discussing discomfort with the third gender)

“Sometimes I feel this was needed. . . I witnessed the death of my friends, colleagues. . . there is so much suffering all around. . . I somehow feel stronger, more ready to face the world. . .”
(P10, on the effect of the outbreak on coping)

“Age brings in experiences, wisdom, acceptance, and much more. . . all my life I have faced hardships, even in daily existence. . . it’s tougher times now, deaths, medicines, hospitalizations all around. . . with my age anyway I have nothing to lose. . . so I try to make maximum out of my life now, irrespective of everything. . . I tell others the same. . .”
(P5, when asked about suggestions for others in the old-age home)

Psychotherapy for the elderly often uses such lived experiences, building upon notions of resilience and post-traumatic growth after disasters/crises, based on existential and humanistic approaches (37). Earlier studies have mentioned age and experience as enabling factors for community inclusion (38). However, our participants felt “othered” in their community, which forms a significant part of the societal stigma that is potentially harmful to coping and mental health.

“They say people who are living on the streets are being targeted for having the infection. I have the additional issue of being a Hijra. They were almost forcibly admitting me to the hospital. . . even without testing. . .”
(P1, when asked about the challenges they face)

There is also a common myth that the elderly do not have sexual needs, and these ideas were challenged by P4 and P7, who mentioned that they “cannot even experience intimacy to soothe us during difficult times as they (their partners) go out

for work, and the risk of infection” is present. The pandemic’s effect on psychosexual health and deprivation of “social touch” remains largely unspoken but is critically detrimental to well-being. As COVID-19 is a highly contagious infection, this has led to doubts relating to sexual transmission and a definitive fear of intimacy. Sexual relationships and sexual well-being can be affected, irrespective of age or gender specifications (39).

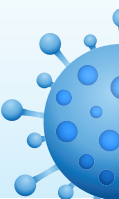
“Our relationship and closeness have literally formed my core strength in the worst of times. He goes out, so we sleep in separate rooms. . . the infection has created an emotional wall between us. . .”
(P3, on relationships during COVID-19)

“Intimacy with my partner is a major comfort. But he goes for work. So, we don’t feel comfortable making love. . . It makes me weak and vulnerable!”
(P7, on how the crisis has affected coping)

It is important to note here that resilience and strength emerging from their relationships and intimacy served as “viable supports” during the pandemic crisis. This is in contrast to models of psychological resilience being conceptualized as “personal internal attributes” based on Western mainstream psychology schools (40). The authors further emphasized the “social functioning” that can be vital for coping and in developing problem-solving approaches during the crisis. In large-scale social threats like the COVID-19 pandemic, the need for social enmeshment and emotional bonding with their partners fostered love, care, and support, which were reflected in our participants.

Disasters in the Transgender Elderly as “Survival Threats”

Overall, the above factors together generated physiological, emotional, and financial pressures for participants. Losing priority and stigma kept them at a “backfoot” for health care, their voices unheard, and the uncertainty of the COVID-19 situation was amplified due to the double fear of “aging” and “being deprived.” Many of the participants reported mentioning that “old people are dying fast,” which they encountered in the media, with detailed information about morbidities that added to their fear. Besides, it is essential to understand that frequent comorbidity of Human Immunodeficiency Virus (HIV), diabetes, and other chronic medical conditions, compounded by neglect, often leads to persistent immunocompromised states in transgender people. These, along with age, can form the two most crucial risk factors for morbidity and fatality in COVID-19 (41). Associated mental illness and substance abuse often worsen the situation. Seven of our participants mentioned that their suffering lacked the audience, though the community was superficially concerned. It made them feel “invisible to society,” resonating with “how they have always felt.” Empathy and compassion were not sensed by the people around them, and even financial support was difficult to access. In the absence of employment and social benefits (such as a pension) for most of them, this made the situation even more dire.



"My neighbors would not want to interact with me. I was old, staying alone, and even basic needs were difficult. . . people knew that, but I hardly even got anyone asking how I am doing. . ."
(P2, while discussing the unmet needs)

"Take care' is the maximum assurance that I have received! Nobody bothered about how I needed to care for myself staying on the streets. . . Even begging didn't help."
(P8, on social indifference to suffering)

There has been a traditional association between the LGBTQ group and disasters. McKinnon et al. (42) mentioned how the voices of this community were largely under-represented by mainstream media during the Brisbane floods or the Christchurch earthquake of 2011. There was mention of similar marginalization during the Queensland floods (43). The same authors have also written about the "Queer domicile" wherein homelessness was a significant offshoot of natural disasters in gender minorities as the administrative policies that respond to these crises remained neutral or respond to the needs of the perceived status quo (44). The *Higashinihon Dai-Shinsai* (The Great Japan Disaster) of 2011, which began with a tsunami and earthquake, led to a lack of shelters, mass stigma, bullying, violence, and social exclusion for the Japanese LGBTQ community, effects that have been vastly under-represented in the literature (45). Systematic research and policies related to the plight of the LGBTQ population in India during disasters also lack standardization. The present study recommends that LGBT rights are incorporated into and allowed for in disaster ethics and disaster preparedness planning. The literature on this subject also documents that many older transgender adults do not have fixed jobs and are dependent on their families, homes, and communities, which decreases their autonomy and increases their risk of abuse. The homeless individual who took part in this study faces overcrowding, lack of quarantine facilities, and proper shelters, an experience shared by thousands of migrants all across India during the lockdown. Their age, gender, and the social crisis are a "triple blow" to their present condition.

"People usually help seniors, don't they! Am I any different because of my gender? Can't I expect the same help from others who are much younger than me. . ."
(P5, on being an "invisible sufferer" during the pandemic)

"There was no respect for age or humanity. . . how can I expect help!"
(P7, while talking about distress)

While these were their vulnerabilities, we will now discuss how transgender individuals have navigated the crisis and the barriers they face.

Coping, Resilience, and Barriers to Care

Five participants in this study were aware of the Pride movement and ongoing Pride month. Two knew that there was some celebration scheduled for their community at this point of the year, and three were unaware. Pride celebrations emerged after the Stone Wall riots in 1969, and mark the ongoing protest

and expression of the social integrity of the LGBTQ community (46). Around 220 pride festivals have been canceled across the world due to the COVID-19 situation, and even though some organizations held events online, there was limited impact and access (47). In India, elderly participation in the Pride Movement has always been scarce (48), which creates a situation of "seclusion within seclusion." The participants looked forward to a regular get-together of their community as a way of coping during the ongoing crisis. While most did not identify the festival with a "name," they were aware of celebrations being canceled due to the pandemic situation. Even local festivities within their community were compromised, which affected their social support. This is a notable reflection of emotional expression in the Indian socio-cultural context. While discussing "gender, depression and emotion," Davar (49) examines Indian folk stories and contrasts the "collective" emotional expressions of Indians rather than the usual homogenized view of singularity. This collectivism was more prominent in the marginalized sector of the population that we studied.

"I know about this place where all of us gather and celebrate. Someone told me it is this time of the year. I wish it could have happened."
(P3, while discussing Pride celebrations during a pandemic)

"I don't know too much about it and what they call [it]. But in our community, we have small celebrations, cooking, singing, and all. . . nobody dared to do all these. . . it will lead to more trouble in society, as such we are always blamed. . ."
(P8, when asked about festivities in the community)

Spirituality and hope emerged as essential themes in seven and five participants, respectively. Ross et al. (38), while studying a group of transgender individuals, mentions that "personal development" and optimism are essential factors in building resilience, even though the study subjects were not older adults. Spirituality and hope for the future play an essential role in coping in our study subjects, forming a part of their "self-identity."

"I used to go to Hanumanji's temple whenever possible, irrespective of all odds. It really helped. There was so much peace there. . ."
(P3, while talking about religious practices)

"God or not, there is a force I believe in and worship. Can't explain! But that gives me hope. . ."
(P10, when asked about spirituality and coping)

The need to identify oneself with society for perceived self-worth, irrespective of disabilities, formed an essential aspect of the community health care needs of the elderly in a systematic review done by Holm and Severinsson (50). A low level of spirituality has been associated with a poor ability to cope emotionally and higher rates of depression in Indian older adults (51).

All the participants agreed that they lacked awareness about the necessary measures and ongoing situation about the pandemic. Only two followed social media updates, and



apart from the numbers projected in the newspapers, they had questions about safety and testing for COVID-19. Three were increasingly dependent on their families while four others worked in shops as manual laborers and domestic help and lost working days during the lockdown. Salary cuts and unemployment have been widespread during the COVID-19 pandemic. Data from the PSB Research group in the United States showed that 30 percent of the LGBTQ community had their working hours reduced and salary decreased, compared to 22 percent of the general population (52). This creates a sense of mistrust and anger at the administration for the participants. Media reports mention increased socio-economic deprivation for the Indian LGBTQ community during the lockdown, a rise in abuse at the hands of their own families, and social harassment, which adds to the pre-existing burden caused by the pandemic (53).

All of the study participants agreed that they felt like an “outcast” even when they repeatedly heard people saying “we are in this together.” Eight of them reported lacking an audience for their problems, which was why they welcomed the interview.

“Thanks to your research that you are asking. . . I felt good sharing these issues with someone, very few bother. . . already old, now more of a burden to the society!”
(P4, toward the end of the interview)

“Media arrives and raises thousands of questions when needed. Nothing changes! Maybe nothing will, but at least you asked. . .”
(P3, while reflecting on the present study)

Social integrity and support are essential components in creating resilience during widespread disasters. These needs were not met in most participants. To summarize, the “dual burden of ageism and third gender” along with marginalizing factors decreased their access to health care and created physically unsafe and emotionally insecure environments, which along with “dependence” and “poor awareness” increased their physical and psychosocial vulnerabilities to the COVID-19 situation.

Our study had a small sample size and is subject to the usual limitations of qualitative research, such as subjective interpretation and reduced generalizability. The ongoing pandemic crisis could also have exaggerated participant responses to questions related to their suffering. However, in a marginalized sector of the population, each voice matters, and our study benefits from a rigorous methodology, analysis, and reflecting and providing a platform for these usually “unheard and invisible” voices. As requested by the participants, the researchers present these “narratives” as representations and accounts of social suffering, rather than mere data.

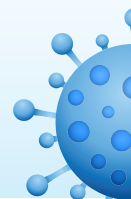
CONCLUSION

India is aging fast, as are the increasing number of gender minorities. Guidance on the care of the elderly by the WHO as well as the Ministry of Health and Family Welfare (MoHFW) in India are comprehensive, but unfortunately fail to mention the already neglected experiences of the transgender community

(54, 55). Wang et al. (41) have recently appealed to the Government and private sector to consider the holistic care of transgender groups, advocating community-based screening for their needs, online consultations, and a reshaping of policies that accommodates their health-care needs and enhances access. Associated with this are HIV management and harm-reduction techniques for substance abuse in this population during the pandemic. *Aging with Pride: The National Health, Aging and Sexuality/Gender* (NHAS) study has proposed the “Health Equity Promotion” model for older transgender adults, based on a bio-psychosocial understanding of their unique vulnerabilities (56). The Coronavirus Preparedness and Response Supplemental Appropriations Act and The Coronavirus Aid, Relief, and Economic Security (CARES) Act passed by the U.S. Congress during the pandemic are inclusive of LGBTQ communities (57). Such models could be adopted by the Indian Government, especially with the numbers of this population increasing. Our study sample was small, but the rich data from the participants, the thematic saturation, and the holistic representation from various backgrounds strengthened the study. These results indicate that the needs of gender minorities are still largely unmet, especially in older adults. However, these findings need to be interpreted in the Indian socio-cultural context. The Indian Pandemic Act of 1897, needs to be overhauled to consider the needs of both seniors and the transgender population, which could help preparedness for similar crises in the future. Banerjee and Nair (23) have discussed the different “vulnerability areas” of transgender individuals during the COVID-19 crisis and suggested interventions to mitigate physiological risks, social discrimination, sexual stigma, substance abuse, and to preserve psychological well-being, economic stability, sexual health, and gender-based equality. The authors highlight the unique needs of the elderly LGBTQ population and foreground the need to prevent ageism, stigma, and appropriate social rehabilitation measures. The under-representation of older adults in India’s LGBTQ movements has been a growing concern in recent years, particularly in terms of their civil rights and socio-economic security. Care homes are often not suited to their needs and can turn into potential sites of abuse. Transgender individuals are not immune to the frailty, cognitive, and sensory deficits of aging and will need similar care. This sensitivity needs to be emphasized at all levels, by active collaboration between physicians, human rights activists, the media, and government administration (58). As the pandemic is still in its early period, the coming months will be crucial for undertaking more systematic research into lived experiences and risks due to COVID-19, apart from focusing on testing and symptom-based management. Similarly, our collective responsibility is to be aware of the unmet needs of this community in terms of social inclusion, care, and support rather than discrimination. Only then can their health emerge as a priority and not an option.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary materials, further inquiries can be directed to the corresponding author/s.



ETHICS STATEMENT

The studies involving human participants were reviewed and approved by JSS Academy of Higher Education & Research, JSS University, Mysuru, Karnataka, India. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

DB was involved in data curation, analysis, and drafting of the manuscript. TSSR was responsible for designing the study, data collection, reviewing, and editing the manuscript. Both authors conceived the study, read and agreed on the final version of the paper.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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APPENDIX

The Key Questions of the Semi-structured Interview Schedule

- What difference did you face between the pre-pandemic and the COVID-19 times?
- How do you think the pandemic has affected your mental well-being?
- How do you think your age affected your perceptions related to the current crisis?
- What challenges did you face due to the pandemic situation?
- What type of support have you received?
- What do you think could have been done to make your experiences better during this time?
- What were the difficulties in seeking psychological care during the pandemic?
- What were your unmet needs?
- How do you think the COVID-19 situation might affect your future?
- What message would you like to provide for the elderly from the same community?



The 'Othering' in Pandemics: Prejudice and Orientalism in COVID-19

Abstract

Pandemics are not just medical phenomena. They affect the society at large, having long-lasting psycho-social implications. Throughout history, they have led to stigmatization, prejudice, "othering," and blame. This amplifies hate and socioeconomic divisions, and the effect outlasts the outbreak itself by years to come. Traditionally, humankind has always fared better to deal with the pathogen causing the outbreak, rather than the resultant stigma and prejudice. In the pursue of biological cures for the infection, this vital social implication is unfortunately neglected. The coronavirus disease 2019 (COVID-19) has emerged as a global public health threat. As international borders are sealed, economies slashed, and billions quarantined at their homes in an attempt to contain the spread of infection, history repeats itself in the prevalent marginalization, blame, and stigma that are more contagious than the virus itself. This commentary traces back through the past to look at examples of orientalism and colonialism in pandemics and the resultant stigma, and also to highlight global perspectives of the prevalent prejudice in this current outbreak of COVID-19.

Keywords: Coronavirus, COVID-19, orientalism, othering, pandemic, prejudice, stigma

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Back in Times: The Case of "Typhoid Mary"

In the early 1900s, a sanitary engineer by the name of George Soper was requested to investigate a strange outbreak in New York. Typhoid, as it turned out to be, and as we today know is a bacterial disease caused by *Salmonella typhi*, was then recognized as an emblem of "poverty and filth." Concomitantly, it was considered to be unique to the slums, homeless, and laborers being equated to dust, dirt, and lack of sanitary hygiene. Parallely, the Long-Island of New York started reporting plenty of new cases of typhoid, and without any apparent known cause. This generated mystery and unsettling emotions about how an apparent "illness of the poor" could affect one of the most affluent and posh sections of the society.

After starting his inquiry, Soper made an interesting observation. A middle-aged Irishwoman named Mary Mallon could be traced back to at least eight of the families who contracted typhoid. She worked as a cook and would change the family the moment a new case of typhoid broke out in them. Mary herself was, however,

completely healthy and showed no symptoms of the disease. Understandably, Soper was excited to pin the source back to where the society thought it belonged to, the lower socioeconomic class. A manhunt followed, Mary was stalked to her residence and finally accused of being responsible for the outbreak. Soper wanted her to undergo medical testing, and when she refused, the police arrested her. Her blood, urine, and fecal samples were collected almost forcibly, and she underwent a detailed physical examination. All these were totally based on a hypothetical conclusion that Soper had made. Though Mary's physical examination was completely normal, her test reports came back showing the presence of the causative *Salmonella* bacterium. This proved her "guilty" in the society beyond doubt. That was the first time that "healthy carriers" were described: people who carry the disease-causing pathogen infecting others while themselves stay asymptomatic. George Soper got the credit for this discovery, while Mallon continues to be a figure of social disgrace known till date as "Typhoid Mary." Mentioned in most medical and epidemiological textbooks, this term stigmatizes a poor, migrant

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woman who was also a talented cook. She had totally no idea that she was carrying the infection, but the violence and coercion against her was justified, which would have been so much against the “code of ethics” that we follow for medical examination and testing. The media and the society including the medical school portrayed her as a “mass-spreader” like a “mass murderer,” accusing her to have infected around sixty cases, three of whom died. The true numbers were sadly never corroborated.^[1]

Mary Mallon continued to be cornered for the rest of her life being tested and questioned multiple times for something she knew little about. She was kept in quarantine on Northern Brother Island for 26 years till her death. Her fellow mates and hospital staff never stopped viewing her as “guilty” of being the “carrier of infection.” Typhoid was re-affirmed as an illness of lower social strata as the higher classes heaved a huge sigh of relief. Unfortunately, the illness was not new to the city, but Mallon was labeled as “deadlier” than the bacteria itself. Only much later did Bourdain,^[2] her fellow chef, point out that she had just done her duty in spite of all odds and was totally unaware of being the causative factor for the illness in the families. Her true fault was probably different: setting a reminder for the affluent society that infections did not choose based on wealth and power.

The Concept of “Othering” and Social Stigma

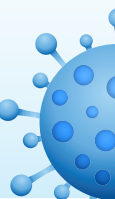
“Othering,” originally a philosophical concept relating to distinction of personal identity from the “other” thereby creating a sense of “self,” has eventually generated the “we/us versus they” dichotomy of the social divide.^[3] Edmund Husserl, the founder of phenomenology, conceptualized “the other” through intersubjectivity, that explains the differences between races, castes, ethnicity, religions, etc.^[4] Eventually, othering has formed the basis for labeling and disenfranchising the “vulnerable” minorities based on any characteristic, thus leading to the alienation and marginalization of “the other.” Over the years, territorial conflicts, violence, communalism, military disputes, diseases, famines, social divisions, and racism have been rooted in the processes of othering and social stigma. Throughout history, “othering” has also led to the genesis of imperialism, colonialism, sexism, gender dichotomization, and cultural subordination (the “subaltern natives,” who are socially, politically, and geographically beyond the hierarchy of power and hence exploited by the privileged sections).^[5] Goffman while hypothesizing stigma, emphasizes on the social discredit of an individual or a group by virtue of them being “undesirable other” by the society.^[6] Socio-political and economic hierarchy, generalized apathy, discrimination, and blame perpetuate this othering further, especially at times of crisis like wars or epidemics, where the “othered” are held responsible for the “social condition.” This plays an important role in the attributional bias that makes the higher socioeconomic

classes assure, secure, and safe by displacing the prevalent tension onto the discriminated lot. This can further give rise to self-stigma among those who are “othered,” leading to their impoverishment, human rights violation, and social injustice: all of which can have intergenerational effects and serious psychosocial consequences.^[7] The subsequent section deals with the perpetuation of othering at times of infectious disease outbreaks.

“Othering” in Pandemics: Perspectives from History

Pandemics repeat themselves in time. The basic evolutionary need is to live and thrive, the same applies for the pathogens causing these diseases. Death of the human host is only a small fraction of the outcome. The resultant morbidity, social chaos, widespread panic, and crashing of public health infrastructure are the main offshoots of such large-scale outbreaks. After the initiation, eventually, there is an uneasy bio-psycho-social symbiosis with time for the mutual survival of both humankind and the pathogen. However, the psycho-social impact is far beyond just the organs affected or the symptoms. Such illnesses do not discriminate between social, racial, ethnic, or economic classes, and the impact is widespread. Conventionally, whenever a pandemic has struck the world, there has been stigma, prejudice, and marginalization with harmful effects for months to follow.^[8] Here are few examples of the same.

During the classical “pestilences” or the Bubonic Plague of the 13th century, the Catholic Church blamed the Jews for poisoning the water and spreading the illness. The “Black Death” was proposed as an alleged attempt by them against Christianity and the “guilty” included the vulnerable and impoverished sections of the society. Many were not treated, not received at hospitals, and simply left to die based on their socioeconomic position. There are descriptions of corpses piling up to close one end of the road, but still they were not touched or even buried based on the fear that they are contagious even after death.^[9] Areas such as Basel and Strasbourg witnessed the burning of many Jewish people as the punishment for the “plague.” Even Camus has spoken about increased “death anxiety” in the rich which leads to “death denying behaviors” such as “othering” and blame.^[10] Similarly, people in Rome, Italy, faced such persecutions being labeled for being responsible for the plague. Their movements were restricted, rights were curbed, and they were termed as “Zingaris” (a pejorative term for the Romans).^[11] In addition, in the medieval Europe those who were practicing alternative forms of medicine and faith healing were accused of “witchcraft” and many were burned or buried alive with the same blame. Historical estimates set the number of prosecutions to be around 1 lakh, though the exact numbers are unclear. The majority were, however, women from low-income families.^[12]



Eventually, the germ theory and the advent of microscope helped the society understand that specific pathogenic agents are responsible for illness, not a particular “class” of people. However, soon enough, the science of microscopy was buried in colonialism. The “Tropical regions” were prone to various vector-borne diseases which horrified the Anglo-European colonizers. Mosquitoes, ticks, bugs, and rodents were associated with Asian and African colonies, and the fear was rampant that Western countries will eventually contract them. As a result, people who were degraded or punished in their own countries would be deputed for duties in these colonies with poor access to health care and restrictions on return.^[13] The Asiatic Cholera (1817), the Asiatic Plague (1846), and the Asiatic flu (1956) are examples of diseases being tagged with certain “areas” even though the outbreak was all over the world. On similar lines, *Vibrio cholerae*, the causative agent of cholera, was linked to the intestinal tract of a colonized native’s “tropical” body as the outbreaks were more pronounced in the Indo-Gangetic belt. It was further termed as “Indian Cholera,” linked to poor dietary and sanitary conditions, “waste” lands, and “nonsophisticated” men.^[14] The other classical example would be that of leprosy, which has traditionally been a disease of stigma, hate, and marginalization. The affected were considered “sinners” and were socially outcast, as the upper classes did not want to publicly notice them. As a result, they were victims of neglect and faulty treatment. Even gender separation was attempted to prevent reproduction, as it was wrongly considered to have a genetic basis.^[15]

The Root of Stigma: Epidemic Orientalism and Coronavirus Disease 2019

The World Health Organization (WHO) now has clear guidelines to name an infectious disease. It needs to have generic terms, irrespective of the origin and people affected.^[16] However, even of late, the Hong Kong flu and Middle East respiratory syndrome are examples of such “epidemic orientalism.” Humans pay the price for being “social” beings as the hate mongering has always been the inevitable accompaniment of a biological disaster. Epidemics and pandemics tend to be labeled with specific regions, race, class, ethnicity, or even sexual orientation. Infections have historically blurred origins and stigmatized the affected. Naming an outbreak is important as that is how the illness is recognized and called globally. In every reference or discussion, it sets the reminder of prejudice and marginalization. With use over years, people forget its true origin and only remember the “tag” associated with it. Such has happened with “Typhoid Mary” as mentioned before. One of the most stigmatizing infections, acquired immunodeficiency syndrome caused by the human immunodeficiency virus, was long known as “gay-related immunodeficiency.”^[17] Also termed as the “Gay Plague,” it was theorized as a punishment for sexual “deviation”

in America of the 1980s.^[18] This belief has held on to its ground in the legislation of many countries which prohibit homosexual men from donating organs or blood.

History repeats itself. The modern world has rarely seen a global and contagious outbreak like the coronavirus disease 2019 (COVID-19). Within 7 months of its origin, the novel coronavirus has taken the world by its knees affecting international borders, economy, the daily routine, and movement of civilization.^[19] The epicenter of this pandemic was in the Wuhan province of China and since then, it has been termed as the “Chinese virus” or the “Kung Flu.”^[20] Such terms even when used on a lighter note turn viral, as already information on COVID-19 is spreading faster than the virus itself. Used in social media forwards as jokes or memes, these terms quickly turn into pejorative labels for a region or a country. As a result, Chinese settlements in many countries are being blacklisted with avoidance of even Chinese food and goods. People with Mongoloid features are being cornered and stigmatized in the South-East Asian countries and the United States. Various countries have accused China of being the source of the virus and mis-managing the initial wave of infection, leading to the global pandemic.^[20] Conspiracy theories have been rampant about coronavirus being used as “biological weaponry” to destabilize the powerful nations of the world. It has subsequently perpetuated anti-Asian sentiments and xenophobia besides the panic related to COVID-19. The penetration of these theories went to such an extent that the WHO and Centers for Disease Control and Prevention had to give official statements on the falsity of the information.^[21] This again is in historical resonance to the Church’s vague accusation of the Jews to “produce” the plague for harming the faith of Christianity. Various politicians from Europe have also mentioned the role of migrants and refugees in “carrying and spreading” the infection, leading to the dismal state of COVID-19 in many European countries such as Italy, Germany, and Spain.^[22]

In low- and middle-income countries like India with preexisting and prominent caste, racial, and class divisions along with a markedly heterogeneous population, the pandemic situation is even worse. “Social distancing” has incited the old evil of untouchability and people from certain regions are being discriminated against.^[23] Racist comments are hurled at them with threats of eviction. Even health-care staff including doctors have faced the brunt, being prevented from entering apartments and losing social circles. They are believed to be “close to infection” and hence carriers.^[24] Although the nonresident Indians were returned to the country, thousands of migrant laborers, daily wage workers, and homeless are stranded on different parts of the country struggling basic amenities of living. Many are walking down hundreds of miles to reach their homes due to unavailability of any transport. They are more afraid of not able to reach their families, losing their jobs, and dying due to the hunger rather than the COVID-19 panic.^[25] Relief



camps and measures taken to provide food and shelter to this already-vulnerable population are ongoing but slow to keep up pace with the increased numbers. Added to that is the mass panic, hoarding of medical goods and medicines, and plethora of misinformation that further leads to anxiety and stigma.^[26] Certain recent incidents such as hosing down of migrant workers in Uttar Pradesh to “disinfect” them and the increased number of COVID-19 cases in the Tablighi Jamaat meet in Nizamuddin, New Delhi, have fueled the fire of social-class-based and communal disharmony.^[27,28] People act more irrationally when anxious, and this can contribute to the discriminating, blaming, and competitive behavior. A recent Indian study using the Fear of Coronavirus Scale has demonstrated that fear and generalized xenophobic (communal) attitudes are inversely related to the mental well-being during the pandemic, while collectivism promotes it. The authors highlighted an important area of concern in this socio-politically heterogeneous country, where misinformation and rumor can easily lead to fear-mongering, social prejudice, and communal sentiments, that can be as damaging to public health as the virus causing the pandemic.^[29] India like many other South-East Asian countries is on the verge of a community transmission, when all these factors essentially promote the spread impeding the containment measures.

Conclusion

We had long back taken the shelter of science to understand that disease-causing pathogens just need a human body to thrive, irrespective of the typologies. Unfortunately, science itself has been modified to suit the clutches of stigma. Each pandemic will eventually be over, but the resultant social distress and discrimination will last long. The classical example is that of Mary Mallon, who, as mentioned before, lived her life being equated with an illness that lasts till date. Even today, as we fight COVID-19 with the main strategies of social distancing and quarantine, the administration is desperate to enforce the public compliance by stamping the doors, tattooing their bodies, and making their identities public. While all of these are in good faith and isolation is indeed necessary, such social coercion is totally against human rights and moral code of ethics. We do not know what state COVID-19 will leave us in. Irrespective of the numbers affected, the virus might hopefully decrease in virulence and the pandemic will eventually cease someday. The label of this prejudice and social stigma will however outlast it by years, probably till another such infection originates and amplifies them. The human race has fared much better with such diseases than with its internal “blame game” and “othering.” Pandemics might flare up “hate,” but the society propagates it. Viewing this scenario through the lens of “social psychiatry,” it is obviously much beyond the diagnostic categories or psychiatric disorders: preventive approaches using community awareness, social tolerance, and anti-stigma interventions are necessary

to protect mental well-being, as much as the medicines or psychotherapy needed to treat them. To fight a global health crisis like COVID-19, humankind needs to be united and that is only possible if it stops viewing an infection through the lens of “socio-politico-economic divisions.”

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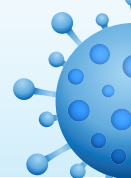
Nil.

Conflicts of interest

There are no conflicts of interest.

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NOTE: The data, and views, in this Viewpoint have been updated, and are accurate, to the best of knowledge of the Authors as of 13 August 2020.



“Unheard Voices of the Pandemic”: Psychosocial Vulnerabilities of the Indian Migrant Population during COVID-19 Crisis

“The habit of despair is worse than despair itself”

Albert Camus, *La Peste* (The Plague), 1943, pp. 62.^[1]

Khandelwal, in his comprehensively drafted review in this issue,^[2] aptly highlights one of the touching aspects during the ongoing outbreak in India – the crisis of the migrant workforce (pp. 18–19). Besides making us aware of the immense importance of health care and emergency service workers, the virus has also showcased the sad reality of the migrants, who play a pivotal role in the Indian economy. The coronavirus disease 2019 (COVID-19) pandemic has surged into a global health threat within months of its emergence, as every nation faces unique challenges to deal with the outbreak. India, being under constant “internal migration” for employment and living, has faced significant difficulties with the care and provisions for its migrant labor force. This commentary glances at few aspects of the “despair” of this vulnerable section of the population, through the lens of the “*Social determinants*.”^[2]

The Long Way Back to “Home”

To quote Dr. Chinmay Tumbbe from his book “India Moving: The History of Migration,” “A little bit of India moves with every migrant worker.”^[3] The Indian migrant workforce (daily wage workers and laborers) range roughly between 100 and 125 million, who have left their places of origin, families, and homes, to find work and livelihood wherever possible.^[4] “*It is an obligation for us Saheb, not a choice! Would you really want to stay away from your newborn son for years? But, at the end of the day, it is me who have to feed*

him,” as mentioned by one of the migrant workers from Bihar residing locally, involved in a construction worksite at our Institute.

Some of us are also migrants, living away from home, for years altogether, and we can all resonate this common realization, i.e., living away from “home” is never easy, especially when “home” in our sociocultural context signifies much more than just an accommodation. It is a nurturing place of emotional bonds, family ties, and memories that make a significant part of our identity. During times like this, when the pandemic threat looms large, being at the comfort of home also provides psychological resilience, which the migrant workers are largely deprived of. Ironically, they are as much prone to the physiological effects of the infection, as they are to the psychosocial and economic offshoots of the “sudden lockdown” in an effort to contain it. Some suffered from salary cuts, and many became unemployed; however, what all of them wanted was at least to reach their homes, which was the real challenge in absence of transport. As rightly mentioned in the article,^[2] many of them were forced to walk miles on a “*long and arduous journey*”, driven by hunger and lack of basic living amenities, in the absence of any policy or plan to safeguard their interests. As the lockdown progressed through the four phases, it has been pointed out that “*their plight became evident by the heart rending stories that started trickling in the print, as well as the social media.*”^[2] Assuming that they are as much a citizen of this country as anyone of us, a prudent question arises: How did they differ from the Indians stranded abroad who

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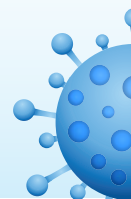


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were flown back promptly at the initiation of COVID-19 crisis or the students who were returned home from their coaching centers at Rajasthan, Kerala, etc.? Eventually, special trains were arranged for the migrant workforce, but even then, their travel has faced immense ambiguity and inequality over time.

The “Vicious Cycle” of Infringements

Each kind of work has its own dignity. However, the migrant workers are mainly involved in manual labor in extremely difficult and threatening conditions, irrespective of the climatic or environmental outbursts. Even though, we are traditionally trained to respect the ideals of visionaries such as Gandhiji, Hegel, Marx, and Luther King, the intensive and under-paid labor of the migrants often tend to be overlooked by the administration, deprived of human and socioeconomic rights, blinded by societal apathy and dealt with through “sympathy” and “charity.” Migrant labor and mental illness have always had a close bi-directional relationship; the above-mentioned factors contributing toward the “social and minority stress.”^[5] We agree with the view mentioned in the review^[2] that the migrant workforce will continue to suffer from chronic physical and psychosocial morbidities even in the aftermath of the COVID-19 pandemic, due to the “*vicious cycle of poverty, poor health and inability to access any kind of health care.*”^[2] It is unfortunate to realize how we, the so-called “socially affluent” class have taken their back-breaking work to “be granted,” and considered their social upliftment as an option, rather than a priority. For the migrant workforce, work is an important source of satisfaction, self-esteem, and dignity, which is the best that they can do being away from home and susceptible to a contagious outbreak. Human rights and dignity are equally applicable to this population, repeatedly violated in the overcrowded stations and streets, where thousands of them get stranded in unsanitary and unhygienic conditions. When the World Health Organization has recurrently emphasized on the three-pronged approach of “social distancing, hand hygiene, and respiratory hygiene” as the main strategy to fight against COVID-19, each of these seems a “luxury” for the migrant workers, when masks, soaps or even water tend to become “rare commodities” for this section of the population. Many of them have also turned homeless, which itself tends to be a unique vulnerability for an illness like COVID-19 with high human-human transmission. It is important to understand, that as the COVID-19 crisis progressed in the country, most of these migrants were “obliged” to go back home; more for survival than for comfort. Many of them work in metropolitan cities with a high cost of living, where survival is nearly impossible with the bare minimum money they are left with, compounded by the socio-economic infringements. In fact, viral detection (through active testing) and quarantine options are also minimally available for them.

The “Vulnerable and Deprived”

Dr. Ravi Srivastava, Honorary Director of the Center for Employment Studies, Institute for Human Development, Delhi, has recently and quite relevantly described the migrant workforce as “people from nowhere,” characterized by four “D”s: Dirty, dangerous, difficult and the most consistent one, discriminated.^[6] All of these terms represent the socioenvironmental situations that they live and work in, as well as how the society perceives them. The National Sample Survey (NSS) shows that most of the migrant laborers are from the rural areas and belong to the poorest socioeconomic classes. Even though they form the economic backbone of construction and agricultural sectors, the “we versus they” dichotomy of the classical “class divide” has always stigmatized and “othered” them to form the outcast in terms of rights, health care, and legal provisions. The Indian Pandemic Act, 1897 already needs a major overhaul and as has been mentioned,^[2] integrating psychosocial equality, mental health interventions, and identification of the “at-risk populations” need active incorporation into the public health response to disaster management.

The virus, unlike humans, does not discriminate based on socioeconomic class, race, color, or ethnicity. The societal “blind-eye” to the safety of the “migrant workforce” has started to “boomerang” us of late, when many of them are returning to their respective places, being the “carriers” of infection. Sadly, they are being blamed for this too, which is a social blow even for those who could return to their homes. The current crises that the migrant workers are facing, is also an amplification of their distress during the otherwise “normal times.” Most of them are exploited and deprived of the legally minimum wages that they deserve. They have no rights to contest the transparency of their salaries and become increasingly accountable for their financial indebtedness to various employers. Added to that is their dire living and working circumstances. We cannot agree more with Khandelwal when he remarks that in line with the United Nations (U. N.) Sustainable Development Goals (SDP), “*a society is considered civilized when it is judged by how well it looks after its disadvantaged citizens.*”^[2] COVID-19 might be yet another opportunity for us to do so, before it is too late. The world is well aware by now about the shockingly tragic incident in Aurangabad, when 16 migrant workers were overrun by a goods train when they were resting alongside the railway track.^[7] Some of us, who are safely sheltered in our “social distancing,” might be too naïve to question the choice of the resting place of these unlucky “migrant workers” and blame their idiosyncrasy as a reason for their untimely and painful death. *What the society however fails to realize is that for years together the train of “discrimination” has been running them down under the tracks of its so-called “civilization,” as they lose their lives and livelihood every other day.* Humanity, collectivism, and care are



the common tools required to fight a global crisis, as much as biological cures or vaccines. Societal as well as administrative apathy toward the impoverished only add to their misery, which in turn can turn back on us at a large. Unfortunately, it required a microscopic (COVID-19) virus to open our “blindfolded” eyes!

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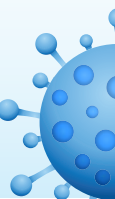
Conflicts of interest

There are no conflicts of interest.

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Note: The data and views in this Commentary are updated, and accurate, to the best of knowledge of the Authors as of 10 June 2020.



LETTER TO THE EDITOR

WILEY

Covid-19 and Namaste

To the Editor-in-Chief

The novel coronavirus (SARSCoV-2) has emerged as a major pandemic stretching the healthcare resources of most countries of the world. In this context, it is imperative that social distancing and good hand hygiene is practised to stem the transmission of this highly contagious virus.

The WHO's standard recommendations to prevent infection spread include regular hand washing, covering mouth and nose when coughing and sneezing, thoroughly cooking meat and eggs and to avoid close contact with anyone showing symptoms of this respiratory illness.¹ Also shaking hands or any form of hand-to-hand contact should be avoided as cross-transmission of organisms occurs through contaminated hands.²

In most countries of the World, handshake, fist bump, high five and hugs are some of the different methods of greeting each other,

which leads to physical proximity and contact, facilitating rapid propagation of infections such as Covid-19.

Alternatively, other non-physical greeting forms can be explored like Namaste, which is used in Indian subcontinent since hundreds of years to greet people with folded hands, while maintaining a fair distance from each other [Figure 1]. An individual in addition to saying "Namaste" presses his hands together in front of the chest and respectfully greets the other person. This form of greeting does not involve any physical touch between individuals and gives a sense of parity to all the parties.³

In addition to following general principles of meticulous hand washing, rapid transmission of infections both in hospitals and the community can be overcome by adopting the no-touch salutation Namaste and other such forms like bowing the head as done in some Asian countries.

KEYWORDS

Covid-19, Namaste, pandemic


CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS CONTRIBUTION

Prashanth Kulkarni: Conceptualization-Lead, Methodology-Lead, Resources-Lead, Software-Lead, Writing-original draft-Lead, Writing-review & editing-Equal; Shruthi Kodad: Supervision-Equal, Validation-Equal, Visualization-Equal; Manjappa Mahadevappa: Visualization-Equal, Writing-review & editing-Equal.

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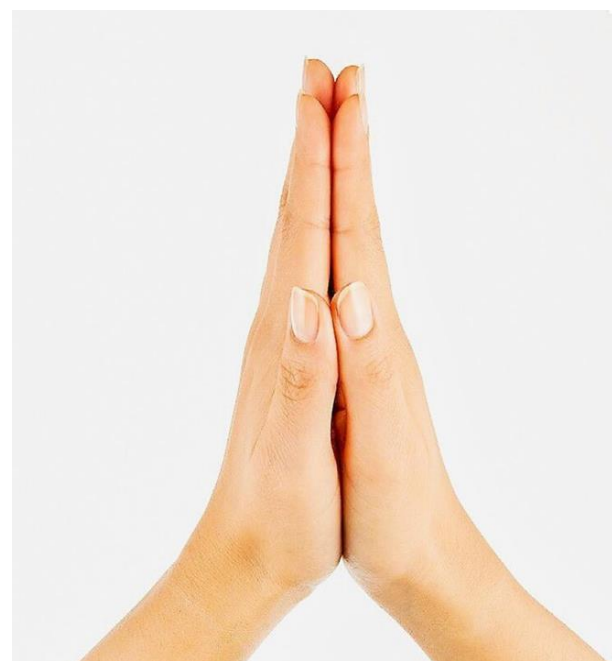


FIGURE 1 Namaste

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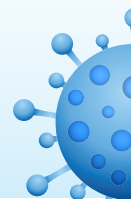
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Guest editorial

The Silent victims of the Pandemic: Children and adolescents during the COVID-19 crisis

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“Children are not the ‘faces’ of this pandemic. But they risk being among its most-affected victims.” – World Health Organization [1]
COVID-19: The Problem Statement

The World Health Organization (WHO) declared Coronavirus disease 2019 (COVID-19) as a pandemic on the 11th of March 2020. Besides affecting global public health, outbreaks like this have long-standing psychosocial offshoots. Travel has been widely restricted, economies slashed, jobs lost, and billions quarantined at their homes in an attempt to control the outbreak. Awareness about the disease, its symptoms and the three-pronged strategy to contain it (social distancing, hand and respiratory hygiene) have been given prime importance by the WHO and consequently by all the nations of the world. WHO had declared, "This is the first pandemic caused by a coronavirus, and we have never before seen such a large-scale infectious outbreak!" [1] In fact, within months of its emergence, the virus took the world to its knees, affected human lives, society, and livelihood alike. With more than seven million affected and nearly five lakhs succumbing to the infection, so far, the numbers are rising [2]. The need to protect citizens drove the Governments to take extreme draconian measures to contain the spread of the virus. Governments ordered residents to stay in a 'lockdown' amidst this public health emergency. The complete and historical four-phased lockdown enforced in India encompassed closure of public and social places, schools and educational institutions, religious places, and others. This created mass panic and anxiety in people residing all over, already affected by the fear and uncertainty the pandemic posed. Though every sector has faced unique challenges due to this unprecedented situation, certain populations are exceedingly vulnerable. In these uncertain times, special groups like children, adolescents, the elderly, and people with co-morbidities (diabetes, hypertension, and others) are known to be affected more than the general population [3]. Alongside this, children were largely affected by the burden of anxiety passing from parents and media onto them [4]. Though the number of children infected by the virus is seemingly lower than other age groups [3], the psychological and social impact on children is known to be higher and will probably have long term consequences. Increased anxiety, the uncertainty of the pandemic situation, lack of peer support, and chronic trauma can all lead to detrimental psychosocial issues for the children and adolescents.

The unique vulnerabilities of the population

Children and adolescents are in a constant physiological and psychosocial phase of development. Children progress through the first five stages of Erickson's psychosocial model to transition into adulthood. During this phase, children encounter various situations and either accommodate or assimilate learnings to develop positive virtues or remain stagnant [5]. This makes the "stress" encountered by children and adolescents as a part of the normal developmental process. This stress can be classified as - normative stress and non-normative stress [6]. The former is normal developmental stress and enables children to develop positive coping strategies [6]. The latter, non-normative stress, is experienced by children who go through traumatic or unusual experiences, for example, abuse and violence. The ability to handle stress depends on gender, socio-economic status, cultural background of the child, and resources available [7]. The developmental effects are seen in the physical, psychological, and social domains. Children in whom negative events summate (hunger, poverty, violence, abuse all at once), the rate of maladjustment multiplies [6]. The pandemic is an example of the latter category. Stress affects children tremendously and has a bearing on their long-term development as adults.

The pandemic so far has affected over 1.29 billion children and adolescents in over 210 countries [8]. The children from low and middle income (LAMI) countries are at a higher risk. The children from the disadvantaged or marginalized sector of the society like migrants, slum-dwellers,



homeless children, orphans, children diagnosed with mental illness, disabilities, children living in institutional or residential care are at a greater risk of succumbing to mental health consequences. The children living in an environment at risk of violence, domestic abuse of any nature directed towards them or their loved ones, and/or a witness to this would have a larger risk of psychological distress. Lack of peer contact, limited understanding of the global crisis in younger children, and disrupted daily structure can add to the social stress. In this paper, we discuss the various psychosocial and emotional issues and strategies to handle them to ensure positive psychosocial development.

Psychosocial and emotional considerations

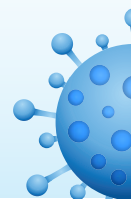
The direct effects of the pandemic/virus on the mental health of children and adolescents are seen in the children testing positive for SARS-CoV-2 (causative agent of COVID-19), close contacts of cases, or children of health care workers involved in the care of COVID-19 positive patients. The psychological effects of the illness in older children and adolescents are that of anxiety, depression, fear of death, and fear of loss of loved ones similar to those faced by adults [3]. During the first phase of the pandemic, Wang et al. [9] conducted a general population-based online survey where 54 percent reported having moderate to severe mental health problems, out of which depression and anxiety were the major ones. However, younger children do not have a complete understanding of the situation and are unable to express their emotions. In them, symptoms like poor sleep with nightmares, poor appetite,

physical discomfort, agitation, inattention, clinginess, and separation problems are red flags for psychological distress [10]. Social distancing, masking, and hand hygiene are difficult to enforce in younger children and children with disabilities as they do not understand the need for these measures. The need for parents to help them understand and practice is a challenge. The habitual (stimulus-response) associated with repeated positive reinforcement for practicing and punishment or negative reinforcement, diminishes the ability of the brain to perform goal-directed (action-outcome) activity [11]. Hereby understanding compulsions can precede obsessions to develop Obsessive-compulsive disorder (OCD). Repeatedly telling children – "wash your hand every time you touch something" might induce habitual learning, in turn increasing the risk for OCD. This might also influence their cognitive and personality development.

Digital learning: A 'dual-edged' sword

Schools are anchor points to children for numerous reasons [12]. To reduce risks of the pandemic spread, most countries have declared a complete or partial lockdown. This sudden change in social milieu has various effects on children. The closure of schools disrupts their daily routine. A structure is important for children with Autism spectrum disorders (ASD), Attention Deficit Hyperkinetic Disorders (ADHD), and neuro-developmental abnormalities, and its disruption might worsen pre-existing behavioral problems like frustration and irritability. The children on speech therapy, social skill training, and others would be unable to achieve goals in the specified time duration; this would delay achieving milestones that are of prime importance in motor, social and cognitive development. Children going to school is not only about education, but also gives them the opportunity to meet their friends, develop a peer group, and involve in physical/extra-curricular activities. The lockdown has led to social isolation and a sedentary lifestyle by restricting physical movement. This also has an impact on hobbies, sports, and extra-curricular opportunities they would have in school. Schools are also a primary source of nutrition to those from underprivileged families, some of whom solely depend on schools for their nutritional supplement- through school meal programs. The closure of schools in this case also results in hunger and malnutrition in this group of vulnerable children.

The closure of schools has prompted urban schools to shift learning to digital modes – Audio visual-based to continue the learning process. The effects of digitalization will be discussed subsequently. Children with disabilities who cannot engage themselves in digital modes and those from underprivileged families with a lack of appropriate access facilities face the maximum brunt. Digital learning has also been used in adults who are enrolled in colleges. In schools, children are usually prohibited from bringing any electronic gadgets and face the consequences like confiscation of the device or other non-corporal punishments, if non-compliant to the instructions. But with the advent of the pandemic, all reservations of electronic gadgets have seemingly taken a back seat. Teachers appreciate the continuation of the learning and its advantages to be of larger importance. The balanced effects of digital learning in children has not been studied previously. In line with the studies of problematic cell phone use in children and adolescents, one should be mindful of the long duration of permission for using gadgets, increased privacy, and access to internet for educational reasons unknowingly would have negative effects on the visual and psychological well-being. An inverse relationship between problematic cell phone use and mental health has been observed. But it has not been established if there is a



causal or consequential relationship between the two. The access and privacy might nudge them to experiment with social media, which can snowball excessive feed of misinformation and unhealthy use of technology. The premature exposure to varied digital content without an adequate understanding of the associated risks puts them at a higher risk of cyber-bullying, exposure to explicit content, online exploitation, and abuse. The psychological issues associated with problematic cell phone usage are sleep disturbances, preoccupation with social media feeds, depression, anxiety, suicidality, substance use, and a higher propensity for addiction [13]. The use of the internet and gadgets also inversely associated with physical activity [14]. Though done with all good intentions, along with the positives of continuation of school, children and adolescents are at a high risk of experiencing the negative effects of prolonged use of internet. Lockdown has also led to a prolonged 'entrapment' in that sense when many families are faced with a challenge to channelize the activities of their children. Pre-recorded classes and online demonstrations though innovative, are far from the dynamic environment of the 'school', which is also emotionally nurturing for the child. Hence, many of them tend to lose interest in academic schedules, further promoting 'digital screen time' and behavioral addiction.

Parental stress and the child's mental health

“Man and woman power devoted to the production of material goods counts a plus in all our economic indices. Man and woman power devoted to the production of happy, healthy, and self-reliant children in their own homes does not count at all. We have created a topsy-turvy world” – Looking back at John Bowlby’s words in A secure base: parent-child attachment and healthy human development [15], which is accurate in the current scenario.

The government and health care professionals are focusing on containing the spread of the disease and the mental health concerns though an important backbone of public health, has sadly been in the backseat. The current situation of the pandemic has obliged parents to embrace the multi-modal role of caregivers, teachers, friends for their children who are homebound. Parents, apart from taking care of all aspects of the child, also must take care of household chores, their jobs and face the stress of the pandemic. The stress is experienced at both personal and dyadic levels. The parents are also faced with economic and financial stress, some have lost their jobs, and this particularly has been seen to affect the marginalized

sectors. Especially in most patriarchal families, 'work for home' and 'work from home' are difficult to balance for the mothers, the primary caregivers of children. The increased stress levels are also associated with higher levels of domestic violence, child abuse, child trafficking, and maltreatment evidenced by the number of calls reported by child helpline numbers globally. Thus, it becomes all the more important to ensure adequate care for children and adolescents. The parents are of utmost importance in maintaining a homogeneous milieu. Studies have looked at the relationship between stress and psychosocial health of children and adults. However, the risk and protective factors at the interplay between the child and parental mental health have been less focused on. A study in Italy had identified the stress of quarantine as one of the most crucial factors influencing the child and parental mental health. The lockdown and unavailability of human resources like teachers, peers, and others involved in caregiving leads to the parents being burdened and at increased risk of experiencing stress and negative emotions, which can negatively affect their children's wellbeing [16]. All efforts should be made to educate the parents to handle this situation in better ways to prevent the short term and long-term psychological issues in children and adolescents. The knowledge, attitude, and practice of mental health care measures in their children thus assume overt important during these critical times, beyond just the physical safety from the virus. Family forms the most important part of a child's socio-ecological sustenance, and hence during such biological disasters, families play a vital role in coping and resilience of the child.

Sexuality and intimacy: The untold crisis

The adolescents are in a phase of psychophysiological stress owing to the hormonal, physical, psychological, and sexual development. The changes in puberty, need for socialization with peers, attending get-togethers and parties, identification and exploration of their sexual interests and needs, being attracted to others: all of these help in developing self-esteem, healthy body image, developing a social and sexual identity as well as foster intimate relationships [17]. The need for 'touch' or close personal communication has been studied in neuro-biological and psychosocial development of humans [18]. The risk of infection from a contagious illness like COVID-19, the need for social distancing, social segregation, and travel restriction, have all led to the genesis of 'touch hunger', which amplifies in children and adolescents. Borrowing from Bowlby's attachment theory and Harlow's classical anthropological experiments with primates, this 'deprivation of social touch' can be



important in the genesis of chronic stress [19]. Chronic stress has been implicated in involving the Hypothalamic-Pituitary-Axis (HPA) and hence affect immunity [20], the most important factor in COVID-19. Adolescents and children suffer increasingly from this 'touch hunger' that can affect their emotional wellbeing and cognitive development. The phase of chronic stress associated with social disconnectedness can affect adolescent psychosexual development, similar to those studied in other chronic illnesses. However, the core effects of the pandemic on sexual development can only be predicted. The pubertal growth might be reduced due to stress and low physical activity. The increased sexual urges (sexual frustration) following touch deprivation might result in excessive masturbation, indulging in pornography, and other high-risk behaviors. This, in-turn results in a high number of gender-based sexual abuse (GBSA), impulsive sexual behavior, higher risk for sexually transmitted illnesses, early marriage, and teenage pregnancies. This will negatively affect psychosexual development; some of these negative events might also put adolescents at higher risk for psychiatric illnesses like depression, post-traumatic stress disorder, anxiety, insomnia [21]. Though digital intimacy has been advocated in the COVID-19 times, traditional beliefs about personalization of 'sex', restricted access, and discomfort with technology use can make these practices less acceptable. Adolescents are also at the risk of online fraud and sexual exploitation.

Post-pandemic aftermath

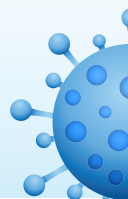
We have already discussed the vulnerabilities of childhood and adolescence during the pandemic. The post-pandemic aftermath on the development of children and adolescents is not a single outcome. The effects of the stress caused by socio-economic conditions can only be extrapolated and assumed. The first to look at is the age at which the stressful event occurs, the intensity and chronicity of stress. Acute stress at high intensity or chronic stress of varying intensities – like the pandemic causing stress in children and adolescents will have long-lasting effects on the brain and can induce persistent changes in behavior [22]. Though stress is seen globally, the environment within the family and other social factors determine the aftermath of the pandemic. Complex post-traumatic stress is often an offshoot of such chronic stressful situations of an outbreak with multi-dimensional vulnerabilities. It is under-detected and normalized in the Indian socio-cultural context but, if untreated, can affect the self-image, personality, impulsive traits, addiction behaviors, interpersonal relationships, and social trust. If intervention or buffering of the stressful situation is done, it will promote resilience [20] and pro-social behavior [22]. The development of child and adolescent during and after the pandemic is in the hands of parents, relatives, teachers and health professionals. The promotion of growth and psychosocial wellbeing needs more focus. It is true that COVID-19 and consequent lockdown have brought about increased family and personal time, something that was perhaps long due. Integrating the child's world into the family, quality time spent together, and structuring the days can help in familial cohesion and personal growth. Such concepts of optimism and collectivism have been used in positive psychology for post-traumatic growth following disasters [23].

The way forward: Proposed interventions

1. The parents should monitor the duration of daily use of gadgets, also keep a watch on the use of social networking and other illegal content.
2. Ensuring secure web access is important, as well. Parental supervision to ensure safety needs to be complemented with adequate involvement and interaction with the child fostering a positive environment. Digital learning needs to be carefully balanced with parent-assisted academics.
3. Maintaining regular routines for children (school/learning, free time/relaxing, bedtime, etc.) and create new opportunities for joint activities (entertainment, leisure, and creative activities online or offline).
4. The quality time and attention given to younger children to help them express their feelings (anxieties, fears, boredom) to their caregivers and alleviate their anxieties through this supportive environment.
5. Adolescents need to be provided with their emotional space and peer connectivity.

Behavioural changes are expected to be more in them in such unprecedented situations, which can be dealt with dialogue rather than directive measures.

6. In these times of stress borne by families, we believe that parental behaviors of reinforcement are better appreciated than limitations or



punishment imposed on children. A positive and nurturing environment during this time of stress in the long term will help the child attain adequate socio-emotional development, the virtue of trust, and form secure relationships in adulthood.

7. Building resilience helps children manage everything from disappointments to life traumas. If adequately supported by healthcare professionals, families, teachers, and other social connections, children and adolescents can appropriately overcome their distress and prospectively stabilize emotionally, physiologically [3] and avoid severe long-term consequences [16].
8. To include daily indoor physical activity – like Yoga, aerobics, or other forms of exercise in their daily routine.
9. To encourage the development of new hobbies like – arts, literature, dance, music, and other handcrafts. The parents can assist children in helping them acquire new skills or develop already existing ones. Certain positive structures developed now can go a long way for personal growth, even post-pandemic.
10. Social protection measures need to be moved online and help to rescue children facing abuse and violence.
11. Specific child helpline numbers need to be established with adequate volunteers to cater to the needs of hunger, poverty, shelter, clothing, and other basic needs for children and adolescents. Such helplines can be integrated with the existing mental health helplines of central institutes and the Indian Ministry.
12. Adequate care for maternal antenatal, perinatal, and post-natal care in terms of hospital assisted deliveries, neonatal care, vaccination, and primary health care measures should be available.
13. Children need to be educated about the need for social distancing, using masks and other personal protective equipment, hand hygiene. An age-appropriate explanation for the pandemic situation is necessary. Debunking myths related to COVID-19 will be of paramount importance as this age group serves as important vectors for snowballing health-related misinformation.
14. The younger children need to be spoken to in a calm and reassuring tone with affirmative statements to ensure they understand the need to isolate without being scared. They need to be encouraged to keep in touch with loved ones through phone/video calls. Social connectedness plays a vital role in coping for children, especially with their peers.
15. Children in quarantine should be given adequate opportunities to contact their parents, have activities to keep them occupied indoors, and enjoy recreations of their choice to reduce the stress experienced.
16. Children and adolescents with pre-existing mental health disorders or intellectual disabilities need increased care and supervision. Teleconsultation with the treating physicians, continuing psychosocial management, home-based behavioral management, and empathy are the key strategies for their care. Red flags of suicidality, excessive aggression, and seizures need urgent professional help. Awareness and prompt action related to the same will be necessary.
17. Information, education, and communication (IEC) activities for the community awareness and primary care health workers related to child mental health care: advocacy can be a joint liaison between the media and physicians. Simple yet socio- culturally sensitive infographics in multiple languages can help both the children and their parents in understanding the COVID-19 situation.

Conclusion

The Coronavirus disease 2019 (COVID-19) has emerged as a global health threat. Though the 'at-face' risk of infection for the children and adolescents are documented to be less, they often bear a major brunt due to the pandemic and consequent lockdown. Restricted access to mental health care, social distancing, consistent entrapment with families that can foster neglect and abuse, as well as challenges in education and training, are among the main psychosocial offshoots of the present crisis. Increased pressure on the families and schools, as well as the anxiety, fear, and economic recession post-pandemic can affect their care and wellbeing. Many educational institutions and courses have considerable ambiguity regarding their continuation and examinations, which can set a 'new normal' for the younger population even in the post-pandemic aftermath. As the lockdown has been relaxed in many countries, social distancing is not an option for the children of many families, as the seniors might need to attend jobs. Added to that, is the psychosexual aspects, deprivation of 'social touch' and chronic 'traumatization'. Those with neurodevelopmental disorders, ADHD, or other mental disorders share increased susceptibilities, which are often neglected as optional priorities during the pandemic crisis. Stress-related coping can be dysfunctional for some, which can increase the risk of substance use, impulsive sexual behaviors, and suicidality. Keeping in mind the special mental health care needs of this population, the policies need to shape



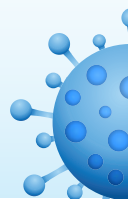
accordingly. Health care at all levels need to sensitive to their needs, liaising with the parents and schools for appropriate IEC approach. Mental health needs to be a priority, not an option as it can have far-reaching consequences for the psychosocial and cognitive development of the children. Systematic research can address the population-level risk and their unmet needs in the months to come, which will be vital for administrative regulations and prevention of abuse. Such plans can help preparedness for such futuristic crises. The pandemic is still in its early stages, and this might be a global chance to re-look into the vulnerabilities of the child and adolescents to prevent physiological and emotional morbidities for years to come.

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The “Untold” Side of COVID-19: Social Stigma and Its Consequences in India

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“Imagine a society of saints, a perfect cloister of exemplary individuals. Crimes or deviance, properly so-called, will there be unknown; but faults, which appear venial to the layman, will there create the same scandal that the ordinary offense does in ordinary consciousnesses. If then, this society has the power to judge and punish, it will define these acts as criminal (or deviant) and will treat them as such.”

—Émile Durkheim, *Rules of Sociological Methods*, 1895, p. 123¹

The Canadian sociologist Erving Goffman theorized that social stigma is an attribute or behaviour that socially discredit an individual by virtue of them being classified as the “undesirable other” by society.² There has been a long association of social stigma with illness. Through the process of othering, social stigma segregates the healthy from the ill. It creates stereotypes and prejudice. “Othering,” originally a philosophical concept given by Edmund Husserl, describes the reductive action of labeling and defining a person as a subordinate in terms of category.³ This generates a “we versus they” dichotomy that helps

in the establishment of a socioeconomic hierarchy. During times of social crisis (pandemics in this case), it can lead to discrimination and blame. Those who have any association with the illness are discriminated against and socially isolated, with their human rights being violated. The unknown factors about illness create fear, myths, and rumours around



them that heighten social stigma. This can negatively affect the treatment and prevention of the illness. Especially, pandemics of infectious disease outbreaks have had a historical relationship with stigma and prejudice. Mary Malon, in the 18th-Century England, became infamous as “Typhoid Mary,” guilty of spreading the infection amongst affluent families, though she was unaffected. The concept

of “asymptomatic carriers” came quite later; however, the textbooks still bear her name associated with an illness.⁴ Transmission of infections has always been associated with “poverty, filth, and class,” to maintain a false sense of assurance and safety for the higher sections of society. The “pestilences” of bubonic plague, Asiatic flu and cholera, Middle East respiratory syndrome, and Ebola outbreak in Africa, all have been associated with polarization, racism, blame against certain ethnicities, and resultant psychological distress.^{5,6} The concept of naming illnesses by the country or place of origin has been termed as “epidemic orientalism” and is considered to be a form of social labelling.⁵ Even acquired immunodeficiency syndrome (AIDS) had been termed as the “Gay Plague,” being theorized as a “divine punishment” for homosexuality.⁷ The tradition is reflected in the legislation of many countries that still prevent homosexual men from donating organs and blood. Research has shown that the fear and uncertainty of unknown infections affect human behavior significantly. Panic, illogical beliefs, aggression, blame, and “othering”

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are some of the unhealthy offshoots.⁸ The need to hold someone accountable based on power and social hierarchy has been explained by the social attributional theories.⁹ Through decades, humans have paid the price for being “social beings” by fostering hate-mongering as an inevitable accompaniment of biological disasters.

The outbreak of coronavirus disease 2019 (COVID-19) has created social stigma and discriminatory behavior towards individuals who are perceived to have any contact with the disease. This is one of the most large-scale outbreaks known to the modern world. It has affected more than 10 million globally and killed nearly 516,000—the numbers rising as we speak.¹⁰ Pandemics such as these are much beyond just biological phenomena. They create lasting psychosocial consequences that persist longer than the infection itself. Besides the direct psychological impact of stress, fear, anxiety, and mass hysteria, COVID-19 has led to the emergence of significant stigma, “othering,” prejudice, and blame that have strained both inter-regional and international relations. From the very time of its origin at Wuhan, China, the infection has been termed as “Chinese virus” or “Kung Flu,” which later fostered conspiracy theories about biological warfare, which strained international relations. Ironically, social stigma has spread faster than the virus itself. This commentary briefly glances at the resultant social stigma of COVID-19 pandemic in India, the vulnerable populations, and the impact of it on the society at large. It then highlights the ways forward to mitigate this “social evil” associated with the outbreak.

The Victims of Social Stigma During the COVID-19 Pandemic

The stigma around COVID-19 stems from the fact that a lot is unknown about it. Scientists, researchers, and medical professionals around the globe are still working at a breakneck pace to figure out the strategies to deal with the novelty of this virus. The fear of the unknown has overwhelmed humankind evolutionarily. Human beings tend to distance

and segregate themselves from the unknown. Deviant has been branded and stigmatized in all eras of human history, particularly in the history of medical science. Whenever there has been a lack of explanation, be it scientific or supernatural, the affected individuals have been segregated, labelled, and stigmatized, and therefore, ostracized as a consequence.

Social stigma towards the segregated appears to be normal behavior to the common mass. It gains social acceptance amidst the chaos of the unknown. Institutional segregation of those who are affected by a disease, at present COVID-19, further strengthens the stigma. We are aware of the social stigma experienced by those who are admitted to institutions for mental illness, leprosy, HIV Aids, or tuberculosis, even today.^{11,12} Even the prevention of COVID-19 demands segregation; terms like quarantine, social distancing, and isolation have become an integral part of the household vocabulary. Hospitals have been allocated particularly for the treatment of COVID-19, separate laboratories been assigned, quarantine zones been set, containment zones have been created, and the country has been divided into color zones depending on the incidence rate. Indeed, these are steps to flatten the ever-rising graph. However, since a pandemic is much more than a biomedical phenomenon, all these steps have their own social implications as well. For example, the Air India crew members who brought hundreds of stranded Indians back home experienced being stigmatized by their neighbors when their homes were stamped “quarantined.”¹³ Similar experiences have been reported by home-quarantined individuals when the Delhi Government decided to put up notices outside their home.¹¹

Incidents of social stigmatization towards those who are affected with COVID-19, including their family members, have been rampant. Individuals who have succumbed to the illness have been denied their last rites. In many cases, the families have refused to accept the bodies, and the state governments have performed the cremations instead.^{14,15} As an action towards such ostracizing behaviors, some states of India even is-

sued orders to bring criminal charges against anyone obstructing the performance of the last rites.¹⁶ Many incidents have come to light where the survivors have been isolated by the neighborhood, forcing them to live a life that is far from ordinary. Being labelled with multiple tags like “super-spreader” only worsens their suffering.¹⁷ The medical symptoms of COVID-19 subside, leaving behind the society to ostracize the survivors for days innumerable.

The stigma is directed not only towards those who have recovered from COVID-19, those who are undergoing treatment, or who are presumed to be affected or who have succumbed to it or their families. The brunt of social stigma is also faced by frontline workers, medical practitioners, nurses, police personnel, etc. They have been forced to leave the neighborhood and denied access to their houses and the families have been threatened. The insurmountable atrocities that they have been undergoing to win this race against the virus have been ignored. Instead, social stigma has overpowered the goodwill of those for whom they are fighting.¹¹ The way mental health practitioners are labelled as *paagolon ka doctor* (doctor for the mad person), the frontline workers who are tending to those affected by COVID-19 are being stereotyped against.

Social stigma towards certain marginalized groups like the homeless or the migrant laborers has also been witnessed. On returning home after months of being stranded in various parts of the country, the workers and their families have been singled out, sneered at, and harassed by the community members. At some places, they have been cast off even after completing the mandatory 14 days’ quarantine.¹⁸ Similarly, in the wake of the spurt of cases following a religious gathering in Delhi, the social media was flooded with communalistic and provocative sentiments.¹⁹ In a country like India, with a history of multiple communal riots, such stigmatization might bear significant consequences. The Government of India issued an advisory on April 8, 2020, asking its citizens to act more responsibly in such a critical time and to refrain from stigmatizing any community or area.²⁰



The “Dual” Burden: Struggle with COVID-19 and Related Social Stigma

Social stigma towards different stakeholders during a pandemic like COVID-19 might play a significant role in undermining social cohesiveness, enforcing social segregation.²¹ The International Federation of Red Cross, WHO, and UNICEF issued guidance to prevent and address the social stigma around COVID-19.²¹ The report identifies the impact social stigma might have on both treatment and prevention of the disease.

There have been multiple instances reported in various states of India where individuals have not reported their history of foreign travel or symptoms of COVID-19 due to the fear of facing social boycott and discrimination, leading to low testing and high mortality rates.^{22,23}

According to public health experts, the social stigma associated with being diagnosed is creating a fear among the public and is acting as a deterrent to the effective management of the disease, particularly in the urban setup.

The stigmatization is taking a heavy toll on the mental health of the frontline workers as well as those who are recovering or have survived the disease. Media has reported the influence of isolation and discrimination on suicides in India.²⁴ Experiencing isolation and stigma from social boycotting and religious discrimination can increase the risk of loneliness and self-harm.²⁵ Data related to suicides during the COVID-19 period in India is scarce. As per the cases reported in the media, 168 out of 326 non-coronavirus-related deaths in India (data till May 9, 2020) are due to suicide²⁶; however, the source of this statistics has not been clearly mentioned. Reverse migration, the two-months-long lockdowns, and fear of job loss are making individuals vulnerable to self-harm and depression. Social stigma, as well as the self-inflicted stigma associated with the pandemic, is further catalyzing the process. However, these are largely media reports that can have their inherent bias. Systematic population-based studies over the next few months after the pandemic will help us estimate the actual risk of suicide attributable to COVID-19.

In an unprecedented event, hundreds of nurses (more than 350, as on May 17, 2020) quit their job from multiple private hospitals in West Bengal in two days.²⁷ Most of these nurses belong to other states, and they started returning to their native states. While the experts are still at a loss in understanding what led to such a mass resignation, fear of treating those who are affected with COVID-19 and the social stigma associated might have encouraged such unfortunate behavior.

Mitigating the Social Stigma: The Way Forward

Social stigma might threaten the basic structure based on which a society grows. In times like this, when “physical distancing” and “physical isolation” are much-required steps to keep oneself and the loved ones safe and healthy, society might need to act together to stand against all things, be it COVID-19 or the stigma associated, that challenge its cohesiveness.

Wording Sensitive

Historically, it has been seen that the terms that are used in connection to a disease, *pagal* (mad) for individuals with mental illness or *pagalkhana* for hospitals treating mental illness, can possibly shape the lens through which society is likely to perceive that disease. Illness creates othering. Coining terms to address those who are affected with COVID-19, or for that matter, any illness, widens the gap between self and others, instead of bridging it. It thus becomes critical to consider the words that are used in relevance to COVID-19 by not only medical professionals but also organizations like WHO and UNICEF, public directives and notices, promotional campaigns and advertisements, and media.²⁰ For example, “a person suffering from COVID” is more appealing than “COVID positive.” Terms like “coronized,” used in casual humor, can be perceived as labelling. Acknowledging the affected as victims of the pandemic, rather than the source, is helpful. Also, the frontline COVID warriors need community support and encouragement rather than discrimination.

Amplifying the Voices

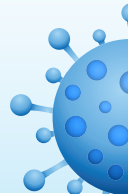
It is relevant to involve and amplify the voices of those who are affected by COVID-19 the most, to develop stigma-mitigating strategies. It would involve those who have recovered from it, those who are undergoing treatment, their families, families of those who have succumbed to the disease, as well as frontline workers. Their lived experiences of COVID-19 and other intersecting stigmas can contextually inform public health strategies to mitigate stigma. Furthermore, the stories of recovery are likely to create hope in public that might help individuals come out with their symptoms instead of hiding them. As identified earlier, social stigma is deterrent to testing for the disease. Thus, learning from the survivors that recovery is possible would encourage people to deal with this stigma.

Furthermore, the everyday struggle of the frontline workers should also be focused on. Their experiences, when remaining unheard, might not generate the gratitude that they deserve from society. The life risk that is undertaken by them to provide us with a safe and healthy society stays in the background, while we express stigmatized behavior towards them.

Acting Responsibly

It is not only on the government and frontline workers to act responsibly in a critical circumstance like this. Apart from them, political leaders, media, and, most importantly, the citizens need to act responsibly and do their parts sincerely in fighting the pandemic and related stigma.

One must stay informed. Stigma can be heightened by insufficient knowledge. It is thus necessary to spread the knowledge about COVID-19 (e.g., what causes it, how it is transmitted, treatment, and prevention) without using medical jargons. While social media can be a useful platform to reach the maximum people while lockdown is practiced, its use must be done responsibly. In the past, the misuse of social media had created further stigma than reducing it.²⁸ At the same time, journalistic reports that focus on an individual’s behavior or role in



“spreading the virus” might create stigma among the public. Such publication must be dealt with sensitively, keeping in mind the disruption it might create in the life of those who are involuntarily forced under societal scrutiny. The Ministry of Health and Family Welfare, Government of India, has also issued a directive that highlights the importance of the responsible role the citizens need to play to empower the community to respond effectively and appropriately in the face of adversities.²⁹ Knowledge, attitudes, and practice (KAP) can actually be improved through community awareness. Based on the Zika outbreak model, Banerjee and Nair have proposed a community-based psychosocial toolkit that involves all levels of health care, with an active health-media liaison, to improve the information–education–communication (IEC) activities during the COVID-19 pandemic.³⁰

Engaging social influencers such as religious leaders and celebrated actors and cricketers, and their take on COVID-19 and stigma, might also be influential in fighting stigma. The recently launched “Break the Stigma” campaign, featuring Amitabh Bachchan, is one such initiative undertaken by the Government of India.³¹ Such steps would not only ease the struggle of the survivors against the stigma but would also deal with the infodemic of misinformation and rumor that is playing a crucial role in creating stigma and racism. Understanding the crisis in humanitarian perspectives is a collective responsibility. The “we versus they” dichotomy mentioned before can only add to a set of common processes and conditions that amplify group-based inequalities and marginality. Knowledge, awareness, care, and empathy are probably the generic but neglected pillars to change “othering” into inclusiveness, collectiveness, and belonging for better coping and resilience against the ongoing crisis.

Conclusion

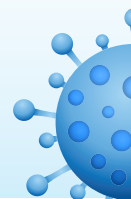
At this juncture, when the number of individuals affected with COVID-19 has crossed six lakhs in India,¹⁰ we are in dire need of more than just information to reduce the tension related to the pandemic

and to mitigate the stigma surrounding it. Multilevel strategies are required to address the underlying stigma drivers and facilitators.³² An intersectional lens can improve the understanding of the ways in which COVID-19 stigma might be intersecting with gender, race, immigration status, and health status, among others.³³ We had long taken the shelter of science to understand diseases and their pathogenesis. But, unfortunately, stigma exists beyond scientific understanding of diseases, at all societal levels. This is aided by misinformation and xenophobia during pandemics. Certain sections of the society are already vulnerable—for them, being targeted by society is a “dual pandemic” apart from COVID-19 itself. Very few times in history has the human race faced such uncertainty about itself. The pandemic will eventually cease, but the resultant stigma might prevail in the society for times unknown. Historically, pandemics have flared up hate but not “caused” it. It is unfortunate to see a civilization dealing better with medical rather than social management of infectious outbreaks. As COVID-19 is still in its early stages, unchecked stigma can lead to dire psychosocial comorbidities, the risk of psychiatric disorders and suicidality being one of them.²¹ Pandemics or epidemics do not discriminate based on sociopolitical, ethnic, or economic divisions. More than ever, society requires its solidarity and cohesiveness to deal with this pandemic. By reducing the stigma around this pandemic, its prevention, and containment, we might be able to develop immediate and long-term strategies to build empathy and social justice for the days ahead. COVID-19 just gives us one more such opportunity to strengthen our social resilience

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Psychology of Misinformation and the Media: Insights from the COVID-19 Pandemic

Abstract

The coronavirus disease 2019 (COVID-19) pandemic has emerged as a significant and global public health crisis. Besides the rising number of cases and fatalities, the outbreak has also affected economies, employment, and policies alike. As billions are being isolated at their homes to contain the infection, the uncertainty gives rise to mass hysteria and panic. Amid this, there has been a hidden epidemic of “information” that makes COVID-19 stand out as a “digital infodemic” from the earlier outbreaks. Misinformation and fake news are invariable accompaniments to this “information pollution” which can add to the anxiety, fear, uncertainty, and agitation and lead to faulty treatments, noncompliance to precautionary measures, prejudice, and stigma. Research shows that distress and panic during pandemics can propagate and promote misinformation in various ways along with increased digital screen time and unhealthy use of technology. In that context, media is considered to be a “double-edged sword” and can either add to the misinformation burden or aid in the awareness and health communication during such a biological crisis. Lessons from past outbreaks portray media, especially social media, as a useful tool to promote health literacy and control the outbreak. This article looks at the impact of information during COVID-19, the psychology behind spread of misinformation, and finally, a balanced view of the role of media in such disasters, proposing ways for its healthy integration into public and social health.

Keywords: Coronavirus, coronavirus disease 2019, health, media, misinformation, pandemics, social media

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“Whoever controls the media, controls the mind.”

(Jim Morrison)

Introduction

While the last few months witnessed a global health threat named coronavirus disease 2019 (COVID-19), the spread of information about the pandemic was much faster than the virus itself. There has not been 1 day since the World Health Organization (WHO) declared COVID-19 as a “public health emergency” that people have not come across messages, memes, or videos related to COVID content, going widely viral on the social media.^[1] Added to that is the plethora of information about the outbreak statistics (number of cases and causalities in every single geographical distribution), being fed daily to the common masses. As billions are isolated or quarantined at their homes, in an attempt to contain the infection,

“digital screen time” exposure has increased with much more penetration of media.^[2] Subsequent to the same, every single day “information pollution” about COVID-19 adds to the already existing uncertainty and panic about the virus and lockdown. In our daily lives, we have seen people with eyes glued to their television, laptop, or mobile screen busy consuming news feeds related to the coronavirus. This often assumes a “compulsive” nature, with the need to stay updated on every single facet about the illness, that further increases the psychological discomfort and physical unrest.^[3] Keeping this in background, this review looks at the significance of information during COVID-19, the psychology behind spread of misinformation, and finally, perspectives on a balanced role of media in such disasters, proposing ways for its healthy integration into public and psychosocial health.

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Information and Coronavirus Disease 2019: Role of Media

Contrary to popular belief, COVID-19 is not the first “digital infodemic.” In the recent past, the outbreaks of Zika in Brazil, Ebola in Africa, influenza in Europe, and Nipah in India had similar bidirectional relationships with media.^[4,5] However, the degree of “media panic,” the amount of media consumption, and the consequent change in public reaction have been paramount during COVID-19, especially considering that the modern world has been unprepared for such a large-scale biological disaster. Harding in “*Pandemics, Plagues and Panic*”^[6] highlights how the spread of an outbreak and the resultant human behavior can be influenced significantly by the flow and vectors of information. Any piece of news attaching an existing belief or theory to the ongoing “topic of interest” can serve as a potential vector (for example: during COVID-19, the well-known antiviral effect of garlic according to Ayurveda has been generalized to garlic being considered as an antidote of coronavirus, which is definitely a false news propagating vector). Identifying such vectors is useful in debunking misinformation. Health communication and understanding of public health depends a lot on how the data about an illness are interpreted by the masses.^[7] Within every bit of news, there can be a potential admixture of “fake information” with the major challenge being teasing out both separately. This health-related misinformation becomes all the more crucial during a pandemic like COVID-19 when the “fear of an unknown infection without a definitive cure” mixed with “an anxious mind” tends to easily accept “fast solutions and theories,” irrespective of visible loopholes in their logic and reasoning.^[8] One senseless forward of a wrong message in wrong hands can snowball the spread, increasing the acceptability as it moves along the chain. Often, names of credible public health agencies such as the WHO and Centers for Disease Control and Prevention are tagged along wrongly to make the piece of false news more credible and acceptable.^[9] Similar things were being circulated during the first wave of infection in China, implicating “biological weaponry” in the manufacture of coronavirus. It unfortunately remained viral on various social media platforms for more than 2 weeks till the WHO finally discredited it.^[10]

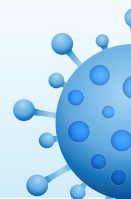
Misinformation and Rumors: Mechanism of Spread

There is a certain price we pay for being social beings. This includes the continued sharing of misperception and faulty interpretations of information. Like the Aesop’s Fables where a boy starts chasing a crow after hearing from a stranger that the crow has his ear, we all tend to follow lucrative and hope-generating information in times of fear and crisis, irrespective of the authenticity of evidence. Fake news or rumors are sometimes socially useful half-truths

with strong emotional overtones that help it spread fast, gripping human minds to create “common” consciousness and agency, but with dire social consequences.^[7]

Health-related misinformation has been studied extensively in health communication and cognitive psychology. Jamuna Prasad, a social psychologist, was the first to establish a relationship between high levels of anxiety and the spread of false news.^[11] Later, multiple studies have established the link between various forms of disasters, human-made or biological, and rumor mongering.^[12,13] At times of uncertainty, people rely on knee-jerk speculation and prejudice. Based on the theories summarized by a systematic review of literature on health-related misinformation,^[14] here are some psychological perspectives as to why the snowballing of fake news occurs, with examples from the current pandemic.

1. False but commonly held beliefs: A message on social media that ginger and turmeric can cure COVID-19 went viral after an accidental text. Although it is a commonly held belief that ginger has antiviral properties, there is no evidence about its effectiveness in fighting coronavirus
2. Generalization of other false beliefs to the current crisis: A common false belief is that the consumption of hot water helps combat multiple illnesses. Not surprisingly, it is wrongly believed that hot water can kill coronavirus
3. Cultivation theory: Repetitive exposure to consistent and regular news (fake or true) can “reiterate, confirm, and modify” values, beliefs, and perceptions of reality. How the news is portrayed is important. This is commonly how advertisements work
4. Social learning theory: New behaviors can be fostered by imitating and observing popular or idealized others in the media. Certain stereotypes, mannerisms, and choices of celebrities tend to get popular in community cultures through this mechanism
5. Theory of negativity bias: The prohibition or negation of certain acts is often accepted as preventive measures. For instance, decreased consumption of chicken or seafood has led to a marked reduction in their sales. This is more acceptable as a preventive strategy to most people than wearing masks or maintaining good hand hygiene
6. Modeling of rumor: A hearsay or rumor becomes a learned behavior for fear of social deprivation. If a majority of members in one’s social network are doing something, it is easier to blindly follow them
7. Overanalysis and faulty interpretation of science: Phenyl/cresol/autoclave is known to kill viruses. The same logic is being used for coronavirus without any evidence. Furthermore, there are half-baked theories about reptiles and birds spreading the virus. The widespread hoarding and use of hydroxychloroquine (HCQ) immediately after it came



in news has led to many inadvertent side effects and mortality^[15]

8. Motivated reasoning: Human beings, usually, accept things in keeping with their culture and traditions. For instance, Indians are more likely to believe that herbal remedies made of tulsi (holy basil) and triphala (ayurvedic herbal formulation) are effective, even if there is little scientific evidence to support the claim. Similarly, religious or local customs often compound the practices related to the disease outbreak
9. Fear reasoning: Human beings fear the “unknown” or “uncertain.” In such cases, the anxious mind cooks up its own remedies and tends to accept the most irrational or logically bizarre facts. That explains why antibiotic sale has increased considerably due to self-medication and prescriptions, even though they have no efficacy against coronavirus. Hoarding of protective medical equipment, antivirals, and sanitizers has not only led to panic but also their unavailability for hospitals and patients who need them
10. Boomerang effect of social media: Hundreds of fake videos about the outbreak in India, mass burials in China, virus spreading through cattle, etc., on various social media platforms bear testament to the perils of senseless sharing. Conspiracy theories like coronavirus being used as a biological weapon or biowaste may make for stimulating debates, but eventually, they add to the global panic and hysteria.

The Impact of Information during Pandemics

“We have sold our priced jewelry to go to this treatment camp. They charge high for each vial of medicine. It is also far from our house. Many people from our village told it works and we can prevent corona infection. Now my son is so ill after taking this tonic. Doctors are not able to help much” (mentioned by a lady from rural Assam).

“People don’t talk to me anymore. They move away when they see me. My neighbors give me a strange look. I fail to explain them my role in the whole process. It makes me frustrated when I return home” (from a doctor working in a COVID-19-designated hospital in Karnataka).

“I was too scared. I just wanted to get the medicine to save my elderly mother. It was all over the news. I got lot of messages that it must be taken by all at risk to stay safe” (son of a senior citizen, who had cardiac arrest after taking inadvertent dose of HCQ in West Bengal).

These excerpts have been slightly modified for anonymity and reproduced with informed consent from the individuals. They are obtained from the crisis calls made to the National Institute of Mental Health and Neurosciences COVID-19-related mental health helpline.

The excerpts mentioned above are both from general public in urban and rural areas as well as frontline health workers,

all of whom were the victims of misinformation and related stigma.

The impact that information or misinformation can have on human behavior is remarkable. It can range from faulty treatment, noncompliance to precautionary measures, panic, mass hysteria, agitation, and competition for health-care resources.^[16] On the other hand, relevant and timely information has shown to improve preparedness for infectious diseases and strengthen public health infrastructure.^[17] One of the main related platforms, social media, thus can be a “double-edged sword.” A review by Kadam and Atre^[18] points out that social media reach has risen three times during the lockdown period in India, with COVID-19-related search spiking significantly. The inherent insecurity and lack of daily structure that strikes people during lockdown makes them feel inadequate without the constant feed of health-related information. It is indeed extremely challenging to ensure a fine balance between the “toxic overuse” of technology and the healthy and systematic harnessing of health data. Many distress calls that the helplines of our tertiary mental health-care center cater to nowadays are related to compulsive use of the Internet and social media leading to health anxiety, somatic complaints, anxiety, depressive disorders, agitation, and insomnia. On a different note, children and adolescents being exposed to more “online time” tend to develop technology and gaming addiction. It is vital to remember that certain unhealthy habits will long outlast the pandemic to cause continued problems in life. Furthermore, anxiety and apprehension about an unknown illness might increase irrational decisions and inadvertent self-medication. One such popular example is the selective appearance of HCQ in the media as a “life-saving” drug against COVID-19 which has overshadowed the strictly prescribed guidelines for its use and the weak scientific evidence for its widespread use against the coronavirus.^[15] Such a selective portrayal of scientific literature generalizing the effects of treatment in its early phases, especially during a crisis like pandemic, can quickly generate a “false hope” with overuse against the recommended safety guidelines. Furthermore, social media-related “blame” can also lead to stigma, marginalization, communalism, and violence, especially at such times of crisis.^[19] In India, people from the North East, certain religious communities, and lower socioeconomic classes like the migrants and homeless have already been victims of such stigmatization related to COVID-19 in our country.^[20] This labeling of “outsiders” in these polarized populations can further increase the social unrest during the already difficult situations. Furthermore, the generation of “self-stigma” in the minority groups increases stress, delays the detection and treatment of mental comorbidities, and perpetuates the vicious cycle of social prejudice.^[19]

“Digital Balance”: The Integrative Role of Media and Technology

Information dissemination definitely has its own merits. It cannot be looked into as an “all-or-none” process. History has proven that continued and timely liaison between media personnel and scientific community can help immensely for the information-education-communication outreach in the community.^[21] The increased use of social media can be a powerful tool for debunking misinformation itself. The linkage of various media platforms with scientific databases such as PubMed and Google Scholar can provide appropriate search guidance, and content analysis of the

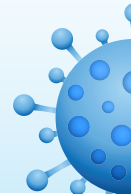
search data gives useful information about the search trends, the popular “sought for” information, and the unmet need for data.^[22] Those can then be harnessed for authentic updates and fighting false news. Social media owing to its increased penetration, popularity, and consumption is uniquely equipped to aid public and mental health during such times. Various proposed ways of this integration are summarized in Table 1.

Awareness for healthy use of technology can be spread by social media itself with administrative reforms regulating unnecessary forward and rumormongering related to the ongoing pandemic.^[2] In the short run, such regulations

Table 1: Role of social media during pandemics

Role of the social media during pandemics	Processes involved
Fighting false news and misinformation	Using diagnostic and referral health tool (example: Facebook preventive health tool) Individualized approach for evaluation, testing, and counseling based on reported symptoms Highlighting and debunking rumors and providing relevant data Integrating data from search engines (like Google QHub) to understand and study trends of misinformation
Enabling digital health literacy	Prevent information overload and content related to xenophobia, stigma, and prejudice Video conferences and webinars Live platforms (like Facebook and Instagram) for awareness campaigns Liaison between journalists and physicians
Helping research during crisis	Search data can be pooled and studied to understand the unmet needs Community public health research
Resource and psychological preparedness during pandemics	Liaising with public health platforms (WHO, CDC, ICMR, etc.) and forums like “Worldometer” to update statistics and trends of ongoing infection Integrating essential service location and contact tracing using special applications Counseling, mental health crisis intervention, and suicide prevention
Crisis communication Fighting stigma	Identifying priorities, providing relevant facts, and precautionary measures Assisting community awareness campaigns through advertisements and promotion Incorporating popular/public figures in the media IEC activities
Facilitating public health needs	Socioculturally and linguistically sensitive infographics Geolocation facilities for identifying hotspot zones and caseloads “COVID-free” content for recreational purpose Special services for those in quarantine Training and health communication between tertiary and primary health care Social connectedness in community and enhancing mutual support Mitigating loneliness
Addressing mental health	Increasing “COVID-free” content to reduce panic Fostering optimism and hope Humanizing mental illness Providing authentic information of mental disorders and treatment Advocating and promoting mental well-being through media programs (especially for the vulnerable groups and those with preexisting psychiatric disorders) Counseling using cyberspace Sensitive reporting of suicides (including celebrity suicides)
Aiding healthy use of media	Advocate healthy use of technology Regulated timelines and content

IEC=Information-education-communication, CDC=Centers for Disease Control and Prevention, WHO=World Health Organization



are imperative. In the long run, destigmatizing pandemics, preventing prejudice in community, and addressing the collective anxiety need to be the goals of the government. Recently, the Regional Outreach Bureau of the Ministry of Information and Broadcasting, Government of India (GOI), had launched a digital media and messaging campaign drive related to COVID-19 for the rural areas.^[23] The messaging service focused on the following targets: maintaining

good personal hygiene, abiding by the lockdown rules, ensuring social distancing, targeting mental and physical health, prevention of rumormongering, and downloading the Aarogya Setu app. The messages were also made in local languages and dialects to cater to the sociolinguistic diversity of the country. The audio version of the same was popularized by all the telecommunication companies which played the message compulsorily during any call

Table 2: Proposed channels of media communication during a pandemic

Channel	Benefits	Challenges
Radio and television	Widespread High consumption	Takes time to get the warnings Limited use at night
Telephone (fixed and mobile)	Messages delivered quickly Simplest method of communication	Problems of authenticity Does not reach many areas Network connectivity issues Difficulty for some groups in telephonic expression of distress
SMS	Quick Messages can be sent to groups	Congestion Does not reach nonusers Local language problems Elaborate discussion/detailed communication is not possible
Cell broadcasting	No congestion Can address a group simultaneously	Frequent network interruption Does not reach nonusers Local language problems
Satellite radio	High penetration	Cannot be used to educate masses Only good for specific points Not widespread
Amateur/ community radio	Excellent for rural, poor, and remote communities	People lose interest if used only in case of disaster Not widespread (limited penetration into rural areas)
Internet/web network	Interactive Multiple sources can be checked for accuracy of information Increasing penetration	Bandwidth issues Issues with handling of technology More prone to misinformation bias (less filters) Difficult without technical assistance in sensory and cognitive impairment

Table 3: Responsible reporting of suicides by media

Preferred ways of reporting	Practices to be avoided
Accuracy of information	Personal assumptions, biases, and “tales” of suicide
Authentic sources of help-seeking	Conspiracy theories
Facts and risks of suicide	Detailed and repetitive reporting
Suicide prevention methods	Sensationalizing, fantasizing, or normalizing suicides
Vulnerable groups at risks for suicide	Reporting self-harm as “heroic” or “constructive”
Expert opinions for qualified professionals/ first-person accounts of coping	Generation of fear, stress, and panic
Sensitive and humane interviewing of the bereaved	Extensive debate and discussion with multiple professionals about the same incident, which generates confusion
Peer debriefing and support among the media personnel to deal with trauma	Avoid using “catchy” or sympathetic headlines/phrases
Factual reporting of the suicide event (especially celebrity suicide)	Coercive questioning of the bereaved on camera
	Avoid visual content (photographs, videos, social media links, etc.) whenever possible
	Excessive emphasis of personal life and contextual information
	Judgmental comments
	Explicit details of methods used

Modified from WHO (2017). Preventing suicide: A resource for media professionals, update.^[30] WHO=World Health Organization



and also appropriate advertisement on audiovisual and print media. The Aarogya Setu (Health Bridge) application, developed by the National Informatics Center, was introduced by the GOI to spread awareness and connect essential COVID-19-related health services to the people of India.^[23,24] It is a tracking app that uses smartphone's global positioning system (GPS) and Bluetooth features to track the coronavirus infection. It tries to determine the risk if one has been in the proximity of a COVID-19-infected person, using geolocation and containment zone data. Although debates have persisted about the "coercive nature" of its use and security concerns, it has definitely been a novel use of technology during the pandemic for the greater good. The various modalities of media with their respective challenges are summarized in Table 2.

The pandemic has also led to increase in suicidality and self-harm attempts. Although systematic studies are yet to emerge, various reports have been published globally including India.^[25,26] Besides the usual psychological impact of stress, isolation, and panic on suicide, media reporting can also have a significant effect on suicide prevention efforts. Extensive coverage, portrayal of information, fantasizing suicide in vulnerable groups, and drawing inconclusive evidence between the pandemic and suicidality can all lead to misinterpretation and public chaos. The "Werther effect" is already a well-known manifestation of "copycat suicides" in vulnerable consumers of media. Studies have consistently found a relevant association between how suicide is portrayed in the media and the effects on the viewers/readers. On the other hand, the protective effect of media is paramount in suicide prevention.^[27] Also known as "Papageno effect," this involves responsible reporting of suicides (especially during disasters and for popular figures), educating the audience about prevention strategies, raising awareness about the early signs of self-harm, encouraging prompt detection and management, targeting at-risk population during the pandemic, and finally, enhancing care for those already suffering from psychiatric disorders.^[28] Liaison between the media outlets and suicide prevention helplines along with those for woman, child, and elder safety can not only decrease self-harm but also age- and gender-based abuse that has increased during the ongoing crisis. It is also important to remember that media professionals themselves get affected with suicide reporting and vivid visual content, with studies showing a high prevalence of insomnia, acute stress, depression, and complex posttraumatic stress disorder in them.^[29] Hence, peer support, counseling, and managerial sensitivity are prime necessities at all hierarchical levels in media organizations. Public health agencies like the WHO has clear guidelines for suicide reporting by the media, especially in sensitive situations.^[30] Few facets of the same are highlighted in Table 3. These are, however, more commonly overlooked than implemented.

Conclusion

Irrespective of profession or socioeconomic background, it becomes the collective responsibility of stakeholders at all levels to join the fight against health-related false news that can have devastating public health and social consequences. Societies can never be fully informed or secure, so rumors are inevitable, particularly during the present times. However, providing active and relevant rebuttal will help in tackling this "unwarranted fatalism" of information. Importantly, we need to understand that we do need information, but "loads of statistics" about every single aspect of "the virus" make no sense to the masses. They will do more harm than good. Maintaining a conscious and informed distance from social media can help increase the "COVID-free" time which is so necessary for the mental well-being.^[31] Technology can rather be used for social connectedness than isolating people in their own "digital spaces" that can add to loneliness, isolation, and depression. When the viral caseload is peaking globally, the most desired plan is obviously to prevent COVID-19 from invading our "mental peace." In keeping with those lines, "digital distancing" can be best practiced through these words of Abraham Lincoln, "Discipline is choosing between what you want now and what you want most."^[32]

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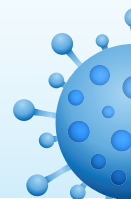
Nil.

Conflicts of interest

There are no conflicts of interest.

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NOTE: The data and views in this Perspective are updated, and accurate, to the best of knowledge of the Authors as of August 3, 2020.

The Role of “Attributions” in Social Psychology and their Relevance in Psychosocial Health: A Narrative Review

Abstract

Assigning motives or reasons to situations and actions have been the basic premise of human existence. Attributing cause to an action makes it logical and easier to comprehend. In social psychology, attribution is the process through which individuals explain the causes of behavior and events. Various theories and models have been proposed to explain this concept, starting from the early works of Fritz Heider in the early 20th century and further advances by Harold Kelley and Bernard Weiner. Attributional concepts can be used in a wide arena of behavioral science ranging from mental health stigma-related interventions to consumerism, corporate and jury psychology, and finally, attributional bias in psychosis and learned helplessness in depression. Attribution theories are viewed as the relevant concepts in the exploration and explanation of a wide repertoire of psychopathologies, especially for culture bound syndromes. Research into the translational use of attributional theories has declined in the recent years, the models being criticized for being mechanistic and reductionistic in approach. Nevertheless, the role of “attributions” in social psychology remains equally important today to explore the various facets of human behavior and reactions. The article explores the relevance of attributions in the fields of psychosocial health. It discusses various theoretical perspectives and frameworks premised on attributional models and narrates the understanding as well as the applications of the relevant theories in the realms of stigma research and consumerism. The criticism and implications in mental health are highlighted thereafter.

Keywords: Attribution theory, mental health, psychosocial, review, social psychology, stigma

Introduction

Humans are inherently motivated to assign causes to their actions and behaviors. Since evolutionary times, the discoveries and explorations of humanity have been based on this instinctive need. Assigning a cause to an action necessarily justifies it and makes it rational and understandable. Social psychology deals with this aspect of human need using the models of attribution theories. The motives, sentiments, intentions, and processes that define and guide these attributions are explained through the various models. As civilization has progressed, attributions have shaped anthropological and sociological constructs, to guide human bonds, conflict, social structures, and interpersonal interaction. Starting from politics to consumerism or prejudice, “attributions” have been fundamental in studying the phenomena. Even in psychiatric disorders, attributional models help understand psychopathology

and genesis of culture-bound syndromes. Though popular in the earlier century, research related to attribution theories has diminished over time. Keeping this in background, this narrative review attempts to revisit these models, their effect on human behavior and limitations.

Attribution is the process of inferring the causes or origins of various events or behaviors that take place in our lives. Individuals formulate attributions to comprehend and attach meanings to their life experiences. These experiences have a substantial impact on the kind of interactions people have with each other. Heider was the first to theorize about attribution in the field of psychology; however, Weiner *et al.*, developed a theoretical framework that has become a relevant research paradigm in the realm of social psychology. Heider shed light on naïve or common sense psychology in which he viewed people as amateur scientists who attempt to understand and

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decipher other's behaviors by collating information unless they deduce a rational inference or explanation. According to Fiske and Taylor,^[1] attribution theory deals with how the social perceiver pieces together information to arrive at causal explanations for events. It examines what information is gathered and how is it combined to form causal judgment.

Attributions: Typology

Attribution can be classified along two dimensions: Internal and external and stable and unstable. By coalescing these two dimensions of attributes, one can categorize a particular attribution as being internal stable, external stable or external unstable.

Internal versus External

In a "dispositional versus internal" attribution, people infer that the event or the behavior is the result of one's abilities, feelings, and traits. In an "external versus situational" attribution, people tend to center their explanations of events and behavior around factors in the social milieu. For instance, a man is acting aggressively and violently. If his behavior is attributed to his innate aggressive drives and temperament, then this attribution will be internal or dispositional as it focuses on the inborn tendencies of the man. However, a plausible explanation could also pertain to the contextual factors of the man such as a sultry weather, or a deficit of necessary resources to lead a fulfilling life and so on. This is an instance of external or situational attribution.

Stable versus Unstable

Stable and unstable attributions are also distinguished. Individuals are said to make stable attributions when they infer that a behavior is due to stable or unchanging factors. On the contrary, while making an unstable attribution, one tends to explain the occurrence of the behavior or event by unstable or temporary factors.

Theoretical Frameworks Centered Around Attribution

Heider's common-sense psychology (1958)

Heider believed that humans are innately intuitive psychologists who build diverse causal theories of human behavior and because these theories are premised on sociopsychological foundations, people can be viewed as naïve psychologists. His idea carries three underlying principles. First, humans have proclivities to perceive that every behavior is intentional rather than just random. Thus, our search for the causes of a particular behavior is always focused around the purpose of discovering the motivating factor of that action. Heider and Simmel^[2] had explored this tendency in an experiment. Their study suggested that participants who were asked to explain and describe the

movement of abstruse geometric figures described them as if they were humans with intentions to act in a particular fashion. Secondly, people have a tendency to conjure theories about causality to be able to predict and regulate the surroundings. We look for more stable and unchanging characteristics in people, situations and behaviors. Finally, whilst determining the causes for different behaviors, we distinguish between personal and contextual factors explaining the occurrence of a given behavior. Scherer^[3] for instance suggested that people construct assumptions about the stable personality traits of strangers, on the basis of their voices on the telephone.

Jones and Davis's theory of correspondent inference (1965)

This theory throws light on an individual's propensity to infer that an individual's behavior corresponds to a fundamental disposition or personality trait. People like to form correspondent inferences, primarily because a dispositional cause is stable and enhances the predictability of an individual's behavior, thereby elevating one's sense of control over the world. Individuals rely on the five sources of information or cues while forming correspondent inferences. Primarily, freely chosen behavior is more suggestive of a disposition than is behavior that is influenced by external threats or constraints. In addition, behavior with effects that are relatively exclusive to that behavior rather than shared across various behaviors reveal more about dispositions. People assume that others are aware of noncommon effects and that the specific behavior was performed with intent to produce the relatively exclusive or noncommon effects, this behavioral tendency is called outcome bias.^[4] Further, socially desirable behavior tells us a little about a person's disposition as it is likely to be maneuvered and governed by societal norms and values. On the contrary, socially undesirable behavior is generally counter normative and thus provides a better basis for making a correspondent inference.

Individuals construct more confident correspondent inferences about other's behavior that may produce pertinent consequences for one's self; behavior which holds hedonic relevance. Such inferences are also formed about behavior that is high in personalism or behavior that apparently has a direct intention to harm or benefit us. Jones and Harris^[5] found that students making attributions for speeches made by other students were likely to make more correspondent inferences for freely chosen socially unpopular positions, for instance, freely choosing to make a speech supporting Cuban president of the time, Fidel Castro. In another experiment,^[6] it was found that the participants tended to construct more correspondent inferences about an out of role behavior. However, correspondent inference theory is not devoid of certain limitations.^[7] The theory contends that correspondent inferences are significantly contingent on the attribution of

intentionality; however, unintentional behavior can form a strong ground for a correspondent inference. The concept of uncommon effects is also problematic. This theory also postulates that individuals examine the commonality of effects by drawing a comparison between chosen and nonchosen effects, while research suggests that people do not attend to nonoccurring behaviors and hence would be unable to perceive the commonality of effects accurately.^[8]

Kelly's covariation model (1967, 1973)

It is a prominent theory in the repertoire of attribution theories. In the course of discovering the causes of behavior, people act like scientists. They distinguish a factor that covaries most closely with the behavior and determine that factor as a causal agent. He proposed that there are three factors to influence the way we behave. First consensus, a factor that implies the extent to which other people behave in the same way in a similar situation. Second, consistency is reflective of the extent to which the person behaves in the same way every time the situation occurs. Third, distinctiveness refers to the extent to which person behaves in same way in similar situations. Hesketh^[9] assessed the impact of Kelly's theory on the self-attributions made by 82 unemployed in a field study. The field study also explored the relationship of self-esteem and locus of control to the attributions for success and failure. Kelley's theory was supplemented by the findings from the laboratory study, but only two of the twelve predicted relationships were found in the field study. Low distinctiveness (weak work-related skills) was associated with strong attributions to the lack of ability and low consistency (past job seeking activities successful) with strong attributions to bad luck. As predicted the unemployed with high self-esteem and an internal locus of control attributed failure to lack of effort and credited their success to ability. Unemployed with low self-esteem and an external locus of control attributed success to unstable factors, but failure was not attributed to lack of ability. Possible reasons offered for the lack of support for Kelley's theory in the field study included the influence of group identity, individual differences in the perception of the stability and locus of causes, the greater realism of the field setting, and the inadequacy of the assumptions underlying the model.

Weiner's Attribution Theory

This is one of the chief and notable theories, for developing the dimensions pertaining to the experiences of attribution, integrating attribution with emotional processes, and enlightening the affective processes as well as the experiences of attribution which are embedded in achievement behavior and other concrete domains of experience. Weiner contended that there are two key factors in eliciting attributions: Unexpected versus expected events and nonattainment versus attainment of a goal. Oliver and Desarbo^[10] suggest that outcomes that can be interpreted as successes or failures (e.g., good and bad)

elicit causality inferences along three dimensions, namely of locus, stability, and controllability. Locus is a familiar location of a cause internal or external to the person; stability refers to the temporal nature of a cause, varying from stable (permanent) to unstable (temporary), and controllability is the degree of volitional influence that can be exerted over a cause. Weiner also argues that although there are a several perceived causes for a particular event, the specific type of cause attributed to any event holds lesser importance than it is latent dimensionality. Russel's research findings align with this explanation. He asked participants to indicate the most probable cause for a particular event and then rate the cause on the basis of locus, stability, and controllability dimensions. The dimensions tended to predict outcomes better and more accurately than the specific causes noted.

Utility in Accounting for the Perceptions of Patients with Mental Illness

Several theoretical frameworks for understanding bias and stigma attached with mental health ailments have been drawn from attribution theory. The cardinal view of attribution theory is that people are motivated to understand and gain awareness of their surroundings.^[11] In the application of the theoretical perspectives of attribution in the context of mental illness stigma, people are attempting to seek for the grounds that have given rise to an ailment. However, to the observer, there is often an apparent lack of the cause of a mental ailment as a result of which, the people may attribute the cause of the mental illness to the person, which may yield a misbelief that people diagnosed with a mental illness are accountable for the ailment they are dealing with and lack in self-control and competence in looking after themselves and their well-being. Thus, such perceptions can reinforce discriminatory behavior and attitudes against people with psychological disorders. According to Weiner *et al.*,^[12] when a cause is considered to be unstable, it is believed that person has the ability to recover. As opposed to this, if the cause of the problem is perceived to remain unchanged over a span of time, the person is not viewed; the problem is not seen as recoverable or curable. The advancement of the idea that mental illness is caused by biological factors instead of being determined by the psychosocial factors may give rise to the impression that mental illness is stable over time. Previous literature contains some evidence which supports the idea that people perceive mental illness as something from which people cannot recover due to which individuals experiencing such ailments struggle to lead fulfilling lives.^[13]

Attribution Models in dealing with the Mental Health Stigma

There have been various attempts in the past to modify attributions as well as the resulting emotions, by targeting the problematic attribution directly.^[14] Changing attribution



may require provision of information that contests the present belief system. The attribution model posits that a when disability or disease which is viewed as uncontrollable, it induces feelings of pity and increases prosocial tendencies. Thus, educational efforts inculcate collective sense of sympathy and elevated assistance. This is further supported by a Crandall's study^[15] in which he explored public attitudes about obesity. The findings of the study suggested that by providing information that enables participants to believe that there are various biological and genetic factors at play that influence one's metabolism, a central issue in the problem of obesity, the participants can be made to perceive obesity as an uncontrollable condition. Fat-phobic attitudes diminished after imparting such information.

The Concepts of “Learned Helplessness” and “Perpetual Salience”

Seligman and Maier described “learned helplessness” based on their experiments on dogs in which they were classically conditioned to electric shock (which they could not escape) and subsequently failed to escape in a similar situation. They argued that this concept applied to human psychopathology. In context of attribution theory, individuals who “attribute” negative outcomes to internal, stable, and global factors reflect a view in which they feel no control of their situation. It is suggested that this particular “attributional bias” might alter mood state and bring about melancholia and clinical depression. When people try to make attributions about another's behavior, the information processed is focused on the target individual. Their perceptions at that time are lacking accountability for most of the external factors that might affect that individual.^[16] The gaps tend to be skipped over and the attribution is made based on the perceived information that is most salient. The most salient information dominates the perception at a given point of time. For individuals making behavioral attributions about themselves, the situation and external environment are entirely salient, but their own body and behavior are much lesser so. This tends to lead to an external “attribution” to their own behavior, neglecting the internal locus of control, a concept often known as “perceptual salience.”

Attribution and Culturally Bound Syndromes

Culture plays a vital part in the understanding of psychopathology as well as its origins and evolutions. Certain psychiatric disorders and mental health concerns are exclusive to a particular culture. These disorders are referred to as culture specific or culture bound syndrome. Culture bound syndrome was first used as a term in the fourth edition of Diagnostic and Statistical manual of Mental disorders. In the Indian context, some disorders are viewed as manifestations of culture specific syndromes. Some prevalent culture bound psychiatric abnormalities include Possession syndrome, Dhat syndrome, Koro, Bhanmati, Gilhari syndrome, Culture Specific Suicide (Sati,

Santhra), Compulsive spitting and Jhinjhinia, Ascetic syndrome, and so on.

Attributions play an integral role in the comprehension of the culturally bound syndrome and enables us to attach meaning and formulate rational perspective around such concerns. Every culture provides explanations and causal attributions for somatic symptoms. Such explanations establish expectations that determine the manner in which individuals perceive their bodies and the kind of symptoms they identify and report to others. The prevalence of explanatory models and prototype may also impact the rates of prevalence of specific clinical presentations of several symptoms.^[17] Symptomatic attributions and interpretations are continuously evolving instead of being stagnated. They are malleable and tend to reorganize cognitively in the process of psychological adaptation and social positioning. Specific somatic symptoms are related with popular cultural explanations that have been illustrated on the basis of somatic syndromes. For instance, loss of semen in the urine is associated with the “Dhat syndrome” in India based on the cultural belief that semen concentrates vital energy.^[18] Certain symptoms may be more pertinent and prevalent as they are a part of the illness prototype of a specific culture. Cultural models not only influence symptom reporting but can also shape psychopathological processes. Hinton *et al.*^[19] conducted study among South Asian migrants in the United states. The findings of their study described an array of culture specific vicious cycles whereby ethno-physiological concepts have an interaction with memories and bodily conditioning engendering disabling symptoms.

Thus, the social and cultural processes can propagate particular meanings and interpretations of psychological distress which may further direct help seeking behavior. Cultural models can have an impact on cognitive processes such as attention, interpretation, and coping through which, cultural models can modulate symptom experience, reporting, help seeking behavior, adaptation, treatment response or disability.

Attribution and the Field of Consumerism

According to Weiner's attribution theory,^[20,21] a consumer would first evaluate the product outcome or event as either good or bad which determines its success or failure. It is also suggested that primary evaluation will result in a primary effect. The customer seeks to discover the reason behind a product's success or failure by making an attribution that will give rise to attribution-dependent emotions. Causal attributions and the underlying dimensions of locus, stability, and controllability generate differentiated affective reactions which are considered to exist along with initial primary effect produced by the goodness or badness of the product. Consequently, general affective reactions associated with the outcome get diversified as more complex attributional thinking is included in the process.^[21]



Oliver and Swan^[22] suggests that a summary judgment is formed which encapsulates the common satisfied/dissatisfied responses. Attribution processing is seen as impacting satisfaction through the means of definite emotional responses supplementing the main evaluation which influences the satisfaction/dissatisfaction through primary affect. Folkes^[23] conducted a study which highlights that attribution theory predicts that the perceived reason for the product's failure influences how the consumer reacts thus suggesting the importance of the theory in consumer psychology and how vital it is to comprehend consumerist behaviors and attitudes.

Criticism

Attribution theory has been largely criticized as being mechanistic, subjective, and reductionistic for making assumptions that individuals are generally rational, logical, and systematic thinkers. The fundamental attribution error, however, demonstrates that most are “cognitive misers” and “motivated manipulators.” It also fails to address the social, cultural, and historic factors that shape causal attributions. This has been further criticized and explained in the branch of “discourse analysis,” that uses qualitative methods including language and descriptions extensively to understand psychological phenomena. A common example is that what we speak and how we categorize our language based on our sociocultural milieu explain our attribution style that is otherwise unexplained by the original attribution theory. The subjectivity can be considered as a narrow lens of “intellectualization” that limits the causal attribution of humans into “set” patterns, disregarding the flexibility and pragmatics of changed thinking and patterns of causality.^[24]

Utility in Clinical Practice

Attribution theories form an important interface between social cognition and behavior. As clinical practice fundamentally depends on understanding the nuances of human behavior, “attributions” might help us understand the thought processes, causes of certain specific “reactions,” and finally help in behavioral and social modifications. A common example in daily life is the use of cognitive behavior therapy for dysfunctional thoughts or public stigma reduction measures based on the prevalent knowledge-attitude-practice in the community. Even in criminology and the field of terror management, attributional theories help in exploring and understanding intentional and unintentional behaviors, which form a vital component of social responsibility and legal implications. The “folk-conceptual theory of behavior explanation” posits “belief” and “desire” to be fundamental for “intention” in an individual, with gets transited to “intentionality” through skill and awareness.^[25] Hence, essentially five requirements are considered necessary for an action to be “intentional.”

- It needs to be based on desire for an outcome
- One needs to believe about the action's relationship with that outcome

- The above two parameters need to result in an intention to perform the particular action
- Presence of required skills to perform it
- Awareness of the action being performed.

Further, “cause” explanations and “reason” explanations based on subjectivity and rationality can be used to construct the context, outcome, consequences, and expression related to a certain action or belief, be in a healthy person or in someone suffering from a psychiatric disorder. Sexual myths and attributions are common examples, where sexual knowledge and practices can be heavily influenced by the “causes” and “reasons” attributed to sexuality, which has varied sociocultural connotations. It is highly individualized and may also form the basis for various sexual dysfunctions and disorders. Similarly, “attributions” can shape the concepts of self-esteem, self-identity (including gender or cultural identities), and self-stigma, which is an important barrier in the path of help-seeking for psychological wellbeing.^[26] In daily interaction with clients, attributions form important relationship between triggering events, mediating stigma, emotional reactions, and discriminating behavior. This is helpful in understanding any form of age, gender or race-based “othering,” xenophobia and prejudiced stereotypes against certain groups, communities, and populations.

Few important areas where attribution theories can be practically applied are summarized in Table 1.

Conclusion

Attribution theory can be seen as a viable concept for the explanation of a wide array of psychopathologies. The importance of this theory in clinical psychology cannot be overemphasized. Questionnaires such as Attributional Style Questionnaire and Content Analysis of Verbatim Explanation are fundamentally based on this theory to assess individuals with different mental state and their corresponding attributional styles. Although the construct validity and the subjectivity of the offshoots of this theory have been largely criticized, it still forms a unique avenue of stigma research, consumer experience and satisfaction (used in marketing), and as explanatory models for mental illness. Mental health-related stigma, especially self-stigma forms a significant deterrent to any therapeutic service. Interventions targeting this are primarily focused on changing a person's attributional styles and the way they perceive their “abnormal behavior.” Even in criminal psychology, attribution theory has been traditionally used to determine the “situational or dispositional” attitude of the juror toward the defendant. Literature on the applications and importance of attribution theories in mental health has been limited over the last decade, with more emphasis given on the neuroscience of social cognition, one of its related offshoots. However, understanding of attribution theories in social psychiatry and psychology might help in appreciating the cognitive and social processes behind the various psychiatric disorders, which might shape



Table 1: Practical applications of attribution theories in various areas of clinical practice

Area/field	Applications
Understanding psychopathology/symptoms ^[24,27]	Cognitive biases of depression/anxiety disorders/substance use disorders Genesis of delusions/hallucinations Culture-bound syndromes Somatoform disorders Sexual dysfunction and disorders Personality disorders (especially borderline, antisocial) Paraphilias Gender identity disorders
Formulating management plan ^[28,29]	Autism spectrum disorders, separation anxiety Behavioral modification/CBT Social skills training Modeling and social learning Interpersonal therapy Psychoeducation
Stigma-reduction measures ^[30,31,32]	Understanding controllability attribution with public attitudes Community measures (using drama, art, and education) to reduce misattributions for mitigating public stigma Use of media for IEC activities Understanding psychology of misinformation/disinformation Use of disease targeted and culture-specific infographics
Positive psychology ^[33,34]	Addressing self-stigma, burnout, and stress in health-care professionals Enhance self-esteem and modify coping strategies Foster collectivism through motivational attributions Re-attributional modeling to reduce xenophobic attitudes
Industrial psychology ^[23,35,36]	Leadership psychology and training Utility in consumerism science and sales management Advertisement, brand management, and marketing Performance analysis Administrative policy-making for social change based on prevalent “causal” attributions Education strategies, learning, and curriculum building
Social rehabilitation ^[30,37]	Applications in political psychology, estimating public perceptions, election campaign behaviors, and policy reactions Motivational enhancement Action orientation Morality and cultural salience
Terror management and Criminology ^[38,39]	Culture and context-specific understanding of disability and appropriate social engagement Understanding personality attributions and genesis of psychopathy Motive estimation “Dual-component cultural anxiety buffer” to understand terrorism based on worldview and self-esteem (which are based on “reason” attributions)
Understanding and addressing stigma in special populations	Exploring and understanding fanaticism, radicalism and related beliefs HIV LGBTQ population Racism Age, gender, caste and ethnicity-based discrimination

CBT=Cognitive and behavioral therapy, IEC=Information education communication, HIV=Human immunodeficiency virus, LGBTQ=Lesbian gay bisexual transgender queer



management strategies beyond medications and also help in compliance to treatment.^[40] Like any other psychological theory, it might have its own share of biases and errors, but in-keeping with the basic human need of assigning causes to their actions, “Attribution theory” stands as a strong pillar to explain, describe, and explore this very facet of human nature and much more beyond.

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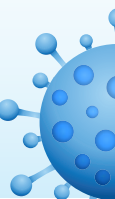
Nil.

Conflicts of interest

There are no conflicts of interest.

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Guest Editorial

“Too Far or Too Close...”: The changing scenes of sexuality during the pandemic

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“The only unnatural sexual behaviour is none at all”. (Sigmund Freud, 1970)

The Premise of the pandemic

The above-quoted words of the renowned psychoanalyst resonate more than ever in the present times. The unprecedented threat of the Coronavirus disease 2019 (COVID-19) has engulfed the world since the beginning of this year. Besides its immense public health impact, it has rarely happened before that the 'basic structure' of human lives has been re-ordered for 'new norms'. The pandemic, the consequent lockdown, the ongoing rise in the case-curve, the fear of infection, social distancing, and stigma have generated 'emotional distancing' and eventually leads to social disconnectedness (Wang et al., 2020; Banerjee and Rai, 2020). With more than 34 million cases globally, and fatalities crossing one million, the pandemic has been a persistent threat to human sustenance. It has challenged the social fabric of life and living (World Health Organization COVID-19 Situation Report as on 2nd

October 2020). The pandemic's psychosocial offshoots have been well-researched and can increase the risk of depression, anxiety, insomnia, post-traumatic stress, and impaired quality of life. The various psychosocial factors contributing to the same are isolation and quarantine, the global lockdown and travel restrictions, the plethora of misinformation, the 'morbid' fear of the infection in the masses, and financial plights. Added to that are the vulnerabilities of specific special populations like the age, gender minorities, the socially impoverished, and the frontline workers (Xiong et al., 2020). The 'life-changes' due to COVID-19 and containment measures have affected physical proximity and intimacy, thereby altering the relationship dynamics among millions of couples and families. This brings us to the sensitive yet stigmatized area of 'psychosexual health', one of the highly affected areas during the pandemic, but at the same time less spoken about. Sexual relations and sexuality have been important determinants of relationship dynamics, psychological resilience, and well-being: more than ever necessary attributes during the present times of crisis. Furthermore, considering the established fact that

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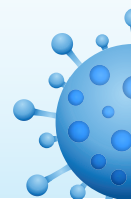
COVID-19 is a highly infectious disease, it generates a cascade of fear, guilt, and physical separation, especially in those exposed (like the frontline workers), that can alter the sexual dynamics and sexuality, thereby impacting psychological well-being and general health. In that sense, this pandemic is an 'eye-opener' for us to understand and appreciate the integration of sexual health into public health, for the greater good.

Psychosexual Health and Infectious outbreaks: The Intersections

Sexual health, as defined by the World Health Organization (WHO), is "not merely the absence of disease, dysfunction or infirmity. Sexual health requires a positive and respectful approach to sexuality and sexual relationships, as well as the possibility of having pleasurable and safe sexual experiences, free of coercion, discrimination, and violence"(WHO, 1975).

The pathways to hamper psychosexual health during a biological crisis such as COVID-19 can be multi-faceted, depending on demographic factors, interpersonal relationships, and situational contexts. Throughout history, global infectious outbreaks have had critical implications on sexual and reproductive health at all levels: individuals, systems, and society. Traditionally, sexuality and pandemics' intersections have been compounded by stigma, prejudice, and ostracization (Tsiamis et al., 2018). Thus, the critical question arises: when an outbreak is claiming millions of lives globally, what can be the possible reason to discuss intimacy and sexuality at that juncture? Sadly, humankind is more used to 'snapshotting' distress, leading to the short-sightedness for long-term reactions. 'Social touch' being an irrevocable part of human development, relationships and intimacy can get significantly affected by the ongoing

pandemic, which might continue affecting the lives of millions for years to come (Cascio et al., 2019). Decades back, during the bubonic plague, classically termed as the 'Black Death', Tsiamis et al. (2018) quoted the "fear of infection disrupting love and lives". His article the "The Knights Hospitaller of Rhodes and the Black Death of 1498: a Poetic description of the Plague", describes how newly married couples were physically separated during the outbreak that affected their mental status. They were mentioned to 'crave for the proximity' of their partners, which they believed will generate 'fresh air'. On the other hand, history has numerous examples when the 'spread of an infectious disease' has been linked to illicit sexuality, immorality, and 'bad air'. As always, public health has been overshadowed by the age-old myths and misinformation related to sexuality, stigmatized 'intimacy', and 'sexual abstinence' was regarded as an effective strategy in controlling the plague in the European sub-continent during the Victorian era (Cantor, 2001). These decisions of 'immoral standards' of sexuality being responsible for 'a disease' have both socio-cultural beliefs and religious connotations wherein 'Bad air', 'Bad emotions', and 'Bad interactions' were the equivalents of sexual discourse, sexual thoughts, and sexual practices respectively. It was theorized by the German physicians that 'ill feelings' that included sexual attraction might be the breeding ground for 'infectious agents' and thus diseases (Karras, 2017). On the other hand, there has been reported an increase in incest, promiscuity, and exogamy (marrying outside clan or community) in the post-pandemic aftermath after the plague in 13th Century Europe. As a paradoxical reaction to the suppression of sexual intimacy, the industry of prostitution bolstered manifesting as a surge in sex-parlours and 'royal safeguards' as places for safe and consensual sex (Cantor, 2001). Hatcher



(1977), while describing the plague in England, mentioned an increase in sexual practices between newly married and elderly couples.

This increase could be conceptualized in various ways (Cohn and Cohn, 2003; Karras, 2017):

- ♦ A coping mechanism- the pandemic resulting in losses at a financial, personal, and societal level, leading to incorrigible frustration and adaptation of a coping strategy debatably maladaptive as Maslow's hierarchical model's basic needs were not being met.
- ♦ A revolt against the orthodox blame put by the Medieval Church on the society.
- ♦ An existential bewilderment resulting from the introspection of the personal mortality and purpose with prevailing uncertainty of life and togetherness.
- ♦ Increased sexuality arising out of sexual frustration and 'social touch' hunger.

The gender and sexual minorities were more vulnerable, especially to the religious organizations, as the 'Divine Will' and the need for 'sanitary legislation' claimed them to be 'unholy sinners' responsible for the breeding of infections (Byrne, 2004). From the idea of 'sex and intimacy' being responsible for the pathogenic spread of infections and the discriminatory idea of morality, we have evolved into 'biological' understandings of pandemics. This has led to a better appreciation of the emotional distress and frustration resulting from chronic deprivation of love, affection, and sexual desire during the disease outbreaks, primarily when physical proximity generates the 'fear and taboo' of infection. The level of permissible intimacy during a pandemic has been a concern even in the earlier related outbreaks of Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). An increase

in familial discord, sexual dysfunctions, and arousal disorders have been reported as a long-term psychosocial offshoot of the SARS pandemic (Chua et al., 2004). It is understandable that under stressful circumstances, especially when one of the partners works in a 'high-risk' area, there tends to be increased performance anxiety, stress about sexual practices, impaired perceived sexual satisfaction, and associated mood changes. The rise in substance use and intimate partner violence, which have been growing concerns globally during the entrapment due to pandemics, can further compound couples' sexual and reproductive health (Bradbury-Jones and Isham, 2020). Adverse pregnancy outcomes like miscarriages, abortions, and intrauterine growth retardation have been reported earlier in SARS, MERS outbreaks, and even during the present pandemic, which add to the uncertainty and stress of child-births (Schwartz and Graham, 2020). Any new infection with 'novel' ways of transmission thus has a chance to generate fear, stigma, and physical distancing that can impair sexuality and quality of relationships. This tends to be all the more critical during pandemics, as sexual well-being has been significantly linked to positivity, hope, personal growth, and optimism: attributes most needed during the present times.

Sexuality and intimacy at times of COVID: A neglected horizon?

Undoubtedly sexual well-being is one of the neglected constructs during the pandemic. Bearing the already existing prejudices related to disclosure and discussion of sexuality, especially in certain cultures, the associated problems are also under-reported. SARS-CoV-2 is a highly contagious virus with extensive aerosol transmission and can persist for a long on fomites and inanimate surfaces (Singhal, 2020). This makes 'fear of intimacy' a relevant consequence. Both the



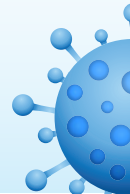
partners' desire and arousal might be discrepantly leading to an alteration in the relationship dynamics. While on the other hand, many have expressed increased sexual practices with thousands stranded at home for a prolonged duration, leading to increased abortions and unplanned pregnancies. Coercive sexual practices amounting to domestic violence have been rising and can have profound psychosocial consequences (Nair and Banerjee, 2020). Sexual and reproductive rights are vital components of human rights and need to be safeguarded during difficult times. Especially populations like those who are separated from their newly-wed spouses, partners who are stranded apart like never before, the frontline workers with increased risk of exposure, the gender minorities (Lesbian, Gay, Bisexual, Transgender, Queer population), those with pre-existing psychiatric disorders and finally the commercial sex workers, face unique challenges concerning the 'safety and quality' of sexual practices during this pandemic. Arafat et al. (2020) performed a multi-centric online survey to explore the effects of COVID-19 induced lockdown on subjects' psychosexual health in India, Nepal, and Bangladesh. This was one of the first studies to explore this neglected impact of the pandemic worldwide. The majority of the subjects were sexually active during the lockdown, while 10% showed an increase during the 'unlocking' period.

The authors highlighted the importance of understanding the psychosexual impact of the outbreak, especially in developing countries with varied socio-cultural dimensions. They advocated sexual health as a vital modality of psychological resilience. Another Indian study with the physicians reported an increase in depression, anxiety, and sleep disturbances, which were adversely related to relationships and family dynamics (Chatterjee et al., 2020). Roy et al. (2020)

assessed the knowledge, attitude, and perceived mental healthcare need in 662 Indian adults and reported misinformation related to the modes of infection spread, social media exposure, and disinformation to be directly linked to perceived stress, anxiety, paranoia about contracting COVID-19 and sleep disturbances; all of which impaired interpersonal relationships. Social distancing has led to enhanced emotional distress in adolescents in an age-structured impact study (Singh and Adhikari, 2020). During the historical three-month lockdown in India, sentiment analysis from Twitter revealed fear, disgust, and stigma related to intimacy (Barkur and Vibha, 2020). These statistics apart, many of us who work on the frontline may have experienced or heard about the persistent 'fear and guilt' of transmitting the infection to our closed ones, leading to burnout, stress, and depression. The authors would urge reflective participation from the audience to appreciate the effects of 'social distancing', one of the many consequences of which is chronic deprivation of 'social and affective touch', popularly known in the literature as 'touch hunger' (Cascio et al., 2019). It is a well-researched concept with neurobiological and psycho-behavioural implications, which can surface during times of distancing, travel restrictions, and 'fear' of social interactions to impair psychosocial well-being.

Finally, Banerjee and Rao (2020), in their recent review in the Indian Journal of Psychiatry, have comprehensively detailed the intersections of sexual well-being and the ongoing pandemic highlighting the at-risk populations, and have focused on various ways rather than 'complete abstinence' that can be advocated as 'safe sexual practices' during the ongoing times. Few of these vital attributes related to sexuality and intimacy to consider during times of COVID-19 are (Banerjee and Rao, 2020):

- ◆ Fear of intimacy and travel history leading to complete sexual abstinence



- ◆ Uncertainty and misinformation related to the sexual spread of the virus
- ◆ Chronic 'social and intimate touch deprivation' leading to 'touch hunger' and its psychosocial offshoots.
- ◆ Possibilities of marital discord/issues with couple interpersonal relationship
- ◆ Rise in coercive sexual practices and intimate partner violence: compounded by substance abuse
- ◆ Knowledge-attitude-practice gap related to healthy sexuality during pandemics
- ◆ The rise in sexually deviant practices
- ◆ Loneliness, isolation, chronic stress, grief, depression, anxiety: contributing to disinterest in sex
- ◆ Increased unprotected sex and rise of abortions, unplanned pregnancies
- ◆ Possible increase in sexual dysfunctions, performance anxiety, and altered perceived sexual satisfaction (increased in those with pre-existing psychiatric disorders)
- ◆ High-risk sexual behaviours
- ◆ Indiscriminate sexual practices without precautions can contribute to the spread of infection
- ◆ 'Digital sex' as a 'dual-edged sword': Healthy versus compulsive use of pornography; implications of cyber-safety and digital security during online sex

The 'New Normal' of sexuality: Ways ahead

Based on Maslow's hierarchy, sexuality is one of the 'basic needs' for survival, which, if not satisfied, leads to a state of despondence and inability to graduate to higher needs and thus result in a significant hindrance to the desire of self-actualization. Therefore, sexuality is a primal instinct for survival and sustenance and cannot be neglected while promoting health practices. As mentioned before, the virus's aerosol spread makes any form of in-person sexual activity a potential risk. The literature on the sexual transmission of the virus is still unfounded, though that remains

a legitimate fear in many minds. During such 'fear and panic', like any other human interactions, intimacy has also borrowed a digital platform to set the 'new normal'. The use of pornography and digital sexuality has increased, while long-distance relationships have derived a renovated significance (Turban et al., 2020). Sexual abstinence (referring to complete cessation of all forms of sexual activity) cannot be considered a universal solution for obvious reasons, and sexual intercourse and foreplay have often been reported as 'stress-relievers' and factors helpful for coping (Rao et al., 2012). It is vital to remember that situations like COVID-19 cause 'obligatory' sexual abstinence due to fear or concerns of infection instead of voluntary sexual abstinence, which is entirely different in context. Pre-existing marital issues can be amplified as there might be discordance of opinion related to sexual practices between the partners. Chronic sexual repression affects performance anxiety and sexual confidence, which can eventually lead to arousal disorders, anorgasmia, premature ejaculation, and erectile dysfunction (Banerjee and Rao, 2020). Fear of intimacy can lead to emotional distancing from the partner, which perpetuates loneliness, maladaptive coping, and sleep disturbances, all of which are independent risk factors for depression, anxiety, and chronic diseases like diabetes, hypertension, cardiovascular illness, etc. (Lotfi et al., 2020). Especially infectious disease outbreaks are times when one critically needs to weigh between sexual abstinence and intercourse practices, based on the risks involved.

The Center for Disease Control and Prevention (CDC) recommends a minimum distance of six feet to avoid transmission, which is impossible for intimate relationships (CDC, 2020). Safety of sexual intercourse is to be ascertained individually for a couple: asymptomatic, have been



practicing precautions, have no history of travel or after exposure: then touching, hugging, kissing, and intercourse are likely to be safe. After community transmission in many countries, asymptomatic carriers are rising, which poses a threat to health in general and sexual health in particular. If symptomatic self-quarantine is necessary without bed-sharing or any form of intimacy till at least 7-14 days after the symptoms started, or till full resolution of all symptoms or at least up to 72 hours of being fever-free without any medications (Planned Parenthood, 2020).

Under such circumstances, few propositions for alternative healthy sexual practices can be (Farid, 2020; Banerjee and Rao, 2020; CDC, COVID-19 and HIV, 2020):

- ◆ Masturbatory practices with hygiene caution as followed in sexually transmitted diseases (STD)
- ◆ Informed decision making by both the partners
- ◆ Digital sexuality which needs to involve consensual agreement, protection from online extortion, cyber-bullying and with obvious concerns of cyber-safety
- ◆ Unique strategies to prevent sexual abuse of children and adolescents
- ◆ Sexual practices with a quarantined partner
- ◆ Usual sexual practices with minimum acceptable risk, with the standard precautions (Risk-reduction counseling)
- ◆ Awareness about the stress, performance anxiety, and symptoms of sexual disorders
- ◆ Reduction in the number of sexual partners
- ◆ Special safety precautions for the commercial sex-workers
- ◆ Finally, mutually consented exploration of sexuality and alternate sexual practices (that can involve non-penetrative sex, kissing, fondling, etc. and various other connotations of foreplay)

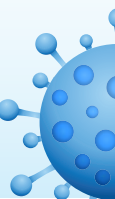
Again, intimacy, love, and affection in relationships equated with 'sexual intercourse' is a grossly inappropriate and reductionistic approach. Under trying times, regular connectedness via virtual media in those separated and spending 'quality couple time' for those living together can foster emotional support and closeness, vital parameters to fight social isolation and loneliness. The pandemic has not been all about 'distancing.' Several families have got a renewed chance to nurture lost time and mend broken bonds while living together during the lockdown. Many couples have explored each other's company like never before, strengthening their communication and sharing of happiness. Such activities might not be strictly 'evidence-based' but are pragmatic, help building resilience, improve relationships, and finally promote healthy sexuality. Consent is a vital factor, especially for minors, and awareness and prevention of any form of sexual abuse are of paramount importance.

Epilogue

"A loveless world is a dead world."

(Albert Camus, 'La Peste', 'The Plague', 1947)

COVID-19 is a situation which has also allowed nurturing and mending relationships as people spend more time together, realizing the importance of vitality and the importance to be with loved ones, as man is but a social animal with an advanced neocortex but nevertheless regulated by the centers of hunger, fear, and sex. Darwin's theory of evolution has translated over the longitudinal course of time and has shown structural and physiological changes translating across species, the same may not hold true for more meta concepts like intangible mindsets and thought process. In a country which has been the epicenter of the earliest civilizations known to man, one of



the most populous countries and the land of origin of the 'Kamasutra'; India still ironically shies away from discussions about sex and sexual practices. The socio-cultural acceptance of sex only being the act of physical intimacy and rigidity to adapt to contemporary concepts of intimacy are roadblocks in applying many of the concepts discussed above (Rao et al., 2012). Thus, concepts of digital intimacy may be perceived as perverted, obscene, and unacceptable. In that context, even with the use of technology for psychosexual well-being, the partners need to discuss and tailor it according to their beliefs, values, and ideals. The learning from past pandemics is that sexuality and relationships are severely disrupted due to many factors aptly conceptualized in the bio-psychosocial framework of psychiatric illness (Schwartz and Graham, 2020). Acknowledging the magnitude of morbidity arising from psychological dysfunction, including psychosexual health impairment, provides a holistic perspective that will act in tandem with physical health. With that background, the skeptical stance of challenging the need to study or discuss sexual health in the presence of more serious physical health consequences, including death and the need for critical care, is unfounded. More systematic research exploring lived experiences and consideration for the vulnerable populations might help awareness in this neglected area, improve the sexual health in the community and integrate its importance in public health interventions and policies that will help even in the post-pandemic times and during such futuristic crises.

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COVID Research & Publication Compendium

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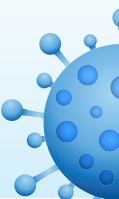
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Psychosocial Framework of Resilience: Navigating Needs and Adversities During the Pandemic, A Qualitative Exploration in the Indian Frontline Physicians

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Introduction: Frontline healthcare workers (HCW) have faced significant plight during the ongoing Coronavirus disease 2019 (COVID-19) pandemic. Studies have shown their vulnerabilities to depression, anxiety disorders, post-traumatic stress, and insomnia. In a developing country like India, with a rising caseload, resource limitations, and stigma, the adversities faced by the physicians are more significant. We attempted to hear their “voices” to understand their adversities and conceptualize their resilience framework.

Methods: A qualitative approach was used with a constructivist paradigm. After an initial pilot, a socio-demographically heterogeneous population of 172 physicians working in COVID-designated centers were purposively sampled from all over India. Following in-depth virtual interviews using a pre-formed semi-structured guide, the data was transcribed and translated verbatim. The interview was focused on their challenges, needs, and processes of coping and support. Charmaz’s grounded theory was used for analysis supplemented by NVivo 10 software.

Results: Fear of infection, uncertainty, stigma, guilt, and social isolation emerged as the main challenges. Simultaneously, their “unmet needs” were flexible work policies, administrative measures for better medical protection, the sensitivity of media toward the image of HCW, effective risk communication for their health, and finally, social inclusion. Their resilience “framework” emerged as a process while navigating these adversities and consisted of three facets: forming a “resilient identity,” managing the resilience, and working through the socio-occupational distress. The role of mental well-being, social network, peer support, problem negotiation, and self-care emerged as the key coping strategies.



Conclusion: The study findings support the global call for better psychosocial health and quality of life of the frontline HCWs. Their “unheard voices” explored in the study can anchor subsequent resilience-enhancing interventions and policies. Guidelines focusing on the psychological wellbeing of frontline HCWs need to be grounded in their unmet needs and lived experiences.

Keywords: healthcare workers, physicians, COVID-19, resilience, psychosocial, challenges, frontline workers

INTRODUCTION

The unprecedented global crisis caused by the Coronavirus disease 2019 (COVID-19) pandemic has disproportionality affected many sections of the society. For obvious reasons, health care workers (HCW), especially those working on the frontline, are uniquely vulnerable to both the physiological and psychological offshoots of the outbreak (Chew et al., 2020; Greenberg et al., 2020; Vizheh et al., 2020). Even in the earlier Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and recently the Zika and Ebola outbreaks, the HCWs have faced overwhelming difficulties, chronic stress, high risk of infection and uncertainty, impaired quality of life and disturbed interpersonal relationships (Paladino et al., 2017; Simas et al., 2020; Xiao et al., 2020). Since the declaration of COVID-19 as a pandemic, multiple quantitative studies from various countries have explored the plight of the frontline physicians and reported increased rates of depression, anxiety, sleep disturbances, post-traumatic stress, and adjustment problems (Que et al., 2020; Spoorthy et al., 2020). With understaffing, rising caseload, and mental health-related stigma, the situation is even direr in a low and middle-income country (LMIC) like India, where the physician: patient ratio is 1:1,456 against the World Health Organization (WHO) recommendation of 1:1,000 (Paul and Bhatia, 2016). Considering the socio-cultural diversities and varied response to stressful situations, it is vital to understand the “unheard voices” of those fighting the pandemic at the upfront and qualitative approaches are better in that regard. Especially while navigating this adversity, it is important to appreciate their “processes of resilience” and strategies to improvise. According to Manning (2013), individuals who continue to manage hardships and flourish in personal and social lives are considered to be resilient; however, this concept of resilience has been highly contextualized based on the research settings and populations in whom it has been studied (Fletcher and Sarkar, 2013). Psychological resilience is the ability to emotionally cope with a crisis to return to the pre-critical state. It is said to exist when an individual uses “mental processes and behaviors in promoting personal assets and protecting self from the potential negative effects of stressors.” (De Terte and Stephens, 2014). The other way of looking at resilience is as a “psychological capital” that helps one stride through stressors and losses by the means of humor and hope (Pedro-Carroll and Jones, 2005). Emmy Werner, one of the first researchers who used the term resilience in 1970s after studying children in Hawaii, highlighted the need to understand resilience as a “fluid process” rather than a dichotomous construct that is built through constant interaction of an individual with his/her stressors and

eventually helps in tiding over the adversity (Werner, 1971). Resilience research during biological disasters, maltreatment, abuse, violence, catastrophic life events, and poverty has focused on understanding the “processes” of resilience, so that it can be further enhanced through interventions (Grotberg, 1997; Werner, 2005). As resilience is considered as a dynamic interaction between individuals and the ongoing environment (Fletcher and Sarkar, 2013), we planned to explore the “lived experiences” of the frontline physicians, irrespective of their specialties, in terms of their challenges, unmet needs and further construct a “conceptual framework” of their psychological resilience during the ongoing crisis. Though HCW include many more specialties, it will be used interchangeably with physicians/doctors for the purpose of this study.

METHODOLOGY

Design and Sample

We adopted a qualitative design for the study with a social constructivist paradigm, especially as the objective was to gather “rich data” from the participants in terms of their lived experiences and explore the processes of their resilience. As opposed to the positivist approach in quantitative studies, social constructivism views knowledge to be constructed through constant interaction with others as human development is socially based (McKinley, 2015). In that way, social “realities” can be multiple based on the context, communication and interpretation all of which form the approach in qualitative research (which is based on social constructivism) (Walker, 2015). Qualitative methods have been shown to provide a substantial contribution to understanding the concept of resilience (Ungar, 2003). This is usually achieved through exploring lived experiences, phenomenological interpretation, understanding “minority voices,” constructing meaning of the “undefined” and member-checking of the results to establish trustworthiness (Ungar, 2003). We conceptualized resilience as a dynamic process that is difficult to be scaled or quantified and hence the approach to explore it needs to be “grounded” within the experiences of the population who use their resilience to navigate through the adverse situations. After being approved by the JSS-AHER Institutional Ethics Board, a semi-structured interview guide was designed based on detailed discussion among the researchers, existing literature related to the potential challenges faced by the frontline HCW, and clinical experience of the researchers (**Box 1**). It consisted of open-ended questions related to the experiences of the physicians while working in COVID-designated hospitals (as decided by the Government



BOX 1 | Semi-structured interview guide used for the study.
Difficulties during the pandemic:

- How have the COVID-19 times been different for you (personally & professionally)?
- In what ways has the pandemic affected you and your loved ones?
- How do you feel about the ways you have been affected during this outbreak?
- What were the challenges that you faced as a physician during these times?
- How did you feel when you faced these challenges?
- How has the COVID-related lockdown impacted your clinical work, self-care and care for your family?
- What are the various factors that have led to these effects (that you mentioned above)?

Needs during the pandemic:

- How do you feel things could have been different during the outbreak (personal & professional front)?
- Based on the challenges mentioned above, what were your expectations from individuals/society/government?
- How did you feel about these expectations?
- What do you think your fellow healthcare workers felt during similar situations?
- How were those expectations met/not met? How did you feel about the same?

Coping during the pandemic:

- What were the positive things for you during the COVID-19 outbreak?
- How did these 'positive aspects' help you?
- How do you think your fellow healthcare workers fare during the pandemic? What factors may have helped them?
- Regarding the 'challenges' that you mentioned earlier, how did you deal with them?
- If you have overcome all/some of them, how did you do so?
- How has the pandemic changed you (as a healthcare worker and individual)? How do you feel about it?
- What would you suggest to others in similar situations of crisis?

of India) (Government of India, 2020), the adversities that they have faced, their perceived needs while working, and how they attempted to overcome these hardships, including their sources of support, sense of control and narratives of the “process” of coping. The guide was supplemented by open-ended probes, prompts, and regular memo-writing to maintain the data trail. Only the salient questions have been mentioned in **Box 1** for the sake of clarity. We theorized resilience as a flexible construct that lies on a dynamic continuum with inter-relationships between socio-cultural development and personal capacity building while exposed to stressful conditions, which can be altered and enhanced through various processes. The study used a theoretical and purposive sampling technique (Corbin and Strauss, 1990). The contact details were obtained through professional networks and directories of the national medical associations (Indian Psychiatric Society, Indian Medical Association), and snowballing was used to maximize sampling. We selected physicians of any specialty who were consistently working in a COVID-designated hospital (dealing with COVID-positive inpatients and outpatients) for at least 2 weeks. The time limit was arbitrary to exclude HCW, who are temporarily posted in COVID-wards on an *ad hoc* basis. Those who had

been diagnosed with COVID-19 anytime in the last 6 months were excluded, which would alter their perceptions differently. All physicians were assessed by two independent psychiatrists (with a clinical consensus) before the interview to rule out any diagnosable mental health condition, in which case they would be excluded from the study. This was done as psychopathology could have been a potential confounding factor biasing the content of interviews, especially when it was related to the processes of coping during a stressful situation. Besides, a long, unbiased in-depth interview would not have been pragmatically and ethically possible with them. International Classification of Diseases (ICD)-10 was used for clinical diagnosis. A total of 28 participants were excluded in this way. Their symptoms may have been related to the professional stressors of the pandemic, however, the details of their diagnoses are not mentioned as they do not fall within the scope of this study. Irrespective of the participation status, they were provided required treatment by the psychiatrists involved.

Participants were sought based on varied ages, gender, all areas of India, practice settings, specialties, and socio-economic backgrounds. The contacts were initially mailed regarding the purpose, objectives, and nature of the study. Participants provided explicit informed consent, with whom virtual (Google Meet/Zoom/Skype) one-to-one detailed interviews were conducted over 1–2 sessions based on mutual convenience. The average session lasted 112 + –9.5 min. The open-ended questions of the interview guide were supplemented by various probing and supplementary queries to further obtain “rich” information, that forms the essence of qualitative research. However, the need and extent of probing varied between participants and were also based on the pragmatic feasibility of a virtual interview platform. All sessions were recorded with consent and conducted by the first three authors in English and Hindi. The initial pilot was done on 10 physicians, subsequent to which the interview guide was modified accordingly. The study was conducted between April–August 2020 and continued till the thematic saturation of data was obtained. To maintain anonymity and confidentiality, data sets were identified with a serial number/code and no names/identifiers were used. Furthermore, access to the participants’ interview recordings was strictly limited to the researchers. The participants were offered if they wanted to review the recordings or wished certain parts to be eliminated.

Analysis

Charmaz’s grounded theory approach was used to analyze the data (Charmaz, 2006). Initially, all the interviews were transcribed and translated verbatim (with cross-translation) to ensure integrity. Subsequently, a frame-to-frame analysis was performed to obtain common contents or “codes,” which was the process of initial coding. Subsequently, focused coding and axial coding were performed to coalesce and condense codes into relevant themes and form a meaningful hierarchical structure between the resultant categories, themes, and codes, respectively. To enhance the level of clarity, causal references were looked for in the data and organized into a structure/process of relationships, which was important for exploring resilience. All



steps of coding were done independently by the first two authors, who were certified in qualitative research. Through analysis, a constant comparison was made between the obtained themes and the actual “excerpts” back-and-forth to keep the results “grounded” in the data, along with syntheses of the themes based on rigorous discussion between the researchers. Though most of the coding was done manually as immersion into “rich data” is necessary for sound qualitative research, NVivo 10 software was used for assisting and organizing the analysis¹.

The conceptual process of resilience was focused on during analysis. Thematic saturation was obtained with 162 participants, but 10 more were interviewed for super-saturation. Triangulation and respondent validation were further used to ensure study rigor (Krefting, 1991). The latter involved presenting the initial results to 60 participants from different ages, areas, and settings to discuss whether they truly “reflected” their perceptions and processes of coping during the crisis. Based on their subsequent inputs, further interviews were conducted, and interpretations were made accordingly. The entire analysis took 3 months to be complete.

RESULTS

The findings suggest how the physicians all over India working on the frontline faced the challenges and adversities during their service, their unmet needs and the “conceptual process” of their psychological resilience. Though we tried to keep the sampling as heterogeneous as possible, the participants were mostly married males practicing in Government set-ups of urban areas. The zonal representation in the sample was fairly equal, with more general physicians in the sample. Most physicians were young, in the age range of 20–30 years. The mean age and experience of the sample were 29.2 ± 3.8 years and 16.7 ± 4.2 years, respectively. The socio-demographic details of the participants are highlighted in Table 1.

Besides the challenges faced and the perceived needs, the results also reflect how the process of facing these hardships and the vulnerable state had helped their coping and resilience evolve through time. There were three facets to this:

- The resilient “identity or self” that was formed harnessing social support, rooted in morality, gratitude, and a sense of purpose (duties of a physician) that provided hope.
- The resilience “management” which occurred through regular dialogue with self and stress-management strategies that helped in problem-solving and negotiation with adversities. The sense of “togetherness” in the “physician community” enabled collectivism, which supplemented by their past training and stressful life-experiences helped them build resilience. Finally, the assumption of a “vulnerable or sick role” throughout the chronic stress of their challenges helped decrease expectations, promoted self-care, and reduced self-stigma.
- Working through the “distress” was facilitated by self-commitment and care (adequate sleep, diet, hobbies, small

TABLE 1 | Socio-demographics of the participant physicians.

Attribute	Category	No. (N = 172)
Age (years)	20–30	42
	30–40	83
	40–50	29
	>50	18
Gender	Male	110
	Female	62
Marital status	Single	62
	Married	95
	Divorced/separated	15
Region (India)	North	32
	South	68
	East	30
	West	32
	Central	20
Specialty	General physicians	74
	General Medicine/Pulmonologists	52
	Intensive care specialists	25
	Other specialties	21
Experience (years)	0–5	25
	5–10	34
	10–20	92
	>20	21
Area of practice	Urban	98
	Semi-urban	53
	Rural	21
Set-up of practice	Government set-up	110
	Private organizations	47
	Private practice	15

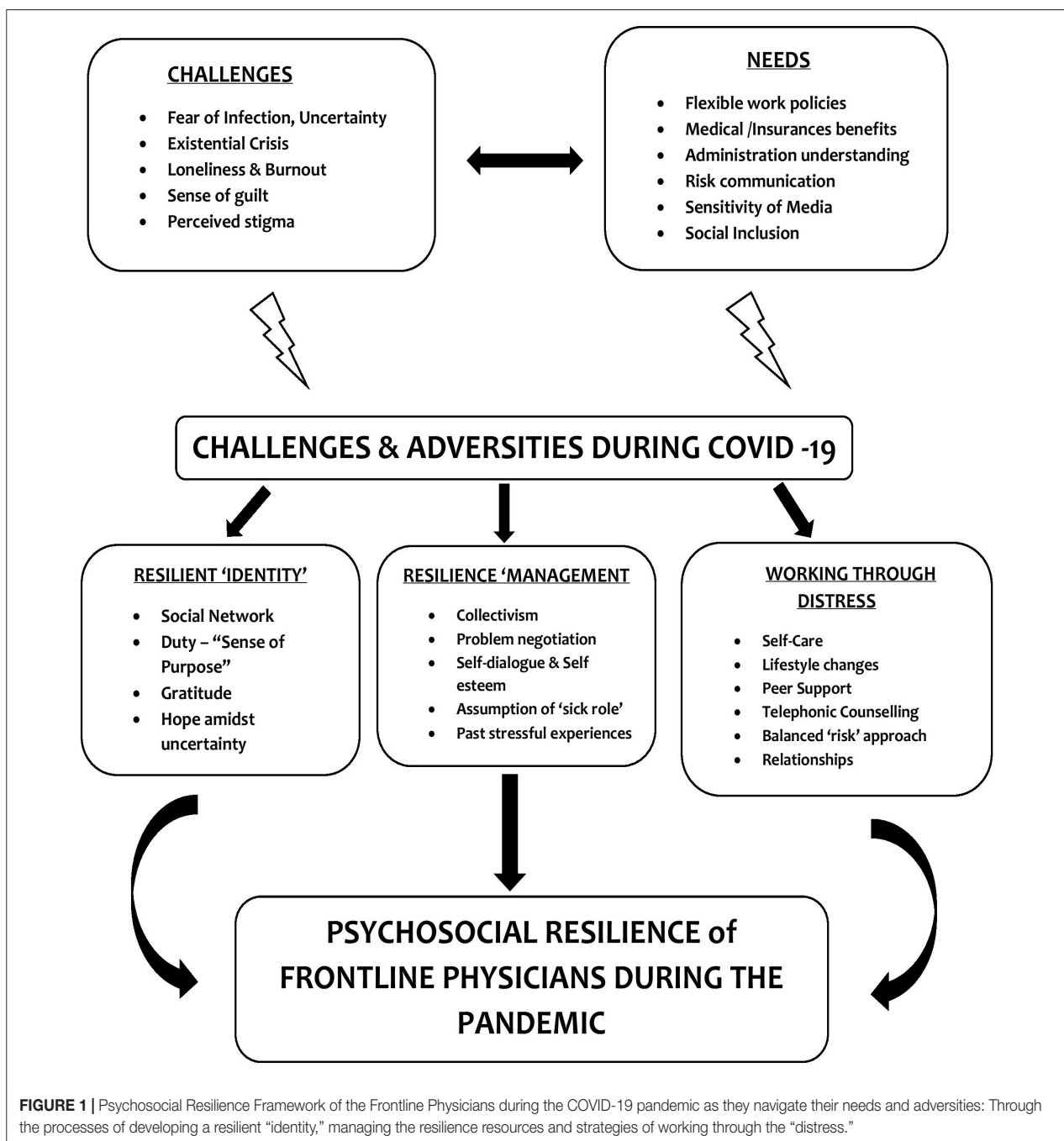
celebrations, festivities, etc.) that boosted self-confidence and positive lifestyle changes. They also drew their strength from their relationships, which was complemented by peer support, which proved valuable for their understanding, empathy, and validation. Telephonic sessions also helped them “work through” the adversities, and mental health was considered to be an important component of well-being. Finally, the participants agreed that facing the difficulties with a balanced and pragmatic approach was the only way to build resilience, as resilience and stress were bi-directional.

The above-mentioned processes together formed the “conceptual framework” of the psychosocial resilience developed by our participant physicians while facing their challenges and adversities (Figure 1). This was grounded in their verbatim data obtained during the in-depth interviews.

Table 2 summarizes the key categories and themes, supported by the verbal excerpts from the participants. As the sample was large, we present only a few of the relevant excerpts in the results. The detailed participant-responses will be made available on reasonable request directed to the authors. Though there were no marked differences in the themes based on the gender, lady HCWs reported more challenges in work-life balance (“work from home” vs. “work for home”), especially those who were mothers. A greater proportion of them reported guilt of spreading the infection and social stigma compared to their male

¹www.qsrinternational.com





counterparts. While exploring resilience, we did not find any difference between the male and female HCWs.

DISCUSSION

Challenges Faced by the Physicians

Our study identified the various key factors involved in building the process of resilience for the physicians working on the frontline. One of the prime challenges was perceived stigma and avoidance, which have been observed in healthcare since the beginning of the pandemic. Bagchi (2020) mentioned

about the condemning of more than 200 incidents of COVID-19 related attacks on health care workers by 13 medical and humanitarian organizations. Globally, the frontline HCWs have faced “social ostracism,” othering, discrimination, restrictions to public resources, and eviction from their apartments (Galbraith et al., 2020). Public fear and avoidance of them have been highlighted as an under-recognized form of stigmatization (Taylor et al., 2020). Media reports in India have occasionally portrayed doctors as “carriers of infections” and hence feared in the community (Bloomberg Quint, 2020). Since the beginning of the pandemic, xenophobic sentiments, and social prejudice were directed toward certain populations, especially the frontline



TABLE 2 | Categories, Themes of analysis and supporting verbal excerpts from the participants.

Categories	Themes (frequency)	Verbal Excerpts
Challenges	<ul style="list-style-type: none"> • Fear of infection and uncertainty (80%) • Existential crisis (65%) • Loneliness and burnout (69%) • Sense of Guilt (53%) • Perceived stigma (71%) 	<ul style="list-style-type: none"> • “Each day is difficult. It’s like living with a constant sense of apprehension and guilt of infecting my family.” • “I haven’t met my parents for months now. I stay separate to keep them safe. I have lost my colleague. Don’t know if I will lose them too...” • “People have started looking at me with “disgust”! It feels as if a doctor is always a carrier unless proven otherwise...”
Unmet Needs	<ul style="list-style-type: none"> • Flexible work policies (88%) • Medical/Insurance benefits (70%) • Administrative understanding (60%) • Effective risk communication (43%) • Sensitivity of media (82%) • Social inclusion (90%) 	<ul style="list-style-type: none"> • “We are already understaffed. I haven’t got a single-day leave in the last 6 months. it can’t go on like this...” • “The wards are not sanitized regularly. If the authority doesn’t organize, how will be managed such a caseload!” • “Doctors are not immune. We work most closely with COVID patients. The degree of our risk estimates and shift rotations are mostly chaotic... that adds to our stress...” • “All that we need in such difficult times is some empathy. Many of my colleagues are being evicted from their apartments or looked down upon...” • “Doctors are being portrayed in a negative shade. this needs to stop! The popular media has a huge role to play in improving our status...”
Processes of Resilience		
Resilient Identity	<ul style="list-style-type: none"> • Social network (55%) • Duty: “Sense of purpose” (67%) • Gratitude (42%) • Hope amidst uncertainty (49%) 	<ul style="list-style-type: none"> • “I am really thankful to my friends and family, who helped me move on, even from miles away...” • “I have seen the sufferings, deaths and grief myself, it makes me feel I can make a difference, save lives...” • “My duty and oath as a physician are my strengths, my hope...”
Resilience management	<ul style="list-style-type: none"> • Collectivism (39%) • Problem negotiation (73%) • Dialogue with self and self-esteem (59%) • Assumption of “sick role” (52%) • Past stressful experiences (66%) 	<ul style="list-style-type: none"> • “I kept writing letters to myself... that was my stress-buster.” • “Now, I realize the importance of ICU duties and prolonged shifts. The training helps me gear up so much now...” • “There are multiple things at stake. I try my best to organize and prioritize at the end of the day... it helps me cope...” • “While working in COVID-wards, we have to consider ourselves “vulnerable,” “potentially” sick: this stops too many expectations.” • “I just keep telling myself, it’s a susceptible period, not to be too hard on myself...”
Working through distress	<ul style="list-style-type: none"> • Self-care (73%) • Lifestyle changes (40%) • Peer support (84%) • Telephonic counseling (34%) • Balanced “risk” approach (47%) • Relationships (72%) 	<ul style="list-style-type: none"> • “Indulging in my hobbies and maintaining a schedule has helped me de-stress...” • “I felt my colleagues and co-workers understand my status best. I felt validated...” • “Even weekly discussions with the counselor was fruitful. I felt there was an “audience” to my voice.” • “Risk was inevitable since the pandemic started. You can’t avoid it, just try ways to minimize it...” • “You don’t cope till you face the risk. Face it in a pragmatic way that helps in the face of such distress...”

workers. These have been compounded by misinformation related to the spread of infection, suggested remedies, and fear of “accessing healthcare facilities.” (Bhattacharya et al., 2020; Menon et al., 2020). With marked cultural diversities, pre-existing mental healthcare stigma, and varied societal beliefs, the perceptions toward HCW in India have been quite mixed. Such societal attitudes generate self-stigma in physicians, according to the Health-Stigma-Discrimination model, which facilitates internal hate, minimizes interactions, and causes social exclusion, further compounding isolation and burnout (Stangl et al., 2019). Guilt about transferring the infection to their loved ones, physical separation, and existential questions about the future of their families emerged as important themes in our study. This emotional insecurity also stemmed from a lack of perceived physical safety, as lack of adequate essential medical protective devices (PPE) has been reported as a consistent concern in the earlier studies from the United States (U.S.), China, and Saudi Arabia (Almaghrabi et al., 2020; Liu et al., 2020; Santarone et al., 2020). The constant fear of getting infected, decreased testing rates, and lack of leaves enhance the uncertainty, which along with “a helpless witness of daily suffering” in patients,

creates “vicarious trauma” for the HCWs that impairs coping and accentuates chronic, complex trauma. Resource constraints, stigma related to mental illness even among physicians, and rising COVID-caseload in recent months potentially add to the burden.

Needs

Based on the unprecedented global crisis created by the pandemic, the needs of the HCWs can be heterogeneous. Our participants welcomed the study as they felt that it provided an “audience” to their “unmet needs” and were quite expressive about the same during the interviews. A possible reason could be that the researchers were also physicians, which could have acted as a “peer support.” Flexible working hours, insurance coverage, and adequate medical safety are concerns that have been resonated worldwide (Taylor et al., 2020; Vindrola-Padros et al., 2020), but assume renewed significance in developing countries. One of the first studies done on Indian physicians during Lockdown highlighted the need for administrative assurance, financial security, recognition and societal understanding as important factors for altruistic coping (Chatterjee et al., 2020). Recognition and support of staff in healthcare are vital factors for



confidence, motivation, sense of achievement, and occupational security (Abu Sultan et al., 2018). Interestingly, social inclusion, timely risk communication by the infection control committee to the HCWs, and the presence of “medical trust” in the system were the predominant needs reported in our study. With a widening treatment gap and lack of primary – tertiary collaboration, this can be a significant concern in India. The benefits of periodic mental health screenings, digital peer support groups, and counseling sessions have demonstrated benefits in other pandemic-struck countries like China and Italy (Di Tella et al., 2020; Liu et al., 2020). Our participant HCWs perceived that their “emotional needs” lacked ears and, with the added stigma, further isolated them from the mainstream. Such social exclusion has been shown to increase apprehension and uncertainty, which can potentially increase experiential avoidance, enhancing stress (Seçer et al., 2020). As pointed out by Banerjee et al. (2020) in the systematic and advocacy review of the Indian Psychiatric Society (IPS) related to COVID-19 and psychological well-being, the need for safeguarding physical, financial security and psychosocial healthcare of frontline physicians are supposed to serve as important parameters in the fight against the pandemic. Though the guidelines of the Ministry of Health and Family Welfare (MoHFW), Government of India (GOI) mention the “selfless service” and critical roles of frontline HCW including nurses in the community and call upon for national stigma-mitigating techniques, our study indicates that the practical implementation of such guidelines is still a way to go. The available guidelines for psychosocial wellbeing during emergencies focus more on categorical definitions of distress and fail to tap into the resilience of the frontline workers. A study by San Juan et al. (2020) contrasted guidelines with lived experiences of practicing HCWs in United Kingdom and reported that understaffing, mental exhaustion and busy schedules often prevented them from accessing the available interventions. Future research can focus on exploring the gaps in the current guidelines when compared to the unmet needs and perceptions of HCWs in India during the pandemic crisis.

Resilience as a Process

Most of our participants mentioned resilience as a continuum developed through experiencing and facing an unprecedented crisis, aided by social support and past encounters with stress. Traditionally, schools of thought have debated on the static versus dynamic views of resilience, which pave the way for resilience-building strategies and interventions (Werner, 2005; Fletcher and Sarkar, 2013). Our findings grounded in the experiences of our physicians support the “learned resilience” hypothesis (Ryff, 2014), conceptualizing the framework through a “resilience identity,” managing the gradual development of resilience and working through the ongoing distress. Hence it is a process that can be intervened with therapeutic strategies, adaptive coping, resilience training, stress counseling, etc. It has also been related to secondary trauma faced by the HCWs, which can cause biopsychosocial impairment and decisional inefficacy in physicians during the pandemic (Vagni et al., 2020). Based on the conceptualization of resilience in our study as mentioned before, our results suggested that the consistent living

through hardships and adversities of the COVID-19 crisis with responsible risk-taking helped pave the way for problem-solving, personal efficiency, and coping in the physicians.

An overarching theme in our study was a physician’s duty and moral obligation to serve during crisis situation, which provided the physicians with a “moral sense of purpose” and formed the basis of a resilient self. HCWs derived hope and gratitude from the same with further help from their social connections. This engagement process has been theorized during COVID-19 to help combat loneliness and isolation, turning them into resilient and self-subserving “solitude” (Banerjee and Rai, 2020). Further, our participants also reported the timeliness of activating these social supports in order to prevent reaching the breaking point. Based on their prior experiences, reframing of hardships was a vital factor. Few studies of resilience and resources in HCWs done earlier have identified work as “personal gratification” and “doctor’s duty as a resilience among challenges” in HCWs (Ardebili et al., 2020; Liu et al., 2020). The latter study though done on a much smaller sample, was one of the first to identify that a physician’s “training, oaths, and values” were related to coping and resilience in such crisis situations. Social constructivism in qualitative research can have various approaches. Nyashanu et al. (2020) used interpretive phenomenological analysis (IPA) to study the lived experiences of 40 frontline HCWs in Midlands, United Kingdom. They worked mainly in the private care homes and domiciliary care agencies. Death of colleagues, fear of infecting others, unreliable testing and shortage of staff were reported as important concerns in the study. The participants felt that poor preparedness for the pandemic crisis had affected their coping adversely. Psychological preparedness as well as advance public health measures have been suggested as vital strategies to deal with the pandemic burden in a socio-culturally heterogeneous and populous nation like India (Banerjee, 2020). The HCWs in this study also added to this by mentioning that public understanding and social support during the initial phase of the COVID-19 crisis had boosted the process of their resilience. A community-based psychosocial toolkit based on the Zika virus model that was proposed to deal with the pandemic burden in India also includes resilience building among frontline workers through sense of purpose, social support and social cohesion at all levels of healthcare (Banerjee and Nair, 2020).

The next attribute was managing the “*praxis of resilience*” through an enhanced sense of self-esteem and maintaining it through self-dialogue. Socio-cultural diversities existed in our sample interviewed from various parts of India, and the ways, as well as processes of coping varied but there, was a commonality in “problem negotiation” (confronting and reframing the problem areas). Based on Cognitive-Behavioral principles, this is considered as a healthy problem-solving approach that involves perceived self-efficacy (Brown et al., 2012). Further, many HCWs assumed a “sick role” considering themselves exposed to the infection, which helped them reduce personal expectations and perceived guilt. The sick role has shown to be beneficial during the chronic crisis as per sociological theories and help attributes the impaired performance and socio-occupational shortcomings of sick or vulnerable individuals to the ongoing adverse



situations, which creates a “shielding” from enhanced roles and responsibilities during a crisis situation (Shilling, 2002). Hope and adaptation to a different lifestyle were reported by more than half of our participants as coping mechanisms which they thought would fetch them more experience during the post-pandemic aftermath. “New normalization” and using gained experiences to adapt to the pandemic stress have also been reported in a qualitative study from Iran where 97 HCWs including emergency services, physicians, nurses, pharmacists, laboratory personnel, radiology technicians, etc. reported change in personal lifestyle, new experiences in the pandemic era, negative emotions, learning to deal with them and finally need for mental health interventions as the major themes of their lived experiences while working during the outbreak (Ardebili et al., 2020).

Also, based on each of their training and experiences, they developed a “resilience model” consisting of mutual support among the peers, empathy, and positivism that generated hope in spite of adversities. Earlier studies on lived experiences during pandemic reported positivism and collectivism as powerful coping strategies that also help in the reduction of stigma. Xenophobia has been a growing concern during the pandemic, compounded by misinformation, which has been shown to increase fear of infection and can be potentially mitigated by collectivistic attitudes and personal growth (Ahuja et al., 2020). Xenophobic attitudes and social stigma was experienced by a greater proportion of lady HCWs in our study. This has been resonated earlier as well, where “amplification of social inequalities, paternalistic discourses and professional overshadowing of personal lives” were prominent among female NHS frontline health workers (Yarrow and Pagan, 2020).

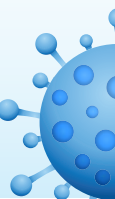
Finally, our participants agreed on the “gray line” of calculated risk-taking as part of occupational hazards with the strategic precautions, which boosted medical and emotional security. Most of them admitted that when “escape from stress” is impossible, facing it helps in the process of coping, whereas avoidance makes it chronic. The ongoing adversities of working in a pandemic situation helped them sustain personally and professionally. They discussed retaining a positive image while facing vulnerabilities and stressors on a pre-planned support system, through digital connectedness with peer groups and enjoying their hobbies and small celebrations. Studies have shown that groups with similar occupations can emphasize better during the crisis, which was resonated by the strength derived by our physicians from peer-support. “The risk with reason” approach helped our participants “work through the distress” aided by hobbies, support, spirituality or positivism, and the HCWs were quite open to discussion of how to focus on diet, nutrition, sleep, and lifestyle through generic measures, aided in resilience. Positive risk-taking has been related to risk-perception during infectious disease outbreaks, which in turn influence psychological wellbeing. Studies from China and Italy have shown how health risk perception can be influenced by empathy, self-efficacy and positive imagination (Commodari et al., 2020; Ding et al., 2020). The HCWs participants in our study also mentioned that a “careful balance between risk adaptation and medical safety measures” helped them face the prolonged stress of work during the

pandemic and they faced reduced personal susceptibility to the infection. Self-care and management have been considered as a dynamic interaction between an individual and his/her stressful circumstances that determine overall health and well-being. The well-known concept of micro-resilience is also related to self-care, self-esteem, and internal locus of control (Ryff, 2014). These factors can help in fostering resilience through the lifespan, which forms the “psychological capital” during a crisis. Our study also revealed that the simple measures of telephonic counseling provided validation and an “emotional audience,” which went a long way for emotional support. This has been the basis for the telecare model in china for HCWs in hospitals of Hubei province, where the pandemic first appeared. In short, the overall process of resilience was highly contextualized and related to the socio-occupational environment, but irrespective of the personal strategies used, the results help in conceptualizing a common ground in the “resilience-framework” of physicians during the ongoing outbreak. Such focused social support and understanding of the distress faced by HCWs during crisis times can help reduce social stigma and improve social connections. This has been termed as an “epidemic of empathy” that has the potential to bring together science and humanism that might be beneficial even after cessation of the pandemic (Barello and Graffigna, 2020). As discussed before, empathy, optimism and self-efficacy can also improve personal health-risk perception, which is vital for psychological resilience during pandemics (Commodari et al., 2020).

The study has the usual limitations of qualitative work, including generalizability and subjectivity. Besides, we only included physicians in the sample, while HCW also consists of nurses, para-medical staff, and other allied professionals. However, the study sample was large and heterogenous in socio-demographics, from all parts of India. Also, the rich data of the lived experiences of the physicians and rigorous analysis are the added strengths of the study. Besides this, we had to exclude some participants as they were diagnosed to be psychiatrically ill by independent psychiatrists prior to the commencement of the study. Only clinical interview was used though diagnosis was established through a consensus. The authors agree that some of these mental health issues could have been contributed by the psychosocial stressors of working during COVID-19. However, the objective of the present study was to explore resilience framework and coping in HCWs and pre-existing psychopathology would have colored their subjective perceptions during the pandemic, which form the main data of this qualitative study.

CONCLUSION

The psychosocial well-being of the physicians strengthens the healthcare infrastructure, which is vital for any country. With growing caseload, increased work-burden, and resource constraints, the quality of life of HCW assumes exaggerated importance in developing countries like India. To the best of our knowledge, this is the first study from any LMIC to explore



the “voices” of those directly working with COVID-19 patients and conceptualize their processes of resilience. Santarone et al. (2020) highlighted the importance of incorporating the needs and perspectives of HCW into resilience-building strategies that can involve mental health screenings, peer support, sensitive workplace infrastructure, and social security. Stigma-mitigating strategies need to be a collective responsibility for all levels of stakeholders, including sensitive reporting by the media. Bhattacharya et al. (2020) while discussing the consequences of social stigma in India, mentions the “dual burden” of the pandemic and prejudice in HCWs, suggesting the need to amplify their voices for psychosocial management and administrative policymaking. The “resilience framework” derived in the study can be integrated into digital psychotherapeutic interventions involving cognitive-behavioral, interpersonal and humanistic principles. The post-pandemic aftermath is uncertain, and various public health agencies have globally called for the safety and resilience-building of the frontline HCW (Banerjee et al., 2020; Galbraith et al., 2020; Xiao et al., 2020). This study provides a small step toward that “call” and obviously warrants further systematic, population-based, and mixed-method research into the emotional and psychosocial well-being of the HCW, their mental health issues, hardships at work, and finally the ways of coping, which can shape tailored interventions and legislations. There is also an urgent need to tailor the existing guidelines for the psychosocial wellbeing of the frontline HCWs based on their unmet needs and lived experiences. This much-needed approach

can potentially anchor the ongoing fight against the pandemic and help preparedness for such futuristic crises.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, on reasonable request.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the JSS University, Mysore, India. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

DB and AJ share the corresponding authorship. DB, TS, and AJ were responsible for the data collection and curation. DB and TS were involved in data analysis. DB and RK wrote the first draft of the manuscript. All authors had conceptualized the study and design, had full access to the data and take responsibility for data integrity and analysis, responsible for the reviewing, editing, and final approval of the manuscript.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Sexual functioning during the lockdown period in India: An online survey

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ABSTRACT

Aim: This study aimed to evaluate the impact of lockdown on sexual functioning in India. In addition, impact of lockdown on relationship with the partner and mental health was evaluated.

Materials and Methods: An online survey was conducted using changes in sexual functioning questionnaire, Patient Health Questionnaire-4, and a self-designed questionnaire.

Results: The mean age of the participants was 41.5 (standard deviation: 11.2; range: 22–77; median: 39.5) years, with the majority being males 385 (85.6%). The participants reported that lockdown led to reduction in the frequency of sexual intercourse and also touching the partner (fondling, caressing, touching, or kissing) when not indulging in sexual intercourse. Majority of the participants reported improvement in the overall relationship, communication with the partner, and interpersonal conflicts. About two-fifths of the participants reported engaging in sexual intercourse more than twice a week or more. About one-fifth screened positive for psychiatric morbidity, with 14.2% screened positive for anxiety, 14.8% screened positive for depression and 8.7% screened positive for both. In both genders, presence of depression and anxiety were associated with lower sexual functioning in all the domains.

Conclusion: Lockdown led to a reduction in the frequency of sexual intercourse, and reduction in the frequency of intimacy in the form of fondling, caressing, touching, or kissing partner when not doing sexual intercourse. However, lockdown led to the improvement in overall relationship and communication with the partners and a reduction in interpersonal conflicts.

Key words: COVID-19, lockdown, sexual dysfunction

INTRODUCTION


Novel coronavirus 2019 (nCoV/SARS-CoV-2/COVID-19) outbreak has posed extreme challenges for survival to humanity. To deal with the COVID-19 infection, most of the countries went through a phase of “lockdown” and are now

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gradually unlocking. During the initial phase, “lockdown” led to no entry/exit movements, and the persons were required to stay wherever they were. Lockdown was considered as both preventive strategies and an emergency strategy to save the lives of the vulnerable or at-risk persons. Government of India implemented “lockdown” with effect from March 25, 2020, across the country to control the spread of COVID-19.^[1] Lockdown had a significant negative impact on the mental health and overall functioning of the person.^[2] Additional strategy which was recommended to tackle the spread of COVID-19 infection included social distancing, which possibly impacted the interaction with others.

Lockdown for a man meant staying at home for a longer duration of period and availability of longer time to interact with the spouse.^[3] Lockdown for women meant an increase in the workload for women, because of everyone being at home throughout the day, higher work pressure, more chances of domestic violence, and interpersonal relationship issues.^[3] Considering the impact of lockdown on domestic violence, the World Health Organization issued an advisory against domestic violence.^[3] However, despite increase in the workload, the “lockdown” gave women more opportunity to spend time with their spouses.^[4]

Lockdown possibly provided more opportunity for sexual intimacy for the couples.^[4] Few studies from different parts of the world have evaluated the impact of social distancing, quarantine, and lockdown on sexual activity.^[5-7] An online survey from the United Kingdom, which involved 864 participants showed that, during the period of self-isolation/social distancing, about two-fifth (39.9%) of the participants engaged in sexual activity at least once per week. The presence of sexual activity was associated with being a male, of younger age, taking alcohol, being in a marital relationship or a domestic partnership, and longer duration of self-isolation/social distancing.^[8]

Another study from Turkey, which evaluated the sexual functioning of 58 females, showed that, compared to 6–12-month period of prepandemic time, the frequency of sexual intercourse during the pandemic increased significantly, and there was a significant improvement in the female sexual functioning index score, compared to that during the time before the pandemic. However, when compared before a pandemic, there was a significant reduction in the use of contraception and desire to become pregnant during the pandemic. In addition, this study showed that there was an increase in menstrual disorders during the pandemic.^[7] A study from Italy evaluated the sexual satisfaction of 1515 respondents who were quarantined. This study showed a reduction in the frequency of sexual intercourse during the period of quarantine, compared to the earlier. However, the majority of the participants reported sexual desire to be similar (39.2%) or

more than (40.66%) to the previous times. A majority of the participants (78.88%) reported indulging in autoerotism, and this was similar (29.44%) to or more than 39.74% than earlier. There was an increase in the consumption of pornography and marked reduction in sexual satisfaction during the period of being quarantined. It was also seen that sexual dissatisfaction in men was associated with age, whereas in females, it was associated with age, a higher level of depression, and knowing people positive for COVID-19.^[5]

Little is known about the impact of the COVID-19 pandemic on sexual functioning in people from India. Over the period, many myths have also emerged related to sexual intercourse (such as sexual intimacy with partner can lead to spread of COVID infection) and pregnancy (transmission of COVID infection from mother to the newborn during the process of birth) during the COVID times.^[9] These can influence the sexual intimacy. Accordingly, there was a need to evaluate the impact of lockdown on sexual functioning. This online survey evaluated the impact of lockdown on sexual functioning, which had not been determined yet in the Indian context. In addition, impact of lockdown on relationship with the partner and mental health was evaluated.

MATERIALS AND METHODS

This was an online survey conducted using Survey Monkey® platform through a link which was sent to people using either Whatsapp® or E-mail, using the nonprobability snowball sampling. Initially, the links were circulated by the researchers to their contact and the people receiving the survey link were requested to forward the link further. People receiving the survey link were at freedom to participate or not to participate in the survey. Similarly, there was no compulsion to forward the survey link to others on those receiving the survey link. These were ensured by the nonprobability snowball sampling in that after the initial circulation of the survey link, the direct involvement of the researcher was absent.

The survey invitation mentioned that the participants would have the right not to participate in the survey, and participation in the survey would imply providing informed consent. The participants were also informed that the responses will be anonymized, and there was no chance of them getting identified. The survey link was circulated during the period of May 14 to June 6, 2020. To be included, the participants were required to be aged more than 18 years. The survey was carried out using bilingual (English and Hindi) questions.

Clicking on the invitation link implied providing consent for participation in the study.

The Ethics Committee of the Indian Psychiatric Society approved the study, and the survey was conducted under



the aegis of Research, Education, and Training Foundation of the Indian Psychiatric Society.

Instruments used

Changes in Sexual Functioning Questionnaire (CSFQ):^[10] The CSFQ is a reliable and valid measure of sexual functioning, which is useful in both clinical and research settings. This is a structured questionnaire designed to measure illness- and medication-related changes in sexual functioning. The scale has separate male and female versions, both of which have 14 items, with each item rated on a 5-point Likert scale. English and Hindi version of the scale, which were available, were used. Permission was sought from the original author of the scale, for use.

A self-designed questionnaire was used to evaluate the effect of lockdown on the relationship with the partner and frequency of sexual intimacy in the past and during the lockdown.

Patient Health Questionnaire-4 (PHQ-4):^[11] The PHQ-4 is a self-administered questionnaire, which has the depression and the anxiety modules, to screen for depression and anxiety, respectively. This questionnaire has excellent reliability and validity, sensitivity and specificity of 88% for major depression.

Data were analyzed using SPSS 20.0 (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp., 2011), and the descriptive analysis in the form of frequency, percentages, the mean and standard deviation (SD) was calculated. Comparisons were made by using *t*-test and Chi-square test.

RESULTS

During this survey period of May 14 to June 6, 2020, 514 responses were received. All the responses which were received from outside the country, verified using the IP addresses were excluded. Similarly, responses received from people below 18 years were also excluded. Responses which were incomplete were not considered for the final analysis. The entries were also checked for duplicacy, and in case of doubt, such responses were excluded. Out of the response received, 26 responses were incomplete, 1 was from a participant <18 years, 6 were from outside India, and 31 were from those who did not have a partner. All these responses were deleted. Finally, 450 responses were found to be complete in all aspects and were analyzed. Majority of the participants were male, married, and postgraduates. The mean age of the participants was 41.5 (SD: 11.2) years. Small proportions of the participants were suffering from chronic physical illness and were on any regular medications. Majority of the participants were spending more than 1 h/day on the screen media [Table 1].

To understand the impact of lockdown on sexual functioning, the participants were asked to keep the month of December

2019 in mind (to give the responses for the time before lockdown), while responding the questions enquiring about prior sexual functioning. Lockdown led to reduction in the frequency of fondling, caressing, touching, or kissing partner when not indulging in sexual intercourse and reduction in the frequency of sexual intercourse [Table 2].

When enquired about the impact of lockdown on the overall relationship with their partner, the majority of the participants reported improvement in the overall relationship, communication with the partner, and interpersonal conflicts [Table 3].

Majority of the participants reported lack of privacy issues (54.1%) during the lockdown period. However, one-third of the participants reported some privacy issue (32.8%) and a small proportion of them reported significant privacy issues (13%). In terms of availability of contraception, a majority (76.7%) reported no worries related to the availability of contraception; a small proportion reported worries related to contraception “somewhat (17%)” and “very much (6.3%).”

As per the assessment of PHQ-4, 14.2% screened positive for anxiety, and 14.8% screened positive for depression. A small proportion (8.7%) screened positive for both, and overall prevalence of psychiatric morbidity (depression, anxiety, or both) was 20.4%.

As is evident from Table 4, less than half of the participants of either gender reported, “much” or “great” enjoyment or pleasure in their sexual activity at the time of assessment. Only about two-fifths of the participants reported engaging in sexual intercourse more than twice a week or more. Other details are shown in Table 4. Similarly, only a small proportion of the females reported indulging in various sexual activities. The mean CSFQ score for males was 44.9 (SD: 9.5), and that for females was 40.2 (SD: 11.8). Overall, female had significantly lower scores on all the domains except for the pleasure domain [Table 4].

In both the genders, presence of depression and anxiety were associated with lower sexual functioning in all the domains [Table 5].

DISCUSSION

This online survey evaluated the sexual functioning of the people during the lockdown period using a self-designed questionnaire and CSFQ. Findings of the present study suggest that lockdown due to COVID-19 pandemic has led to a reduction in the frequency of sexual intercourse, and reduction in the frequency of intimacy in the form of fondling, caressing, touching, or kissing partner when not indulging in sexual intercourse. Further, the present study suggests that lockdown led to an improvement in overall



Table 1: Sociodemographic profile of the participants

Variables	Frequency, n (%) / mean (SD)
Age (years) and range (median)	41.5 (11.2), 22-77 (39.5)
Number of participants aged >65 years	20 (4.4)
Sex	
Male	385 (85.6)
Female	65 (14.4)
Marital status	
Married and living with spouse	389 (86.4)
Married and living away from spouse	35 (7.8)
Unmarried but in a live-in relationship	4 (0.9)
Divorced	4 (0.9)
Single	17 (3.8)
Others (did not specify)	4 (0.9)
Education level	
Up to matric	2 (0.4)
Intermediate	4 (0.9)
Graduate	143 (31.8)
Postgraduate	301 (66.9)
Occupation	
Student	2 (0.4)
Business	27 (6.0)
Housewife	12 (2.7)
Professional	260 (57.8)
Self-employee	155 (34.4)
Retired	13 (2.9)
Type of family set-up	
Husband and wife only	76 (16.9)
Husband, wife, and children	172 (38.2)
Husband, wife, children, and parents	158 (35.1)
Joint/extended family	40 (8.9)
Did not response	4 (0.9)
Do you have a personal bedroom	
Yes	410 (91.1)
No	40 (8.9)
Are you suffering from any chronic physical illness	
Yes (for example-hypertension, diabetes mellitus, chronic obstructive pulmonary disease, asthma, and rheumatoid arthritis) [#]	68 (14.8)
Are you receiving any regular medication for any illness	
Yes	33 (7.2)
Time spent watching television, using social media, laptop, facebook, whatsapp, twitter, etc.	
Up to 1 h/week	53 (11.8)
1-3 h/day	165 (36.7)
3-6 h/day	150 (33.3)
6-9 h/day	55 (12.2)
9-12 h/day	15 (3.3)
>12 h/day	12 (2.7)

[#]Hypertension (n=11), diabetes mellitus (n=6), diabetes mellitus and hypertension (n=3), hypothyroidism (n=2), chronic pain (n=16), PCOS (n=1), coronary artery disease (n=1), chronic kidney disease with asthma (n=1), depression (n=1). SD=Standard deviation, PCOS=Polycystic ovary syndrome

relationship with the partners, communication with the partner, and reduction in the interpersonal conflicts. In terms of psychiatric morbidity, the present study suggests that the prevalence of psychiatric morbidity is about 20.4%, with 8.7%, fulfilling the diagnosis of both depression and anxiety. On CSFQ, less than half of the participants reported enjoyment or pleasure in their sexual activity. About two-fifths of the participants reported engaging in sexual intercourse more than twice a week or more. When the findings of the present study are compared with an online survey from the United Kingdom, which reported the frequency of sexual activity of once per week in 39.9% of participants during the period of self-isolation/social distancing, it can be said that the frequency of sexual

intercourse in participants from India was higher than that reported from United Kingdom,^[8] despite participants in the present survey reporting reduction in frequency of sexual intercourse. These differences could be attributed to various psychosocial factors, demographic factors, personal/individual differences, timing of the survey with respect to the pandemic, availability of the partner, and possibly giving socially desirable answers. Our findings are also supported by the survey conducted in Italy, which also reported a reduction in the frequency of sexual intercourse during the period of quarantine, compared to the earlier.^[2] This study also showed that majority of the participants indulged in autoerotism, similar to or more than the earlier; increase in consumption of pornography



Table 2: Comparison of sexual activities before and during the lockdown period

	Prior to lockdown (n=450), n (%)	During the lockdown (n=450), n (%)	Chi-square test (P)
Time spent in watching porn/reading erotic material per week			
Nil	181 (40.2)	178 (39.6)	12.263 (0.092)
<15 min/week	101 (22.4)	82 (18.2)	
15-30 min/week	76 (16.9)	64 (14.2)	
30-60 min/week	39 (8.7)	47 (10.4)	
1-2 h/week	31 (6.9)	38 (8.4)	
2-3 h/week	6 (1.3)	19 (4.2)	
3-6 h/week	8 (1.8)	10 (2.2)	
>6 h/week	8 (1.8)	12 (2.7)	
Frequency of masturbation and sexual self-pleasuring acts			
More than once per day	11 (2.4)	15 (3.3)	4.578 (0.333)
Once per day	27 (6.0)	33 (7.3)	
Few times in a week	113 (25.1)	109 (24.2)	
Few times in a month	169 (37.6)	144 (32.0)	
Never	130 (28.9)	149 (33.1)	
Frequency of fondling, caressing, touching or kissing partner when not doing sexual intercourse			
More than once per day	118 (26.2)	124 (27.6)	9.883 (0.042*)
Once per day	66 (14.7)	54 (12.0)	
Few times in a week	142 (31.6)	115 (25.6)	
Few times in a month	84 (18.7)	94 (20.9)	
Never	40 (8.9)	63 (14.0)	
Frequency of sexual intercourse			
More than once per day	14 (3.3)	21 (4.7)	2.163 (<0.001***)
Once per day	42 (9.6)	46 (10.2)	
Few times in a week	175 (39.1)	168 (37.3)	
Few times in a month	188 (41.5)	143 (31.8)	
Never	31 (6.5)	72 (16.0)	

*P<0.05; ***P<0.001

Table 3: Impact of lockdown on the relationship with the partner

Variables	Very much improved, n (%)	Somewhat improved, n (%)	Not changed, n (%)	Somewhat worsened, n (%)	Very much worsened, n (%)
Overall relationship with my partner during lockdown period	129 (28.7)	124 (27.6)	156 (34.7)	33 (7.3)	8 (1.8)
Level of communication between you and your partner during the lockdown period	155 (34.4)	119 (26.4)	146 (32.4)	24 (5.3)	6 (1.3)
The interpersonal conflicts between you and your partner during lock-down period	98 (21.8)	119 (26.4)	187 (41.6)	40 (8.9)	6 (1.3)

and marked reduction in sexual satisfaction during the period of being quarantined.^[2] However, in our study, there was no significant change in the frequency of masturbation and sexual self-pleasuring acts or time spent in watching pornography or reading erotic material per week. Our findings also do not support the findings from Turkey, which evaluated females and reported an increase in the frequency of sexual intercourse during the pandemic.^[7] In fact, we found that higher level of dysfunction in females. These similarities and differences in sexual behavior during the period of lockdown/self-isolation and quarantine in different countries can be attributed to a difference in cultural factors, which possibly influence sexual behavior. Besides these other factors, such as individual/personality factors, timing of the survey, sampling technique, and socially desirable responses could have influenced the frequency of sexual intercourse. In addition, the prevailing myths and incorrect beliefs in the society, with respect to

the sexual intercourse and spread of COVID-19 infection.^[12] The reduction in the frequency of sexual intercourse or avoidance of sexual intercourse may also be attributed to the fear of spreading the infection or contracting infection to or from the asymptomatic partner. The present study also suggests that a lower score on various domains of CSFQ was associated with higher severity of depression and anxiety scores. However, this should not be interpreted as a cause and effect relationship, as psychiatric morbidity may be a cause or effect of reduced sexual functioning. Previous studies have also reported a negative impact of psychiatric morbidity on the sexual functioning.^[13]

The present study suggests that lockdown led to an improvement in the relationship with their partner. This improvement can be attributed to a possible reduction of the stress and availability of time. A previous survey from India, which evaluated the psychological impact of lockdown, also



Table 4: Sexual functioning as assessed by change in sexual functioning questionnaire

Variables	Male frequency, <i>n</i> (%)/ mean (SD) (<i>n</i> =385)	Female frequency, <i>n</i> (%)/ mean (SD) (<i>n</i> =65)	Chi-square test/ <i>t</i> -test (<i>P</i>)
Compared with the most enjoyable it has ever been, how enjoyable or pleasurable is your sex life right now?			
No enjoyment or pleasure	46 (11.9)	10 (15.4)	1.234 (0.873)
Little enjoyment or pleasure	56 (14.5)	11 (16.9)	
Some enjoyment or pleasure	109 (28.3)	18 (27.7)	
Much enjoyment or pleasure	101 (26.2)	14 (21.5)	
Great enjoyment or pleasure	73 (18.9)	12 (18.5)	
How frequently do you engage in sexual activity (sexual intercourse, masturbation, etc.) now?			
Never	40 (10.4)	11 (16.9)	13.541 (0.009**)
Rarely	51 (13.2)	12 (18.5)	
Sometimes (more than once a month, up to twice a week)	110 (28.6)	25 (38.5)	
Often (more than twice a week)	140 (36.4)	9 (13.8)	
Everyday	44 (11.3)	8 (12.3)	
How often do you desire to engage in sexual activity?			
Never	25 (6.5)	6 (9.2)	3.888 (0.421)
Rarely	42 (10.9)	11 (16.9)	
Sometimes (more than once a month, up to twice a week)	103 (26.9)	19 (29.2)	
Often (more than twice a week)	132 (34.3)	19 (29.2)	
Everyday	83 (21.6)	10 (15.4)	
How much now frequently do you engage in sexual thoughts (thinking about sex, sexual fantasies)?			
Never	11 (2.9)	7 (10.8)	29.973 (<0.001***)
Rarely	51 (13.2)	16 (24.6)	
Sometimes (more than once a month, up to twice a week)	91 (23.6)	26 (40.0)	
Often (more than twice a week)	127 (32.9)	9 (13.8)	
Everyday	105 (27.35)	8 (12.3)	
Do you enjoy books, movies, music or artwork with sexual content?			
Never	53 (13.8)	8 (12.3)	11.136 (0.025**)
Rarely	88 (22.9)	23 (35.4)	
Sometimes (more than once a month, up to twice a week)	110 (28.6)	23 (35.4)	
Often (more than twice a week)	81 (20.9)	9 (13.8)	
Everyday	53 (13.8)	2 (3.1)	
How much pleasure or enjoyment do you get from thinking about and fantasising about sex?			
No enjoyment or pleasure	28 (7.3)	7 (10.8)	6.459 (0.167)
Little enjoyment or pleasure	63 (16.4)	17 (26.2)	
Some enjoyment or pleasure	108 (28.1)	18 (27.7)	
Much enjoyment or pleasure	122 (31.7)	13 (13.8)	
Great enjoyment or pleasure	64 (16.6)	10 (15.4)	
How often do you have erection related or unrelated to sexual activity (male)/how often do you become sexually aroused? (female)			
Never	62 (16.1)	5 (7.7)	11.092 (0.026*)
Rarely	60 (15.6)	19 (29.2)	
Sometimes (more than once a month, up to twice a week)	90 (23.3)	19 (29.2)	
Often (more than twice a week)	88 (22.9)	10 (15.4)	
Everyday	85 (22.1)	12 (18.5)	
Do you get an erection easily? (male)/are you easily aroused? (female)			
Never	18 (4.7)	7 (10.8)	37.558 (<0.001***)
Rarely	29 (7.5)	18 (27.7)	
Sometimes (more than once a month, up to twice a week)	71 (18.4)	17 (26.2)	
Often (more than twice a week)	96 (24.9)	11 (16.9)	
Everyday	170 (44.2)	12 (18.5)	
Are you able to maintain an erection (male)/do you have adequate vaginal lubrication during sexual activity (female)?			
Never	17 (4.4)	7 (10.8)	21.537 (<0.001***)
Rarely	37 (9.6)	10 (15.4)	
Sometimes (more than once a month, up to twice a week)	61 (15.8)	19 (29.2)	
Often (more than twice a week)	111 (28.8)	19 (29.2)	
Everyday	159 (41.3)	10 (15.4)	
How often do you experience painful, prolonged erection? (male)/how often do you become aroused and then lose interest? (female)			

Contd...

Table 4: Contd...

Variables	Male frequency, <i>n</i> (%)/ mean (SD) (<i>n</i> =385)	Female frequency, <i>n</i> (%)/ mean (SD) (<i>n</i> =65)	Chi-square test/ <i>t</i> -test (<i>P</i>)
Never	256 (66.5)	31 (47.7)	10.822 (0.029*)
Rarely	78 (20.3)	20 (30.8)	
Sometimes (more than once a month, up to twice a week)	23 (5.9)	9 (13.8)	
Often (more than twice a week)	21 (5.4)	4 (6.2)	
Everyday	7 (1.85)	1 (1.5)	
How often do you have an ejaculation? (male)/how often do you experience an orgasm? (female)			
Never	45 (11.7)	3 (4.65)	23.879 (<0.001***)
Rarely	46 (11.9)	21 (32.3)	
Sometimes (more than once a month, up to twice a week)	85 (22.1)	19 (29.2)	
Often (more than twice a week)	137 (35.6)	13 (20.0)	
Everyday	70 (18.2)	9 (13.8)	
Are you able to ejaculate when you want to? (male)/are you able to have orgasm when you want to?			
Never	27 (7.0)	17 (26.2)	57.228 (<0.001***)
Rarely	42 (10.9)	22 (33.8)	
Sometimes (more than once a month, up to twice a week)	81 (21.1)	12 (18.5)	
Often (more than twice a week)	139 (36.1)	7 (10.8)	
Everyday	95 (24.7)	7 (10.8)	
How much pleasure or enjoyment do you get from your orgasms?			
No enjoyment or pleasure	21 (5.5)	5 (7.7)	22.899 (<0.001***)
Little enjoyment or pleasure	36 (9.4)	18 (27.7)	
Some enjoyment or pleasure	86 (22.4)	16 (24.6)	
Much enjoyment or pleasure	142 (36.9)	11 (16.9)	
Great enjoyment or pleasure	100 (25.9)	15 (23.1)	
How often do you have painful orgasm?			
Never	281 (72.9)	9 (13.8)	87.946 (<0.001***)
Rarely	57 (14.8)	28 (43.1)	
Sometimes (more than once a month, up to twice a week)	27 (7.1)	17 (26.2)	
Often (more than twice a week)	11 (2.9)	8 (12.3)	
Everyday	7 (1.8)	3 (4.6)	
Mean score for the pleasure domain	3.2 (1.3)	3.3 (1.2)	0.788 (0.431)
Mean score for the desire (frequency) domain	6.1 (2.2)	6.8 (2.1)	2.423 (0.016*)
Mean score for the desire (interest) domain	10.0 (2.7)	8.6 (2.9)	3.970 (<0.001***)
Mean score for the arousal (excitement) domain	11.1 (3.1)	9.4 (3.2)	4.203 (<0.001***)
Mean score for the orgasm (completion) domain	10.7 (2.9)	8.7 (3.2)	5.010 (<0.001***)
Mean total CSFQ score	44.9 (9.5)	40.2 (11.8)	3.557 (<0.001***)

P*<0.05; *P*<0.01; ****P*<0.001. SD=Standard deviation, CSFQ=Changes in Sexual Functioning Questionnaire

Table 5: Correlation of sexual functioning with psychological morbidity

Variables	Anxiety	Depression
Females		
Pleasure	-0.307 (<0.001***)	-0.341 (<0.001***)
Desire (frequency)	-0.130 (0.006**)	-0.114 (0.017*)
Desire (interest)	-0.147 (0.002**)	-0.149 (0.002**)
Arousal (excitement)	-0.174 (<0.001***)	-0.141 (0.004**)
Orgasm (completion)	-0.209 (<0.001***)	-0.166 (0.001**)
Total CSFQ score	-0.196 (<0.001***)	-0.167 (0.001**)
Males		
Pleasure	0.315 (<0.001***)	-0.345 (<0.001***)
Desire (frequency)	-0.215 (<0.001***)	-0.177 (<0.001***)
Desire (interest)	-0.109 (0.022*)	-0.077 (0.103)
Arousal (erection)	-0.155 (0.002**)	-0.133 (0.009**)
Orgasm (ejaculation)	-0.237 (<0.001***)	-0.214 (<0.001***)
Total CSFQ score	-0.230 (<0.001***)	-0.211 (<0.001***)

CSFQ=Changes in Sexual Functioning Questionnaire. **P*<0.05; ***P*<0.01; ****P*<0.001

reported a positive impact on the relationships.^[2] There are also reports of increase in domestic violence and worsening

of relationship between couple during the lockdown period.^[14,15] Hence, considering this negative impact of lockdown, it can also be said that the improvement in relationship, as noted in the present study could have been influenced by sampling bias and those with actually relationship issues, possibly not participating in the survey.

However, the prevalence of depression and anxiety in the present study was lower than that reported in the previous survey from India, which was conducted about a month before the current survey.^[2] This difference could be due to the use of a brief version of PHQ in the present study, which could have led to lower prevalence of psychiatric morbidity. Other possible reason could be the fact that, at the beginning of the pandemic, there was a significantly higher level of stress, which possibly reduced with passing time and hence led to a reduction in the prevalence of psychiatric morbidity. Accordingly, it can be said that lockdown has not led to only negative consequences for the general population but has also led to some of the positive consequences in



terms of improvement in the communication between the couple. Accordingly, while evaluating patients presenting with various psychological issues, it is important to enquire about both and negative aspects of lockdown, and making the patients aware about the positive aspects may help in dealing with patients who only talk about the negative consequences and the associated distress.

Findings of this survey must be interpreted in light of its limitations. The response rate was limited, and the survey was conducted by using the snowballing sampling technique. In view of this, the findings cannot be generalized to the entire country. The demographic profile of the study sample is not representative of the demographic profile of the nation; hence, the findings can not be generalized to the country. Further, the psychiatric morbidity ascertained in this survey was assessed by PHQ-4, and the same was not confirmed using any diagnostic interview by a psychiatrist. The Hindi version of the CSFQ has not yet been validated. It is possible that some of the participants would have given socially desirable answers. The survey was limited to those able to read either English and/or Hindi. The survey was also limited to those with a smart phone with internet connection or those with a valid e-mail address. In future, attempts must be made to overcome these limitations.

CONCLUSION

To conclude, this survey shows that lockdown led to a reduction in the frequency of sexual intercourse and reduction in the frequency of intimacy in the form of fondling, caressing, touching, or kissing partner when not doing sexual intercourse. However, lockdown led to an improvement in overall relationship with the partners, communication with the partner, and reduction in the interpersonal conflicts. These findings overall imply that lockdown led to improvement in the communication between the couple but led to reduction in sexual intimacy. This suggests that possibly lockdown led to improvement in relationship. Accordingly, in future, there is a need to evaluate the role of stress in day-to-day life on the relationship between couple. Further, there is a need to evaluate the role of stress management techniques in couples facing relationship issues.

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Conflicts of interest

There are no conflicts of interest.

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Uncertainty, Sex and Sexuality during the Pandemic: Impact on Psychosocial Resilience

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Abstract

The Coronavirus disease 2019 (COVID-19) pandemic has been a global unprecedented health threat. Besides the myriad of effects on public health, the psychosocial implications of the outbreak have been far-fetched. Though the increased prevalence of psychiatric disorders, reduced access to care and social vulnerabilities have been highlighted in literature, the immense impact on sexuality and psychosexual health tends to be silent. The World Health Organization (WHO) defines sexual health as “a state of physical, emotional, mental and social well-being in relation to sexuality; it is not merely the absence of disease, dysfunction or infirmity.” Sexual practices and intimacy have been influenced by more ways than one, namely fear of infection, ambiguity about viral spread, misinformation, physical distancing, travel restrictions, intimate partner violence and deprivation of ‘social touch’. The frontline workers, socio-economically impoverished groups, age and sexual minorities are especially affected. Sexual and reproductive rights are compromised due to reduced help-seeking, panic and stigma related to the outbreak. Psychological resilience helps one navigate through stressful situations and assumes a special importance during the ongoing crisis. This chapter reviews the multi-faceted intersections between sexual health and resilience, highlights the possible roles of pandemic-related uncertainty and advocates for certain guidelines to promote and preserve healthy expressions of sexuality for coping during COVID-19.

Keywords: sex, sexuality, sexual health, COVID-19, pandemic, coping, resilience

1. Introduction

Very few global catastrophes have been as unprecedented as the Coronavirus 2019 (COVID-19) crisis. The pandemic caused by the severe acute respiratory syndrome coronavirus – 2 (SARS-CoV-2) started with its epicenter in Hubei (Wuhan province), China in December 2019. As of today, the virus has affected 137 million people across the world claiming the lives of 2.94 million, the numbers rising as we speak [1]. More than a year has passed since COVID-19 was declared as a pandemic by the World Health Organization (WHO), and presently many nations are threatened by the second waves of infection, though several vaccine rollouts have begun globally. Besides the public health burden that has received primary importance, the emotional and social effects of such a large-scale crisis are

far-fetched. Long-term uncertainty, lockdowns, travel restrictions, fear of infection, social chaos, stigma towards those infected, apprehension and grief have been the psychosocial offshoots of the pandemic which are discussed several times in literature [2, 3]. The morbidity of psychiatric disorders such as depression, anxiety, post-traumatic stress, insomnia and adjustment disorders has increased based on various studies from both developing and developed nations [4–6]. Especially the vulnerable populations such as frontline workers, age and gender minorities, socio-economically disadvantaged groups, homeless individuals, migrants and those suffering from the infection have disproportionately shared the brunt of the pandemic [2, 7, 8]. Though several of these issues have been discussed in academic, social and policy discourse, one of the basic facets of human existence has largely been silent in research. This is the need for ‘social touch’, physical proximity and intimacy which comprise sexuality and sexual health. An infectious disease pandemic is bound to affect sexual and reproductive rights as well as health in multiple ways due to the fear and risks of infection [9]. Further, partners have been separated due to lockdowns, travel has been restricted, and the ‘assuring’ nature of intimate touch is now feared and tabooed. Lifestyles and work patterns have changed with prolonged entrapment within families on one hand and long-term physical distancing on the other, all of which have the potential to influence relationship dynamics [10]. Sexuality has also increasingly shared the virtual platforms with rise in pornography use [11]. The rigorous measures of using face masks, social distancing and respiratory hygiene advocated by all global agencies to curb the viral spread have ‘masked’ emotions, distanced loved ones and caused global exhaustion and frustration [12]. Nevertheless, these precautions need to be followed and continued as crucial strategies to fight the pandemic. As expected, a highly contagious infection like COVID-19 has generated fear of couple intimacy, guilt of transmitting the infection to partners/spouses (especially in the high-risk workers), impacted relationships and increased intimate partner violence (IPV) [12–14]. Psychosexual health forms a vital component of emotional wellbeing and coping during such crisis and can be markedly affected by this prolonged uncertainty during the pandemic period. With this background, this chapter looks at the various dimensions of sex and sexuality during the COVID-19 pandemic, the intersections with psychosocial resilience and anxiety management, and finally highlights strategies for safe sexual practices to navigate through these adversities.

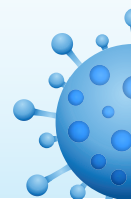
2. COVID-19 and psychosexual health: multi-dimensional intersections

2.1 Glancing back at the “Plagues”

“A loveless world is a dead world. The plague makes us long for the warmth of our loved ones.”

Albert Camus, The Plague (La Peste), 1947 [15].

Pandemics have a history of social disruption. Since the bubonic plague of the 13th Century, the Spanish Flu, Human Immunodeficiency Virus (HIV), Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), to the modern-day Ebola and Zika virus outbreaks, linking infectious disease outbreaks to promiscuity, low socio-economic status and lack of hygienic standards were common [16, 17]. Moral standards were imposed by the society and these illnesses were historically viewed with religious and political overtones [18]. Even without a pandemic, sexuality has historically been influenced by social, political, and religious beliefs, with stringency regarding its practice suggested across most



of the communities [19, 20]. Legal and religious ascendancy over sexual expressions have been modified over time, leading to a more permissive attitude, however, sexual expression still remains a taboo and is governed by the socio-legal norms significantly [20]. Delamater in his article [21] pointed out that family and religion are the two most important influencers of sexual expression. The controls exerted may result from the societal perspective of the purpose of the sexual activity, thereby putting down rules for appropriate sexual behaviour. The normative control, comprising of codes of conduct, is seen to have an enormous impact in shaping sexual attitude and behaviour. The codes include social, personal, and peer codes, variably influencing the permissiveness towards sexual expression [21]. Similar regulations surround infectious disease outbreaks. Hence sexual expressions have often been considered 'unsanitary' and associated with 'spread of germs' [19, 20, 22]. Sexuality and sexual expressions have been discussed several times in literature with relation to pandemics. "Poetic description of the plague" highlights newly married couples being segregated in rooms, not allowed to communicate during the classical "black death". "Fear of infection" was seen to "disrupt love and lives" more so in affluent social classes who feared hospitalization and death [22]. Cantor mentions about illicit sexual relationships and immorality being perceived as social reasons for the plague and physicians advising complete sexual abstinence as a solution [23]. In the medieval Europe, coercive sexual relationships, incest and prostitution were seen to rise during the plague and religious blames were allegedly put forth against homosexual individuals for disobeying the "Divine Will" and "sanitary legislation" that supposedly led to the propagation of the illness [24].

In Land, Kinship and Life-Cycle [25], Smith highlights the increase in punishment for fornication during the periods of plague (1349–1350), and sexuality was perceived as a driving force for the spread of infectious illness. However, there is also mention of a spurt in sex-parlors and prostitution as the plague waned off, due to the "need for being connected and expressing their sex drive" in the population which served as coping factors. Social distancing measures were looked down upon by the public during the Spanish Flu of 1918, where innuendos like "you are your safest sexual partner" and "I want to be quarantined with you" gained popularity [26]. It can be concluded from these texts that though there was a social 'aversion and ban' blaming unrestricted sexuality for the spread of infections, traditionally it has been considered to be healthy coping factor for the general public, irrespective of the restrictions.

With changing understanding of pandemics and epidemics, social thoughts have also been modified with time. Sexual dysfunctions, impaired perceived sexual satisfaction, reduced sexual interest, heightened performance anxiety and marital problems were noticed in longitudinal studies done during SARS and MERS [27, 28]. Adverse reproductive outcomes and compromised reproductive rights were seen in vulnerable populations during Ebola and Zika virus outbreaks, especially in the migrants and Lesbian Gay Bisexual Transgender Queer Intersex (LGBTQI) groups [29, 30]. The psychosocial models of care adopted for Nipah infection in India and Zika virus in Brazil involved sex education, healthy and safe expressions of sexuality during the crisis, prevention of viral spread and coping through social connectedness [31, 32]. This assumes enhanced importance during crises such as COVID-19 as sexual wellbeing is linked to better physical health, hope, personal growth, optimism and positivity.

2.2 How has COVID-19 impacted sexuality?

Systematic literature on how COVID-19 has impacted psychosexual health is lacking. Few predominant dimensions have been conceptualized [33]:



- Fear of sexual intimacy, lack of perceived satisfaction and ambiguity about safe sexual practices
- Worsening of symptoms, treatment and distress of those already suffering from sexual disorders and dysfunctions
- Cyber-sexuality and consumption of pornography

The various possible factors impacting sexuality and sexual health during COVID-19 are depicted in **Figure 1** and we propose that each of them adds to the uncertainty and anxiety related to this global outbreak. Impaired psychosexual health in turn can impact psychological resilience and coping with this persistent multi-faceted stress.

Panzeri et al. [11] conducted an online survey between April–May, 2020 to explore relationship quality between cohabiting couples. Out of 124 participants, more than two-thirds were women and most couples did not report differences in sexuality. However, women reported reduction in satisfaction, pleasure, arousal and desire primarily due to concerns of worry, stress and lack of privacy. Qualitative data in this regard is more informative and is yet to be analyzed from this study. Another study with similar design conducted by Arafat et al. [34] in three South-Asian countries of India, Nepal and Bangladesh had male predominance in participation. 45% of the respondents mentioned that COVID-19 had affected their sexual life and though the frequency of sexual interactions changed little after lockdown, the quality of sex and perceived sexual satisfaction were affected more. Half of the sample however reported improvement in emotional bonding and coping during lockdown and this was related to more time spent together, better ‘family time’, less work burden and reduced social commitments. A cross-sectional study from Turkey [35] assessed sexual dysfunction and sexual behaviour in 245 volunteers and reported that sexual intercourse had decreased in men post-pandemic. Sexual avoidance and solitary sexual behaviours (pornography use, masturbation) increased more in the males but the couples who

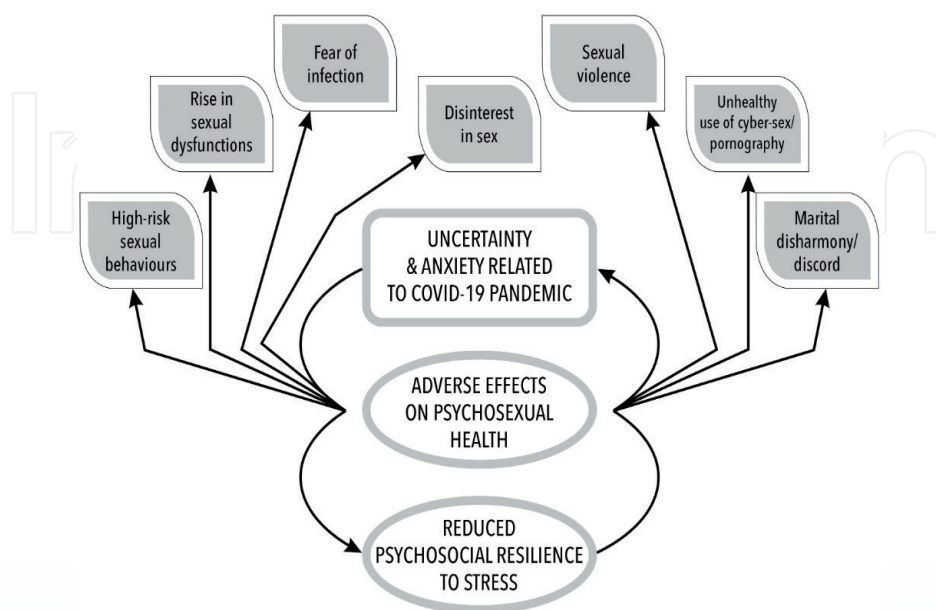
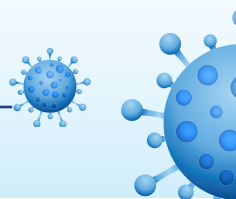


Figure 1.
Multi-faceted intersections between COVID-19 related uncertainty/anxiety, sexual health & psychological resilience.



spent more time together had better sexual interactions and healthier coping strategies with lower depression/anxiety scores. In another larger but preliminary study from Italy on 1,515 individuals through Facebook and Instagram, 40% respondents revealed enhanced sexual desire during the lockdown [36]. However, both frequency and quality of sexual behaviours decreased in couples over time with increase in autoerotic interactions. Sexual satisfaction decreased significantly throughout the lockdown and was associated with increased pornography use, male sex, depression scores and unhealthy ways of coping (such as binge-eating, harmful use of technology, etc.)

In the absence of larger longitudinal studies, it has been hypothesized that psychiatric comorbidities (especially depression and anxiety disorders), a consistent fear of contracting the infection and uncertainty related to the global crisis alter sexual desire and interest [12, 33, 37]. These discrepancies have varied socio-cultural connotations as manifestations of sexuality itself can be quite heterogeneous. While for some individuals, need for 'social touch' and intimacy are vital to cope, in others the moral underpinnings about mortality, grief and death anxiety can lead to sexual aversion [38]. Discrepancies in these perceptions within a couple can lead to impaired relationships and discord. Besides, body dissatisfaction, body image perceptions, 'fat talk' and weight gain have also increased during this pandemic due to lack of physical activity, altered sleep-wake cycle and change in dietary patterns, all of which can influence sexual intimacy [39, 40]. The "Dual Control Model of Sexual Response" can be used to explain the differential impact of uncertainty/anxiety on sexual reactions of individuals. Individual variations in sexual arousal and inhibition patterns may decide what effect stressful situations would have on their sexual cycle [41]. Due to these differences, there can also be increased sexual violence and coercive sexual practices. Global data already shows a significant rise of intimate partner violence (IPV) across the world [42]. Sexual frustration and dysfunctional coping strategies can be further compounded by increased substance abuse during the pandemic that can perpetuate the cycle of violence and discord in relationships [42].

SARS-CoV-2 is more infectious than its earlier congeners with new mutant strains being more pathogenic [43]. Aerosol and fomite spreads are rapid and survival of the virus on various inanimate objects can last up to three weeks [44]. Besides, since the advent of the pandemic, there has been a plethora of misinformation and rumor mongering all across media about its pathogenesis, origin and treatment. This adds to the fear, uncertainty and ambiguity in safe sexual practices [45]. Various global agencies have already issued guidelines in this regard [46, 47]. The readers are encouraged to go through Banerjee and Rao [37] as well as Pennanen-lire et al. [33] for comprehensive reviews of COVID-19's sexual impact and summary of safe sex guidelines during this crisis. Sex education and risk reduction counseling are considered to be most important with permissible sexual contact within equal-risk and quarantined partners. Informed decision making, emotional support, mutual consent and respect between couples are called for. Ultimately healthy sexuality is much more than mere intercourse and is based on a biopsychosocial understanding of desires, needs and consequences.

2.3 Changing approaches and needs

Few considerations are vital. For newly married couples or partners who have never been separated before for such prolonged periods, the challenges are much more. The same applies to frontline workers and their partners as the fear, apprehension and stress will understandably be more for them. Complete sexual abstinence (including lack of any form of foreplay) though ideal cannot be considered to be a pragmatic and feasible solution in all [48]. Chronic sexual repression can also

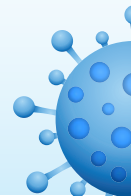


impact self-confidence, sexual performance, increasing the prevalence of anorgasmia, arousal complaints, erectile dysfunction (ED) and premature ejaculation (PME) [49]. Impaired sexual dynamics in the couple can in turn cause loneliness, anxiety, sleep problems and poor coping that further impact resilience and add to the vicious cycle of uncertainty during the pandemic crisis [33]. Besides continued sexual abstinence has shown to impair couple communication and pre-existing psychiatric conditions. It also carries a risk of high-risk sexual behaviours, gambling disorders, alcohol abuse and compulsive masturbatory practices [49, 50]. Cybersex has been the 'new normal' of sexuality with various pornography platforms delivering free premium content during the lockdown. While it helps with safe and anonymous expression of intimacy and deals with uncertainty to some extent, it carries the obvious concerns of socio-cultural acceptance, ease of technology use, risks of data theft, cyber-security threats, risks of sexual extortion, cyber-harassment and cyber-bullying (especially for the minors) (discussed later).

The Lesbian Gay Bisexual Transgender Queer Intersex (LGBTQI+) population is disproportionately affected during this pandemic and their sexual rights compromised. Besides the usual brunt of social stigma, prejudice and financial stressors during the outbreak, social cohesion within their groups is adversely affected by lack of cultural gatherings, PRIDE festivals and travel restrictions which lead to a double-edged 'minority stress' [51]. The various dimensions of this 'othering' during COVID-19 have been highlighted by Banerjee and Nair [52] as social inequality, sexual stigma, stereotyping, gender-based discrimination, marginalization and misinformation about their 'gender roles'. This can lead to multi-faceted effects during the pandemic impairing their psychosocial resilience. In the Love and Sex in the Time of COVID-19 survey, Stephenson et al. [53] explored changes in sexual behaviour and HIV prevention approaches in gay, bisexual and other men who have sex with men (GBMSM). Among 518 participants, the awareness about HIV prevention was high but there was no decrease in the number of sexual partners during the lockdown. High sexual activity was associated with binge drinking and substance abuse. The authors called upon for comprehensive HIV prevention plan for this group utilizing tele-health services. In another qualitative exploration of the lived experiences of older transgender adults from India, social disconnection, stigma, ageism, sexual difficulties and "survival threats" emerged as the main themes [54]. Social rituals, spirituality and acceptance of "gender dissonance" were the predominant coping factors during the pandemic whereas mental healthcare and social inclusion were the perceived unmet needs. In today's world of human-rights based approach to mental health, it is necessary to consider safe, appropriate and free sexual expressions to be integral to psychosexual health and intervention strategies need to be socio-culturally sensitive rather than being moralistic or paternalistic in their approach. The next section deals with various facets of emotional resilience during the COVID-19 pandemic and their crossed paths with psychosexual health.

3. Psychosocial resilience during the pandemics: living through the adversities

Spencer defines resilience as the ability to adapt to stress and adversity adequately [55, 56]. Psychological resilience or simply resilience basically refers to individual psychological, social, environmental, cultural, and physical resources associated with this adaptation [57]. Essentially, it is a dynamic process that protects a person by modifying his/her responses to the stressful life events [58]. Thus, its importance during crisis situations is indubitable. Pandemics comprise of one such situation. Resilience enables a person to stride through the crisis, by maintaining



health and functionality, or by “bouncing back” to the premorbid functioning after the crisis, or by even growing at an individual level afterwards [59]. The complications with pandemics are manifold. They affect the population at large, usually last long as exemplified in the past by Spanish Flu and now by Covid-19, and interspersed with acute exacerbations, thereby limiting the resources in general [60]. There needs to be a constant dynamic interaction between one’s individual resources, environmental resources and stressors for the resilience to develop [61]. There exists literature showing an inverse relationship between psychological resilience and psychological distress in natural catastrophes like earthquake, hurricane, etc. [59]. A number of factors in this current pandemic can be outlined, that are linked to poorer health, social and psychological outcomes. The factors include constant need for safety measures like masks, sanitization, emergence of novel viral strains with uncertainty and fear regarding the future, lack of a rock-solid preventive or curative measure, physical distancing and separation from social contacts and loved ones, home confinement, and financial insecurity including loss of job, to name a few. Hence, the role of developing resilience is all the more important in this context to fight and sail through this situation.

This brings us to the question of how is resilience developed. The answer is simply by enhancing the psychosocial resources, strengthening them, and using them in the process. [62] Certain individual traits like hope, motivation, humour, personal skills are shown to improve resilience [63]. A recent qualitative study on the frontline healthcare workers during Covid-19 found out that “resilience framework” comprised of “resilient identity” formation by social network, sense of purpose, gratitude, hope, “resilience management” by professional collectivism, problem negotiation, assumption of vulnerable role, and “working through distress” via self-care, risk minimization, peer and social support, lifestyle changes and relationships [64]. Across literature, the role of social and interpersonal relationships has been emphasized in strengthening resilience. Perceived family support, organized family dynamics, peer support, support from a significant other are found in two studies as predictors of greater resilience during Covid-19 [65, 66]. Social support encompasses not only the size but also the quality of social network, social connectedness being an integral component. Social connectedness is shown to be associated with lower perceived stress in a study on the Austrian citizens [67]. Sexuality, as a concept, embraces intimacy, pleasure along with physical sexual interactions [68]. Positive sexual health as highlighted by Pennanen-Iire et al. (2020) confers emotional and psychological benefits [33]. While regular sexual interaction with partner improves both physical and mental health, the intimacy aspects also enhance sense of belonging, security, hope, mood, well-being, and ultimately resilience.

4. Sexual health and emotional resilience

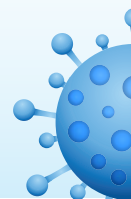
In this section, we elaborate the link between psychosexual health and resilience. The World Health Organization (WHO) defines sexual health as “a state of physical, emotional, mental and social well-being in relation to sexuality; it is not merely the absence of disease, dysfunction or infirmity. Sexual health requires a positive and respectful approach towards sexuality and sexual relationships, as well as the possibility of having pleasurable and safe sexual experiences, free of coercion, discrimination and violence” [68, 69]. Expression of sexuality impacts people’s day-to-day lives and improves general well-being [70]. To begin with the components of sexuality, that includes both physical and emotional aspects of sexual interactions and interpersonal bonding, let us discuss the role of touch.



“Touch” is a fundamental facet of interpersonal connectedness and sexual encounter. It is known to give rise to positivity and bonding [71]. Social touch can include expressions of intimacy, expectations, care, well-being, and mood [72]. Social touch is closely related to affective modulation via release of oxytocin, vasopressin, mu-opioid receptor stimulation, stimulation of coupling between ventromedial prefrontal cortex (vmPFC) and periaqueductal gray (PAG). Sexual touch implicates other areas as well, like anterior cingulate cortex (ACC), limbic system, nucleus accumbens (NA), and PFC [72]. There is also a role of serotonin on the positive affect of affiliative touch, discriminative affective touch, social dependency [73–75]. Biological studies have found significant role of NA, medial PFC, ventral tegmental area and serotonin on resilience [76]. Thus, it can be said that social and sexual touch improves resilience via biological and psychological mechanisms.

During the Covid-19 pandemic, separation of partners, physical distancing practices, fear of illness have given birth to “touch starvation” or “touch hunger”, which is all the more relevant for frontline workers, infected individuals and alike [72]. This deprivation is seen to be associated with disruption of resilience, and increase in stress and trauma [77]. Chronic touch deprivation is also seen to impede immunity by expediting autonomic activation in response to stress and the adverse effect of covid-19 on the physical system is likely to be enhanced by the pre-existing immune deficit. Poor physical health and sexuality affect each other in a bidirectional way [33, 73]. Sexual activity is seen to have positive impact on the autonomic nervous system, cardiovascular system, cognitive faculty, and immunity [78–81]. Sexually active people, in one study, have been shown to have high salivary IgA antibody levels [78]. Regarding the mechanism of sexual activity in improving mental health, studies postulate a role of hypothalamo-pituitary-adrenal (HPA) axis, endorphins, endogenous sex hormones, oxytocin and prolactin [82]. Role of HPA axis in stress modulation and thus resilience is well-documented in the literature. Behavioral effects of sexual activity encompass improvement in stress, anxiety, negative self-image, poor self-esteem and low confidence [82]. Sex is shown to have positive influence on trust, intimacy, emotion expression and use of mature defence mechanisms [83], and ultimately global well-being. Covid-19 has affected sexual function of individuals at multiple levels, including desire, arousal, orgasm, satisfaction, genitopelvic pain symptoms [11, 33]. Details of the possible aetiology of the different sexual dysfunctions during the current pandemic is beyond the scope of this chapter.

There is an increase in virtual sexual activities and masturbation because of the possibility of disease transmission or lack of cohabiting partner [84]. There are certain other aspects of sexuality that must be reviewed. Relationship dynamics is naturally one of them. Expression of intimacy and relationship dynamics have been affected in this situation due to various reasons. Getting housebound, loss of outside recreational activities, alteration of routine, breach of personal space and lack of private time due to constant presence of other family members, anxiety and stress due to social and economic uncertainty are to name a few [11, 66]. There is evidence of worsening of previously strained relationships due to forced cohabitation and poor social network support, further taking a toll on mental health and resilience of the individuals [85, 86]. A recent study among 789 participants in the U.K. showed that many of them used sex more often to cope during the lockdown as compared to before [87]. However, that was associated with less adherence to social distancing regulations and better emotional comfort. Younger age, living with partners/spouses, and male gender were associated with coping through sexual practices. Thus, it has been emphasized



that maintaining sexual health is important to avoid the secondary health hazards arising out of Covid-19 [33]. More at risk of negative health effects are the minorities like LGBTQ community. Stigma, discrimination, higher risk of immunocompromise and infection, economic constraints, decreased access to healthcare, loss of opportunities of community bonding and connectedness put them at a higher risk of stress and its unfavourable outcomes, hampering resilience [52, 88].

Connectedness is as significant as all other components of sexual health, as mentioned in the previous section. Though individual sexual health encompasses more personal connectedness and bonding with the partner, it does not function as a stand-alone and here social connectedness comes in. Social connectedness leads to social cohesion, strengthening of the “social capital”, positive effects on the mental health and development of resilience [89, 90]. Community-based exercises are now being evaluated to develop community resilience [89], and the significance of community resilience in fighting a global pandemic cannot be overemphasized [91]. The discussion on sexual health is incomplete without talking about sexual rights. Fulfilment of sexual rights is duly acknowledged in by the WHO while defining sexual health [68]. Both inaccessibility and violation of sexual and reproductive health rights have been noticed across many countries during this pandemic, in terms of access to contraception and abortion, cessation of sexual education, sexual violence, etc. [92]. This may lead to increased vulnerability of the individual [93], shacking resilience and health. **Figure 2** depicts the multiple facets of sexual health and their association with psychological resilience.

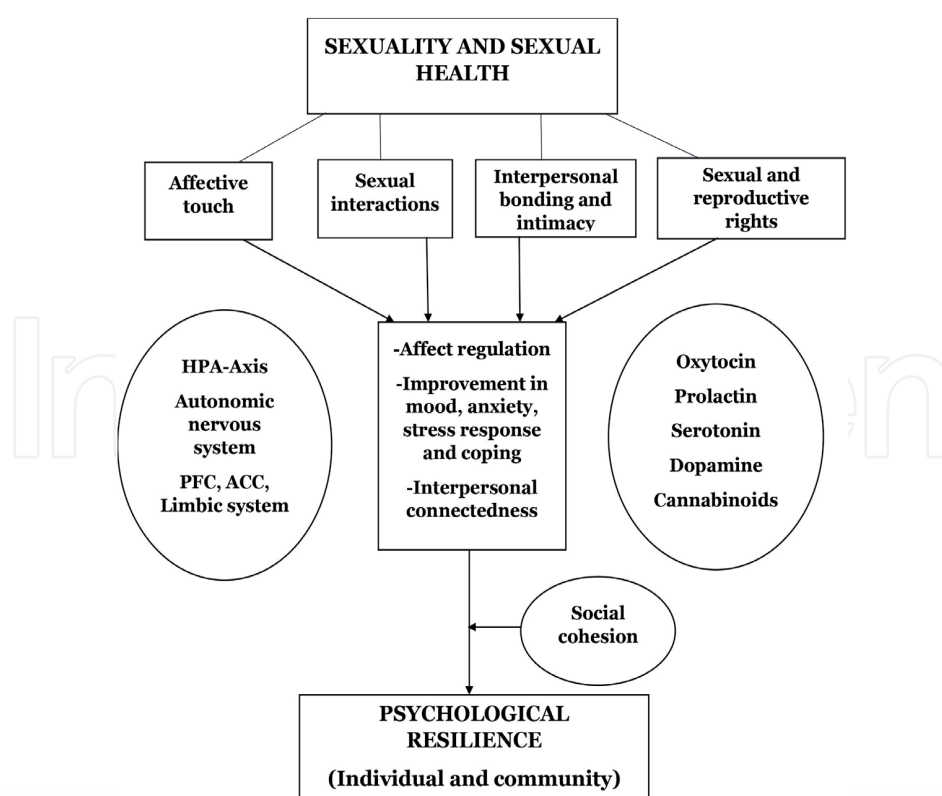


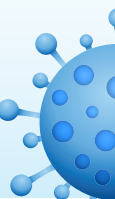
Figure 2.
Associations (neurostructural, physiological and neurochemical) between sexuality, sexual health and resilience.



5. Dealing with uncertainty during crisis: strategies to improve psychosexual wellbeing

Healthy expression and practices of sexuality along with preserved sexual rights help in emotional bonding and resilience. This has been discussed in the previous sections. Nearly after a year of the pandemic, many nations are being threatened at present with the second wave with resurgence of cases and repetition of precautionary measures such as lockdown. The risks of separation, fear of intimacy and re-living trauma of the recent past can further contribute to the uncertainty and worsen psychosexual health. Deprivation of sexual pleasure has been associated with depressive and anxiety symptoms, loneliness, grief, domestic abuse, substance misuse and poor coping with stress, though direct causal relations are poor [94]. Various public health agencies such as the International Society for the Study of Women's Sexual Health (ISSWSH) and Centre for Disease Control and Prevention (CDC) have advocated guidelines for safe sexual practices [95, 96]. Based on the risks involved with COVID-19, relationship dynamics, dating, sexual activities and expressions of intimacy have been modified. Sexuality has increasingly borrowed virtual forums as digital intimacy has emerged as the "new normal". There has been ambiguity related to presence of SARS-CoV-2 in body fluids. Recent studies have detected it in semen [97] but not in vaginal secretions [98]. However, the study samples were small which question the reliability of the findings. Further, the transmission through non-vaginal modes of sexual intercourse is unknown. As mentioned before, complete or partial abstinence is a possible solution, but pragmatically not always feasible. Masturbation and other self-stimulatory practices using sex toys are safe but needs hygienic measures. Few words of caution deserve mention. In the absence of original data, early pregnancy needs to be considered as an at-risk period for possible teratogenicity of the COVID-19 virus [99]. Also, people with medical comorbidities, without vaccination and immunocompromised states need to better avoid sexual intercourse as a preventive measure, especially if the partner has high risk of exposure.

Digitally mediated sexual interactions through the use of technology include cybersex, electronic sex, chat/cam sex, virtual sex, sexting, etc. With time, the broad rubric of cybersex includes digital sex (online sexting, nudes, mutual virtual masturbation) as well as pornography [100]. Expressing love through digital platforms has been termed as "sexual renaissance of the Gen Z" during the COVID-19 pandemic. Long-distance relationships and travel restrictions have further encouraged sexual experimentation (thirst traps of Instagram, sharing nudes, recording the same, digitally sharing pornography, sexting, etc.) [101]. The consumption and free availability of 'premium' pornographic content have been steadily rising during the pandemic-related lockdown [102]. Various NGOs and human-rights agencies have vouched for the safety and rehabilitation of the commercial sex workers which has further led to them adapting the virtual platform, thus bolstering cybersex. Virtual intimacy is a 'two-way path'. It is fraught with various ethical, moral, cultural and legal dilemmas and social acceptability. Besides, it also needs adequate bandwidth and technology mindedness. Nevertheless, it is a safe and anonymous way of exploring sexuality without the risk of STDs, risk of unplanned pregnancies and fear of infections [103]. Besides, cybersex allows for "an appreciable amount of uncertainty and surprise" that allows for sexual experimentation and eroticism [104]. Online fetish concerts, queer sex parties and LGBTQI+ Pride festivals have been arranged over digital media. However, besides the virtual exploration being devoid of "up close and personal touch" that is restricted during pandemics, it also runs the risk of online extortion, cyber-bullying, cyber-fraud, cyber-security threats, revenge pornography, online sexual harassment, dating scams, and online stalking. This is of



special concern in children and adolescents and has various ramifications based on the legal systems of different countries [105]. Digital sexuality cannot be discussed without talking about the changing ‘faces’ of digital intimacy. Watson et al. [106] has shown that digital modes of contact are being used more frequently now to overcome the problem of physical distance. Video-chat, and phone-call are seen to be most commonly employed method to stay connected. As a midway between the physical closeness and physical distancing imposed during the COVID-19 pandemic, digital intimacy can play an important role, thereby giving expression to the emotional and sexual needs of the people [107]. Doubtlessly, there are many caveats while implementing safe and healthy digital intimacy, including digital theft, inaccessibility of the medium, or lack of knowledge regarding the use [103]. Yet it can be considered as the need of the hour for bonding between partners. Though digital expression of love is unconventional and has not been encouraged socio-culturally [103], the pandemic may pave the path towards a paradigm shift in the concept of intimacy and sexuality all across the world.

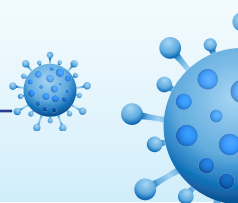
The CDC recommends a minimum distance of 6 feet to prevent viral transmission, which precludes any form of personal intimacy [96]. However, the risk assessment needs to be personalized with mutual consent of the partners/couples. Informed decision making about the frequency, mode and duration of sexual activity should be an informed decision rather than based on misinformation (see the guidelines in **Table 1**). For example, kissing, hugging, fondling, touching and intercourse can be allowed in couples who are asymptomatic, have been practicing precautions and do not have a recent-history of high-risk contact [46, 95, 107]. However, it is important to bear in mind, that nations with a high case-load and rapid rise of cases may have significant number of asymptomatic carriers, the risk of which cannot be neglected. If any of the partners is symptomatic, CDC clearly

Aspects of sexuality	Specifics	Attributes/recommendations
Couples/partners	Solitary activity	<ul style="list-style-type: none"> • Abstinence • Masturbation • Pornography use
	Living together	<ul style="list-style-type: none"> • <i>Sex recommended:</i> with asymptomatic or equally high-risk partners, • For partners with comorbidities: sex only recommended if both of them reside at home • Contraceptive practices for recreational sex • <i>Sex to be avoided:</i> Symptomatic partner and those in quarantine after exposure
	Not living together	<ul style="list-style-type: none"> • Cybersex • Digital intimacy • Pornography
	New partners	<ul style="list-style-type: none"> • In-person sex need to be avoided • Cybersex
	Pregnancy	<ul style="list-style-type: none"> • Possible risk of teratogenicity • More adverse effects of infection
	Individuals with HIV and other STDs	<ul style="list-style-type: none"> • Added protective measures • Sex recommended: only if quarantined together and asymptomatic (with required precautions) • Prioritize PEP

Aspects of sexuality	Specifics	Attributes/recommendations
Sexual interactions	Kissing	• Only in healthy and unexposed couples
	Oral sex	• Only in healthy and unexposed couples
	Vagina intercourse	• Can be allowed
	Anal intercourse	• Allowed, provided faeco-oral transmission can be avoided
	Masturbation	• Safest
	Digital sexual practices	• Safe alternatives: Erotic conversations, mutual masturbation, chat rooms, sexting, cybersex, video dates, nudes, etc.
Sexual disorders and dysfunctions	Basic principles	<ul style="list-style-type: none"> • Stress, uncertainty and panic will increase the disorders • Mental health problems (depression, anxiety, PTSD, etc.) will increase the disorders • Contributed by domestic violence • Treatment need to be prioritized • Tele-counselling • Public awareness about safe sexual practices guidelines during the pandemic • Increase safe home confinement in couples, foster emotional bonding and quality time
	Discrepancies in sexual pleasure/desire	<ul style="list-style-type: none"> • Fear and death anxiety can contribute to differences in sexual interest and perceived pleasure • Chronic stress • Physical distancing
	Erectile dysfunction	<ul style="list-style-type: none"> • Highest risk in older men, frontliners and those with comorbidities • Sensitive to socio-economic stressors • Poverty and stigma • Substance abuse
	Orgasmic disorders	<ul style="list-style-type: none"> • Increased performance anxiety • Reduced perceived sexual pleasure • Anxiety, low mood, irritability, sleep problems, panic due to the pandemic
	Penetration disorders	<ul style="list-style-type: none"> • PTSD, fear of illness and prolonged home confinement due to lockdown • Lifestyle and dietary changes (obesity) • Lack of privacy • Interpersonal discord in couples
Miscellaneous		<ul style="list-style-type: none"> • Mutual respect and consent in couples • Informed decision making • Fighting misinformation and sexual myths • Emotional support • Enjoying quality time • Open and direct communication • Facilitate "COVID-free" time • Seek professional help (couple therapy, sex therapy, IPT, etc.) when needed

PTSD: Post Traumatic Stress Disorder; IPT: Interpersonal Therapy; HIV: Human Immunodeficiency Virus; STD: Sexually Transmitted Diseases; PEP: Post-exposure prophylaxis.

Table 1.
Suggested recommendations for safe sexual practices in various groups during the COVID-19 pandemic.



recommends self-quarantine without any form of intimacy or bedroom sharing for at least 7–14 days after the symptoms have started, or till full resolution of symptoms, or at least being fever-free up to 72 hours without any medicines [96]. A safe approach is to self-quarantine with partners if exposure has already occurred. This involves an acceptable amount of risk with the benefit of physical proximity and support. Adequate testing and treatment are necessary in all cases after proper professional guidance. This is especially vital in couples who have newly entered relationships, are exploring sexuality, have been physically distanced soon after marriage or any/both of them are frontline workers [107]. Adequate precautionary measures, hygiene and risk assessment are necessary in the latter. Adequate contraceptive measures and understanding of the reproductive risks are essential in the sexually active population [95, 107]. Indiscriminate sexual activity and in-person sexual experimentation are better avoided as it involves HIV and other STDs, that can further compound the risk and course of COVID-19. Frequent digital contact between distanced couples has been shown to improve emotional bonding and perceived sense of support. **Table 1** provides a summary of various attributes and recommendations for safe sexual practices during the ongoing pandemic. This is based on all the available guidelines discussed above.

Eventually, resilience is not just about physical proximity and sexuality is not merely about intercourse. Closeness is a process that helps navigate through adversities building up emotional support. As per Banerjee and Rao [37], “communication is the key and informed mutual decision-making” help relationships. The authors also highlight the brighter side of the lockdown when the long-due time of closeness with partners and families has eventually come to reality [107]. This quality time can be spent to “generate love and intimacy, to mend strained relations, and fostering new avenues of trust and hope.” [107] There can be perceived differences in sexual satisfaction between the couples with change of lifestyle and working patterns during the pandemic, and these discrepancies need to be sorted out mutually, and if needed, with professional help. Eventually social cohesion within family calls for understanding differences, respecting gender rights, open and direct communication and informed decision making. The process of sexuality is no different [108]. Besides, there can be socio-cultural adaptations of the guidelines related to sexual practices during the pandemic.

Sexual activity has a positive effect on mental state, cognitive abilities and immunological responses, and needs to be advocated for cohabiting couples during the outbreak [33, 107]. The authors propose that considering the well-researched benefits of sexuality on physical health and psychological resilience, safe sexual interactions need to be facilitated rather than discouraged by all health agencies and professionals to tide over the uncertainty and crisis of these troubled times. Sound sexual health between couples is indeed one of the ways to foster bonding, improve relationships and strengthen support, all of which help positivism and coping during stress [10]. Relationship conflicts and discord are common during these times, and impaired sexual relationships often form a responsible link. Of special mention are people with pre-existing sexual dysfunctions which can get exacerbated due to the fear, change in arousal patterns, altered frequency of sexual encounters, behaviour of their partners and physical distancing [109, 110]. Performance anxiety can be heightened thereby triggering premature ejaculation and erectile problems. On the other hand, increased prevalence of psychiatric disorders like depression, anxiety, PTSD, insomnia, etc. can in turn worsen sexual dysfunctions especially erectile dysfunctions and anorgasmia [110]. The central tenet remains: with social distancing and home confinement, couples need to discuss, decide and agree upon safe and practical ways to foster healthy sexual practices among them to stay connected, resilient and tide through the adversities.



6. Conclusion

The ongoing COVID-19 pandemic and consequent precautionary measures have several long-term implications on sexuality, sexual practices, relationships dynamics, and emotional interactions between couples. The frontline workers, socio-economically vulnerable groups, individuals with psychiatric disorders and sexual dysfunctions, age and sexual minorities are at more risk. Uncertainty and fear of infection are the two persistent factors during this pandemic which has impacted sexuality besides other psychosocial outcomes. Research into the sexual effects of COVID-19 is however still in its infancy. It is known that preserved psychosexual health leads to better coping and resilience but the processes underneath need to be explored during the outbreak. Both population-based longitudinal studies and qualitative methods to understand the lived sexual experiences of cohabiting and long-distance couples are necessary to develop tailored interventions. Safe sexual practices have been recommended in the guidelines including digital intimacy, but their real-life implementation remains challenging. Couple therapies, family therapies, sex therapies, interpersonal therapies and supportive work can help bolstering healthy sexual relationships during these uncertain times of COVID-19 to build resilience both during and after the post-pandemic aftermath.

Conflict of interest

None.

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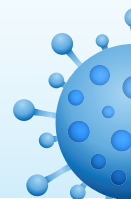
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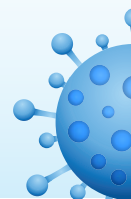
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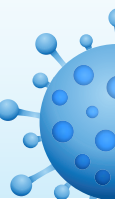
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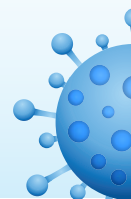
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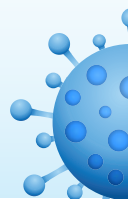
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10. Preventive Strategies

SI No	Title	SDG IMPACT
84	Mask – A Ubiquitous Symbol of COVID19 Scuffle, Dr Pushpa N.B., Kumar Satish Ravi, National Journal of Clinical Anatomy, 10, 1-4, 2277-4025	Goal 3: Good health and wellbeing
85	Obesity, COVID19 severity, and yoga, Dr. Prasanna K. Santhekadur, International Journal of Health & Allied Sciences, 10, 184-185, 2278-4292	Goal 3: Good health and wellbeing
86	A review of the management and safe handling of bodies in cases involving COVID-19, Dr Smitha Rani, Medicine, Science and the Law, 0025-8024	Goal 3: Good health and wellbeing
87	COVID-19 Vaccine Development, Trials and Tribulations, MrsJuny Sebastian., Dr Ravi M.D., Dr Pramod Kumar T M, Indian Journal of Pharmaceutical Education and Research, 54, 457-463, 0019-5464	Goal 9: Industry innovation and infrastructure Goal 3: Good health and wellbeing
88	Evolving potential vaccine candidates amid COVID-19 pandemic: Pipeline to Lifeline, Anshu Kumar Yadav., Dr Akila Prashant., Dr Prashant M. Vishwanath., Surinder Singh., Nirmal Kumar Ganguly, International Journal of Research in Pharmaceutical Sciences, 11, 1323-1333, 0975-7538	Goal 9: Industry innovation and infrastructure Goal 3: Good health and wellbeing
89	The Current Status and Challenges in the Development of Vaccines and Drugs against Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2) Narasimha M. Beeraka , 1,2 SubbaRao V. Tulimilli , 1 Medha Karnik , 1 Surya P. Sadhu , 3 Rajeswara Rao Pragada , 3 Gjumrakch Aliev , 2,4,5,6† and SubbaRao V. Madhunapantula 1, BioMed Research International Volume 2021	Goal 9: Industry innovation and infrastructure Goal 3: Good health and wellbeing



Mask – A Ubiquitous Symbol of COVID-19 Scuffle

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INTRODUCTION

COVID 19 pandemic, the first major global catastrophe of this measure in 100 years, had devastating effects on humanity. The SARS-CoV2 virus of the Coronavirus family responsible for COVID-19 spreads from person to person through small respiratory droplets.^[1,2] The virus colonizes the mouth, nose, and oropharynx of the infected persons gets expelled out when they cough, sneeze, speak, or breathe heavily. These expelled small aerosols are likely to be inhaled and picked up by persons in close contact, especially when <1 m apart. An exposed person can pick up the infection by three possible mechanisms of respiratory pathogen transmission. Transmission can occur through self-inoculation after contact with droplets that settle on surfaces, direct deposition, or inspiration of infectious droplets in the mouth or nose, and deposition on the eyes, as well as through airborne transmission with inhalation of aerosols. Short-range (<2–3 m) aerosol transmission can be difficult to separate from droplet transmission, and long-range transmission for viral respiratory pathogens, including influenza and coronaviruses, remains controversial.^[3,4]

Apart from spreading through aerosols and droplets, COVID 19 is also thought to spread via touching the contaminated surfaces, fomites, etc. However, this is not the common mode of large-scale transmission as in the real-life scenario, the number of viral particles available on contaminated surfaces to transmit infection is much less. This was proved in a study in which the authors tried to mimic actual conditions in which a surface might be contaminated by a patient, no viable SARS-CoV was detected on surfaces.^[5]

Since WHO and Centers for Disease Control and Prevention are yet to identify or endorse any specific or definitive treatment regimens, preventive measures such as maintaining physical distance, use of face cover (mask), hand hygiene, and good ventilation play key roles in helping a person to keep himself safe from COVID-19.^[6]

Handwashing alone can decrease the risk of viral transmission by 55%. A mask can reduce the risk by 68% and with aforesaid measures combined with wearing gloves, risk can be further reduced by 91%.^[7] Eikenberry *et al.*, from their model study, also suggested that wearing masks by the general public can

significantly reduce community spread and hence the death toll.^[8]

Wearing of masks can bring down the chances of viruses entering the healthy person as droplets while also reducing the risk of expulsion from an infected person.^[9,10] Hence in this article, we concentrate on respiratory transmission by droplets and aerosols and its prevention by appropriate use of masks.

TYPES OF MASKS

It is essential to be aware of the type of mask to be used in a health-care setting, community setting, and at home.

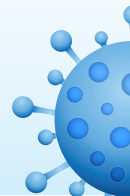
Respirator mask

Respirator masks are designed in such a way that they perfectly fit over the face and there is minimal chance of air escaping from the sides. They were originally designed for people who work in the mining, painting, and construction industries. They provide protection to the wearer against microbes, noxious substances, oil, and gas depending on how tightly the mask is woven and the electrostatic charge incorporated within them. Made of polypropylene material, they are of different kinds based on their ability to resist oil particles. “P” varieties are oilproof and need to be replaced often as pores get clogged by oil particles. They protect all sorts of solid and liquid particles. “R” type is somewhat resistant to oil particles. They also protect against solid and liquid particles. The above said masks are mainly used in industrial settings.

“N” type is not oil resistant. They protect the oil aerosol-free environment. They filter particles that are more than 0.3 μ in size (maximum size of the particle which can pass through the lung). Depending on their efficiency to filter the particulate material, they are called N95, N99, and N100 masks. N95 masks can filter 95% of the particles and N99 and N100 can filter 99% and 99.97% of the particles, respectively. Although coronavirus size ranges from 0.06 to 0.14 μ , they are easily trapped within this mask due to the exhibition of Brownian movement.^[11]

Medical mask/surgical mask

Use of surgical masks dates back to the early 1990s. Initially, they were worn by surgeons to prevent contamination of open



wounds of patients. Often referred to as a face mask, they do not cover the whole face. Surgical masks are meant to protect against large particle droplets, splatter/splashes. They reduce the risk of exposure to the other person from saliva and respiratory secretions that contain microbes expelled from the wearer to the immediate environment and also remind the wearer not to touch his/her mouth and nose, which, in turn, can transfer microbes from contaminated surfaces. Due to their loose-fitting nature and inability to filter very small particles, they do not provide protection against viruses and bacteria expelled out during coughing and sneezing.^[12]

Surgical masks are made of paper or nonwoven material; hence, they are intended to be used only once and to be properly discarded after usage.^[13] They are made of three layers, a melt-blown polymer (usually polypropylene, which acts as a filter and prevents penetration of pathogen in both directions), placed between nonwoven fabric. The outermost layer helps in repelling fluid droplets from the environment, whereas the innermost layer acts as an absorbent and traps the droplets from the wearer. To increase the surface area, to enable the wearer to cover themselves properly from nose to chin, they have been provided with pleats. These masks can be secured via head ties, ear loops, or elastic straps.^[14]

Medical/surgical masks, to be called so, should have a minimum of 95% filtration rate with a droplet size of 3 μ and they are tested for American Society of Testing and Materials (ASTMs) five basic criteria, which are flammability, bacteria filtration efficiency (BFE) *in vitro*, breathing resistance, particle filtration efficiency, and splash resistance.^[15]

Nonmedical mask

With the nonavailability of vaccines and proper treatment regimens, it is essential to follow preventive measures in the war against the new pandemic even at the community level. More than 50 countries in the world have made wearing masks compulsory in public spaces. Since every individual cannot avail and afford N95/medical masks, there is a huge requirement of easily available and affordable masks. Fabric/cloth masks meet the aforesaid criteria. Although they are not as effective as N95/medical masks, they help the person wearing it from contracting the infection in crowded places where social distancing is difficult to maintain. Ideally, it should have three layers of cotton/linen fabric. Two layers are tightly woven and the middle layer is a filter type fabric, preferably nonwoven polypropylene fabric. They can be prepared with a wide variety of materials available [Figure 1] and it has been established that a double layer of 100% cotton fabric is 70% effective in seizing minute particles. The best household materials are pillow covers and 100% cotton T-shirts. It is worthy to note that the doubling of masks increases the pressure drop and makes breathing difficult. The main advantage is that they can be washed and reused.^[16] A manual has been released by the Ministry of Health and Family Welfare, Government

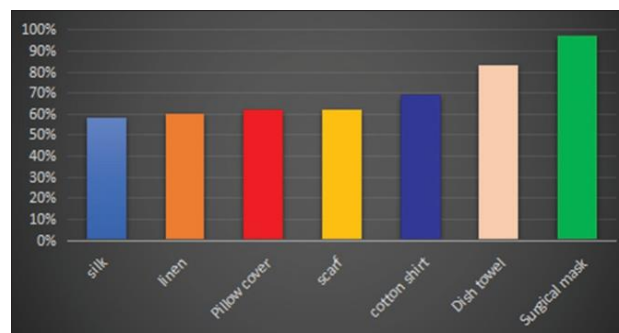


Figure 1: Showing the effectiveness of masks made with different material

of India, on how to make fabric masks at home using easily available cotton fabric as well as the methods of washing and sanitizing them.

Vander Sande *et al.* in their experiments showed that both long-term protection (3 h) and short-term protection were best by filtering facepiece [FFP]-2 against particles, an N95 equivalent compared surgical and homemade mask. Not only the kind of fabric but also the design, fitness to the user's face, type of particle, and the velocity of exposure determine the efficiency of a homemade mask.^[17]

Therefore, while homemade masks may not eliminate the disease, they can significantly control the transmission of disease in the light of a shortage of surgical/N95 masks.^[7,18]

DECONTAMINATION

The prolonged pandemic has inevitably resulted in a sudden surge in the requirement of masks, compelling the use of masks judiciously. While N95/surgical masks are a must for frontline health workers, reusable masks can protect the general public to some extent from infection. Acute shortage and absolute unpreparedness had compelled many nations to adopt desperate measures to decontaminate and reuse N95 masks. Decontamination measures include the use of hydrogen peroxide, ultraviolet (UV) rays, ethylene oxide, heat, and steam.^[19,20]

A recent study showed that the SARS-CoV-2 virus can remain infectious on the outer layer of the surgical mask even after 6 days.^[21] Besides, even accidentally touching a surface for as little as 5 s can result in the transfer of some quantity of the infectious microbes to the hands. Disinfection of masks, especially reusable ones, is therefore crucial. Cloth masks may be disinfected by washing with detergents and bleach, whereas surgical and N95 masks can be best disinfected via hydrogen peroxide followed by UV or heat treatment.^[22-24]

CHILDREN AND MASK

It is observed that all masks are less efficient in protecting children when compared to adults.^[25] Children under 2 years



should not wear masks and those between the age of 2–5 years can wear under proper supervision. According to WHO and UNICEF, older children are expected to wear masks based on the severity of virus transmission in the locality or if they are living with elderly and seriously ill patients. Children over 12 years of age are expected to wear masks like that of adults.^[17]

SAFETY CONSIDERATIONS

The negative effects of wearing masks in otherwise healthy individuals are negligible. Masks are effective only if worn properly. It does not interfere with tidal volume, oxygen, and carbon dioxide concentration in the blood. Often observed negative impact with prolonged use of masks is an increased frequency of development of headache in individuals with a known history of headache.^[26]

Failure to cover the nose and mouth up to the chin will enable the wearer to get exposed to/expel the respiratory droplets. Hanging the mask from the ears, wearing on the chin, and sharing with others should be avoided. Repeated use of soiled masks should be avoided. In the case of single-use masks, they should be disposed of properly after use.^[27]

With the emergence of a second wave of the pandemic, identification of new strains of SARS-CoV-2 and proper preventive measures are crucial to help protect people from the virus. Dreading the loss of approximately 80,000 doctors in due course of time after 5 years, the National Medical Commission has recommended the commencement of MBBS (Bachelor of Medicine and Bachelor of Surgery) classes for the current session from February 1, 2021. It is necessary to take all the preventive measures during this pandemic. In this regard, as stated before, along with proper hand hygiene and social distancing, use of face mask can contribute significantly in reducing disease transmission, thus making it a new norm of daily life. It is not only a matter of protection or prevention as, in the era of consumerism and a complicated human psyche, but the social and psychological impact also cannot be ignored.

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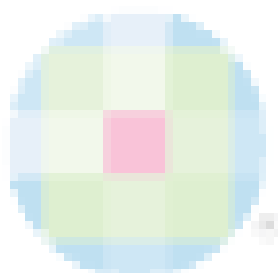
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Obesity, COVID-19 severity, and yoga

Sir,

Obesity has emerged as a master mediator of almost all the inflammation-associated diseases including metabolic syndrome and cancer. Advanced and sedentary lifestyle and the global impact of Western dietary habit created the huge amount of obese population each and every corner of the world. Therefore, obesity is the most common health problem of the 21st century. The sudden resurgence of the global pandemic of severe acute respiratory syndrome (SARS)-COVID-2 and associated COVID-19-related panickiness has led to overnight increase in depression and depression-associated obesity.^[1] Depreobesity has already creating huge disturbances in health status of the normal population as well as already suffering obese population. Home confinement and quarantine have led to frustration, several psychobehavioral problems mainly depression and depression associated over eating habit, consumption of high-calorie diet, which led to further increase in obesity cases.^[2] This post-COVID-19 depreobesity as well as pre-COVID-19 obesity both have a negative impact on SARS-COV-2-infected COVID-19-positive patients health status at this point of time. Many of the recently published studies have clearly established a strong link between overweight, obesity, and risk of COVID-19-associated deaths.^[3-5] These studies distinctly highlighted the global epidemiological information and have provided useful insights into the relationship between overweight/individuals with obesity and their more susceptibility to the SARS-COV-2 infection as well as the severity of COVID-19 disease using meta-analyses of number of published data. All these studies clearly and directly correlated obesity with the increased mortality rate COVID-19 populations.

It is very well-established fact that obesity is the main cause for metabolic syndrome, and in a recent distinguished study, they have established a strong association with metabolic syndrome and COVID-19-associated mortality.^[6] Therefore, metabolic syndrome is a major risk factor of mortality or disease's severity among COVID-19 patients.^[7] Obesity induces various growth factors, cytokines, and inflammatory markers and cytokine storm is one of the major symptoms of SARS-COV-2 infections during COVID-19 severity [Figure 1]. This cytokine storm involves an uncontrolled release of pro-inflammatory cytokines during the disease and it triggers various cellular signaling pathways and immune mediators simultaneously, leading to many series of pathological events.^[8,9] Proper and healthy lifestyle, healthy

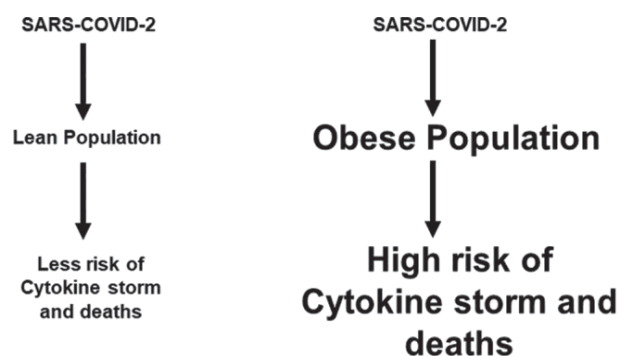


Figure 1: Effect of severe acute respiratory syndrome-COV-2 infection on obese population

dietary habit with good amount of exercise may have beneficial effects on COVID-19 associated deleterious effects. Staying very active, adequate sleeping time, self-health care, coping up with stress and anxiety are very important. Routine meditation and yoga may have additional beneficial effects.^[10] Yoga and meditation have shown huge anti-inflammatory effects and these inflammatory effects are mediated via the downregulation of the nuclear factor-kappa B (NF-κB) transcription factor, which is the master regulator of cellular inflammation and associated signaling pathways.^[11,12] Yoga and meditation not only suppress the NF-κB transcription factor activity but also suppress the cytokine storm, which is triggered by SARS-COV-2 infection.^[13] Therefore, practicing yoga and meditation with other physical activity and exercise may aid during the COVID-19 and also protect every human being from the harmful effects of obesity-associated diseases including this global pandemic of COVID-19.

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Conflicts of interest

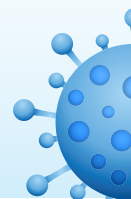
There are no conflicts of interest.

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A review of the management and safe handling of bodies in cases involving COVID-19

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Smitha Rani

Abstract

Wuhan Municipal Health Commission, China, reported a cluster of cases of 'pneumonia of unknown aetiology' in Wuhan, Hubei province in late 2019. The causative organism was eventually identified as a novel coronavirus. Subsequently, the disease spread to more provinces in China, then the rest of the world, and the World Health Organization declared it a pandemic. The virus was named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and the disease was termed COVID-19 (Coronavirus disease). Since then, an increasing number of people have succumbed to this infectious disease. High contagiousness and rapid spread of the disease has been a matter of concern, as it may overburden healthcare systems. Hence, it is vital to implement strict infection prevention and control measures to curb the spread of the disease. This article reviews the guidelines available for the handling of bodies of deceased persons with suspected or confirmed COVID-19, and for their safe disposal. It also provides a summary of recommendations for conducting autopsies in cases where COVID-19 is suspected.

Keywords

Dead body management, COVID-19, autopsy, dead body disposal, funeral guidelines

Introduction

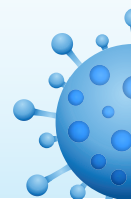
Coronavirus disease (COVID-19) is an infectious disease which was first reported by Wuhan Municipal Health Commission, China, at Wuhan, Hubei province in late 2019.¹ The aetiological agent responsible was termed as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).² Globally, as of 8 June 2020, 6,931,000 confirmed cases of COVID-19 including 400,857 deaths have been reported to the World Health Organization (WHO). Among them, the highest number of confirmed cases has been recorded in the United States of America, amounting to 1,915,712. In India, the total confirmed cases are 256,611 and deaths reported are 7135.³ The case fatality report for COVID-19 is reported to range from 2 to 7%.⁴ As the case fatality rate is dependent on the proportion of deaths from a particular disease compared with the total number of people diagnosed with the disease for a certain period, the above-quoted values must be interpreted with caution. In countries where extensive screening has been performed in the whole population, overall case fatality rates of less than 1% have been reported because the denominator included

many mild or asymptomatic cases. However, in countries where only people requiring hospital admission are screened, case fatality rates have exceeded 5%, because the denominator is much smaller.⁵ With an increasing number of deaths being recorded due to this pandemic, the International Committee of the Red Cross has indicated that deaths caused by COVID-19 could overwhelm local capacity to properly handle dead bodies. It suggested that to overcome this risk, proper preparation and planning is essential so that the dignity of the deceased and surviving family is respected.⁶ While handling mortal remains of COVID-19 cases, balancing the rights of the family and infection prevention and control measures is a crucial factor. This article is a narrative review of the

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currently available guidelines for the safe handling and management of dead bodies in cases involving COVID-19 based on our current understanding of the disease.

Fundamental principles for the management of death related to COVID-19⁷

1. The safety and wellbeing of the staff involved in managing the dead from COVID-19 should be of paramount importance. Hence, implemented protocols should adhere to the advice and latest recommendations from national health authorities and international health organizations, particularly the WHO.
2. To ensure the protection and respect for deceased individuals and their families.
3. To establish the reliable identification of the dead, failing which their proper documentation and traceability are essential for making their future recovery and identification possible.
4. The management of the dead from COVID-19 should not impede the medicolegal investigation of death whenever required by the authorities.

Transmission risk due to handling of bodies with suspected or confirmed COVID-19

There is no evidence so far of transmission of SARS-CoV-2 through the handling of bodies of deceased persons. Although a case of COVID-19 has been reported in a forensic practitioner working in Bangkok, capital of Thailand, there is no scientific confirmation of disease transmission from the corpse.⁸ According to the current evidence, COVID-19 virus is primarily transmitted between people through respiratory droplets and contact routes. In an analysis of 75,465 COVID-19 cases in China, airborne transmission was not reported. Airborne transmission is different from droplet transmission as it refers to the presence of microbes within droplet nuclei, which are generally considered to be particles <5 µm in diameter, that can remain in the air for long periods and be transmitted to others over distances greater than 1 m. In the context of COVID-19, airborne transmission may be possible in specific circumstances and settings in which procedures or support treatments that generate aerosols are performed.⁹ As this is a new virus whose source and disease progression are not entirely clear, more precautions may be necessary until further information becomes available.¹⁰

The potential risk of transmission related to the handling of bodies of deceased persons with suspected or

confirmed COVID-19 is considered low, and can be related to:

- direct contact with human remains or bodily fluids where the virus is present.
- direct contact with contaminated fomites.¹¹

As studies have suggested that the human coronaviruses can remain infectious on inanimate surfaces at room temperature for up to 9 days,¹² there is a possibility that the virus also persists on deceased bodies. Therefore, safety precautions must be adhered to while handling such dead bodies.

Guidelines on the use of personal protective equipment (PPE)

PPE is protective gear intended to safeguard health by minimizing exposure to a biological agent. Components of PPE include goggles, face shields, masks, gloves, coverall/gowns (with or without aprons), head-covers and shoe covers.¹³

PPE for the care of the deceased during the COVID-19 pandemic is listed in Table 1, which is adapted from the guidelines formulated by Department of Health and Social Care, Public Health Wales, Public Health Agency (PHA) Northern Ireland, Health Protection Scotland and Public Health England.⁷

The PPE to be used is based on the risk profile of the healthcare worker. As per the guidelines issued by the Ministry of Health and Family Welfare, Government of India, dead body handling in the mortuary is considered to pose a moderate risk; hence wearing an N95 mask and gloves is recommended. To perform an autopsy, which is a high-risk procedure, it is advisable to wear a full complement of PPE. For transporting dead bodies, wearing a triple-layer mask and gloves would suffice. A triple-layer medical mask is a fluid-resistant disposable mask protecting the wearer from droplets of infectious material. An N95 respirator mask is a respiratory protective device with high filtration efficiency to airborne particles. The filtration capacity of these masks exceeds those of triple-layer medical masks. As these provide a much tighter air seal than triple-layer medical masks, they are designed to protect the wearer from inhaling airborne particles.¹³

Medical masks/respirators such as FFP2, FFP3 or N95 can be used without removal for up to 6 h while caring for a group of patients with COVID-19; however, extended use may increase the risk of contamination with COVID-19 virus and other pathogens. They need to be replaced if they become wet, soiled or damaged, or if they become difficult to breathe through. If the mask is exposed to the splash of chemicals, infectious



Table 1. Personal protective equipment (PPE) for the care of the deceased during COVID-19 pandemic.

Personal protective equipment (PPE)	Low-risk Procedures*: Admission of Deceased/ Preparation for viewing/ Release of deceased	Medium-risk Procedures**: Rolling deceased/ Undressing deceased/ Significant manual handling	High-risk Procedures: Autopsy/Other invasive procedures
Disposable gloves	Yes	Yes	Yes
Disposable plastic apron	Yes	Yes	Yes
Disposable eye protection	Yes	Yes	Yes
Shoe/shoe protection (ideally boots that can be easily disinfected)	Yes	Yes	Yes
Disposable gown	No	No	yes
Fluid-resistant (Type IIR) surgical mask (FRSM)	Yes	No	No
Filtering face piece respirator (FFP)***	No	FFP2 or FFP3	FFP3

*If procedure likely to cause droplet contact, use medium-risk procedure

**If procedure likely to generate aerosols, use high-risk procedure

***ECDC (European Centre for Disease Prevention and Control) recommends the use of FFP3 masks for performing aerosol-generating procedures. In case of shortage of Class 3 respirators, the use of Class 2 respirators (e.g. FFP2) may be considered, on a case-by-case basis and after assessing the risks of the procedures required.

substances or body fluids, or if it is displaced from the face, or if the front of the mask is touched to adjust it, it needs to be changed. Medical mask reprocessing is not advised. Respirators could be reprocessed using methods such as hydrogen peroxide vapour, ethylene oxide or UV radiation lamps; however, these methods are not validated. If cotton gowns are used by health workers, they can be reprocessed by machine washing with hot water (60-90°C) and laundry detergent. If machine washing is not possible, linen can be soaked in hot water and soap in a large drum, and stirred using a stick to avoid splashing. The linen then needs to be soaked in 0.05% chlorine for approximately 30 min. Finally, it should be rinsed with clean water and dried in sunlight. The use of plastic aprons or disposable laboratory coats is not recommended for aerosol-generating procedures. Goggles and face shields can be reused after cleaning using soap or detergent and water, followed by disinfection using either sodium hypochlorite 0.1% or 70% alcohol wipes.¹⁴

Guidelines for packing and transfer of the body from the isolation room, ward or other settings to a mortuary, crematorium or burial ground in non-autopsy cases

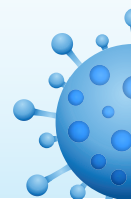
Personnel who interact with the body (e.g. healthcare or mortuary staff, or the burial team) are required to apply standard precautions, including hand hygiene before and after interaction with the body and the environment, and use appropriate PPE according to the level of interaction with the body.¹⁰

All tubes, drains and catheters on the body must be removed. Any puncture holes or wounds (e.g. resulting from the removal of the catheter, drains, tubes, or otherwise) are disinfected with 1% hypochlorite and dressed with impermeable material. It is essential to plug the oral and nasal orifices of the body to prevent the leakage of body fluids. If the family of the deceased wishes to view the body at the time of removal from the isolation room or area, they may be allowed to do so with the appropriate standard precautions.¹⁵

As per the guidelines issued by the WHO,¹⁰ there is no need to disinfect the body before transfer to the mortuary area; also, body bags are not necessary. However, they may be used for other reasons, for instance, if there is excessive body fluid leakage. However, as per the guidelines issued by the Ministry of Health and Family Welfare of the Government of India,¹⁵ the body needs to be placed in a leak-proof plastic body bag. The exterior of the body bag has to be decontaminated with 1% hypochlorite. The body bag is then wrapped with a mortuary sheet, or a sheet provided by family members. The body is then either handed over to the relatives or taken to the mortuary.

If zipped body bags as described are not available, the body can be wrapped in a minimum of two layers of thick, leak-proof plastic sheets, secured with adhesive tapes.¹⁶

All used or soiled linen should be put in a bio-hazard bag, and the outer surface of the bag disinfected with hypochlorite solution. Used equipment should be autoclaved or decontaminated with disinfectant solutions as per established infection prevention control practices. All medical waste must be handled and disposed of following biomedical waste management rules.¹⁵



Guidelines in the context of unidentified bodies infected with COVID-19

Personnel involved in the examination and identification process of human remains known or believed to be infected with COVID-19 are required to wear appropriate PPE. Remains infected with COVID-19 may pose a cross-contamination hazard to unprotected people, hence visual recognition by next of kin should be strictly controlled and should abide by the necessary precautions to be taken, including the wearing of PPE.⁷ In the case of unidentified and unknown dead bodies, samples – i.e. facial and multiple body photographs, fingerprints of both hands, scalp hair with the root by extraction by forceps including the hair bulb for DNA analysis – should be preserved for later identification.¹⁶

Embalming bodies infected with COVID-19

The WHO states that embalming is not recommended to avoid excessive manipulation of the body.¹⁰ At the same time, some jurisdictions have identified that it can be accomplished with the appropriate use of infection prevention and control precautions (including PPE) and avoiding aerosol-generating procedures at all times during the embalming process.^{17,18}

Environmental cleaning and disinfection

Environmental surfaces, where the body infected with COVID-19 was prepared, should first be cleaned with soap and water, or a commercially prepared detergent solution. Surface disinfection with 0.1% sodium hypochlorite with the contact time of 30 min or 62–71% ethanol significantly reduces coronavirus infectivity on surfaces within 1 min exposure time. It is expected to have a similar effect against the SARS-CoV-2.¹²

Personnel should use appropriate PPE, including respiratory and eye protection, when preparing and using the disinfecting solutions, and items classified as clinical waste must be handled and disposed of appropriately according to legal requirements.¹⁰

COVID-19: Funeral guidelines

As per the WHO directive, people who have died with COVID-19 can be buried or cremated. Family and friends may view the body after it has been prepared for burial, as per their religious customs. However, they should not touch or kiss the body and should wash their hands thoroughly with soap and water after viewing. Those tasked with placing the body in the grave, or funeral pyre, should wear gloves and wash hands with

soap and water after removal of the gloves once the burial is complete.¹⁰

Public health recommendations on physical distancing, including avoiding common greeting practices such as hugging and handshakes, apply during funerals and visitation services too. Public Health Agency of Canada recommends a 2-m distance for those observing the preparation of the body, higher than the 1-m minimum suggested by the WHO.¹⁹

Individuals under isolation or quarantine and those who are at high risk of contracting the infection such as children, older people (>60 years old), and anyone with underlying illnesses (such as respiratory illness, heart disease, diabetes, or compromised immune systems) should take measures to ensure that they are physically distancing, or avoid attending the funeral services. Alternatively, death care providers should consider the use of virtual technologies (e.g. telephone, video conference and video recordings) in place of in-person services and gatherings. These technologies allow for broader inclusion and participation, thus improving the bereavement process.¹⁹

Psychosocial considerations associated with death due to COVID-19

Psychologically, the disease can have a tremendous impact on bereaved families, as the time available before cremation is reduced and the number of family members able to attend the funeral is restricted. Insufficient knowledge about how the disease is transmitted and how infection can be prevented has led to the stigmatization of victims and their families, to such an extent that opposition to the burial of the COVID-19 victims has been reported.^{20,21}

Repatriation of dead bodies infected with COVID-19

Given the global public health response to COVID-19, there are currently very few flights available to transport human remains because of travel restriction policies practised within countries affected by the pandemic. As per the Canadian guidelines, human remains identified as those that have died with COVID-19 can be safely repatriated to Canada. In all cases, appropriate documentation must be received with the remains. Two options for repatriation of remains exist for people who were suspected or confirmed to have had COVID-19:

1. the body is cremated, or
2. the body is transported in a hermetically sealed container.



If the remains have been cremated or are transported in a hermetically sealed container, no additional infection prevention and control measures, including PPE, is required by the transportation staff. A screening officer must inform a quarantine officer if there are reasonable grounds to suspect that the human remains arrive in a damaged state (e.g. the hermetic seal appears broken, the container has been damaged, or appears to have been compromised). Quarantine officers and screening officers should follow standard procedures for handling repatriated remains of a person presenting with a communicable disease.¹⁹

Autopsy in suspected COVID-19 cases

Micro-organisms are classified into four hazard groups by the Advisory Committee on Dangerous Pathogens (ACDP) based on pathogenicity to humans, the risk to laboratory workers, transmissibility to the community and whether effective prophylaxis is available.²² SARS-CoV-2 has been categorized as an HG3 (Hazard group 3) organism. Other viruses within HG3 include rabies, poliovirus, dengue virus, hepatitis virus B, C, D and E, HIV 1 and 2.²³

The team performing these post-mortem examinations should ideally include the pathologist, the anatomic pathology technician and a circulator. The presence of a circulator is beneficial but not essential. The circulator assistant carries out auxiliary tasks such as sample labelling. Suitably experienced autopsy pathology trainees (as assessed by senior staff) may be involved in HG3 autopsies with adequate supervision. No specific infection risk to pregnant trainees has been identified; however, they may decide not to undertake autopsy work. Using PPE is vital in such autopsies. Typical surgical masks are not considered to provide sufficient protection. Valved fold-flat and moulded protection masks are over 95% effective and are suitable for use in anticipated COVID-19 cases. Whole-body suits with individual respirators seem to provide almost complete protection, although these are impractical and not necessary.²⁴

Adequate ventilation is needed where HG3 autopsies are being performed, with enough separation from the rest of the mortuary. Natural ventilation with at least 160 l/s/patient airflow or negative pressure rooms with at least 12 air changes per hour (ACH) and controlled direction of airflow when using mechanical ventilation is a requirement.²⁵

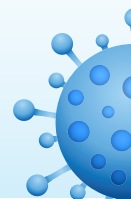
Whole-room ventilation or down-drafts at work stations are acceptable, and the following universal precautions in autopsy dissection practice must be practised:²⁶

- Round-ended scissors and PM 40 blades with blunted points should be used to minimize the risk of prick injuries, and a single practitioner should be operating within the body cavity at any given time.
- Unfixed organs must be held firm on the table and sliced with a sponge. Care should be taken to protect the hand.
- An oscillator saw with suction extraction of the bone aerosol into a removable chamber should be used for sawing the skull; alternatively, a hand saw with a chain-mail glove may be used.
- Needles should not be re-sheathed after fluid sampling. Needles and syringes should be placed in a sharps bucket.
- It is essential to have all necessary equipment to hand, to avoid the need to leave the area to find additional items.

To reduce aerosol-generating procedures during an autopsy, the use of containment devices is recommended whenever possible (e.g. biosafety cabinets for the handling and examination of smaller specimens). High-pressure water sprays should not be used, and if the intestine needs to be opened, this should be done under water.²⁷

If the autopsy is being performed for suspected COVID-19 case, the recommended post-mortem specimen for testing is to collect nasopharyngeal swab and lung swab from each lung. If the diagnosis of COVID-19 was established before death, collection of these specimens for COVID-19 testing may not be necessary. The specimens need to be stored at 2–8°C for up to 72 h after collection. If a delay in testing or shipping is expected, specimens need to be stored at –70°C or below.²⁸

Formalin-fixed and formalin-fixed paraffin-embedded tissue specimens, obtained at autopsy, can be used to establish a post-mortem diagnosis of COVID-19 infection by using immunohistochemical and molecular techniques. The collection of fixed tissues can be particularly important when conventional swab-based testing methods are not available or have provided inconclusive results. A minimum of three representative sections of the lung parenchyma – preferably from different locations – and a minimum of two sections of the airway, to include trachea, bronchi, or both airways should be collected. Tissues collected should be of 5 mm thickness and should be placed in 10% buffered formalin, in a volume that is approximately 10 times greater than the volume of tissue for 3 days for optimal fixation. Serologic tests for SARS-CoV-2 look for the presence of antibodies. It typically takes 1–2 weeks after COVID-19 illness onset for antibodies to develop; in some people this may take longer. Per FDA guidance, antibody tests have not been validated for



diagnosis of COVID-19 infection, and antibody tests by themselves are of limited value in the immediate diagnosis of a patient where COVID-19 infection is suspected.²⁸

One of the effects of the pandemic on medicolegal work, as reported in Italy, is that within 2 months of the outbreak, medicolegal autopsies drastically decreased by 70%. There are a number of possible reasons for this; for example, the system is generally under pressure, there is a lack of protective equipment in some cases, and forensic autopsy rooms may be inadequate and unable to guarantee sufficient negative pressure or other fundamental prerequisites for the safeguard of environmental and operator health.²⁹

Full medicolegal autopsies are therefore not being performed, except in extreme circumstances, and frequently with targeted dissection and percutaneous sampling of fluids, as described in several protocols from across the world.^{16,29}

Conclusion

This article has reviewed the available guidelines for the safe management of bodies infected with COVID-19, to aid body-handlers who are expected to come into contact with them. The guidelines discussed are based on our current understanding of COVID-19 and may change as more information about the disease becomes available. The awareness of the general public regarding safe handling practices will go a long way in preventing and addressing social stigma associated with COVID-19.

Declaration of conflicting interests

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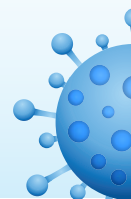
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COVID-19 Vaccine Development, Trials and Tribulations

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ABSTRACT

The coronavirus disease 19 (COVID-19) is a pandemic viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Currently, COVID-19 has affected 210 countries and territories around the world. But there is no clinically approved antiviral drug or vaccine against COVID-19. Governments, private manufactures, academic institutions and non-profit organizations are working hard at a breakneck pace to develop a vaccine for COVID-19. However, vaccine development is very lengthy and expensive process, typically takes many years to produce a licensed vaccine. Because of the high failure rates and cost factors, developers generally follow a linear development sequence with multiple pauses for analysis of data. But in view of the COVID-19 pandemic, development steps need to be executed parallel before confirming the outcome of the previous step. In the current review, we summarize the process involved in the COVID-19 vaccine development and its challenges.

Key words: Candidate Vaccine, Corona Virus, COVID-19 Vaccine, SARS-CoV-2, Vaccine Clinical Trial, Vaccine Development.

BACKGROUND

The coronavirus disease (COVID-19) is an infectious disease caused by the newly identified virus, SARS-CoV-2. The coronavirus family is known to cause illness in humans, from common cold to severe or even fatal diseases such as Middle East Respiratory Syndrome and Severe Acute Respiratory Syndrome (SARS). As COVID-19 is pandemic and spreading globally, there is an increasing demand for vaccines, medicines, personal protection equipments and diagnostics kits and reagents. At this stage, no specific vaccine or treatment is available.¹ The outbreak was declared on 30th January 2020 as a Global public health emergency of international concern. However, many ongoing clinical trials are evaluating potential treatment options and vaccines. Normally, a candidate vaccine

needs to go through pre-clinical stages as well as multicenter clinical trials involving populations across the globe to create large data to prove its efficacy and safety.^{1,2}

Stages of Vaccine Development

Vaccines are one of the most cost-effective public health interventions and therefore, an essential component in the public health. Vaccines are very special as they promote health, protect individuals, communities and entire populations and saving lives rapidly thereby showing their positive impact.³ But the development of a new vaccine is a complex process and takes an average of 10-15 years to establish efficacy, safety and quality.⁴ According to Centre for Disease Control and prevention (CDC) of Dept. of Health and Human services, United States

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of America (USA), there are six different stages for a vaccine development.^{5,6}

1. Exploratory Stage: This is an intensive research phase and is designed to identify the natural or synthetic antigen that helps to treat or prevent a disease. The antigen might be live attenuated, killed or subunits of a particular virus/ bacteria.^{5,6}

2. Pre- Clinical Stage: At this stage, the researchers use a cell culture or tissue culture systems and animal testing to determine the candidate vaccine's expected immunity. Many candidate vaccines fail at this stage because of inadequate immune response or safety issues.⁵⁻⁷

3. Clinical Development Stage: During this Stage, the sponsor of the candidate vaccine submit an application to the regulatory agency of the particular country requesting permission to the conduct the testing in humans. This application is a summary of the findings such as animal study data and toxicity data, clinical protocols for studies to be conducted, manufacturing information, data of any prior human experiments (if any) and information about the investigators. Once the regulatory agency reviews this documents and grant permission, the candidate vaccine must undergo three phases of clinical testing in humans. Additionally, the institute that conducted the study needs an institutional ethical committee approval for conducting the study.⁵⁻⁷

Phase 1: At this stage, researchers test the candidate vaccine in a small group of healthy volunteers to determine whether the vaccine is safe and to determine how it works in the human body. This phase lasts for several months and approximately 70% of the drugs entering this phase move to the next phase of clinical trial.⁵⁻⁷

Phase 2: During this phase, hundreds of human subjects are enrolled with an aim to get more information on safety, immunogenicity, immunization schedule and dose size of the candidate vaccine. This phase lasts several months to two years and approximately 33% the candidate vaccines entering this phase move to the next Phase of the clinical trial.⁵⁻⁷

Phase 3: In this phase, thousands of human subjects are enrolled and it aims to measure the safety and effectiveness of the candidate vaccine. Average time taken for this phase of the clinical trial is 1-4 years and approximately 25-30% of the candidate vaccines entering this phase move to the next stage of the clinical trial.⁵⁻⁷

4. Regulatory review and approval: Once the candidate vaccine successfully completes all the three clinical trial phases, the vaccine developer applies to

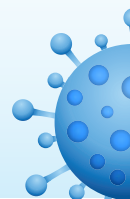
the respective regulator agency to get an approval for manufacture and marketing of the candidate vaccine.⁵⁻⁷

5. Manufacturing: The approved manufacturing units provide proper infrastructures, personnel and equipment necessary to manufacture large quantities of vaccines. The vaccine manufacturers are required to demonstrate that each vaccine batch meets the regulatory requirements as per the tests specified by the respective national regulatory authority (NRA). At this stage, the NRA is also responsible for the release process of official vaccine lots, based on the information and data provided by the manufacturer and confirmatory tests.^{3,5-7}

6. Quality Control: The marketing authorization holders must adhere to the policies and procedures that enable them to track whether the candidate vaccine is having anticipated performance. Post marketing safety studies (Phase 4 Clinical trials) are one way to understand the safety and efficacy of the marketed vaccine. Several thousands of people are enrolled and to try to get more safety information such as rare/very rare adverse events, delayed adverse events and adverse events while administering vaccine combinations.⁵⁻⁷

National regulatory authority is responsible to ensure that the vaccines used within their country is of good quality, of known potency and safe. All these processes are very complex in vaccine development as the public trusts in vaccination programs are key to the success of any immunization programs. A highest standard is expected for any vaccines as the general public has low tolerance for vaccine related adverse events since vaccines are given to a healthy population for prophylaxis purpose compared with drugs which are used to treat sick people.^{3,7}

There are many challenges existing for vaccine development. Vaccine trials often pose ethical concerns. There is a hike in the emergence of various infectious diseases and many vaccines are in pipeline, mostly in the area of Influenza, Malaria, Ebola, SARS and now COVID-19. Pharmaceutical companies are investing money on vaccine research and development by giving preference to vaccine candidates, which are profitable as the average cost involved in a vaccine development ranges from \$600 million to \$1 billion USD. This high cost hinders innovations in the area of biotechnology for vaccine development despite the need of the community. Delay in obtaining regulatory approval also greatly influences vaccine release, as the regulatory authority requires time to review the submitted data.⁸ Generally vaccine development follows a linear pattern of steps that are time consuming. Rapid development requires multiple steps to run in parallel without waiting



for outcomes and therefore the risk of losing money on a failed vaccine is significantly higher. Additional problems occur with trials being conducted during a pandemic such as identifying sites or the ethical problems with placebo control. It would work well if there is an international funding system supporting development, large volume manufacture, fair allocation to high-risk populations and insulating private sector developers from significant financial problems.⁹ The difference between development of vaccines during traditional and outbreak paradigm are presented in Figure 1 (Source: Lurie N *et al.* Developing Covid-19 Vaccines at Pandemic Speed NEJM 2020)

COVID-19 Vaccine Candidates

Currently, in view of the ongoing pandemic of COVID-19, there is lot of interest in developing a vaccine for this disease. Three clinical trials {two from China (ChiCTR2000031781 and ChiCTR2000030906) and one from USA (NCT04283461)} are in clinical trials and 67 are in pre-clinical phase. A Phase 1 clinical trial evaluating an investigational vaccine (mRNA-1273) has begun at Kaiser Permanente Washington Health Research Institute in Seattle. Another vaccine INO-4800 backed by the Bill and Melinda Gates foundation has also entered phase 1 trials in USA. A list of ongoing vaccine development studies is described in Table 1.¹⁰ Different vaccine types of Corona vaccines such as live attenuated coronavirus vaccine, inactivated coronavirus vaccine, S protein-based, vectored vaccines, DNA vaccines and combination vaccines against coronaviruses are in development.¹¹⁻¹⁵

Live attenuated coronavirus vaccines: Attenuating or weakening the wild virus/ bacteria in a laboratory by repeated culturing develops live attenuated vaccine (LAV). The immune response following the administration of LAV is identical to that produced

by a natural infection. As of now, LAV of SARS-CoV are not developed, but the systems are developed to generate cDNA encoding the genomes of CoVs.¹¹⁻¹⁵

Inactivated coronavirus vaccine: Inactivated vaccines are produced by growing bacteria or viruses in a culture medium and inactivating them using high temperature or chemicals such as formaldehyde. The development of inactivated vaccine requires high titers of specific infectious agent (in this case, SARS-CoV-2). This process needs extensive precautions and has some safety concerns especially for production workers. There is also a possibility of incomplete inactivation, which may be a potential public health threat.¹¹⁻¹⁴

Sub Unit Vaccines: Subunit vaccines are developed by growing the whole organism in culture media and then further processing it to purify the components to be included in the vaccine. Subunit vaccines are categorized into three groups: protein-based, polysaccharide and conjugate vaccines.¹¹⁻¹⁵

S Protein-based Coronavirus vaccine: Among all the structural proteins of the SARS-CoV-2, S- protein is the main antigenic component responsible for immune response in a host, neutralize antibodies and/or provide protection against infection. But these S protein-based vaccines may cause a harmful immune response, which may lead to liver damage raising safety concerns about the usage of this vaccine.¹¹⁻¹⁵

Vectored vaccines against Coronavirus: Many research groups reported evaluation of vaccine utilizing other viruses as vectors for SARS-CoV proteins, including rabies virus, chimeric parainfluenza virus, vesicular stomatitis virus etc. results of vectored vaccines further demonstrate the induction of S protein-based Nabs are enough to confer protection.¹¹⁻¹⁵

DNA vaccines against Coronavirus: Results of DNA vaccines for coronavirus demonstrated a strong immune response induction in animal models, specifically in mice. However, data on human subjects are limited.¹¹⁻¹⁵

Combination vaccines: These are also evaluated for the ability to produce immune response to SARS-CoV-2 by administering two doses of S protein encoded DNA vaccine, followed by administration of inactivated whole cell virus. Results of the study showed more immunogenic response in mice than either type of vaccine alone.¹¹⁻¹⁵

Geographical distribution of COVID-19 Vaccine Research and Development: As per Coalition for Epidemic Preparedness Innovations (CEPI) analysis, 46% of developers of active vaccine candidates are in North America, 18% in China, 18% in Asian countries excluding China and Australia and the remaining is in

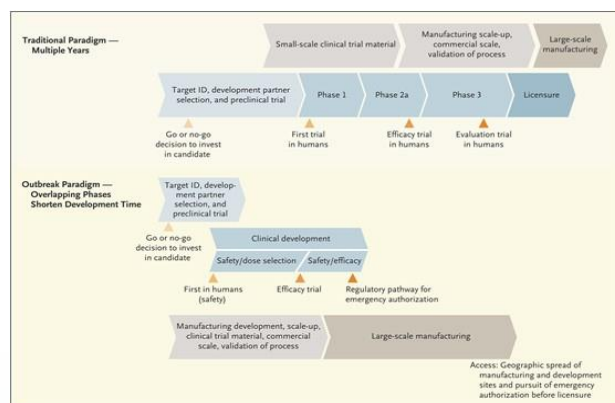
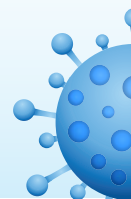


Figure 1: Vaccine development during traditional and outbreak Paradigm.



Table 1: List of COVID-19 candidate vaccines as on 11th April 2020.¹⁰

SI No	Platform	Type of candidate Vaccine	Developer
Clinical development stage – Phase 1 and II			
	Non- Replicating Viral Vector	Adenovirus Type 5 Vector	CanSino Biological Inc. and Beijing Institute of Biotechnology (Phase 2 ChiCTR2000031781 Phase 1 ChiCTR2000030906)
	DNA	DNA plasmid vaccine Electroporation device	Inovio Pharmaceuticals (Phase 1 NCT04336410)
	RNA	LNP- encapsulated mRNA	Moderna/NIAID (NCT04283461)
Preclinical development Stage			
	DNA	DNA with electroporation	Karolinska Institute / Cobra Biologics (OPENCORONA Project)
	DNA	DNA plasmid vaccine	Osaka University/ AnGes/ Takara Bio
	DNA	DNA	Takis/Applied DNA Sciences/Evvivax
	DNA	Plasmid DNA, Needle-Free Delivery	Immunomic Therapeutics, Inc./EpiVax, Inc./PharmaJet, Inc.
	DNA	DNA plasmid vaccine	ZyduScadila
	Inactivated	Inactivated + alum	Sinovac
	Inactivated	Inactivated	Beijing Institute of Biological Products/ Wuhan Institute of Biological Products
	Inactivated	TBD	Osaka University/ BIKEN/ NIBIOHN
	Live Attenuated Virus	Deoptimized live attenuated vaccines	Codagenix/Serum Institute of India
	Non- Replicating Viral Vector	ChAdOx1	University of Oxford
	Non- Replicating Viral Vector	MVA encoded VLP	GeoVax/BravoVax
	Non- Replicating Viral Vector	Ad26 (alone or with MVA boost)	Janssen Pharmaceutical Companies
	Non- Replicating Viral Vector	MVA-S encoded	DZIF – German Center for Infection Research
	Non- Replicating Viral Vector	Adenovirus- based NasoVAX expressing SARS2-CoV spike protein	Altimmune
	Non- Replicating Viral Vector	Ad5 S (GREVAX TM platform)	Greffex
	Non- Replicating Viral Vector	Oral Vaccine platform	Vaxart
	Non- Replicating Viral Vector	MVA expressing structural proteins	Centro Nacional Biotecnología (CNB-CSIC), Spain
	Protein Subunit	Capsid-like Particle	AdaptVac (PREVENT-nCoV consortium)
	Protein Subunit	Drosophila S2 insect cell expression system VLPs	ExpreS2ion
	Protein Subunit	Peptide antigens formulated in lipid nanoparticle formulation	IMV Inc
	Protein Subunit	S protein	WRAIR/USAMRIID
	Protein Subunit	S protein +Adjuvant	National Institute of Infectious Disease, Japan
	Protein Subunit	VLP- recombinant protein + Adjuvant	Osaka University/ BIKEN/ National Institutes of Biomedical Innovation, Japan



	Protein Subunit	Native like Trimeric subunit Spike Protein vaccine	Clover Biopharmaceuticals Inc./GSK/ Dynavax
	Protein Subunit	microneedle arrays S1 subunit	Univ. of Pittsburgh
	Protein Subunit	Peptide	Vaxil Bio
	Protein Subunit	Adjuvanted protein subunit (RBD)	Biological E Ltd
	Protein Subunit	Peptide	Flow Pharma Inc
	Protein Subunit	S protein	AJ Vaccines
	Protein Subunit	li-Key peptide	Generex/EpiVax
	Protein Subunit	S protein	EpiVax/Univ. of Georgia
	Protein Subunit	S protein (baculovirusproduction)	Sanofi Pasteur
	Protein Subunit	VLP- recombinant protein nanoparticle vaccine + Matrix M	Novavax
	Protein Subunit	gp-96 backbone	Heat Biologics/Univ. Of Miami
	Protein Subunit	Molecular clamp stabilized Spike protein	University of Queensland/GSK/Dynavax
	Protein Subunit	S1 or RBD protein	Baylor College of Medicine
	Protein Subunit	Subunit protein, plant produced	iBio/CC-Pharming
	Protein Subunit	Recombinant protein, nanoparticles (based on S- protein and other epitopes)	Saint-Petersburg scientific research institute of vaccines and serums
	Protein Subunit	COVID-19 XWG-03 truncated S (spike) proteins	Innovax/Xiamen Univ./GSK
	Protein Subunit	Adjuvanted microsphere peptide	VIDO-InterVac, University of Saskatchewan
	Protein Subunit	Synthetic Long Peptide Vaccine candidate for S and M proteins	OncoGen
	Replicating Viral Vector	Measles Vector	ZydusCadila
	Replicating Viral Vector	Measles Vector	Institute Pasteur/Themis/Univ. of Pittsburg Center for Vaccine Research
	Live attenuated virus	Measles Virus (S, N targets)	DZIF – German Center for Infection Research
	Replicating Viral Vector	Horsepox vector expressing S protein	TonixPharma/Southern Research
	Replicating Viral Vector	Live viral vectored vaccine based on attenuated influenza virus backbone (intranasal)	BiOCAD and IEM
	Replicating Viral Vector	Influenza vector expressing RBD	University of Hong Kong
	Replicating Viral Vector	VSV vector expressing S protein	IAVI/Batavia
	RNA	LNP- encapsulated mRNA cocktail encoding VLP	Fudan University/ Shanghai JiaoTong University/RNACureBiopharma
	RNA	LNP- encapsulated mRNA encoding RBD	Fudan University/ Shanghai JiaoTong University/RNACureBiopharma
	RNA	Replicating Defective SARS- CoV-2 derived RNAs	Centro Nacional Biotecnología (CNB-CSIC), Spain
	RNA	LNP- encapsulated mRNA	University of Tokyo/ Daiichi-Sankyo
	RNA	Liposome- encapsulated mRNA	BiOCAD
	RNA	mRNA	China CDC/TongjiUniversity/Stermina
	RNA	mRNA	Arcturus/Duke-NUS
	RNA	mRNA	BioNTech/FosunPharma/Pfizer
	RNA	saRNA	Imperial College London
	RNA	mRNA	Curevac
	VLP	Virus-like particle, based on RBD displayed on virus-like particles	Saiba GmbH
	VLP	Plant-derived VLP	Medicago Inc.
	VLP	ADDomer™ multiepitope display	Imphoron Ltd and Bristol University's Max Planck Centre



	Unknown	Unknown	ReiThera
	Unknown	Unknown	BioNet Asia
	Unknown	Unknown	ImmunoPrecise
	Unknown	Unknown	MIGAL Galilee Research Institute
	Unknown	Unknown	Doherty Institute
	Unknown	Unknown	Tulane University

Europe. Developers of COVID-19 vaccine candidates are distributed across 19 countries. Which account for over three-quarters of the world population. No public information is available on the development of COVID-19 candidate vaccines in Latin America or African region.¹⁶

World Health Organization (WHO) Prequalification for vaccines: Candidate Vaccines that are procured by United Nations agencies and for financing by other agencies, including Global Alliance for Vaccines and Immunization (GAVI), require WHO Prequalification. The process of prequalification by WHO assures the quality, safety, efficacy and suitability of vaccine for immunization programs for low and middle-income countries. Hence, WHO encourage the vaccine developers and manufacturers to be aware of the process of prequalification even at the early stages of vaccine development. Licensure by the NRAs, or European Medicine Agency in case of Europe, is required prior to the consideration of prequalification process.¹⁷

CONCLUSION

Currently, the spread of COVID-19 has become a humanitarian and economic crisis. To tackle this crisis, it is very important for multiple professional expert groups from industry, regulators and other global bodies to work together to develop vaccines, get licensee to manufacture and reach population in need. However, considering the time taken for vaccine development, it is likely that no vaccine will be available for another year. Some vaccines were developed relatively rapidly such as the H1N1 vaccine but those for Ebola, Zika and SARS did not. The Ebola and Zika epidemics ended before the vaccine was developed and funding was stopped, causing financial losses to the manufacturers and setting back other vaccine development programs. Hence, researchers also stress the need of strong international coordination and co-operation among vaccine developers, regulators, funders, policy makers, public health authorities and governments to ensure the safe and effective manufacture of COVID-19 vaccine in sufficient quantities, which is accessible to the global community.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

COVID-19: Coronavirus Disease 19; **SARS-CoV-2:** Severe Acute Respiratory Syndrome Coronavirus 2; **SARS:** Severe Acute Respiratory Syndrome; **CDC:** Centre for Disease Control and Prevention; **USA:** United States of America **NRA:** National Regulatory Authority (NRA); **CEPI:** Coalition for Epidemic Preparedness Innovations; **LAV:** Live Attenuated Vaccine; **WHO:** World health Organization; **GAVI:** Global Alliance for Vaccines and Immunization.

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Evolving potential vaccine candidates amid COVID-19 pandemic: Pipeline to Lifeline

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ABSTRACT



Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is globally explored to decode its genomic functionality along with elucidating immunogenic pathways to design and develop an efficient vaccine. Potential immunogenic targets have been screened and validated through preclinical evaluation using experimental models. Computational platform and molecular docking studies are also being conducted to study the immunodynamic mechanisms which involve suitable epitopes of host target cells that respond to the potential vaccine candidate eliciting an immune-mediated reaction. Although SARS-CoV-2 possesses genetic similarities with previously known human coronaviruses, the emergence of novel mutational changes in the immunodominant region of the receptor-binding domain of viral spike protein resulted in high transmissibility and fatality. On a periodical basis, the World Health Organization (WHO) publishes the update on evolving vaccine candidates and encouraging several vaccine developers including multinational companies to join the worldwide campaign against the COVID-19 pandemic. As per the latest WHO landscape draft of evolving vaccine candidates, around 180 teams with respective vaccine candidates across the world are working by utilizing multiple developmental platforms, out of which 35 candidates have entered clinical phase trial and 145 candidates are under the preclinical phase of evaluation. They are also being tested for undesired immunopotentiality without compromising their safety and efficacy. These vaccine candidates along with their advantages and various challenges have been reviewed in this article.

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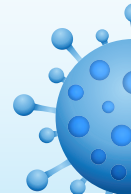
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INTRODUCTION

Viruses have been considered as one of the biological entities responsible for a highly contagious yet infectious form of the disease with the potential to create havoc to human living platforms. Threats of viral attacks are still being recorded as a Public Health Emergency of International Concern (PHEIC) which stimulates international alliances across the globe to prepare for the outbreak, meanwhile encouraging the discovery and development of potential vaccine candidates through solidarity trial. Recently, the entire world is grappling against the viral outbreak, which is a novel form of



human coronavirus (hCoV), COVID-19. Soon after the sporadic outbreak, the virus stepped into cluster transmission and community spread, thereby transmitting across 216 countries following the human chain. Based on the genome sequence of SARS-CoV-2 from several countries, the novel virus appears to be extremely contagious when compared to previous outbreaks of human coronaviruses such as SARS-CoV and the Middle East Respiratory Syndrome-Coronavirus (MERS-CoV) due to mutations in the Receptor Binding Domain (RBD) of one of the Spike protein S1. The S1 subunit is the most variable domain among all the known spike proteins of human coronaviruses (hCoVs) which is also the prominent RBD directly involved in the host-antigen immune reactions. Six RBD amino acids are found to have a critical role in binding to Angiotensin-Converting Enzyme 2 (ACE2) receptors present in the host cells and are different from all known SARS-CoV like viruses which are designated as L455, Q493, F486, N501, S494, and Y505. Out of the six residues, three differ between SARS-CoV-2 (Figure 1) and SARS-CoV, which makes SARS-CoV-2 extremely contagious to humans. The emergence of these novel variations has been attained through natural selection from the reservoir host that was found to be lethal for humans (Wan *et al.*, 2020).

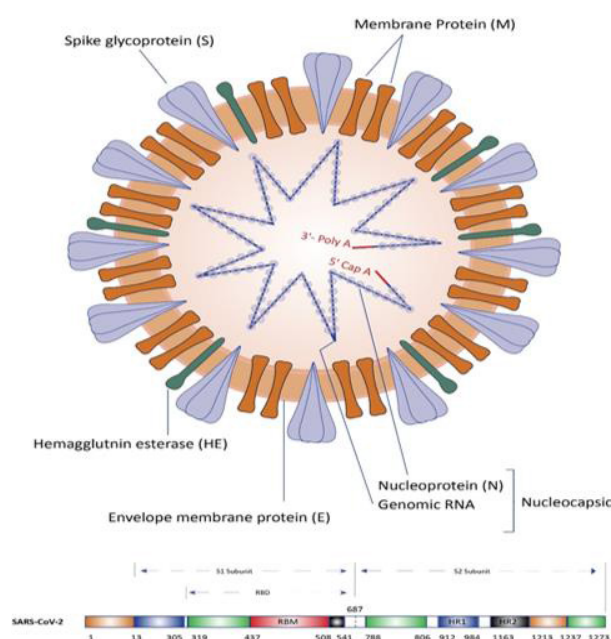


Figure 1: Schematic representation of SARS-CoV-2 structure and Spike protein fragment

A schematic representation of SARS-CoV-2 as depicted in Figure 1 indicates virion, a nucleocapsid composed of positive-sense single-stranded genomic RNA with 5' Cap and 3'-PolyA and phosphorylated nucleocapsid (N) protein within phos-

pholipid bilayer. The viral surface proteins include spike glycoprotein trimer (S), Envelope membrane protein (E), and Membrane glycoprotein (M), which are embedded in a lipid bilayer envelope. The Hemagglutinin-esterase (HE) proteins are located along with other surface proteins in the phospholipid bilayer. The spike protein fragment, which is shown in the figure includes the S1 subunit, S2 subunit, Receptor Binding Domain (RBD), Receptor Binding Motif (RBM), Heptad Repeats (HR) 1 and 2. The site holds antigenicity and a role in eliciting an immune response.

COVID-19: The Need for Vaccines

The outbreak of COVID-19 has triggered scientific communities across the globe for the development of an effective vaccine as well as drugs to manage the disease. As per the latest WHO report updated on 11 September 2020, around 216 countries (territories) are affected with SARS-CoV-2 with total confirmed cases of 2,80,40,853 and confirmed deaths of 9,06,092. To break the chain of transmission and limit the spread towards unaffected regions, interventions in the form of effective vaccines or targeted therapies are in need to combat the COVID-19 global threat. A handful of potential vaccine candidates are in the front line after successfully being tested through different phases of the clinical trial. Yet, several vaccine candidates are still in the pipeline of development utilizing various platforms. To date, no specific and targeted therapeutic module has been approved with international agreement to treat and manage COVID-19 cases.

Multifaceted approaches have been regulated from WHO and concerned authorities to curb the spread of SARS-CoV-2 transmission by isolating positive cases and treating them along with tracing their contacts. Isolating only symptomatic cases was not found to be efficient enough in limiting the spread, since several asymptomatic or presymptomatic cases have been identified as positive with laboratory tests. Same way, high-risk groups such as front line workers, children, geriatric patients above 60 years of age with underlying comorbid conditions must be monitored periodically. Hence, an early and effective vaccine is the need of the time to manage the spread of SARS-CoV-2 and protect from community transmission for saving millions of lives.

SARS-CoV 2-Virus to Vaccine, The most awaiting developmental paradigm

Usually, the development of a vaccine is a long-going process of precisely designed scientific study, including several stages of preclinical and clinical trials that take years to even a decade. The WHO is

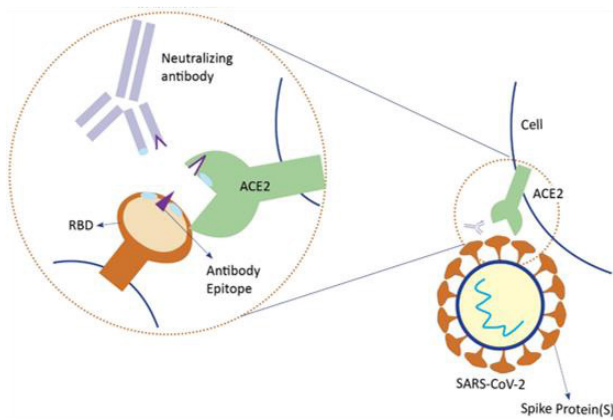


Figure 2: Schematic representation of the interaction between host cell receptor ACE2 and RBD domain of spike protein of SARS-CoV-2 with the production of Neutralizing antibodies

updating the development and progress of several vaccines as a landscape draft on a periodical basis which helps in tracking vaccine trial status. To cope with rapidly spreading SARS-CoV-2, WHO designed “R & D Blueprint for novel coronavirus” which documented a “Large, international, multi-site, individually randomized-controlled clinical trial” to evaluate the benefits and risks of promising vaccine candidates within 3-6 months of trial. As per the latest WHO draft landscape of COVID-19 vaccine candidates update, around 180 vaccine candidates have been registered across the globe to conquer the existing SARS-CoV-2 threat, out of which 35 candidates are undergoing different stages of human phase clinical trials, and around 145 vaccine candidates are in the pipeline of preclinical evaluation.

In the modern history of infectious disease and vaccines, this is the first unprecedented condition when vaccine candidates have entered phase I clinical trials within three months of the outbreak of the virus. The international coalition developed a special strategy to compress the lengthy duration of phase II-III trials from years to months after completing preliminary study from laboratory animals and healthy humans by implementing challenged study which can bypass typical phase III trial (Eyal *et al.*, 2020). To develop the COVID-19 vaccine at a pandemic speed from the limited immunological information available, scientific communities across the world are trying to adapt existing developmental platforms to study possible host responses against various developing vaccine candidates. Several computational study designs based on existing information are being utilized to understand the possible molecular mechanism involved in immunological reactions. Immuno-informatics and molecular docking tools are being used extensively to study

and identify appropriate epitopes that can elicit an immune response so that the same can be used for the development of potential vaccine candidates against COVID-19 (Baruah and Bose, 2020). Several strategies have been embraced in the development of the coronavirus vaccine, out of which surface-exposed spike (S) glycoprotein or S protein is gaining more attention as a potential target that can efficiently induce neutralizing antibodies. Several developmental platforms have been utilized to discover as well as manufacture scalable vaccines for global supply with pandemic speed is described below.

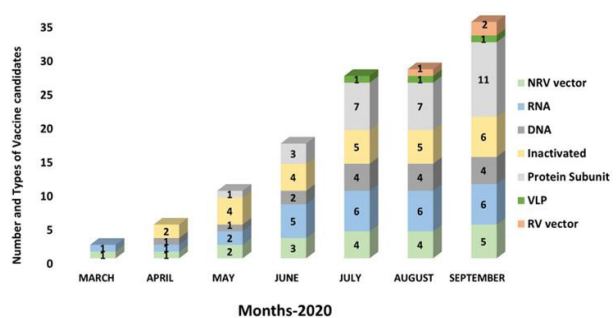
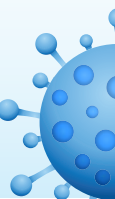


Figure 3: Evolving vaccine candidates for Clinical phase trial- Monthly trend in vaccine development as per the WHO published landscape draft

Whole Virus Vaccines

The category includes live-attenuated vaccines and inactivated vaccines prepared from the whole viral structure. Attenuated whole viruses could be a promising developmental platform for effective vaccines based on its several successful histories in delivering efficient vaccines. Furthermore, it utilizes a novel genetic technique that increases the likelihood to develop comparatively better vaccines despite a high demand to meet global needs. The possibility of working with an inactivated attenuated virus is high due to its feasibility in growing than the wild type virus. A half dozen inactivated vaccines are in the pipeline at different phases of clinical trials, out of which three vaccine candidates are running ahead with phase 3 clinical trial which includes Sinovac, Wuhan Institute of Biological products/Sinopharm, and Beijing Institute of Biological products/Sinopharm (Table 1). The other three vaccine candidates are yet in the middle phase of the clinical trial (phase I/II) which includes the Institute of Medical Biology & Chinese Academy of Medical Sciences; Research Institute for Biological Safety Problems & Rep of Kazakhstan; and Bharat Biotech. There are still 12 vaccine candidates, including both inactivated and live attenuated under the preclinical phase of evaluation. Using live



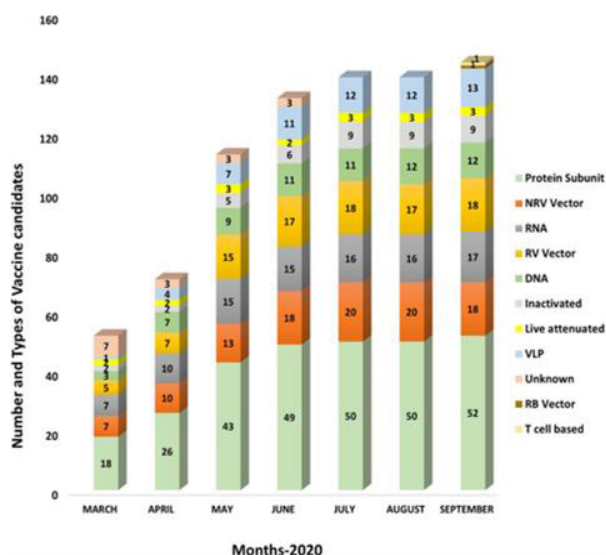


Figure 4: Evolving vaccine candidates for Preclinical evaluation-Monthly trend in vaccine development as per the WHO published landscape draft

attenuated vaccine platform, three developers are conducting preclinical phase evaluation among which Codagenix in Farmingdale, New York, is working in collaboration with Serum Institute of India Pvt. Ltd., an Indian based global vaccine manufacturer, using gene editing principle to weaken SARS-CoV-2. Codagenix has developed a “Codon Deoptimization” technology for viral attenuation which is utilized to explore the COVID-19 vaccine development strategy.

The vaccine named CodaVax-COVID was found to be safe and effective in animal models with a single dose. It is constructed to produce immunity against all SARS-CoV-2 proteins and not just the spike surface protein to elicit a vigorous immune response coupled with long-lasting cellular immunity. Another live attenuated vaccine candidate is in the process of development by Indian Immunologicals Ltd. in collaboration with Griffith University, Australia, adopting codon deoptimization technology. Recently, Bharat Biotech International Limited, an Indian based vaccine developer has developed India’s first indigenous potential COVID-19 vaccine candidate COVAXIN™ in collaboration with the Indian Council of Medical Research (ICMR) using an inactivated vaccine platform. Inherent immunogenicity factor has been one of the significant advantages for whole virus vaccines having the ability to potentiate toll-like receptors (TLRs) including TLR 3, TLR 7/8, and TLR 9. However, live attenuated virus vaccines must be tested extensively to ensure their safe usage (Chen *et al.*, 2020). This is especially an issue with coronavirus vaccines that ren-

ders increased infectivity following whole virus vaccine immunization.

Viral-vector Vaccines

Viruses can be genetically engineered to deliver antigens that can elicit desired immune response inside the host, so-called viral vectors which can be used for the production of vaccines. Viral vector vaccines are presented with advantages over traditional vaccines due to their efficiency in enhancing a wide range of immunogenicity without the application of an adjuvant system which finally prompts a strong cytotoxic T lymphocyte (CTL) response to destroy the virus-infected cells. These vaccines function by supplying the genes to the target cells, highly effective in gene transduction, and efficiently elicit long-term immune response due to high antigenicity, and hence vectored vaccines are more of prophylactic use. The most promising method involves “prime-boost” strategies with other types of vaccines, including DNA vaccines or recombinant antigens. As per the latest WHO published draft, 44 vaccine candidates utilized a viral vector platform in developing both non-replicating and replicating viral vector vaccines, out of which seven candidates are under different phases of the clinical trial.

Four non-replicating viral-vector vaccine candidates are leading ahead with phase III clinical trials, and vaccine developers include the University of Oxford/AstraZeneca, CanSino Biological Inc./Beijing Institute of Biotechnology, Gamaleya Research Institute, and Janssen Pharmaceutical Companies. Around 37 viral vector vaccine candidates are still under preclinical examination that includes 18 non-replicating and 19 replicating vaccine candidates. The University of Oxford in collaboration with AstraZeneca, a UK based multinational biopharmaceutical company, utilized a non-replicating viral vector named AZD1222 derived from the virus (ChAdOx1) which is a deteriorated version of a common cold virus (adenovirus) with the spike coding region cloned into the E1 locus that causes infections in chimpanzees (AstraZeneca, 2020). It contains genetic materials of SARS-CoV-2 spike protein that is genetically modified to make it non-pathogenic towards humans. Due to non-replicating nature, it does not divide inside vaccinated individuals. Yet, it showed a strong immune response from a single dose in an experimental animal which are capable of inducing the human immune system similarly to spike proteins of wild type SARS-CoV-2. CanSino Biological Inc., in collaboration with the Beijing Institute of Biotechnology, has developed a recombinant Adenovirus type 5 vector.

Table 1: Vaccine candidates currently under Phase III Clinical trial

Vaccine platform	Type of candidate vaccine	Route of Administration	Developers/Manufacturer
Non-replicating Viral Vector	Adenovirus Type 5 Vector	IM	CanSino Biological Inc./Beijing Institute of Biotechnology
Non-replicating Viral Vector	ChAdOx1-S	IM	University of Oxford/AstraZeneca
Non-replicating Viral vector	Adeno-based (rAd26-S+rAd5-S)	IM	Gamaleya Research Institute
Non-replicating Viral vector	Ad26COVS1	IM	Janssen Pharmaceutical Companies
Inactivated	Inactivated	IM	Beijing Institute of Biological Products/Sinopharm
Inactivated	Inactivated	IM	Wuhan Institute of Biological Products/Sinopharm
Inactivated	Inactivated + alum	IM	Sinovac
RNA	LNP-encapsulated mRNA	IM	Moderna/NIAID
RNA	3 LNP-mRNAs	IM	BioNTech/Fosun Pharma/Pfizer

In the pipeline of potential vaccine development, another promising candidate from Gamaleya Research Institute of Epidemiology and Microbiology, Health Ministry of the Russian Federation, Moscow is under phase III trial. The candidate named Gam-COVID-Vac is under randomized, double-blinded, placebo-controlled multicentric trial ([Clinical Trials, 2020](#)) Janssen Vaccines and Prevention BV belongs to one of the leading vaccine developers working with non-replicating viral vector vaccine named Ad26.COV2.S reached phase III trial.

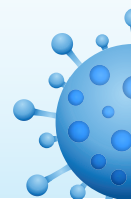
Council of Scientific and Industrial Research (CSIR) funded Indian based Bharat Biotech company in collaboration with Thomas Jefferson University, Philadelphia is conducting extensive preclinical trials in experimental mice and is ready for a human phase trial.

The vaccine candidate was making use of established deactivated rabies vaccine as a mode of delivery for coronavirus proteins which is known to produce a strong immune response to all groups of the population including children and pregnant women ([Biotech and Jefferson, 2020](#)). Another invention of Bharat Biotech in partnership with the University of Wisconsin-Madison (UW-Madison), is CoroFlu, which is based on FluGen's flu vaccine candidate M2SR, which will be incorporated with SARS-CoV-2 gene sequence to develop immunity against

COVID-19.

Subunit Vaccines

These are also called acellular vaccines since they do not contain the whole viral structure. Instead, these vaccines contain only the immunogenic part of the whole virus that might be polysaccharides or surface proteins which are recognized as foreign materials by the host and able to elicit a specific immune response. Although viral subunit vaccines are safe and convenient, yet it shows relatively low efficacy due to the presence of unfavourable epitopes and developers are finding more hopes on protein subunit vaccines since many new studies have been proposed recently, that utilizes the protein subunit as a promising vaccine platform amid COVID-19. Around 63 protein subunit vaccine candidates are in the pipeline, among which 11 candidates are under different stages of phase trials, and remaining more than 50 candidates are still under the preclinical stage of evaluation. Most of them are focusing on the surface-exposed virus's spike protein or S protein for inducing neutralizing antibodies. The S1 subunit serves as the structural scaffold for interaction with host cell receptor ACE2 to induce neutralizing antibodies (Figure 2). Hence, RBD could be a prime candidate for subunit vaccine design, and the S2 subunit of S protein mediates fusion between the virion and host cell membranes leading to the release of viral RNA in the cytosol to initiate replication mech-



anism. During infection with SARS-CoV, the S protein is responsible for inducing protective immunity by stimulating neutralizing-antibodies and T-cell responses. Therefore, full length or a suitable part of S protein could emerge as the most promising vaccine candidate. It has also been reported that neither the absence nor the presence of other structural proteins having the potential to affect S protein immunogenicity or its binding to the ACE2 receptor which is one of the crucial steps for the virus to access the host cell and integrate with the cellular machinery process.

Figure 2 is a schematic representation of the interaction between host receptor angiotensin-converting enzyme 2 (ACE2) with receptor-binding domain (RBD) epitope of the spike protein of SARS-CoV-2 resulting in the production of neutralizing antibodies (NAbs) that blocks binding and fusion of SARS-CoV-2 with host cells and prevents the entry of viral nucleocapsid inside the host cell for subsequent replication, thereby mitigating the adverse consequences due to immune-mediated antigen-antibody reaction. The key residues between RBD and NAb can be identified, which could provide an important implication for the specific vaccines against SARS-CoV-2.

Novavax Inc, a USA-based biotechnology company, developed a protein subunit vaccine that is leading ahead with the late stage of phase II trial. The vaccine candidate NVX-CoV2373 is a full length recombinant SARS-CoV-2 glycoprotein nanoparticle adjuvanted with patented saponin based Matrix-M revealed high immunogenicity in animal models measuring spike protein-specific antibodies (Novavax, 2020). This technology enhances antigen presentation in local lymph nodes and helps in boosting immune response by producing a high titre of micro neutralizing antibodies. NanoFlu, which is a quadrivalent influenza nanoparticle vaccine, which also incorporates Novavax's proprietary saponin-based Matrix-M adjuvant is in its phase II clinical trial in older adults (Inc, 2020). Novavax in coalition with Indian-based vaccine developer Cadila Pharmaceuticals has been working together with virus-like particles (VLP) platform which has been previously used for papillomavirus vaccine.

Moreover, the Mers corona vaccine is in herd phase III of Respiratory Syncytial Virus (RSV) maternal immunization in India. Furthermore, one of the pre-clinical studies from Dynavax Technologies corporation working in collaboration with the University of Queensland, Australia and CEPI (Coalition for Epidemic Preparedness), is trying to develop COVID-19 vaccines by providing its proprietary toll-like recep-

tors 9 (TLR9) agonist adjuvant, i.e. CpG 1018, which is already contained in HEPLISAV-B® [Hepatitis B Vaccine (Recombinant), Adjuvanted], an adult hepatitis B vaccine, initiating the rapid development of a COVID-19 vaccine (Emeryville, 2020; Anges Inc, 2020). Clover Biopharmaceuticals AUS Pty Ltd, a Chinese biotechnology company, is also working in collaboration with GSK and Dynavax for its protein subunit-based coronavirus vaccine candidate SCB-2019 and is currently under phase I clinical trial (Clover Biopharmaceuticals AUS Pty Ltd, 2020). GSK's pandemic adjuvant system AS03 combined with S-Trimer modification over SCB-2019 is developed as a promising candidate that utilized patented Trimer-Tag® technology which has been shown to react with antibodies produced by multiple previously infected COVID-19 patients. S-Trimer developed by Clover resembles native trimeric viral spike protein when analyzed using a rapid mammalian cell culture-based expression system. Another collaborative study headed by Anhui Zhifei Longcom Biologic Pharmacy Co., Ltd in partnership with the Institute of Microbiology, Chinese Academy of Sciences is presently conducting a Phase II trial of its vaccine candidate which is an adjuvanted recombinant S protein (RBD-Dimer) using recombinant DNA technology (baculovirus production). GlaxoSmithKline's (GSK's) adjuvant technology further assists intending to manufacture scalable amount of vaccines amid COVID-19 health crisis (Sano@acts, 2020). There are altogether seven protein subunit vaccine candidates which are under phase I clinical trial from several institutes and/or industries across the globe. In contrast, only 2 to 3 candidates have completed phase I trial.

Nucleic acid Vaccines

These are novel strategies utilized in vaccine development and are composed of purified closed circular plasmid DNA or non-replicating viral vector containing genes that result in the *in-vivo* expression of the encoded protein eliciting both cell-mediated and humoral immune responses. DNA and messenger RNA vaccines are two major types of nucleic acid vaccines that directly get integrated with cellular machinery responsible for protein synthesis such as the viral protein that can elicit an immune response in the form of neutralizing antibodies. Around 40 nucleic acid vaccine candidates are in the pipeline of development, which includes both DNA and RNA vaccines out of which ten candidates are at different stages of clinical phase trials (Figure 3), and around 30 candidates are under preclinical evaluation. RNA vaccine candidates are presently leading ahead in the front line of development, two of which are under phase III trial. In contrast, one of



the RNA vaccine candidates is under phase II trial of development. None of the DNA vaccine candidates has entered clinical phase II trial, but almost 12 of them are in the pipeline of preclinical evaluation (Figure 4).

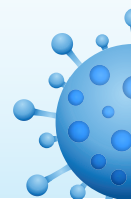
Evolving vaccine candidates amid COVID-19 for clinical phase trial-Figure 3 depicts the monthly developmental updates of potential vaccine candidates at different phases of clinical trials utilizing different platforms. The trending graph indicates progression in the development of the number of vaccine candidates monthly as per the WHO landscape draft. From March 2020, till September 2020, there is a progressive trend in the number of vaccine candidates being included in the clinical phase trial, meantime there is also an increasing trend in the utility of the different possible developmental platforms. In March 2020, only two vaccine candidates entered clinical phase trial utilizing two different developmental platforms which included NRV vector and RNA whereas, in the subsequent months, vaccine developers have taken an interest in utilizing other platforms that included DNA, Inactivated, Protein subunit, VLP, and Replicating viral vector. Recently, vaccine candidates utilizing the protein sub-unit have gained more attention from vaccine developers followed by RNA yet vaccine candidates utilizing the NRV-vector platform, and RNA platform is ahead in the pipeline which started at the earliest and expecting to complete soon shortly.

RNA vaccine is a novel strategy included in the field of vaccine development which works by introducing a synthetic mRNA sequence with a specific length calibrated through the matrix, that is made to code for the disease-specific antigen such as specific viral protein. Once the mRNA strand enters the host cells, it integrates with the host cellular machinery system. It produces antigen which is then displayed on the cell surface inducing acquired immunity to protect against the wild type. RNA vaccines are safe non-infectious, efficient in eliciting reliable immune response with comparatively faster and cheaper scalable production to meet global demand. The explanation for faster approval of the mRNA vaccine is that hCoVs is not being utilized in the developmental work and hence proves to be safely used. (Calina *et al.*, 2020). The RNA molecule trains the cell to synthesize disease-specific antigens which subsequently trains the body to fight against the actual viral antigens. Apart from several benefits, RNA vaccines do possess particular technical challenges, yet the majority of nucleic acid vaccines are based on the mRNA developmental platform. ModernaTX Inc., a US-based manufacturer, is working in collaboration with Biomedical Advanced Research and

Development Authority and the National Institute of Allergy and Infectious Disease (NIAID) for developing mRNA based vaccine candidate (National Institute of Allergy and Infectious Diseases, 2020).

The delivery system, which is a novel lipid nanoparticle (LNP), encapsulates mRNA vaccine candidate that encodes for a prefusion stabilized form of SARS-CoV-2 spike (S) protein. LNPs usually consists of four components which include (i) an ionizable cationic lipid, promoting self-assembly into virus sized particles allowing the endosomal release of mRNA into the cytosol, (ii) lipid-linked polyethylene glycol which increases the half-life of formulation, (iii) cholesterol as a stabilizing agent and (iv) naturally occurring phospholipids to support lipid bilayer. Recent studies demonstrated that LNPs are effective mRNA delivery tools for in vivo studies. BioNTech SE, a German biotechnology company, in collaboration with Pfizer, a US-based multinational company, has developed mRNA-based vaccine candidate 3LNP-mRNAs (Phase II BNT162b1 and Phase III BNT162b2). CureVac, which is also a German-based mRNA company, is developing an mRNA vaccine candidate (CVnCoV) that has entered the phase IIa trial (Curevac, 2020). Imperial College of London, UK, has also developed self-amplifying RNA vaccine candidate LNP-nCoVsaRNA, which encodes for the S glycoprotein of SARS-CoV-2, which is the antigenic viral molecule involved in immune-mediated responses. Indian based Genova Pharmaceuticals has developed an mRNA vaccine that utilizes a patented carrier molecule called Lipid iron oxide (LION) and an adjuvant called GLA-SE.

Evolving vaccine candidates amid COVID-19 for preclinical evaluation- Figure 4 depicts the monthly developmental updates of potential vaccine candidates undergoing preclinical evaluation utilizing various developmental platforms. The graph indicates the monthly trend in the discovery and development of new vaccine candidates approved for preclinical evaluation utilizing several vaccine platforms against the ongoing COVID-19 pandemic. As per the graph, a huge number of vaccine candidates utilizing the protein subunit platform are in the pipeline of development worldwide as per the latest WHO landscape draft published. Initially, at the early phase of vaccine development, protein subunit vaccine candidates were the most preferred platform for preclinical evaluation yet could not enter the clinical phase trial and lag behind NRV vector, RNA, DNA, and Inactivated platforms. In May 2020, one of the protein vaccine candidates first entered phase trial, and now in four months, the platform is most preferred with the highest number of developing vaccine candidates. Apart from



protein subunit vaccine candidates, other platforms gaining interest by vaccine developers include NRV-vector, Replicating viral (RV) vector, and RNA vaccine platforms. Several vaccine candidates using these three innovative platforms are moving ahead to enter clinical phase trials after successful pre-clinical studies. Virus-like particles (VLPs) platform for the development of COVID-19 vaccine candidates has recently gained more attention for vaccine development. VLPs are non-infectious multi protein structures that are engineered to self-assemble from viral structural proteins and could be a promising vaccine candidate with enhanced immunogenicity. The remaining platforms included DNA, Inactivated, and Live attenuated vaccine platforms out of which DNA vaccine platform has been preferred by developers as per the graph indicated. Two more innovative platforms which are Replicating Bacterial vector (RB vector) and T cell-based platforms were choices in developing potential vaccine candidates which include one candidate from each. Overall, there is a progression in the number of vaccine candidates being developed utilizing various platforms and extensive trials across the globe to fight against the COVID-19 pandemic, and the race is still on.

DNA vaccine, otherwise called genetic vaccine, is made up of a plasmid DNA that encodes for the antigen of interest under the control of a mammalian promoter, i.e. Cytomegalovirus (CMV) intron A that can be produced inside the bacterial cells. Inside the host cell, plasmid DNA is presented by antigen-presenting cells (APCs) such as dendritic cells resulting in both humoral and cellular immune response (Coban *et al.*, 2008). Although DNA vaccines suffer lower immunogenicity in higher primates and humans, several studies have been conducted to improve its immunogenicity by modifying the microenvironment of the vaccinated site for boosting its ability to enhance immune-mediated responses. Several DNA vaccine candidates are in the pipeline of development, but until date, none of them has entered phase III clinical trial. Only four DNA vaccine candidates are under the initial stages of clinical trials which are being manufactured by Inovio Pharmaceuticals/International Vaccine Institute, Osaka University/AnGes/Takara Bio, Cadila Healthcare Limited, and Genexine Consortium. Inovio Pharmaceuticals Inc, a US-based leading biotech company in collaboration with International Vaccine Institute, Seoul, Korea, and Coalition for Epidemic Preparedness Innovations (CEPI), are developing a DNA plasmid vaccine candidate with electroporation named INO-4800. INO-4800 contains plasmid Pgx9501, which encodes for the full-

length spike glycoprotein of SARS-CoV-2 (International Vaccine Institute, 2020).

It is a dose defining trial in which intradermal administration of INO-4800 vaccine is followed by electroporation (EP) using CELLECTRA® 2000 device in healthy adult volunteers. AnGes Inc, a Japan-based nucleic acid drugs company has developed a DNA plasmid vaccine candidate (AG0301-COVID19) in collaboration with Osaka University, Japan Agency for Medical Research and Development which is conducting phase I/II trial (AnGes Inc, 2020). Cadila Healthcare Limited, an Indian-based pharmaceutical company, is working by targeting major viral membrane protein using DNA plasmid which upon introduction into the host cells, elicited strong immune response mediated by both cellular and humoral aspects of the immune system. A consortium is established by Genexine, including Binex, International vaccine institute, GenNbio, KAIST, and POSTECH, to develop DNA vaccine candidate GX-19, which is a Genexine's formulation. GX-19 DNA vaccine which was developed in March 2020, works through the genomic pathway in which DNA inserts in the form of the vaccine, commands the body to produce antigen which further induces immune response inside the body in the form of neutralizing antibodies (Han-soo, 2020).

Immunomic Therapeutics Inc. (ITI), a leading US-based Biotechnology Company, in collaboration with leaders from EpiVax Inc. and PharmaJet, is working together to develop a nucleic acid vaccine candidate. The plasmid DNA vaccine is still under the preclinical stage of evaluation. The vaccine candidate further influences their investigational UNITE™ (Universal Intracellular Targeted Expression) platform. EpiVax's in silico T cell epitope prediction tool and PharmaJet's well-established Tropis® Needle-free Injection System specifically targets the delivery to the intradermal layer. Immunomic (ITI) in collaboration with EpiVax and PharmaJet aimed to develop and manufacture scalable vaccine candidate who could be prophylactically and therapeutically suitable while maintaining safety and immunogenicity (Colo, 2020). With DNA vaccines, developers are also analyzing different entry mechanisms that include needle injection with electroporation, needle-free system, intradermal and intramuscular route of administration.

Herd Immunity — key concept to epidemic control

Herd immunity is a form of immunity that describes the indirect protection developed within a group of populations in which a certain group of people develops natural or acquired immunity to infection



which is a key concept for epidemic control. Herd immunity states that only a certain percentage of the population needs to be immune either through overcoming natural wild type infection or induced through vaccination against the infectious agent like a virus, to break the chain of epidemic or pandemic outbreak (Fontanet and Cauchemez, 2020). Overall herd immunity indicates a level or status of population immunity in the given community at which the spread of contagious diseases like COVID-19 declines and stops even after all preventive measures have been relaxed.

However, if the immunity level is still below the herd immunity level and if all preventive measures are being relaxed, then there exists a high possibility of the start of the second wave of infection in the same community (Britton *et al.*, 2020). Through vaccination, the spread of infection can be limited, allowing herd immunity to develop so that the chain of infection from unvaccinated to vaccinated people can be controlled and managed more efficiently. The active immunization to immunologically responding population results in the development of immune memory in terms of neutralizing antibodies. These will be more target specific to fight against subsequent attacks and in persons with impaired immune systems. Herd immunity is also concerned with limiting the spread of infection during the pre-developmental period of vaccine utilizing the body's natural immune system such as in the current pandemic scenario of COVID-19.

With COVID-19 positive cases beyond 30 million across the world, the role of herd immunity in limiting the pandemic chain of transmission seems to be persuasive. Yet, some countries, including India, have recently confirmed the onset of re-infection which was analyzed using genome sequencing to demonstrate that the second wave of infection was because of the emergence of genetically distinct SARS-CoV-2 virus. However, it might help the vaccine industries for policy-making decisions in terms of scaling up the production of an efficient vaccine to meet the global demand.

COVID-19 Vaccine developmental Challenges and possible risks

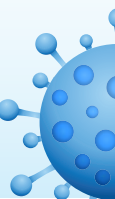
The development and production of safe, efficient, and scalable vaccines to combat the COVID-19 pandemic are yet to face several challenges and multiple risks despite million dollars investments from global economic alliances. Regulatory issues in deploying vaccines among several countries across the world could be one of the significant challenges in this race against COVID-19. Hastening vaccine production during the current pandemic to meet the global need

as an emergency supply might face several issues in terms of vaccine efficacy, adverse medical events if exists, priorities in supply, and many more (Diamond and Pierson, 2020). Vaccine efficacy of 70% in the case of COVID-19 is sufficient enough to control the pandemic. Still, if the efficacy does not exceed beyond 60%, the virus spread continues with the regular pattern, and the world will have to live with this for a long time.

Despite vaccines being developed through extensive trials utilizing several developmental platforms, the risk of triggering antibody-dependent disease enhancement (ADE) with subsequent upregulation of proinflammatory cytokines could be one of the possible adverse events that might be encountered for which clinical management strategies need to be established as per the guidelines. Antibody-mediated immunopathology is one of the serious concerns that might lead to excessive immune activation resulting in the release of cytokines and chemokines that potentially could enhance disease status (Iwasaki and Yang, 2020). Hence, vaccine candidates must not be equipped with undesired immunopotential but at the same time, adequately safe for front line healthcare workers, adults above 60 years with or without underlying comorbidities like diabetes or hypertension. Developed and approved vaccines further need optimized transport conditions apart from scalable production and a well-coordinated international network to deploy across the globe.

Suppose the vaccine is built from an inactivated form of SARS-CoV-2. In that case, churning out for billions of doses could be easy since the industrial technology possibly involved in this process is well established from at least the 1950s (Khamisi, 2020). Nucleic acid vaccine platforms may involve a more straightforward process and likely to make them easier to scale up, but no vaccine with this approach has yet been approved against pandemics. One of the significant challenges is to find appropriate animals that would be infected by the virus in the same way as humans are affected.

In contrast to the regular mice model which might show resistance to the virus, transgenic mice such as Tmprss2 knockout, Stat 1 knockout, human-ACE2 transgenic mice are preferred for experimentation in which HLA (Human Leukocyte Antigen) antigens are expressed. These mice might prove to be useful in understanding the pharmacokinetics of developing vaccine candidates against COVID-19. Developed vaccine candidates will be further subjected to scalable production for emergency usage, and an emergency stockpiling facility will be arranged to



ensure that the vaccine will be made available 24/7 to the high priority groups in case of emergency.

CONCLUSIONS

Several vaccine developmental studies are in the pipeline undergoing extensive human phase trials after the successful preclinical examination. Nine vaccine candidates are ahead with phase III clinical trial utilizing vaccine platforms such as non-replicating viral vector, inactivated, and RNA followed by protein subunit vaccines which are under phase II clinical trial. Besides ongoing clinical trials of multiple vaccine candidates worldwide, multiple approaches for computational study designs and dynamic molecular platforms for understanding the possible immunological reactions that might be involved in vaccine-mediated adverse events need to be carried out.

Meanwhile, the World Health Organization is periodically releasing landscape draft of COVID-19 vaccine candidates that helps in tracking the status of vaccine development globally which also helps scientific communities to design innovative study for the development of new vaccine candidates. With the declaration of global emergency, international alliances across the globe actively joined a worldwide campaign in raising funds for the development of vaccines and deployment across the globe on a priority basis.

World Health Organization is working in collaboration with scientists, investors, and health industries through the ACT (Access to COVID-19 Tools) accelerator to speed up the pandemic response by facilitating equitable access and distribution of effective vaccines to all countries and on a priority basis to health care workers, aged above 60 years belonging to high-risk groups.

On the other side, during the COVID-19 pandemic, several established antiviral drugs are subjected to phase trials to validate its efficacy in treating COVID-19 cases, while waiting for vaccines to be released from pipeline to lifeline. Continuous awareness programs and alerts through social media platforms are also being implemented. Overall, the entire world has joined a campaign to fight against the COVID-19 health crisis favouring the release of pipeline candidates as lifeline medicinal vaccines.

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Conflict of Interest

The authors would like to mention that they do not have any conflict of interest.

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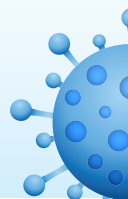
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Review Article

The Current Status and Challenges in the Development of Vaccines and Drugs against Severe Acute Respiratory Syndrome-Corona Virus-2 (SARS-CoV-2)

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Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection causes coronavirus disease-19 (COVID-19), which is characterized by clinical manifestations such as pneumonia, lymphopenia, severe acute respiratory distress, and cytokine storm. S glycoprotein of SARS-CoV-2 binds to angiotensin-converting enzyme II (ACE-II) to enter into the lungs through membrane proteases consequently inflicting the extensive viral load through rapid replication mechanisms. Despite several research efforts, challenges in COVID-19 management still persist at various levels that include (a) availability of a low cost and rapid self-screening test, (b) lack of an effective vaccine which works against multiple variants of SARS-CoV-2, and (c) lack of a potent drug that can reduce the complications of COVID-19. The development of vaccines against SARS-CoV-2 is a complicated process due to the emergence of mutant variants with greater virulence and their ability to invoke intricate lung pathophysiology. Moreover, the lack of a thorough understanding about the virus transmission mechanisms and complete pathogenesis of SARS-CoV-2 is making it hard for medical scientists to develop a better strategy to prevent the spread of the virus and design a clinically viable vaccine to protect individuals from being infected. A recent report has tested the hypothesis of T cell immunity and found effective when compared to the antibody response in agammaglobulinemic patients. Understanding SARS-CoV-2-induced changes such as “Th-2 immunopathological variations, mononuclear cell & eosinophil infiltration of the lung and antibody-dependent enhancement (ADE)” in COVID-19 patients provides key insights to develop potential therapeutic interventions for immediate clinical management. Therefore, in this review, we have described the details of rapid detection methods of SARS-CoV-2 using molecular and serological tests and addressed different therapeutic modalities used for the treatment of COVID-19 patients. In addition, the current challenges against the development of vaccines for SARS-CoV-2 are also briefly described in this article.

1. Introduction

SARS-CoV-2 infection spreads through the respiratory droplets when an infected person is in close contact with other individuals [1]. To date, there are wide ranges of therapies developed and evaluated for the effective management of COVID-19. For instance, the existing treatment methods such as antiviral drugs (remdesivir), antibodies (intravenous hyperimmunoglobulin therapy), anti-inflammatory drugs (statins, dexamethasone), immunomodulatory therapies, anticoagulants, and antifibrotics are reported to exhibit different therapeutic efficacies during COVID-19 treatment [2, 3]. However, currently, there is no single therapeutic modality proven effective apparently to mitigate this disease progression in hospitalized COVID-19 patients [1].

1.1. Structure and Pathophysiology of SARS-CoV-2. Coronavirus exhibits a crown-like appearance due to surface spike (S) glycoproteins when observed under the electron microscope [4]. Coronavirus is composed of a cis-acting RNA genome to foster the viral replication in host cells through RNA-dependent RNA polymerase [5, 6]. Besides, both cis- and trans-acting viral elements participate in spike (S) protein synthesis, coronaviral encapsidation, and packaging into host cells [7]. The spike glycoproteins consist of S1 and S2 heterotrimer subunits, in which S2 subunit significantly conserved with fusion peptide, a transmembrane domain, and a cytoplasmic domain [5] (Figure 1). Mutations in the genes coding for S protein induced the replacement of glycine (G) at 723 positions with serine (S) and isoleucine with proline (P) at 1010 amino acid position. These mutations in S proteins reported were to enhance the invading potential of SARS-CoV-2 [8]. CoV 229E and OC43 strains are detrimental to humans by causing common cold and lower respiratory infections in several immunocompromised patients [9–11]. The coronavirus-induced pathophysiology varies significantly in terms of its impact on alveolar inflammation, neutrophil infiltration, and immune responses during interstitial pneumonia [10, 12–14]. Recent studies have also shown that SARS-CoV-2 infection leads to multiple organ damage, which is due to severe cytokine storm.

2. Modes of Transmission of SARS-CoV-2

Current studies have demonstrated that the infected individual can transmit SARS-CoV-2 virus to an average of 2.2 individuals, which is causing a significant increase in the number of individuals suffering from this disease [15]. Even though the virus is reported to be originated in animals and transmitted to humans, the subsequent transmission is primarily through respiratory mode [15]. Respiratory transmission is either by large droplets with virions of a size larger than $5\ \mu\text{m}$ or aerosols smaller than $5\ \mu\text{m}$ expelled out directly from the respiratory tract by the patient. These infectious droplets are reported to remain suspended in the air for an extended period of time and can travel up to 2 to 3 meters distance before they become inactive [16, 17].

Studies have reported a significant reduction in the risk of respiratory transmission of SARS-CoV-2 if a suitable mask is

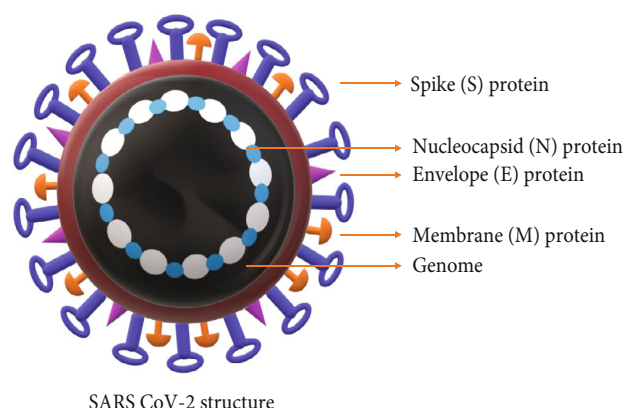


FIGURE 1: Schematic representation of the structure of SARS-CoV-2: SARS-CoV-2 is an enveloped virus containing RNA genome. The envelope contains spike (S) protein, nucleocapsid (N) protein, envelope protein (E), and membrane protein (M).

used [18–23]. Studies have shown a fomite or direct contact-mediated transmission of SARS-CoV-2 [24] when patients share common facilities (restrooms, elevators) and follow a poor hand hygiene [25–28]. Furthermore, the vertical transmission of SARS-CoV-2 has been reported in neonates, where three neonates tested positive for IgM on day 2 after birth while the other tested positive within 16 hours after delivery [28, 29]. Although a case report described transplacental transmission of SARS-CoV-2 [30–33], the transmission from breast milk to infants has not been reported yet. Likewise, the transmission of SARS-CoV-2 through the sexual, fecal, oral, and blood also has not been reported.

S proteins are responsible for the viral particle adherence and docking to the human cell surface receptors such as ACE-II [34]. The binding efficacy of S proteins in SARS-CoV-2 to the ACE-II is “10 to 20 times” stronger compared to the binding efficacy of SARS virus reported in 2002; hence, the spread of SARS-CoV-2 from one person to another is much higher and induces the viral-mediated pathophysiology [35]. Despite several structural similarities between SARS-CoV-2 and SARS virus, the antibodies that were effective against SARS failed to neutralize SARS-CoV-2; hence, targeting SARS-CoV-2 using these antibodies is not feasible, which poses a challenging task to medical scientists to develop a potent and specific approach for mitigating SARS-CoV-2 infection [4].

3. Need for the Improvement of Existing SARS-CoV-2 Detection Methods

Detection of SARS-CoV-2 is the preliminary step in testing, tracing, treating, and the management COVID-19. Therefore, a sensitive and low-cost screening test is highly essential. The existing SARS-CoV-2 detection tests are broadly divided into (a) molecular methods and (b) serological methods. The molecular methods detect “viral RNA” in the biopsy of nasal tissue (collected using a swab) of the infected individual by using reverse transcription polymerase chain reaction (RT-PCR) (Table 1) [36, 37]. Since the collection of nasal swabs can cause irritation to the soft tissues, studies are currently

TABLE 1: List of rapid methods used for detecting SARS-CoV-2.

Diagnostic tests	Mechanism	Sample	Advantages	Limitations
Direct tests				
RT-PCR	SARS-CoV-2-specific hybridization probes are used to target envelope (E), RNA-dependent RNA polymerase (RdRp), and ORF1b and N regions of the virus. This test can detect the virus at least after two days after infection	Upper respiratory tract (URT) and lower respiratory tract (LRT) specimens	This test is a gold standard method for the diagnosis in symptomatic and asymptomatic patients. This test has a high sensitivity (~89%) and specificity (99%)	Needs infrastructure, very expensive, and requires qualified personnel
Reverse transcription loop-mediated isothermal amplification	Exponential amplification of virus-specific genes at a constant temperature	URT and LRT specimens	High sensitivity and specificity	Needs infrastructure, very expensive, and requires trained personnel
Nucleoprotein (NP) antigen detection test	Enzyme-linked immunoassay has a microplate precoated with specific antibodies against SARS-CoV-2 NP and the use of horseradish peroxidase-(HRP-) labeled secondary antibody	URT and LRT specimens and saliva	Simple and rapid technique. No trained personnel and expensive laboratory instruments are required	Less sensitivity (70-86%) and specificity (95-97%) when compared to RT-PCR
Indirect tests				
ELISA	Detects anti-SARS-CoV-2 IgG and IgM by identifying antibodies against the NP and spike proteins	Serum, plasma, whole blood	Widely used technique, inexpensive, easy sample collection, and high sensitivity (~82%) and high specificity (97%)	Needs infrastructure and trained personnel
Chemiluminescent immunoassay	Light-producing chemical reactions estimate the titers of IgG and IgM by the amount of the emitted luminous signal	Serum, plasma, whole blood	High-throughput and sensitive (77.9%) technique	Needs infrastructure and trained personnel
Rapid detection kits	Device with colloidal gold-labeled SARS-CoV-2 recombinant protein and murine anti-human IgG antibodies	Fingerpick blood samples	No need of infrastructure, easy sample collection results in 10-15 min	Low sensitivity (~88.6%) and specificity (~90.63%)

Even though several detection methods have been developed, RT-PCR is considered as the gold standard for detection of SARS-CoV-2. The details presented in the table show various diagnostic approaches that have been developed in the detection of SARS-CoV-2.

in progress to check whether saliva could be used to detect SARS-CoV-2 [38]. Andrew Brooks, the Chief Operating Officer (COO) and Director of Technology Development, Rutgers University Cell and DNA Repository (RUCDR) Infinite Biologics, has developed a saliva test, which requires the COVID-19 suspect to spit the saliva in a cup (Table 1). This test has received emergency use authorization approval from the United States Food and Drug Administration (USFDA). Recent studies are encouraging the collection of saliva as diagnostic fluid sample rather than the nasopharyngeal swab for detecting SARS-CoV-2 [38]. USFDA has authorized 22 companies to distribute these testing kits [39]. However, to date, the Indian Council of Medical Research (ICMR), Government of India, has not approved any saliva-based rapid antigen tests for screening and identification of SARS-CoV-2-infected individuals. World Health Organization (WHO) and the Center for Disease Control (CDC) are currently using more advanced RT-PCR-based tests for detecting SARS-CoV-2 accurately. The testing kits developed by Abbott can take about 5 minutes, whereas the

rapid testing kits designed by other companies usually require more than 30 minutes to produce reliable detection results [39].

Now, Wyllie and colleagues have examined the possibility of using saliva for diagnosis (salivaomics) and concluded that saliva could be used as an alternative for nasopharyngeal swab [40]. PCR data not only provides an absolute quantification of the number of copies of mRNA but also yields key information about the total viral load for efficient assessment of disease severity [40, 41]. Since appropriate standards are simultaneously subjected to amplification in parallel with saliva, the qPCR is considered as a more precise method to decipher the exact viral load [40]. However, the qPCR test is time-consuming and requires expertise to interpret the results [42].

3.1. Serological Tests for the Diagnosis of SARS-CoV-2. Unlike molecular tests, the serological tests can detect the *antibodies* produced against SARS-CoV-2 in the infected or recovered individuals using enzyme-linked immunosorbent assay



TABLE 2: List of various sampling methods currently in the usage for SARS-CoV-2 detection.

Type of specimen used for COVID-19 testing	Stage of sample collection	Description
Upper respiratory specimens: nasopharyngeal and oropharyngeal swabs	Early-stage infections (asymptomatic or mild cases)	Individual nasopharyngeal swabs are reported to be more reliable [49, 60, 78, 79]. Combining nasopharyngeal and oropharyngeal swabs increases sensitivity and reliability for detecting COVID-19 [79–82]
Lower respiratory specimens: sputum, endotracheal aspirate, bronchoalveolar lavage	Later in the course of the disease, the individuals with strong clinical suspicion of COVID-19 test negative with URT sampling [56, 60, 80, 83]	Sputum is not recommended because of an increase in aerosol transmission [84]. Requires consultation by a physician. Invasive sampling method
Oral fluid collection methods (i) Posterior oropharyngeal fluid/saliva (spitting/drooling) (ii) Collection of oral fluid using pipette or sponges (iii) Gargling with saline solutions	Individuals with clinical symptoms tested negative for URT	Less invasive and lower risk of exposure to other upon collection, when compared with the collection of URT specimens, therefore suitable for mass screening But not recommended by WHO as the sole specimen type for routine clinical diagnosis [85–88]
Serum specimens	One collected in the acute phase and the other in the convalescent phase (2-4weeks)	Considered when nucleic acid amplification tests negative
Fecal specimens	Second week after the onset of symptoms	Considered when there is clinical suspicion of COVID-19, but URT and LRT are negative [89]
Postmortem specimens (postmortem swabs, needle biopsy, or tissue specimen)	Collected during autopsy	For pathological and microbiological testing [89–95]

URT: upper respiratory tract; LRT: lower respiratory tract; WHO: World Health Organization.

(ELISA) [43]. The turnaround time (TAT) for serological tests is only 15 minutes; therefore, these diagnostic kits are the preferred choice for the rapid analysis of samples [36]. According to these tests, the presence of IgM indicates “recent exposure”, whereas the presence of IgG indicates “infection in late-stage” [43]. Although serological tests are much easier to execute, they are associated with certain limitations, viz., (a) lack of efficacy to detect the infection at a very early stage due to time gap required to generate antibodies in the body, (b) yielding many false-negative results, and (c) generation of false-positive results if the individual is infected with other related coronaviruses such as HKU1, NL63, OC43, and 229E. Currently, FDA has approved a unique serological test developed by Cellex, USA (Cellex qSARS-CoV-2 IgG/IgM rapid test). Few other companies such as Bodysphere have also announced 2-minute rapid detection methods; however, these tests still require clearance/approval from FDA, USA. The serological test results alone cannot be considered as a confirmatory test, as it requires further validation using molecular tests [39]. Furthermore, the utility of serological tests alone for detecting SARS-CoV-2 is still in debate among medical communities due to their poor accuracy and false positive/negative results [44].

In addition to the above strategies for viral detection, Zhang et al. reported the “CRISPR-Cas13-based SHER-LOCK” (specific high sensitivity enzymatic reporter unLOCKing) technique for SARS-CoV-2 diagnosis. The protocol incorporated the Cas13, which targets the S gene, Cas13 enzyme, and ORF1ab gene [45], but this procedure requires further validation using COVID-19 patient samples. Proce-

durally, the technique involves isothermal amplification of RNA samples using recombinase and polymerase, followed by the incubation of amplified viral RNA with Cas13 enzyme, guide RNA, and reporter. Using a paper dipstick, the distinct band produced by the cleaved reporter is visualized [46].

Council of Scientific and Industrial Research-Institute of Genomics and Integrative Biology (CSIR-IGIB), New Delhi, Government of India, has developed a low-cost “paper-strip based laboratory test” to detect SARS-CoV-2 using CRISPR-Cas9 technology. The test is simple and low-cost (about Rs.500 (five hundred rupees only)) and does not require high-end equipment such as a real-time PCR machine [47]. In addition, this test does not involve the isolation of RNA and conversion of isolated RNA into cDNA and the requirement of PCR reagents etc., which are essential for other molecular testing kits. However, this test requires further validation to establish accuracy and sensitivity and is currently waiting for approval from regulatory authorities in India. At present, a total of 158 RT-PCR kits were validated and approved by the Indian Council of Medical Research (ICMR), Government of India, for screening and testing of SARS-CoV-2-induced COVID-19.

Although the above testing methods could detect the SARS-CoV-2 in infected individuals, the lack of specificity and sensitivity is a major problem and may generate false positive and negative results. Therefore, the prospective research should focus immediately to improve the specificity and sensitivity of SARS-CoV-2 detection methods in clinical samples [36]. One specific approach, which has been gaining medical importance, is the combined detection of SARS-

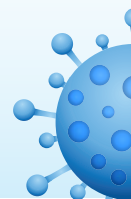


TABLE 3: Key molecular targets of pharmacological agents tested against SARS-CoV-2.

Drugs	Target	Description
Remdesivir	RNA-dependent RNA polymerase enzyme	Used in the treatment of individuals with mild-to-moderate COVID-19 [128, 129] Inhibit viral RNA synthesis It did not reduce mortality, the need for mechanical ventilation, or the duration of hospital stay Used in the treatment of severe cytokine release syndrome In COVID-19 patients, it reduces the use of mechanical ventilation and improves lung function [130, 131] More clinical validations are required [131]
Tocilizumab	Interleukin-6 (IL-6)	HCQ did not effectively prevent COVID-19 infections as it could not slow down the disease progression, pneumonia, acute respiratory distress, and death
Hydroxychloroquine	Target the binding of S protein to ACE2 receptor [132]	The combination is used in the treatment of mild, moderate, and severe COVID-19 infection by suppressing the viral load [128] More clinical validations are required
Lopinavir/ritonavir	3CLpro-CoV protease cleaves polyproteins during viral replication and assembly	Inhibits viral RNA synthesis; more clinical validations are required
Favipiravir	RNA-dependent RNA polymerase enzyme	Inhibits viral RNA synthesis; more clinical validations are required
Triazavirin	RNA-dependent RNA polymerase enzyme	Shows no effect in reducing viral load in COVID-19 patients
Umifenovir	Blocks the viral entry to the host	Recommended for patients with severe COVID-19; reduces lung inflammation, duration of mechanical ventilation, and mortality [134], but not recommended to the patients comorbid with diabetes due to the chances of mucormycosis (black fungus) growth
Corticosteroids—dexamethasone	Proinflammatory genes coding cytokines, chemokines, cell adhesion molecules, inflammatory enzymes, and receptors [129, 133]	

CoV-2 RNA and its viral protein(s) using a signal amplification strategy rather than a “target amplification” procedure. This signal amplification strategy was successfully implemented and demonstrated to be effective in yielding many reliable results in the detection of HPV [48].

3.2. Methods of Sampling for Testing and Tracing COVID-19 Patients. Sampling methods do play a crucial role in detecting SARS-CoV-2. Studies have reported the identification of SARS-CoV-2 in respiratory secretions [49–56], feces or rectal swabs [57–61], blood [43, 60, 62–64], oral fluid [40, 65–67], ocular fluids [68–72], urine [73, 74], semen [75], brain tissue [76], and cerebrospinal fluid [77]. Therefore, the choice of sampling method depends on the clinical presentation and the time since the onset of symptoms. Respiratory tissues are the preferred samples to diagnose COVID-19. Table 2 summarizes various sampling methods used in the detection of SARS-CoV-2.

4. Strategies Targeting SARS-CoV-2: Development of Pharmacological Agents to Mitigate and Treat SARS-CoV-2 Infection

According to WHO, the fatality rate of COVID-19 patients has been increasing across the globe due to lack of selective

therapeutic interventions and potent vaccines [96]. Existing vaccines and drug combinations are either selective to a particular variant of the virus or exhibit systemic toxicity. Therefore, it is crucial to develop potent, pan-specific, and long-lasting vaccines and better pharmacological agents for the prevention and treatment of SARS-CoV-2 infections (Table 3). The combination of alpha-interferon and anti-HIV drugs lopinavir/ritonavir has shown minimal success and proven to be toxic in recent studies [97] (Figure 2). Currently, a broad-spectrum antiviral drug remdesivir (developed by Gilead Sciences, Inc.) is being used for the treatment [97]. A recent study demonstrated the efficacy of two lead compounds 11a and 11b *in vitro*, which were synthesized using a structure-based drug design approach to target viral main protease (M^{pro}), and reported good pharmacokinetic and safety profile in animals [98]. However, further studies are warranted to consider these drugs for clinical use. Similarly, many other studies have also reported the development of drugs targeting various viral proteins and postinfection events [97, 99].

Decreasing the viral load in infected individuals is one of the main strategies and considered by many investigators to reduce the COVID-19 complications. Supporting this idea, interestingly, the fatality rate was reported to be significantly low in pediatric patients as they have relatively low



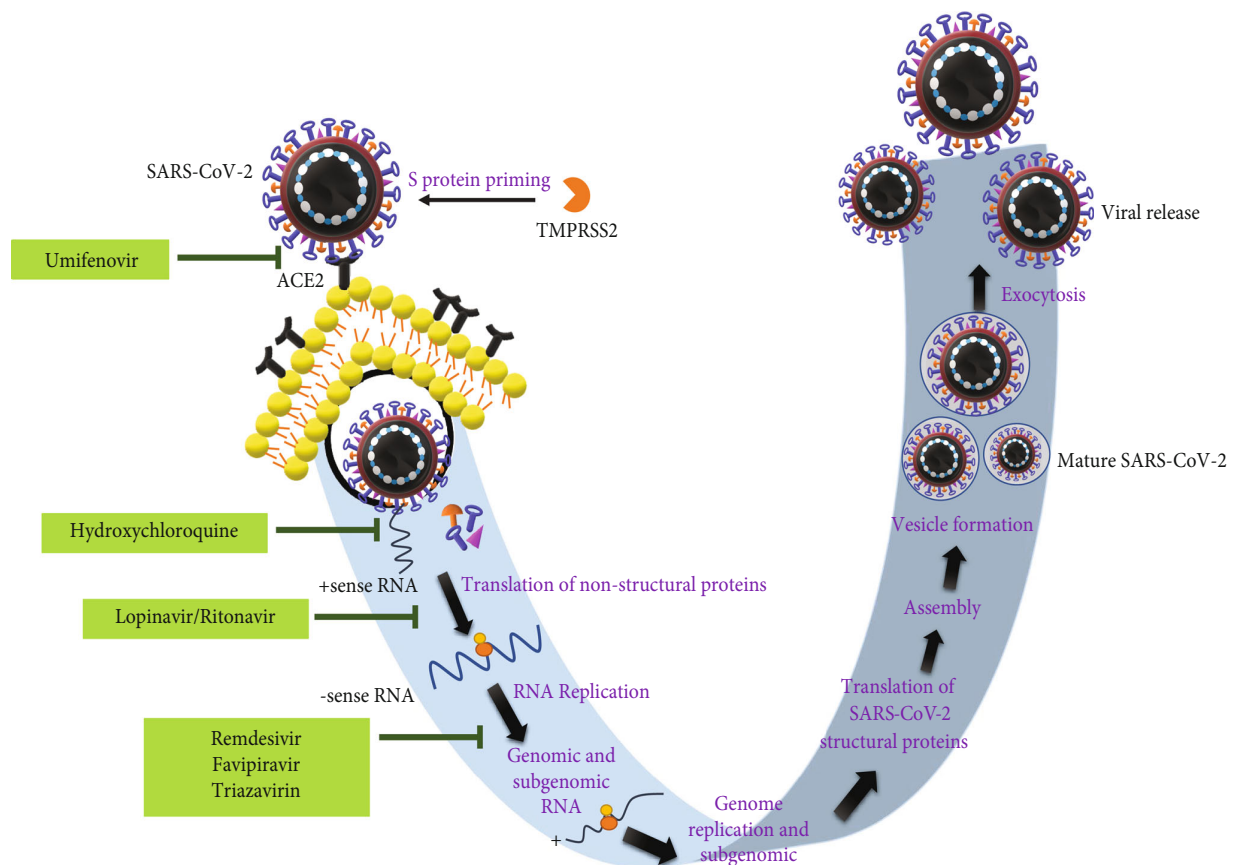


FIGURE 2: The mechanism of action of umifenovir, lopinavir/ritonavir, remdesivir, favipiravir, triazavirin, and hydroxychloroquine in the treatment of SARS-CoV-2-mediated pathophysiology.

seroprevalence compared to adults [97, 99, 100]. Favipiravir is a derivative of pyrazinecarboxamide, which acts by inhibiting RNA-dependent RNA polymerase [97]. Favipiravir is available for the treatment of COVID-19 patients at mild-to-moderate phase. Therefore, a preventive strategy using a potent vaccine is urgently required. However, efforts in developing a potent vaccine are still in progress.

The development of a vaccine requires a thorough knowledge about viral surface glycoproteins (in the case of enveloped viruses such as SARS-CoV-2) and capsid proteins (in the case of nonenveloped proteins) [97]. The genome of SARS-CoV-2 encodes both structural (spike—S; membrane—M, envelope—E, and nucleocapsid—N) and nonstructural proteins that play crucial roles in the assembly and rapid spread of virus among the population [101]. SARS-CoV-2, similar to CoV-NL63, can use ACE-II receptors, which is a characteristic antigenic commonality of several coronaviruses with zoonotic potential [100]. ACE-II is extensively expressed in the gastrointestinal tract where viral shedding is marginally prolonged in the stools due to ACE-II binding. Despite extensive similarities between SARS-CoV and SARS-CoV-2 (>90% similarity between SARS-CoV and SARS-CoV-2 N, E, and M proteins and 76% similarity in S proteins), the available knowledge about key immunological epitopes, which are responsible for antibody and T cell responses, is very minimal [101]. Therefore, developing an effective vaccine against SARS-CoV-2 is still a major challenge.

4.1. Monoclonal Antibodies (MABs) against SARS-CoV-2. COVID-19 patients are characterized by the presence of a dysregulated immune system, hyperinflammation, and very high IL-6 levels. IL-6 is one of the key cytokines implicated in COVID-19 severity and patient mortality [102–104]. Genomic analysis revealed that critically ill patients with COVID-19 exhibit genetic variations in IL-6-mediated inflammatory pathway proteins, which cause life-threatening disease [105]. The accumulation of lymphocytes, inflammatory monocytes, and other mediators such as apoptotic proteins and thrombotic factors results in pulmonary damage in these patients [106–109]. In addition to vascular permeability, the IL-6 can foster endothelial dysfunction; hence, IL-6 is an attractive drug target for mitigating the complications of COVID-19 [110, 111] (Figure 2). For instance, the administration of tocilizumab to COVID-19 patients resulted in the impaired activity of IL-6 α receptors, which consequently fostered good clinical outcomes in these patients [112–114]. This was confirmed by several case reports, retrospective observational cohort studies, and randomized clinical trials. According to COVACTA phase 3 clinical trial, tocilizumab efficiently mitigated COVID-19-induced clinical manifestations such as fever and pneumonia [102–105, 115–117].

Sarilumab is another monoclonal antibody reported to be effective against SARS-CoV-2 by inactivating IL-6-mediated acute inflammatory responses [116–118]. It has proven

efficacy in mitigating cytokine storm. Clinical usage of sarilumab was further confirmed by enhancement in patient survival and mitigation of multiple organ damage in critically ill patients with COVID-19 [119–123].

4.2. Baricitinib and COVID-19. Adaptive COVID-19 treatment trial-2 (ACCT-2) has tested the benefit of combining baricitinib (a specific inhibitor of Janus kinase-1 and Janus kinase-2) with remdesivir in critically ill patients of COVID-19. Both primary and secondary clinical outcomes are reported to be satisfactory [124]. In addition, two reports of Cantini et al. (2020) also concluded the efficacy of baricitinib in inducing the impairment of JAK1 and JAK2, which consequently blocked the immune cascades and viral replication [125–127]. However, the supplemental oxygen through mechanical ventilation is an intriguing subject of research in COVID-19 patients who are receiving baricitinib and dexamethasone.

5. Challenges in the Development of Vaccines against SARS-CoV-2

Recent studies have shown that T cell responses against viral structural proteins are more immunogenic and long-lasting (up to 11 years of postinfection) when compared to non-structural proteins and antibodies [101]. In a recent report, Walls et al. (2020) have identified a set of epitopes in S and N structural proteins that can launch an effective response against SARS-CoV-2 [101]. Furthermore, the authors of this study have incorporated significant details about the epitope associated with MHC alleles so that a wide population range can be covered globally [101]. Virus-specific effector memory T cells can encounter coronaviral strains thereby mitigate the complications of infections [135]. In the case of SARS-CoV and MERS-CoV, these viruses can use non- or subneutralizing antibodies and induce immune responses via the antibody-dependent enhancement (ADE), a kind of Trojan horse mechanism [136, 137]. ADE is involved in several viral infections such as Zika virus, Ebola, SARS-CoV, SARS-CoV-2, and HIV [136, 137]. In the case of SARS-CoV-2, the significant immune mechanism occurs via CD32a-mediated ADE, which limits the efficacy of current vaccination [96]. CD32 is an extensively expressed protein on the surface of monocytes and macrophages (ex. alveolar macrophages), which gets aggregated by IgG.

T cell responses are crucial when compared to the humoral responses as these T cell responses have a significant influence on the recovery from primary infection and avoid reinfection [97]. These immune responses can influence vaccine development against COVID-19. The vaccination should enhance both humoral immunity and cellular responses in order to prevent COVID-19-induced complications [138, 139]. In the first phase, the virus infection can be mitigated to reduce initial viral load and control the spread of SARS-CoV-2 to other respiratory organs. In the next phase, the cellular immune responses become significant and help in mitigating the inflammatory phase of COVID-19 disease. In the case of convalescent plasma therapy, the humoral

response could be triggered by the vaccine to confer protection against SARS-CoV-2 [97].

5.1. Current Status and Challenges for COVID-19 Vaccination. The development of safe and efficacious vaccines against SARS-CoV-2 is a challenging task [4]. Previously, vaccines against coronaviruses were developed using passive/active immunization and used the animal models for SARS-CoV replication. This is due to the nonavailability of authentic animal models for the development of coronavirus vaccines [140–142]. The passive transfer of immune serum can mitigate the SARS-CoV load in naive BALB/c mice [143]. Earlier, Cheng et al. (2005) have reported the efficacy of “SARS-CoV neutralizing antibodies in SARS hyper-immune globulin” isolated from human convalescent-phase plasma for neutralizing the SARS-CoV infection [144]. Human SARS-CoV administration to animal models has been reported to mitigate the outbreaks of coronavirus infection suggesting that future studies should uncover these mechanisms for SARS-CoV-2 infection [4, 145–147]. However, many experimental studies must be conducted to ascertain the activity of MABs for their neutralizing efficacy by analyzing the immune memory repertoire of COVID-19 patients. Even though the usage of antiviral drugs, viz., *protease inhibitors*, *calpain inhibitors*, *nucleoside analogues*, *interferons*, and *siRNAs* against SARS-CoV-2 infection, is reported in recent times, several conflicting results with wide variations in clinical outcomes have been generated, which necessitate a global approach for the development of effective vaccines [148–153]. Therefore, a concerted effort is urgently warranted to develop a potent and clinically viable vaccine against SARS-CoV-2 [154].

Reverse genetics technology may be another important strategy to develop vaccines against coronavirus infections [153]. Recent reports have described the efficacy of both mutant and chimeric recombinant viruses to uncover the function of S protein in coronavirus [155, 156]. Reverse genetics has been widely used to elucidate the “structure/function relationship of viral UTRs at 5′ → 3′ of the genome” and the “function of replicase gene for enzymatic activity” in mediating coronaviral replication and pathogenesis [155, 157]. In addition, this strategy is significantly essential to express foreign gene sequences in place of noncoding genes which can help in the development of attenuated vaccines against coronaviruses [158–161].

5.2. Antibody-Dependent Enhancement (ADE) and SARS-CoV-2 Vaccines. The extensive immune backfiring induced through ADE is one of the critical reactions associated with SARS-CoV-2 infection. ADE is progressively produced from this viral infection followed by the induction of Th2 immunopathology, which further blocks the attempts to develop a safe and effective vaccine against SARS-CoV-2. ADE can modulate the immune reactions and induce sustained inflammation, lymphopenia, and cytokine storm, which further lead to the severe disease and death. ADE also requires prior exposure to similar antigenic epitopes most likely from the circulating viruses [162]. For instance, the neutralizing antibodies exhibit a greater ability to block viral entry, fusion



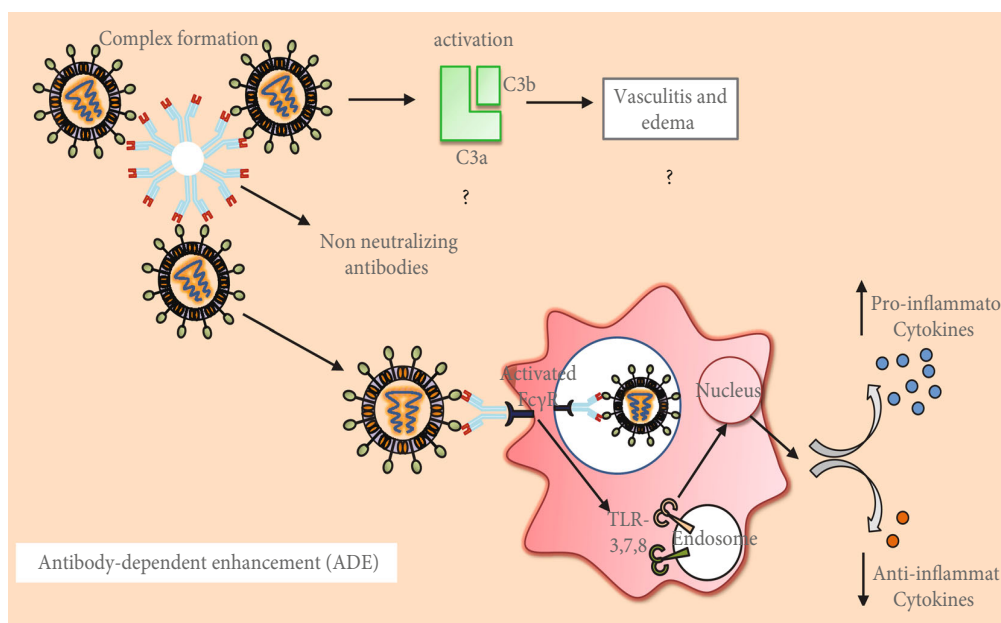


FIGURE 3: The process of antibody-dependent enhancement (ADE) in lung cells. Entry of SARS-CoV-2, which is mediated by ACE-2 receptors on lung cells, further actuates inflammatory cascades through the production of pathogen-specific antibodies followed by ADE. ADE consequently induces lung pathology through the engagement with Fc receptors expressed on several immune cells, viz., monocytes and macrophages. Internalization of ADE-induced immune cascades can foster inflammation and tissue damage by modulating the inflammatory factors in lung cells.

without additional immune mediators, although the Fc region is mandatory for neutralizing the influenza virus [163]. In the case of SARS-CoV, the viral docking on ACE-2 was potentially impaired by the administration of neutralizing antibodies since they can recognize and block receptor-binding domain (RBD) and heptad repeat 2 (HR2) domain on the spike (S) protein [164]. Neutralizing antibodies could foster the immune activities of phagocytes, complement, and NK cells [162]. SARS-CoV-2-specific antibodies significantly can induce lung pathology through ADE engagement with Fc receptors that are expressed on several immune cells such as monocytes, macrophages, and B cells [165]. This process is predominantly independent of ACE-2 expression, pH, and host membrane proteases. Thus, the internalization of ADE-induced immune cascades can foster inflammation and tissue damage by mitigating the anti-inflammatory cytokines IL-10 and TGF- β and enhance the levels of the proinflammatory chemokines CCL2 and CCL3 (Figure 3) [166, 167]. However, the underlying mechanisms associated with ADE-mediated immune reaction in SARS-CoV-2 infection are yet to be investigated for effective vaccine development [136, 165].

5.3. Th2 Immunopathology and SARS-CoV-2 Vaccines. The significant roles of host Th2 immunopathology and Th17 inflammatory responses are responsible for pneumonia and edema in the COVID-19 pathogenesis [168] (Figure 4). Release of IL-17 and granulocyte-macrophage colony-stimulating factor (GM-CSF) exacerbates viral immunopathological events by mitigating Treg cells and enhancing the neutrophil migration with concomitant induction of Th2 responses in the lungs [168, 169]. IL-6-mediated Th17 differ-

entiation can foster lung pathology during SARS infection [170]. Th2-type immunopathology along with eosinophil infiltration has been observed with SARS vaccination against SARS-CoV in mouse models [171]. However, confirmatory studies are yet to be performed for IL-6-mediated Th17 responses during SARS-CoV-2 infection to develop anti-IL-6 monoclonal antibodies as new therapeutic interventions [114, 172]. RBD-based subunit vaccine is expected to be safer compared to other vaccines, which may induce Th2 immunopathology [173].

The attenuated whole virus vaccine may elicit a significant immune response against SARS-CoV-2 because this virus uses ACE-2 receptors to enter into human cells [174]. Another method is to develop a subunit vaccine, which may induce sensitization of the immune system to foster immune response against S protein subunits of SARS-CoV-2 [153, 175]. In addition, recent studies are currently evaluating the efficacy of nucleic acid vaccines against SARS-CoV-2 to combat COVID-19 [176–178].

6. Recent Trends in the Development of Vaccines

As of 13th April 2021, a total of 166 vaccines have been registered; among which, 89 are under clinical trials in humans. A list of vaccines developed against SARS-CoV-2 is given in Table 4 and Figure 5. On 16th January 2021, the COVID-19 vaccines Covishield (Oxford-AstraZeneca and Serum Institute of India) and Covaxin (Bharat Biotech) were launched in India. Initially, these vaccines were made available for healthcare and frontline workers. As of 1st March 2021, these vaccines are also made available for individuals aged above

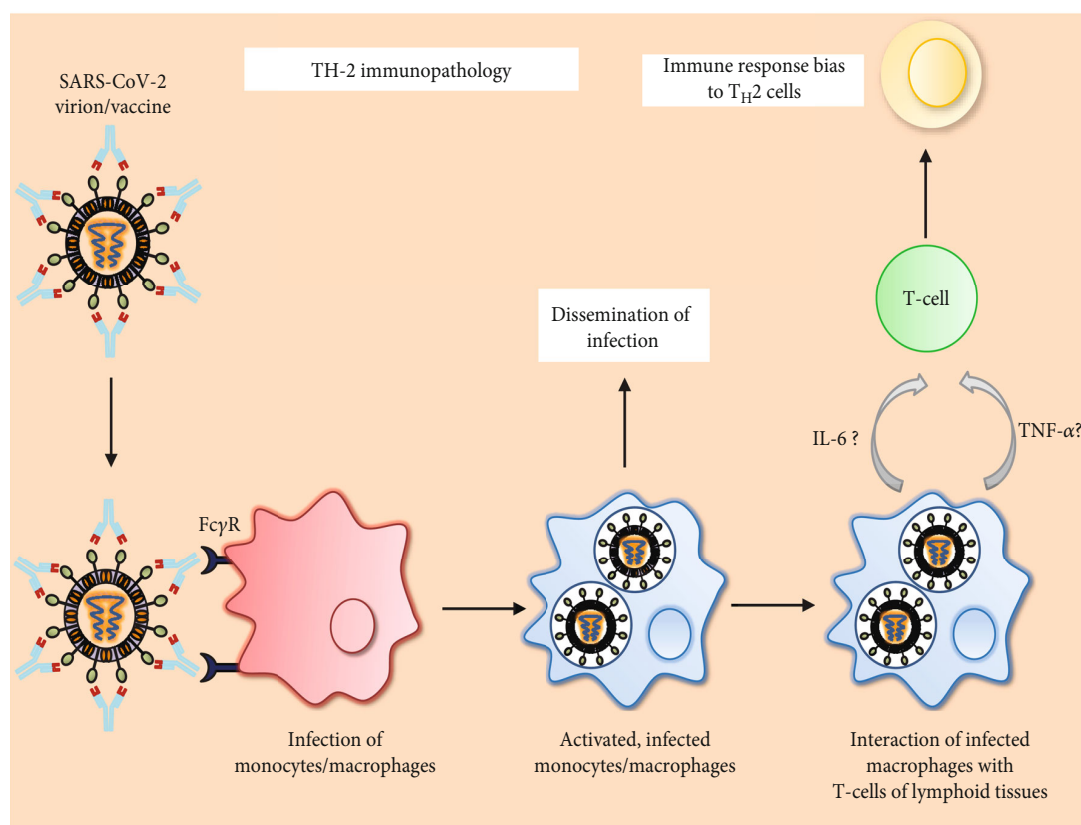


FIGURE 4: Sequence of events involved in SARS-CoV-2-induced Th2 immunopathology: antibody-bound SARS-CoV-2 virion interacts with the FcγR of host monocytes/macrophages. Virus-infected macrophages are not only responsible for various complications of the disease but also interact with T cells of lymphoid tissues in the host, which leads to the aggravated inflammatory responses which were reported in COVID-19.

TABLE 4: Current stage of vaccines and their manufacturer.

Types of vaccine	Vaccine name	Phase	Manufacturer	Country of origin
mRNA vaccine	mRNA1273	Phase 3	Moderna	US
	Comirnaty	Phase 2/3	Pfizer-BioNtech	Multinational
Protein subunits	EpiVacCorona	Phase 3	Vector Institute	Russia
	NUX-CoV2373	Phase 3	Novavax	Australia
	BBIBP-CorV	Phase 3	Sinopharm	China
Inactivated virus	CoronaVac	Phase 3	Sinovac	China
	Name not announced	Phase 3	Sinopharm-Wuhan	China
	Covaxin	Phase 3	Bharat Biotech	India
	Convidecia	Phase 3	CanSino	China
DNA-based vaccine	JNJ-78436735	Phase 3	Johnson & Johnson	The Netherlands, US
	Sputnik V	Phase 3	Gamaleya	Russia
	Covishield (AZD1222)	Phase 2/3	Oxford-AstraZeneca	UK

60 years of age and the ones aged between 45 and 59 years with comorbid conditions like cancer, diabetes, and hypertension. To date, worldwide, approximately 825 million vaccine doses have been administered. However, there is an immediate requirement for safe and effective vaccines as the number of SARS-CoV-2 infected cases is increasing at alarming rates with a current global estimate of 138,027,200 confirmed cases.

6.1. mRNA-Based Vaccines

6.1.1. mRNA-1273. The mRNA-1273, an mRNA vaccine, was developed by Boston-based Moderna therapeutics and the National Institute of Allergy and Infectious Diseases (NIAID), USA. The vaccine encodes the prefusion form of the SARS-CoV-2 spike protein in a lipid nanoparticle vector. Upon administration, mRNA undergoes transcription and

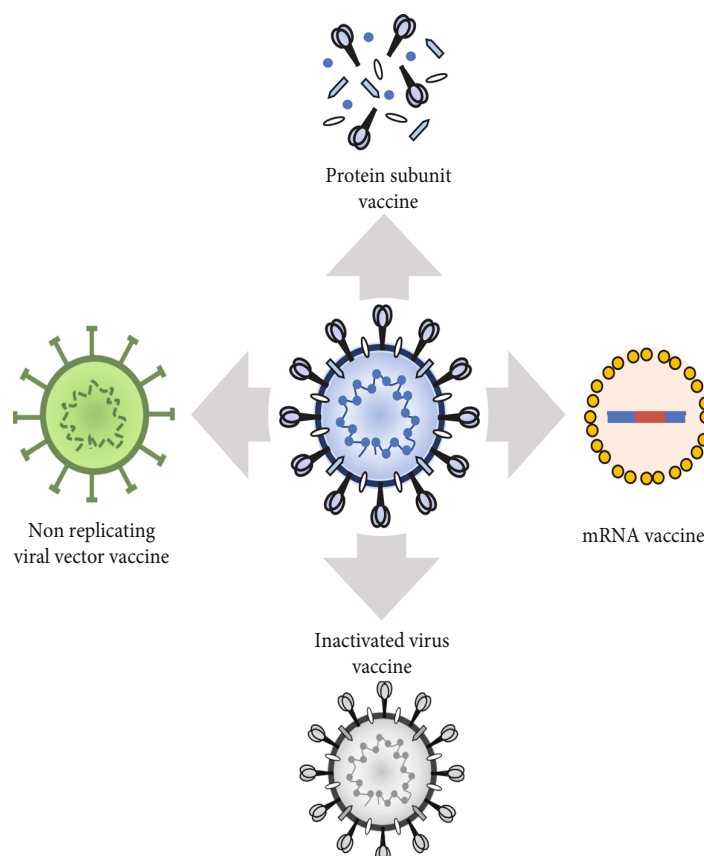
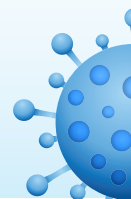


FIGURE 5: Schematic depiction of the four different kinds of vaccines, viz., nonreplicating viral vector vaccine, mRNA-based vaccine, inactivated virus vaccine, and protein subunit-based vaccine.

translation to produce viral antigens. The immune system recognizes these viral antigens and initiates an adaptive immune response against the S protein of SARS-CoV-2. The preclinical studies on BALB/cJ, C57BL/6J, and B6C3F1/J mice showed induction of virus-specific antibodies upon administering intramuscular doses of 1 μ g mRNA-1273, 3 weeks apart [179]. The phase 1 trial began on March 16th, 2020, with 45 healthy volunteers of age between 18 and 55 years. They were administered with three different doses (25 μ g, 100 μ g, and 250 μ g), and the second dose was after four weeks. The trial reported a strong CD4⁺ T cell response and produced neutralizing antibodies, while CD8⁺ T cell responses were recorded by the medium-level dose (100 μ g)[180, 181]. Myalgia, fatigue, headache, chills, and pain at the injection site were side effects recorded only after the second dose of vaccination and were prominent only in the group who had received the highest dose (250 μ g). In a study of 40 older adults (56-70 years or ≥ 71 years), the immunogenic response was similar to 18-55 years, indicating its efficacy and less immunocompetency in all age groups. In the phase 2 trial, 300 young and 300 older adults were recruited to determine the ability of 25 μ g and 100 μ g doses. The data reported significant immunogenic responses at 100 μ g dose. Phase 3 trials began on July 27th, 2020, with 30,420 participants in the USA, where half of the participants (15,210) received two doses of 100 μ g of mRNA-1273 and

other half received the placebo [182]. A total of 196 participants have shown symptomatic COVID-19 illness; among which, only 11 participants were vaccinated with mRNA-1273 indicating 94.1% [183] efficacy without any long-term adverse effects. Pain and redness at the injection site, myalgia, arthralgia, headache, and fatigue were the short-term adverse effects reported after the second dose. The vaccine remains stable at 2°C to 8°C for 30 days, -20°C for 6 months, and room temperature up to 12 hours [184].

6.1.2. BNT162b2. BNT162b2 (Comirnaty®; BioNTech and Pfizer) was developed and manufactured by Pfizer, Biopharmaceutical New Technologies, and Shanghai-based Fosun Pharma. This vaccine has been approved for usage in several countries, viz., Bahrain, Brazil, New Zealand, Saudi Arabia, and Switzerland [185]. In the preliminary trials of this vaccine in BALB/c mice, the effective humoral anti-SARS-CoV-2 immune response was reported without any clinical signs of disease. The immunized mice showed CD8⁺ and CD4⁺ T lymphocytes activation and neutralizing antibodies, which was determined by a GFP-encoded vector on the envelope of SARS-CoV-2 [185]. In phase 1 trials, participants of age groups 18-55 years and 65-85 years showed minimum side effects when administered with BNT162b1 and BNT162b2[185]. Even though high-dose-dependent neutralizing antibodies were produced by both the candidates, BNT162b2 reported to produce less reactivity in older adults



with a 30 μg dose range; therefore, this vaccine candidate is considered for large-scale phase 2/3 studies [185, 186]. The phase 2/3 trial began on July 27th, 2020, with 43,488 volunteers. The study participants included individuals with comorbid conditions. The two-dose immunization with 30 μg of BNT162b vaccine induced neutralizing anti-SARS-CoV-2 antibodies and rendered 95% protection against the disease [187]. The most frequent side effects of this vaccine were fatigue and headache [187].

6.2. Nonreplicating Viral Vector Vaccine

6.2.1. Ad5-nCoV. The replication-defective vector vaccines, which are under phase 3 trial, are Ad5-nCoV, AZD1222, Sputnik V, and JNJ-78436735 [187]. Ad5-nCoV is a vaccine candidate that encodes the S protein of SARS-CoV-2 into host cells. It was developed by CanSino Biologics and the Institute of Biology of the Academy of Military Medical Sciences (AMMS), China [188]. The preclinical studies on BALB/c mice with a dose of intramuscularly or intranasally injected Ad5-nCoV induced humoral response, which subsequently enhanced the levels of neutralizing antibodies against SARS-CoV-2 [188]. Results of phase 1 trial on 108 participants of age group between 18 and 60 showed that doses of 5×10^{10} and 1×10^{11} viral particles/dose were safe and produced good immunogenicity in study participants [189]. In phase 2 trial with 508 participants of age group 18-83, both the doses showed an equal immune response; however, mild adverse effects were reported in 74% and 72% of participants in the lower and higher dose groups, respectively [190]. The phase 3 trial was initiated in September 2020 with a dose of 5×10^{10} viral particles/dose in 40,000 volunteers in Saudi Arabia, Russia, and Pakistan. However, Central Military Commission of China has restricted the use of this vaccine in the military [187].

6.2.2. AZD1222. AZD1222 was developed by Oxford University and AstraZeneca, using a chimpanzee adenovirus (ChAdOx1) vector, which encodes the spike protein of wild-type SARS-CoV-2. In preclinical studies, the intramuscular administration of two doses of AZD1222 to BALB/c and CD1 mice had generated a high immunogenic profile [191]. Subsequent studies have evaluated the efficacy of this vaccine even in pigs. Further analysis using “lentiviral-based SARS-CoV-2 pseudovirus neutralization assay” reported significantly enhanced neutralizing antibodies in the study groups. In the phase 1 study of 1090 healthy volunteers of age group 18-55 years, single or double dose (5×10^{10} viral particles/dose) of AZD1222 exhibited no side effects but produced a strong neutralizing responses against the virus [191, 192]. During August 2020, phase 3 trials were initiated with 30,000 participants in the USA, India, Brazil, Russia, and South Africa [193]. However, due to severe neurological symptoms, the phase 3 studies were temporarily halted in September 2020 [193]. In-depth investigations should be performed to delineate prominent causes for such severe neurological symptoms; however, preliminary phase 3 trial concluded that these effects were due to undiagnosed multiple sclerosis at the time of vaccination, but not related to

the vaccine [193]. The phase 3 study was resumed in other countries, except the USA. Results of phase 3 reported 70.4% efficiency without any severe effects. The vaccine has been approved for use in the UK on November 27th, 2020, in Argentina on December 20th, 2020, and in India on January 3rd, 2021 [194].

6.2.3. Sputnik V. Gamaleya, a Russian Research Institute, developed an adenoviral vector vaccine named Sputnik V [195]. Results of the phase 1/2 trial, which involved 38 participants, have shown an excellent immunogenic profile with mild side effects, myalgia, arthralgia, fever, headache, and minimal pain at the site of injection [187, 195]. Concerns regarding the vaccine's safety and efficacy were raised, as the Health Ministry approved the Russian Federation's vaccine before phase 3 trials. On September 7th, 2020, the phase 3 trial was initiated by recruiting 40,000 individuals across Russia and the Republic of Belarus. After a detailed analysis of 18,794 individuals, 91.4% efficacy was reported from the phase 3 study [195]. However, eight participants were tested COVID-19 positive among the vaccinated group. The vaccine trial has not reported any adverse effects except that some of the individuals experienced mild side effects such as fatigue and headache [187, 195].

6.2.4. JNJ-78436735. It is a replication-defective adenovirus vector (JNJ-78436735) developed by Janssen Pharmaceuticals (Johnson & Johnson) [187]. The vector is engineered for expressing the stabilized prefusion S protein of SARS-CoV-2 in the host. This vaccine was tested in Syrian golden hamsters with a single injection of the vaccine candidate, which resulted in the production of neutralizing antibodies against SARS-CoV-2 and reduced the severity of the disease and mortality. Studies on rhesus macaques reported a significant induction of antibody and T cell-mediated responses. The phase 1/2 trials were initiated in July 2020. Two different doses (0.5×10^{11} /dose or 1×10^{11} /dose) were administered to the participants of two different groups. Whereas the first group is composed of 402 individuals aged 18-55 years, the second group consisted of 394 individuals aged 65 years or above. According to this trial report, only mild symptoms such as fever, pain at the injection site, and headache were reported upon administration of this vaccine. Approximately, 80% of vaccinated individuals showed CD4⁺ T cell responses [187, 196, 197]. Phase 3 studies for this vaccine were initiated in the month of September 2020 with 60,000 individuals. The trial was paused because of the development of severe adverse effects in one of the vaccinated individuals; however, the exact clinical manifestations are not reported. The manufacturer announced the second phase 3 study, which involved recruiting 30,000 adults from Belgium, Colombia, France, Germany, Philippines, South Africa, Spain, United Kingdom, and USA [198].

6.3. Inactivated Virus Vaccine

6.3.1. CoronaVac. CoronaVac is an inactivated virus vaccine candidate with alum adjuvant. CoronaVac was developed by Sinovac Research and Development Co. A recent study reported high immunogenic profile of CoronaVac in BALB/c



mice and Wistar rats. This vaccine reported to induce the activation of SARS-CoV-2-specific neutralizing antibodies. A study was performed on rhesus macaques to determine the efficacy of this vaccine, and the outcome of this study has concluded complete protection against SARS-CoV-2. The phase 2 study was conducted in 600 healthy participants aged between 18 and 59 years, who had received two different vaccine doses (3 and 6 $\mu\text{g}/0.5\text{ ml}$) [199, 200]. As per this study, subjects in both dosage groups exhibited mild adverse reactions and induced more than 90% seroconversion. In the phase 3 trial, a total of 8870 participants from Brazil, Indonesia, and Turkey were recruited and administered with two vaccine doses (2 weeks interval). Finally, this vaccine has been approved in China [187].

6.3.2. Wuhan Institute of Biological Products and Sinopharm Vaccines. An inactivated virus was isolated from WIV04 SARS-CoV-2 strain from a Jinyintan Hospital patient, Wuhan [201]. This vaccine candidate was developed by the Wuhan Institute of Biological Products and Sinopharm by inactivating the virus with β -propiolactone and alum adjuvant adsorption procedure [201]. In the phase 1 trial, three different doses (2.5 μg , 5.0 μg , and 10 μg) were administered to 96 participants of aged 18 to 59 years. In the phase 2 trial, 224 participants were recruited and administered two doses of 5.0 μg each [187]. Administration of the vaccine triggered mild adverse effects but induced the activation of neutralizing antibodies against SARS-CoV-2. This vaccine was approved only in China and in the United Arab Emirates [187, 201].

6.3.3. BBIBP-CorV. BBIBP-CorV is an inactivated virus isolated from 19nCoV-CDC-Tan-HB02 strain of SARS-CoV-2. The vaccine is developed by Sinopharm and the Beijing Institute of Biological Products [202]. Studies on animal models demonstrated the production of neutralizing antibodies against SARS-CoV-2 and rendered protection against SARS-CoV-2 [202, 203]. In the phase 1 study, a total of 192 participants were recruited and administered with one of the three different doses of the vaccine (2.0 μg , 4.0 μg , or 8.0 μg). Fever in 10% of participants was observed as an adverse effect. In the phase 2 trials, a total of 448 participants were recruited and administered either one dosage of 8.0 μg or two doses of 4.0 μg of vaccine at 2, 3, or 4 weeks apart [202]. Results of this trial showed a high immunogenicity and excellent safety profile with 4.0 $\mu\text{g}/\text{dose}$ with an interval of 3 weeks. Furthermore, the vaccine has been examined for its efficacy in a phase 3 trial in Argentina, Bahrain, Jordan, Egypt, and UAE., among 63,000 participants. Two doses of vaccine (4.0 μg) in 3 weeks were administered. The vaccine was approved for public administration in UAE, Bahrain, China, and Egypt [202].

6.3.4. Covaxin. Covaxin is developed by India-based Bharat Biotech. and the Indian Council of Medical Research, Government of India. It is an inactivated virus developed in Vero CCL-81 cells [204]. The vaccine is isolated from an Indian strain inactivated by β -propiolactone along with the alum and imidazoquinoline adjuvant adsorption procedure. The inactivated whole SARS-CoV-2 virion was absorbed into

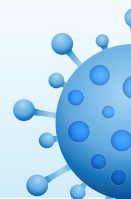
the alum and Algel. This vaccine exhibited a significant reduction in the viral loads and bronchoalveolar infection in animal models [204]. Later, the phase 1 trial was conducted on 375 participants with three different formulations and two different dosages (3.0 μg or 6.0 μg). The vaccine showed a high safety and immunogenicity profile with mild-to-moderate adverse effects with a seroconversion rate of 93.4% in the 3.0 μg dosage group [205]. The phase 3 trials were launched on October 23rd, 2020, in India, with a total of 26,000 study participants of different age groups. The participants have received a vaccine dosage of 3.0 μg in the adjuvant formulation and compared with control groups in the study (2 doses/4 weeks apart). The use of this vaccine has been approved in India and currently in usage for the vaccination of the general public [205].

6.4. Protein Subunit Vaccine

6.4.1. NUX-CoV2373. NUX-CoV2373 is a protein subunit vaccine developed by Novavax. It is a recombinant SARS-CoV-2 S glycoprotein nanoparticle in a baculovirus-Sf9 vector with an adjuvant Matrix M1 [206, 207]. The adjuvant vaccine formulation was investigated in animal models (BALB/c mice), and it has shown a significant increase in the antibody production and strong T cell response [207]. In the phase 1/2 trial, 131 healthy participants received a total of two doses of the vaccine with and without adjuvant. The results of this trial reported a significant increase in the “immune response with vaccine”. Furthermore, anti-S IgG and neutralizing antibody levels were comparatively higher in the vaccinated subjects than those in the convalescent sera of COVID-19 patients [208]. First phase 3 trial was launched on September 23rd, 2020, with 9000 participants in the United Kingdom. Second phase 3 trial of this vaccine was initiated in the US with 30,000 participants in collaboration with Serum Institute of India. The study participants have been receiving a vaccine dosage of 5.0 μg dose with 50 μg of Matrix M1 adjuvant. Results of this study are yet to be announced [208].

7. COVID-19 Vaccines: Choices in a Crisis

Despite having a viable vaccine, the search for a more potent and pan-SARS-CoV-2-specific vaccine continues as the virus is capable of acquiring mutations and exhibits significantly variable pathophysiological effects. For instance, in a recent report, a total of 771 variants of SARS-CoV-2 were identified in India. Moreover, several hurdles, concerns, and queries regarding the safety and quality of the vaccines still persist, for example, (a) the demand for a vaccine against the COVID-19 pandemic far exceeds the supply. Hence, there is a shortage of vaccines to meet the increasing demand; (b) confusion about the safety and efficacy of existing vaccines. In this regard, the efforts have to be made to increase the percolation of information to the public [209, 210]; (c) the feasibility of producing and transporting the vaccine as per the requirement in several countries; (d) whether the vaccine is safer to administer to the “pregnant women and the individuals suffering from chronic health complications such as heart diseases”; and (e) the feasibility of supplying the vaccine



at free of cost or at affordable price for the general public. Therefore, further studies are warranted to address all these queries, which will help to understand more about the vaccine and encourage individuals to attend vaccination camps for timely vaccination.

8. Safety Concerns Pertaining to COVID-19 Vaccines

In general, vaccination is known to induce minimal and transient side effects such as antigen-antibody-mediated reactions, urticaria, fever, and rare skin reactions, which may subside without any major interventions. However, questions about the safety of vaccines arise when the adverse events become a major health concern. Clinical trials of the BNT162b2 mRNA COVID-19 vaccine have been reported to cause minimal local and systemic side effects, viz., pain, redness, fatigue, joint pain, and muscle pain within 1 to 2 days of vaccination [211]. The excipients such as polyethylene glycol (PEG) derivatives may trigger mild anaphylactic adverse reactions upon administration [212]. Anaphylaxis is a serious adverse reaction that can foster asphyxiation, cardiovascular collapse, and multiorgan dysfunction, and sometimes may lead to death [212]. Therefore, it is crucial to delineate prompt recognition of these adverse effects. In general, the anaphylactic reactions are mediated by the mast cell activation via antigen binding and IgE cross-linking. Consequently, these events could trigger the tissue generation of inflammatory mediators such as histamines, prostaglandins, and leukotrienes and foster the development of hives, tachycardia, hypotension, and cardiovascular collapse. Tryptase is higher in blood at the time of both IgE-mediated anaphylaxis and non-IgE-mediated anaphylaxis. The characteristic release of tryptase from mast cells is indicative of the release of inflammatory mediators through mast cells [213]. These effects have raised concerns about the potential adverse risks after vaccine administration in a public community [214]. Therefore, appropriate measures should be taken to minimize these side effects. Further, proper education and awareness about vaccines should be provided to address these concerns and queries associated with vaccine safety and efficacy.

9. Conclusions and Future Directions

SARS-CoV-2 can actuate both innate and adaptive immunities in humans. The uncontrolled inflammatory cascades and blockade of adaptive immune function could induce lung tissue damage at local and systemic levels. Moreover, a drastic decline in the levels of CD4⁺ T cells, CD8⁺ T cells, B cells, monocytes, eosinophils, and natural killer (NK) cells was observed in COVID-19 patients. Significant improvement has been observed in the early detection of SARS-CoV-2 in the infected patients due to the development of new serological testing and diagnostic methods. Furthermore, the vaccine development using immunological approaches to block viral entry and replication is associated with a significant limitation of SARS-CoV-2-induced immunopathology. Although the mRNA-based and DNA-based vaccines and

protein subunit-based vaccines have been developed, the COVID-19-induced immunopathological changes such as *antibody-dependent enhancement* (ADE) and *Th2 immunopathology* have significant implications in developing suitable antiviral agents. Hence, these aspects should be considered while designing a potent vaccine. Furthermore, studies should also focus on developing a drug-antibody conjugate, which can bind to the viral proteins while mitigating the exacerbations in already infected individuals.

Additional Points

Human and Animal Rights. No animal or human was used in this study. All data were collected from open scientific and public sources.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Narasimha M. Beeraka (NMB), SubbaRao V. Tulimilli (SVT), Medha Karnik (MK), Surya P. Sadhu (SPS), Rajeswara Rao Pragada (RRP), SubbaRao V. Madhunapantula (SVM), and Gjumrakch Aliev (GA) collected the literature. NMB, MK, SPS, and SVT collected and prepared tables and figures. NMB, RRP, SVM, and GA conceptualized and developed the sections and proofread the manuscript. All authors reviewed and approved the manuscript before submission. Prof. Gjumrakch Aliev passed away in the month of December 2020. This article is dedicated to late Prof. Gjumrakch Aliev.

Acknowledgments

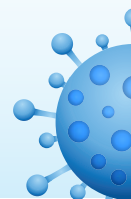
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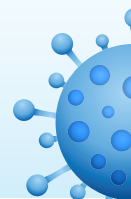
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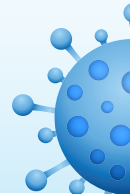
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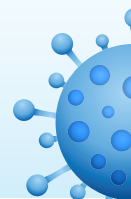
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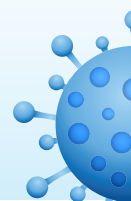


11. Perceptions and Practices related to COVID

SI No	Title	SDG IMPACT
90	Knowledge attitude and practice of personal safety measures adopted by medical practitioners during the covid 19 pandemic, HEMAPRIYA L KUKREJA., MAUREEN PRATIVA TIGGA., NEHA WALI., PRATHAP T., ANIL KUMAR M R., SHREYA CHANDRAN, Journal of Evolution of Medical and Dental Sciences1-7, 2278-4748	Goal 3: Good health and wellbeing Goal 8: Decent work and economic growth
91	THE CURRENT STATUS AND PERSPECTIVES FOR THE EMERGING PANDEMIC: COVID-19, PRITHVI S. SHIRAHATTI., CHANDANA KUMARI V. B., SHASHANK M. PATIL., SUJAY S., TEJASWINI M., LAKSHMI V. RANGANATHA., Dr Jayanthi M.K., Dr Ramith Ramu International Journal of Pharmacy and Pharmaceutical Sciences, 12, 0975-1491	Goal 3: Good health and wellbeing
92	Knowledge, attitude, and practices towards COVID-19 among ayurvedic practitioners of Karnataka, India: a cross-sectional survey, Rufia Shaistha Khanum., Amoghashree., Dr. Sunil Kumar D., Satendra Kumar Verma., Chandan N., Dr Narayana Murthy M.R., International Journal of Community Medicine and Public Health, 7, 4056-4062, 2394- 6032	Goal 3: Good health and wellbeing Goal 8: Decent work and economic growth
93	Pregnant women's knowledge and practice of preventive measures against COVID-19: a study from Mysore city, Karnataka, India, Mamatha Shivanagappa, Yerva Sai Bhavana, Smitha Malenahalli Chandrashekarappa, International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 9, 3622-3625, 2320-1770	Goal 3: Good health and wellbeing



94	Assessment of Clinical Pharmacists' Assistance for Patients With Established Cardiovascular Diseases During the COVID-19 Pandemic: Insights From Southern India, Oliver Joel Gona, Ramesh Madhan, Sunil Kumar Shambu, FRONTIERS IN CARDIOVASCULAR MEDICINE	Goal 3: Good health and wellbeing
95	Knowledge, attitude, and practices toward COVID-19 among the college students in a southern city of Karnataka, NayanabaiShabadi, Chandana Hombaiah, Jose Jom Thomas, Neville Abraham Mathews, RufiaShaistha Khanum, M Shwethashree, M R Narayana Murthy, INTERNATIONAL JOURNAL OF HEALTH AND ALLIED SCIENCES, 9, 343-347	Goal 3: Good health and wellbeing
96	Knowledge and Practice of personal safety measures taken by Medical practitioners during the COVID 19 pandemic, Hemapriya.L, Maureen P Tigga, Prathap.T, Anil Kumar, Neha Wali, Shreya Chandran, Journal of Evolution of Medical and Dental Sciences, 2021, 12	Goal 3: Good health and wellbeing Goal 8: Decent work and economic growth
97	Attitude of Medical Practioners and Their Families Toward Handling of Suspected Covid-19 Patients in Mysore, India Hemapriya L. , Maureen Prativa Tigga ² , Prathap T., Anil Kumar M.R. ⁴ , Neha Wali ⁵ , Shreya Chandran, J Evolution Med Dent Sci / eISSN - 2278-4802, pISSN - 2278-4748 / Vol. 10 / Issue 29 / July 19, 2021	Goal 3: Good Health and Wellbeing Goal 8 : Decent work and economic growth



Knowledge, Attitude and Practice of Personal Safety Measures Adopted by Medical Practitioners During the COVID 19 Pandemic

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Research Article

Keywords: Medical practitioners, personal protective equipment, safety measures.

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Abstract

Introduction: A novel coronavirus (now termed as SARS-CoV 2) was detected as causative agent of severe pneumonia in Wuhan, Hubei Province, China in December 2019. Declared by the WHO as a global pandemic in March 2020, it has created profound changes in global economy and healthcare systems. COVID-19 is transmitted through close contact and droplets with healthcare professionals at significant risk of acquiring the infection, thus requiring to protect themselves. Various measures help in protecting the professionals from contracting the infection. These include hand hygiene, N95 masks, goggles, gloves, gowns, face shields, coveralls and frequent sanitization. Healthcare professionals need to be educated in these various modalities with proper protocols and policies enacted by the health institutions. This study evaluates the knowledge, attitude and practice of various personal safety measures used by the healthcare professionals.

Materials and Methods: After institution ethical committee approval, we conducted an online survey with a preformatted questionnaire consisting of multiple choice questions which assessed the knowledge, attitude and practices adopted by the various healthcare professionals. The survey was done between 1st - 30th of June 2020 and a total of 536 responses were analyzed.

Results: 58.4% of the participants were females, 66% of the healthcare workers worked at a private hospital/ private medical college with 82.1% being located in urban areas. Of the 536 respondents, 90.1% practiced bathing immediately after returning home and 86.8% sanitized their accessories. 86.9% of the professionals used frequent sanitization with use of mask and gloves whereas only 12.3% used full personal protective equipment. 58% of females had used Hydroxychloroquine as prophylaxis whereas only 41% of males used it (statistically significant, $p = 0.005$). Healthcare workers in younger age group (23-40 years) were more likely to maintain distance with family members and government doctors were significantly more likely to do so ($p < 0.001$) as compared to private practitioners.

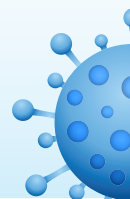
Conclusion: With the medical professionals being at high risk for contracting the infection, the need to provide the healthcare professionals with adequate personal protective equipment is of utmost importance. There is also a need to maintain the well-being of the healthcare professionals as they are the weakest link in the chain.

Introduction

In December 2019 , a set of patients in the city of Wuhan, Hubei Province, China presented with severe pneumonia of unknown origin. Epidemiologically these were linked to a seafood market in the city. On January 7, 2020 the causative organism was identified to be a novel coronavirus - now termed SARS-CoV-

2¹. In March 2020 the World Health Organization (WHO) declared it a global pandemic.²

The coronavirus (COVID-19) outbreak has fundamentally changed the world and also changing



the reality of healthcare workers. This pandemic is creating profound changes in global economy and healthcare systems.³

COVID-19 virus is transmitted between people through close contact and droplets.⁴ The people most at risk of infection are those who are in close contact with or who care for COVID-19 patients. Healthcare workers are at significant risk of acquiring the infection. They are required to protect themselves and prevent transmission in the healthcare setting.

Various measures should be inculcated in day to day life by health care professionals to protect themselves including social distancing, hand hygiene, N95 masks, goggles, gloves, gowns, face shields, cover all's, precautions for aerosol generating procedures and frequent sanitization.

Health care professionals should be educated on when to use which personal protective equipment (PPE), how to put on & take off, how to change them by themselves to prevent contamination and how to properly disinfect and discard this equipment. Health care institutions should have procedures and policies that describe the correct order of donning and doffing PPE in a safe manner.⁵

This study evaluates the knowledge, attitude and practice of the various personal safety measures used by medical practitioners to protect themselves from exposure to this pandemic.

Materials And Methods

Our study is an online survey using a preformatted questionnaire. The institutional ethical committee approval was obtained. We collected data using a questionnaire sent through e-mail or Google form and recorded all responses. The survey consisted of multiple choice questions where we assessed the knowledge, attitude and practices adopted by medical practitioners for their personal safety during the COVID 19 pandemic. All medical practitioners who agreed to participate in the study from the first to the thirtieth of June 2020 were enrolled in the study. We obtained 576 responses. The questionnaire was given as a pilot on 10 subjects to make sure that it was easy to understand and not time consuming.

Based on the feedback obtained, it required no changes. The average time to complete the survey during the pilot was five minutes. The piloted subjects and the subjects who did not complete the questionnaire were excluded and the final number included for analysis after exclusion was 536. Statistical Analysis: The data was compiled and analyzed using MS Excel and SPSS software version 25 at 5% level of significance. The tools of statistics such as – Descriptive statistics, chi-square test, some parametric/non-parametric tests were used for data analysis.

Results

The demographic characteristics of our respondents are tabulated below.

[Please see the supplementary files section to view Table 1.]



Fifty two percent of our respondents reported to have had encountered suspected COVID19 patients. However, only 12.9% were quarantined following such exposure. Five percent of the practitioners were forced to move out of their homes following suspected exposure, in order to minimize risk to their family members. The personal safety measures taken by the various practitioners are tabulated below.

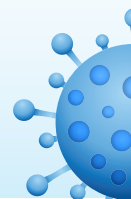
TABLE 2: PRECAUTIONARY MEASURES TAKEN BY THE MEDICAL PROFESSIONALS:

Precautionary measure taken before consulting any patient	Frequency	Percent
Sanitizing and full PPE	66	12.3
Sanitizing, mask and glove	466	86.9
Placing a mask / sanitizer outside the door for use by hospital staff and visitor	408	76.1
Taken Hydroxychloroquine prophylaxis	199	37.1
Taken any online consultation / class because of COVID-19	164	30.6
Bathe immediately reaching home	483	90.1
Sanitize the accessories immediately reaching home	465	86.8
Maintain distance with family members when at home	251	46.8
Advised / administered Hydroxychloroquine prophylaxis to family	128	23.9

Out of the 536 subjects, 86.9% were using sanitization, mask and glove, while only 12.3% were using full PPE as a precautionary measure during their working hours. Almost half the subjects (50.4%) reported interference of PPE in the quality of work sometimes. Twentyseven percent of the subjects felt the interference of PPE with work frequently. There was no significant difference between male and female practitioners regarding the various personal safety measures. Similarly, on comparing the various age groups, designation of practitioners, place of work and area of work; we found no significant difference in the use of personal safety measures.

However, on comparing the different specialties, we found that dentists were significantly more inclined to use full PPE in their practice as compared to others (P value <0.0001).

Female practitioners were more likely to place sanitizers, masks at the entrance of their consulting rooms, as a measure for their own safety,



although not statistically significant. Regarding the use of Hydroxychloroquine prophylaxis, 58% of females had used it as compared to 41% of males, which is statistically significant ($P=0.005$). Practitioners in the age group of 23-30 and 30-40 years were significantly more likely to have taken hydroxychloroquine than older practitioners. However, those in older age group had administered prophylaxis more often to their family members, as compared to younger doctors. Similarly, physicians and general surgeons reported to have taken hydroxychloroquine along with their families significantly more than other specialists. Those in the younger age group, between 23 - 40 years were more likely to maintain distance with their family members, especially physicians and pediatricians. Government doctors were significantly more likely to do so ($p<0.001$) as compared to private practitioners.

Discussion

The coronavirus disease 2019 (COVID19) has become an international health crisis, and the global healthcare system was ill equipped to handle a crisis of such magnitude. The safety of healthcare workers has become the top priority, in order to prevent collapse of healthcare systems and also to prevent transmission of infection from health workers to the community. Medical practitioners are at the highest risk of infection because of frequent close contact with patients who are known or suspected to be infected. A similar situation was seen during the previous SARS-CoV-1 epidemic, where 20% of the cases comprised of health care workers.^{6,7}

Worldwide, over one million people were confirmed to be infected with SARS-CoV-2 by April 2020. Assuming that healthcare workers were infected at the same rate as in the SARS-CoV-1 epidemic, it would foretell the collapse of health care system, especially in developing countries.

There has always been an acceptance that working in a healthcare setting carries a level of personal risk, however, it would seem unreasonable for a healthcare worker to carry out a healthcare activity if there was a high risk of death.⁸ Hence the need for personal protection of frontline warriors is of utmost importance to provide unconditional healthcare services.

Earlier in the pandemic, infection of healthcare workers was as high as 29%, and this dramatically decreased thereafter due to PPE measures put in place to appropriately protect healthcare workers.⁹ Current personal protective equipment (PPE) and infection control guidelines from the World Health Organization (WHO) are based on the assumption that the primary mechanism of transmission is direct and indirect droplet spread.¹⁰

In the current crisis, health-care workers not only have to work harder and longer hours, they often do so in a context where the knowledge and understanding of the novel pathogen is still suboptimal. More than 50% of the subjects in the current study reported interference of PPE in their quality of work. The use of PPE also interferes with vision, difficulty in operating or carrying out procedures. It not only hampers movement and interferes with skills, also, the regular donning and doffing of full PPE add to physical fatigue and psychological stress.¹¹



Aerosol generating procedures may lead to an increase in transmission rates among practitioners. However, the evidence is limited. Infections of health workers following the performance of aerosol generating procedures have been reported, but the exact timing and cause of transmission is unknown.¹² The risk is observed not only during the procedure, but during all periods of contact with the infected patient. Therefore, precautions, and proper PPE usage should be followed not only during procedural periods alone but increase this protection to all times of risk.¹³

While awaiting a vaccine, hygiene measures, social distancing and personal protective equipment are the only primary prophylaxis measures against SARS-CoV-2, but they have not been sufficient to protect our healthcare professionals. Some evidence of the *in vitro* efficacy of hydroxychloroquine against this virus is known, along with some clinical data that would support the study of this drug in the chemoprophylaxis of infection. However, there are still no data from controlled clinical trials in this regard.

In the aftermath of the current pandemic, the exact mode of transmission may still remain controversial as was the case with SARS-CoV-1 and influenza. Urgent further research is required to investigate SARS-CoV-2 transmission, risk factors and strategies to assure the safety of healthcare workers. In the interim, healthcare workers may choose to take a precautionary approach until robust evidence is available.

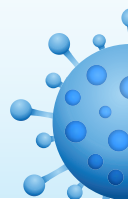
Conclusion

The medical work force is at high risk of exposure as well as increased viral load and although there is a need to balance limited supplies with staff and patient safety, this should not leave the healthcare professionals treating patients with inadequate PPE.

Along with extrinsic organizational, infrastructural and procedural conditions, the intrinsic state and well-being of the health-care worker must also be addressed in order for him or her not to be the weakest link. Personal protection of frontline workers to provide unconditional healthcare services is of utmost importance in the current era as loss of even 1 doctor equals loss of services of almost 1000 patients.

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Competing Interests

The authors declare no competing interests.



Review Article

THE CURRENT STATUS AND PERSPECTIVES FOR THE EMERGING PANDEMIC: COVID-19

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ABSTRACT

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of the extremely communicable viral infection coronavirus disease 19 (covid-19). Initially the virus was found at Wuhan, china which spread across the world exponentially and in a very short span. This outbreak has turned out to be a global health crisis and recently WHO regarded it as pandemic. The origin of the virus is predicted as either the natural selection in animal host prior to the transfer of the pathogen from animals to humans or the natural selection in humans and following transfer. Nevertheless, there is an extensive spread of virus by human to human transfer in the form of droplets. A few antiviral drugs are at the stage of clinical trials to eradicate the covid-19. In this review, a comprehensive approach is put forth to scrutinise the etiology, pathogenicity and transmission of SARS CoV-2. The review also deliberates broadly on the diagnosis and status of therapeutic treatment developed. It also focuses on the preventive and controlling measures from different sectors of the society. The review covers the details reported in 70 studies which were chosen after keyword searches carried out leading to over 884 resulting articles.

Keywords: SARS-CoV-2, Coronavirus disease 19 (covid-19), Transmission, Diagnosis, Therapeutics

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Speedy peer review was done as the subject of the manuscript was related with pandemic.

INTRODUCTION

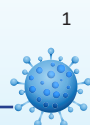
The world has witnessed an array of contagious outbreaks since time immemorial. These outbreaks were caused by a series of bacteria, viruses and other pathogens [1]. These outbreaks were either epidemic, where a small population or community gets affected for a limited duration of time or pandemic, when the whole world might be at risk [2]. Thus, a pandemic is more contagious and dangerous compared to an epidemic and emphasized in this review primarily due to the misinterpretation of the disease in discussion as epidemic at the first mention, which was later declared to be a pandemic [3, 4]. Covid-19 or commonly known as corona virus disease, is caused by a virus, known as Severe Acute Respiratory Syndrome Corona Virus (SARS-CoV-2) [5]. Owing to the health and economic crisis it has created around the globe from a past few months, it can be declared that covid-19 is one of the most pernicious outbreaks of all time [6]. The history dates to 2003, when China officially reported the first outbreak of SARS-CoV-1. It was first spotted in humans in the Guangdong province of southern China in 2002 [7]. Another relative virus, Middle East Respiratory Syndrome Corona Virus (MERS-CoV), was first reported in Arabian Peninsula of Saudi Arabia in 2012 [8]. Both virus outbreaks resulted in significant number of deaths around the globe. In December 2019, China had a cluster of unidentified cause of pneumonia patients in Wuhan, with clinical characteristics significantly like viral pneumonia [9, 10]. According to one study, an exotic animal market in Wuhan city became the centre of the outbreak and there was a rapid increase in the rate of transmission [11]. This led to an immediate examination to characterise the cause of the disease and was identified to be due to novel coronavirus (nCoV). Later, it was named as SARS-CoV-2, by International Committee on Taxonomy of Viruses (ICTV) on 11th February 2020 which is also called as covid-19 [12].

The severity of SARS-CoV-2 is attributed to its life cycle which involves potential natural hosts, intermediate hosts and final hosts. SARS-CoV-2 has great transmissibility and infection causing ability [13] compared to its relative viruses, MERS-CoV and SARS-CoV-1. β-

coronaviruses are a large family of enveloped, diverse-natured, positive-sense and possess single stranded RNA. It is reported to affect both animals and humans, resulting in neuronal, hepatic, gastrointestinal abnormalities chiefly affecting respiratory system [14-16]. Both MERS-CoV and SARS-CoV-1 are responsible for highest reported mortality rates (10% and 40%) in human beings [5]. Being the centre of the pandemic, initially China reported more than 90% of the cases and deaths. However, eventually an outbreak of the disease was observed in places such as Italy, Spain and USA bringing these countries toll on par with that of China. Most of the reported cases were associated with symptoms resembling pneumonia, including cough, fever, myalgia or fatigue [10]. Up to 23rd April, WHO reported 30,90,445 confirmed active cases with 2,17,769 deaths with India reporting 35,043 active cases with 1,154 deaths. According to WHO, the pandemic has spread over 208 countries [17].

The review was planned to report the status of covid-19 pandemic, including its origin and transmission. As it was designed to highlight the available therapeutics, preventive and control measures, a systematic search was conducted using two major databases. Both Google Scholar and PubMed were used to identify published studies related with details about Middle East Respiratory Syndrome Coronavirus (MERS-CoV), Severe Acute Respiratory Syndrome-1 (SARS-CoV-1), and Severe Acute Respiratory Syndrome-2 (SARS-CoV-2). It was completed in accordance with the guidelines given by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

The objectives of the review were planned and independently written by all the 8 authors. The corresponding author was engaged to resolve the conflicting interest in the article. For the collection of published studies, we used the key-words like "SARS-CoV-1", "Covid-19", "SARS-CoV-2", "Detection", "Diagnosis", "Clinical Symptoms", "Infection", "Transmission", "Pharmacotherapy", "Immunotherapy", "Vaccines", "Prevention" and "Controlling measures". In this manner, individual studies were collected and further screened according to relevance to suit the requirement. A total of 884 of studies resulted



from our search criteria and were analysed for duplicates and relevant content. In the first screening, 23 of the studies were removed out of which 19 duplicates and 3 belonged to herbal medications. As the study was strictly designed to report current pharmacotherapeutic agents, ongoing clinical trials and immunotherapeutic agents, herbal medications with no clinical proof were discarded. The remaining 861 studies were grouped

under the planned objectives, in which major selection was carried out. Furthermore, individual authors reported the number eligible studies as 246. A second and last phase of selection was carried out with respect the perspective of the review. Finally, we found only 70 studies that were able to perfectly fit into the perspective of the review article. The scenario of the search identification and selection has been depicted in the fig. 1.

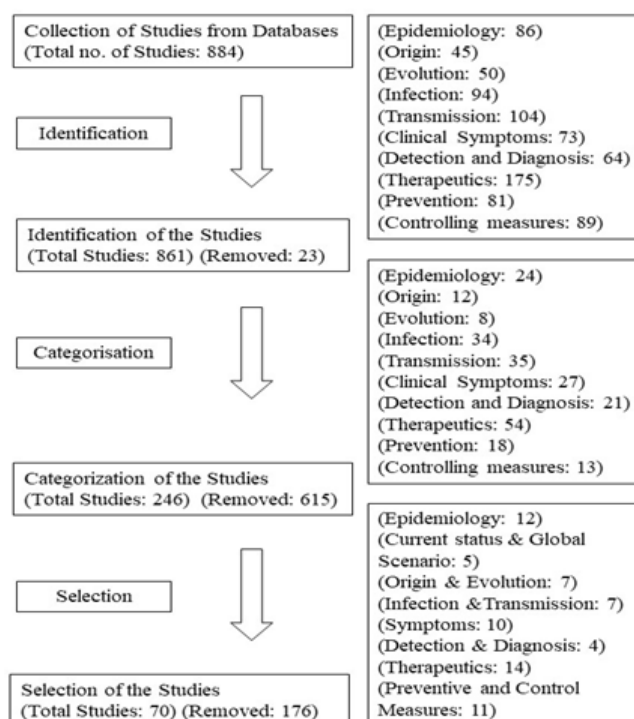


Fig. 1: Flow diagram of the search strategy Created with "BioRender.com"

Current issues and global scenario

It was reported that a total of 44 cases of pneumonia patients of unknown causal agent, from 31 December 2019 through 3 January 2020 in Wuhan city. As the cause was known to be a viral infection there was confirmed cases of SARS-CoV-2, 278 cases in China, 2 cases in Thailand and 1 each case in Japan and Republic of Korea by 20 January 2020 [18]. First case in India was reported on 30 January 2020, almost 649 cases and 13 deaths were reported by 26 March 2020 [19]. Covid-19 is extremely infectious disease with an estimated R0 values of about 2.28 (2.06-2.52), which indicates SARS-CoV-2 is in the epidemic phase and has very strong transmission capacity [20]. Presently, there are about 3 million cases confirmed globally; 1,406,899 infected with 129,311 deaths in European region, 1,213,088 confirmed and 62,404 deaths in America, 176,928 confirmed and 7304 deaths in the Eastern Mediterranean region, 146,449 confirmed and 6037 deaths in Western Pacific region, 51,351 confirmed and 2001 deaths in South-East Asia region and 23,254 confirmed and 903 deaths in Africa as on 29 April 2020 [21]. In India, as on 1 May 2020, there are 25007 active cases with 1147 deaths [22].

Origin and evolution of SARS CoV-2

COVID-19 is also well known as 2019 novel coronavirus, otherwise it is also referred as 2019-nCoV. It was first recognised in Wuhan China and the World Health Organization declared the coronavirus outbreak with an official name covid-19 on 11 February 2020. This virus causes the upper-respiratory tract illness, which was not found to be infecting humans when first identified [23]. In 1937, corona type of virus was first isolated from chickens. Later in the mid-1960s, human coronaviruses were identified for the first time.

Coronavirus is a sense-strand RNA virus; single-stranded enveloped consisting genome of 30Kb [16]. Based on the Coronaviridae family, genera can be divided into four: α , β , γ , and δ . The birds get infected usually by γ and δ genera of coronavirus, whereas the humans and mammals are infected by α and β genera. The novel Severe Acute Respiratory Syndrome coronavirus-2 (SARS-CoV-2) infecting the humans are the β -coronavirus that appears as oval or round and crown shape when observed under electron microscope [24]. Further studies on the genera of coronavirus elucidated that the bats usually are the reservoirs of α and β genera while birds carry γ and δ genera of coronavirus. The studies also reported the progenies of the lineage of β -coronavirus within rhodents [25, 26].

SARS-CoV, MERS-CoV, NL63, HKU1, OC43 and 229E are human coronavirus, among this SARS CoV-2 is the 7th coronavirus infecting humans. Infections by HKU1, OC43, NL63 and 229E cause mild symptoms but the SARS-CoV, MERS-CoV and SARS CoV-2 are associated with severe symptoms and causes disease [27]. Origin of the SARS CoV-2 can have two prospects, firstly its can be predicted that natural selection in animal host prior to the transfer of pathogen from animals to humans. Secondly, we can predict as the natural selection in humans and resulting animal to human transfer. Covid-19 cases were reported initially in Huanan market located in Wuhan, T, which most likely emerged from the animal source owing to its resemblance of SARS CoV-2 to several other coronaviruses. The bat seems to be reservoirs of SARS CoV-like coronaviruses, which were unable to efficiently invade the humans. The mutations in structural covering of spike protein of the virus enabled the access to bind the humans with the aid of ACE2 receptors. As per the first perspective, the animal host would have allowed the natural selection process to effectively cause the necessary changes in order



to escape its host and dwell within the human hosts. There is also a possibility as per the second perspective, that the progenies of SARS CoV-2 hurdled into humans and adapted into genomic characteristics and then spread the infection rapidly through human to human transfer [28].

Infection and transmission

Mode of transmission

The phylogenetic analysis and the protein sequencing from COVID-19 virus exhibited similarity with ACE2 receptors in turtles and pangolins which are genetically closer to humans and bats. It is suspected that these species can be an alternate intervening hosts transmitting SARS CoV-2 to human [29]. The virus can be

transmitted through droplets of saliva, nose discharge and aerosols either from short or long distance by talking, breathing, sneezing and coughing respectively [30]. The person infected can cause transmission through droplets within 1m proximity either by cough or sneeze and the pathogen can enter the healthy person through mouth, nose and eyes. The objects or materials which encountered the infected person or the environment surrounding can also transmit the infection of virus [31]. The virus is present within the droplet mostly reflected as a particle and it cannot be an airborne transmission [32]. Consumption of milk from an infected animal and urine of the animal may also contain virus. The undercooked or uncooked meat consumed directly were also theorised to be main course of transmission [33]. The mode of transmission from primary host to humans has been depicted in fig. 2. [13].

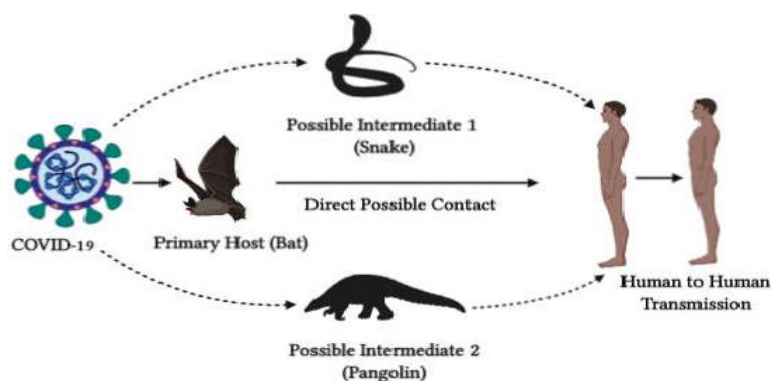


Fig. 2: Mode of transmission of Covid-19 [13] Created with "BioRender.com"

Mode of infection

Structurally, the outermost layer SARS CoV-2 consists of spikes made up of glycoprotein on the surface that helps the virus to invade host cells [34]. The S protein which is recognised by the host ACE2 receptor initiates the virus life cycle in host cell through endocytosis. The endosomal pathway fusion takes place between the viral envelope and the host cell membrane with the release of viral nucleocapsid into the cytoplasm. The RNA of SARS-CoV-2 is released, which gets translated to polyproteins pp1a and 1ab (viral replicase).

Later, the viral proteinase cleaves the RNA replicase to smaller fragments which persuade the structural rearrangements in the cell membrane to form double-membrane vesicles (DMVs). A chain of sub genomic mRNAs is produced by polymerases during the process of discontinuous transcription and the viral proteins are translated pertinently. The combination of viral proteins and RNA genome successively accumulate to form a virion in ER-Golgi intermediate complex (ERGIC). Finally, through secretory pathway, the mature virions are transported and released out of the cell in smooth-walled vesicles as shown in the fig. 3 [13, 35].

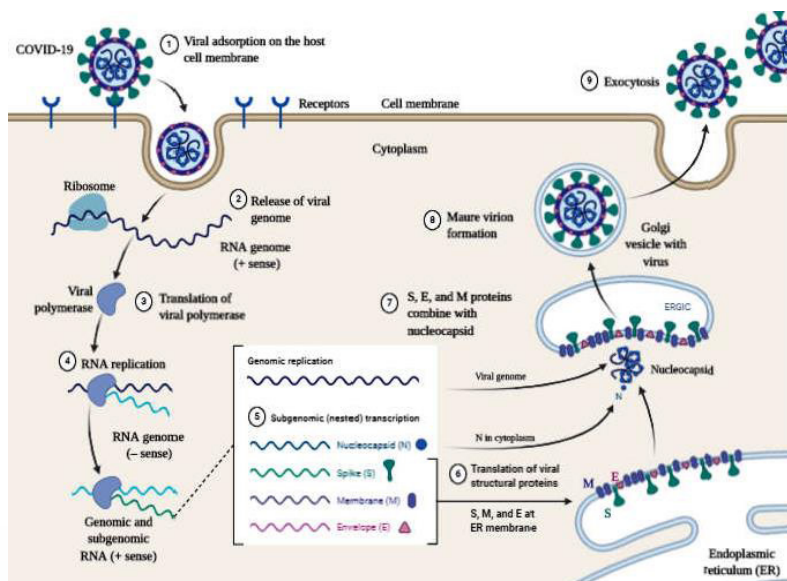


Fig. 3: Mode of infection of Covid-19 [35] Created with "BioRender.com"

Symptoms of infection

Incubation period for covid-19 is 14 d and within 4-5 d one can observe the onset of symptoms. SARS-CoV-2 infection would develop symptoms within 11.5 d in the infected person and although vary between individuals at the onset, most common symptoms are fever, cough, tiredness, eating disorder or also known as anorexia, shortness of breath, excess of sputum production and muscle pain [36]. Least commonly reported symptoms are headache, disorientation, mucus fluid secretions in nasal cavity, sore throat, mucus containing blood stains from the bronchi, larynx, trachea, or lungs, vomiting, and diarrhea [10, 11, 37, 38]. In certain cases, patients also exhibit other common symptoms rarely such as pain in the abdominal region, abdominal distension and recurrent inclination to evacuate the bowels [39]. According to patient's

analysis nausea, vomiting and diarrhea appear at variable percentages [40]. The patients admitted initially of heart palpitation and chest tightness were also found to be infected with covid-19. The patients associated with cardiovascular disease will have high secretion of ACE2 compared to a healthy person and therefore more prone to developing symptoms of infection. The patient infected with SARS CoV-2 with comorbidities such hypertension or diabetes mellitus are in extreme danger. It is recommended that greater care should be taken of people suffering from cardiovascular diseases, hypertension and diabetes mellitus to not encounter Covid-19 positive people [41, 42]. Lately, with close observation of patients infected with covid-19 also exhibited loss of smell that is anosmia, associated with or without parageusia means confusion of the sense of taste [43]. There are also possibility of asymptomatic infections and the transmission of SARS CoV-2, although confirmed yet [44].

Table 1: Available pharmacotherapeutic agents against covid-19

Pharmacotherapeutic agents	Possible covid-19 indication	Mechanism of action	Original indication	Dosage information	References
Hydroxychloroquine/Chloroquine	Off-label use for anti-viral treatment	Increases intracellular pH in host cells, thus inhibiting RNA synthesis. Facilitates the glycosylation impairment of ACE2, by disrupting viral S protein thereby preventing the entry of SARS-CoV-2 into the host cell. Also known to possess anti-inflammatory and immunomodulatory effects	Malaria, HIV, Autoimmune Diseases	Hydroxychloroquine: 400 mg on first day followed by 200 mg for four days, twice, orally. Chloroquine: 500 mg twice for 5 d, orally.	Barlow et al. 2020; Tu et al. 2020; McCreary et al. 2020 [53-55].
Remdesivir	Off-label use for anti-viral treatment	Guanosine nucleoside that specifically inhibits viral RNA replication using molecular mimicry mechanism	Ebola virus, MERS-CoV	200 mg on first day, followed by 100 mg for up to 10 d intravenously	Barlow et al. 2020; Tu et al. 2020; McCreary et al. 2020 [53-55]
Lopinavir and Ritonavir	Off-label use for HIV-1 treatment	Acts as an aspartic acid protease inhibitor that inhibits viral replication hence its life cycle	HIV-1	200 mg-100 mg for 14 d through oral consumption	Barlow et al. 2020; Tu et al. 2020; McCreary et al. 2020 [53-55].
Ribavirin	Off-label use for anti-viral treatment	Nucleoside analog that specifically inhibits viral RNA replication using molecular mimicry mechanism	Hepatitis-A, Hepatitis-B, SARS	400 mg for 14 d, twice a day	Barlow et al. 2020; Tu et al. 2020; McCreary et al. 2020 [53-55]
Nitazoxanide	Off-label use for anti-protozoal treatment	Inhibits hemagglutinin formation hence interferes with viral life cycle. It may also act on the electron transfer activity of pyruvate ferredoxin oxidoreductase enzyme, thus interfering in the protozoan energy metabolism.	Diarrhea	Doses recommended for SARS were based on age groups; 1-3-year olds were recommended with 100 mg, 4-11 y with 200 mg, above 12 y with 300 mg for 5 d, orally.	Barlow et al. 2020; McCreary et al. 2020 [53-55].
Nelfinavir	Off-label use for HIV-1 and anti-viral treatment	Drug binds to the active site of HIV-1 protease enzyme and inhibits the cleavage of precursors of Gag-Pol polyprotein chain, that are essential for the survival of HIV-1 inside the host. The residues left after the molecular process are no longer infectious.	HIV-1	Unknown	Barlow et al. 2020; Shetty et al. 2020; McCreary et al. 2020 [54-56].
Favipiravir	Off-label use for anti-viral treatment	It structurally resembles guanine, and through competitive inhibition, reduces the efficacy of viral replication like remdesivir	Influenza	Unknown	Tu et al. 2020; Shetty et al. 2020 [53, 56].
Ivermectin	Off-label use for HIV-1 and anti-viral treatment	It can dissociate the preformed IMP α . β 1 heterodimer, which aids in the protein displacement. As the protein displacement is essential for the maintenance of viral replication, targeting the protein displacement across the host cell would be a feasible option to inhibit viral life cycle	HIV-1, Dengue	Unknown	Tu et al. 2020 [53].
Nafamostat	Off-label use for anti-viral treatment	Acts as a serine protease inhibitor, inhibits TMPRSS2 associated fusion process, may prevent the entry of	Pancreatitis	Unknown	Shetty et al. 2020 [56].

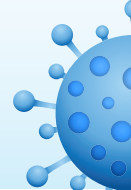
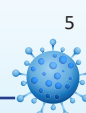


Oseltamivir	Off-label use for anti-viral treatment	SARS-CoV-2 into host cells. Neuraminidase enzyme inhibitor that may prevent the entry of the virus into host cells. Also reduces shedding and infectivity of the virus	Influenza	75 mg	Shetty <i>et al.</i> 2020 [56].
Sofosbuvir	Off-label use for anti-viral treatment	Nucleoside analog that specifically inhibits viral RNA replication using molecular mimicry mechanism	Hepatitis-C	Unknown	Shetty <i>et al.</i> 2020[56].
Zanamivir	Off-label use for anti-viral treatment	Neuraminidase enzyme inhibitor that may prevent the entry of the virus into host cells. Also reduces shedding and infectivity of the virus	Influenza	Unknown	Shetty <i>et al.</i> 2020 [56].
Azithromycin	Antibiotic	The drug acts as an anti-bacterial agent and inhibits bacterial infection, may possess anti-viral properties.	Bacterial Infections	500 mg on first day followed by 250 mg for four days	Shetty <i>et al.</i> 2020[56].
Emodin	Anti-viral drug under investigation	Disrupting viral S protein thereby preventing the entry of SARS-COV-2 into the host cell	Polycystic Kidney Disease	Unknown	Shetty <i>et al.</i> 2020 [56].
Umifenovir (Arbidol Hydrochloride)	Anti-viral drug under investigation	The drug targets hemagglutinin, a glycoprotein present on the surface of the influenza virus. It prevents the fusion of viral membrane with endosome after endocytosis.	Influenza and Arbovirus infection	Unknown	Tu <i>et al.</i> 2020; McCreary <i>et al.</i> 2020 [53, 55].

Table 2: Available immunotherapeutic agents against covid-19

Immunotherapeutic agents	Possible covid-19 indication	Mechanism of action	Original indication	Dosage information	References
Anti-interleukin (IL)-6	Against Acute respiratory distress syndrome	IL-6 can bind to its IL-6 receptor and alternative mRNA splicing. Increased IL-6 content results in reduced lung elasticity and increased bronchoalveolar inflammation. Inhibiting IL-6 may hamper effects of covid-19.	Acute respiratory distress syndrome	Unknown	Tu <i>et al.</i> 2020 [53].
TNF- α inhibitors	Anti-inflammatory	Reduces lung inflammation caused by Tumor Necrosis Factor- α . Blocking these factors would resume normal lung functioning.	Psoriasis, Rheumatoid Arthritis, and Inflammatory Bowel Diseases	Unknown	Tu <i>et al.</i> 2020 [53].
Methylprednisolone	Anti-inflammatory	Consumption would suppress the unwanted immune reactions	Arthritis, Blood disorders	Unknown	Tu <i>et al.</i> 2020 [53].
Fingolimod	Immunomodulating Drug	Through molecular mimicry, it binds to sphingosine-1-phosphate (S1P1) receptors to reduce the T-lymphocytes in lymph nodes, to attenuate the unwanted immunopathogenesis	Refractory multiple sclerosis	Unknown	Tu <i>et al.</i> 2020 [53].
Tocilizumab	Off-label use to hamper unwanted immune response	Monoclonal antibody that binds to IL-6 receptors to block IL-6 pathway	Rheumatoid Arthritis	Unknown	Tu <i>et al.</i> 2020 [53].
NK-Cells	Boosting Anti-Viral Response	Increases the number of cytokines and chemokines, without the help of CD8+and antibodies. Migration towards viral site reduces viral activity.	SARS-CoV-2	Unknown	Tu <i>et al.</i> 2020 [53].
Anti-C5a Monoclonal Antibody	Anti-inflammatory	Anti-C5a treatment could reduce lung injury by reducing vascular leakage and influx of neutrophils into the damaged site.	SARS-CoV-2	Unknown	Tu <i>et al.</i> 2020 [53].
Convalescent Plasma Therapy	Anti-viral response	Antibodies present in the sera from convalescent patients would suppress viremia	Reducing infection	Unknown	Shetty <i>et al.</i> 2020; McCreary <i>et al.</i> 2020 [55, 56].
Thalidomide	Anti-angiogenic, Anti-inflammatory, Anti-fibrotic	Along with the reduction of TNF- α , it reduces multiple inflammatory conditions by suppressing inflammatory cells and pro-inflammatory cytokines	Crohn's Disease, Bechets Disease	Unknown	Tu <i>et al.</i> 2020 [53].
Intravenous Immunoglobulin	Immunomodulatory Activity	Boosts immune system by attenuating the proliferation of inflammatory cells, inhibition of phagocytosis, and interfering antibody mediated cytotoxicity	Neurological, Dermatological, and Rheumatologic Disorders	500 mg for 5 d	Tu <i>et al.</i> 2020 [53].
SARS-CoV-2-Specific Neutralizing Antibodies	Anti-viral	Recovered from patients of COVID-19, these antibodies would significantly reduce the viral infection	SARS-CoV-2	Unknown	Tu <i>et al.</i> 2020 [53].

Table 3: Available cellular therapeutic agents against covid-19



Cellular therapeutic agents	Possible covid-19 indication	Mechanism of action	Original indication	Dosage information	References
Mesenchymal Stem Cells (MSC's)	Anti-inflammatory	Boost immune system by suppressing inflammatory cells and pro-inflammatory cytokines. Produce paracrine factors to aid tissue repairs.	SARS-CoV-2	Unknown	Golchin <i>et al.</i> 2020 [57].
CAR T Cells	Anti-viral activity	Specifically binds to the surface antigen present on the virus and inhibits the viral replication inside the host	Cancer, Hepatitis-B, HIV-1	Unknown	Bachanova <i>et al.</i> 2020 [58].

Table 4: Ongoing vaccine developments against COVID-19

Company/Institution	Estimated timeline	Technology	Stage/Funding	References
Moderna Therapeutics—US National Institute of Allergy and Infectious Diseases	3 mo to early stage (phase 1) clinical trial in US (earliest); much longer for full testing and regulatory approval	Messenger RNA vaccine	Preclinical Awaiting preclinical tests and phase 1 study by NIAID, Funding by CEPI.	Pang <i>et al.</i> 2020 [52].
Inovio Pharmaceuticals	Human testing in the next few months	INO-4800-DNA based vaccine (DNA synthesized in lab, does not require actual virus sample)	Preclinical Funding by Coalition for Epidemic Preparedness Innovations (CEPI), up to \$9 million	Pang <i>et al.</i> 2020 [52].
Novavax University of Queensland	3 mo 6 mo	Nanoparticle vaccine Rapid Response Technology, 'Molecular clamp' vaccine platform (gene added to viral proteins, misleads body to generate antibodies)	Preclinical Preclinical Funding by Coalition for Epidemic Preparedness Innovations (CEPI)	Pang <i>et al.</i> 2020 [52]. Pang <i>et al.</i> 2020 [52].
Vir Biotechnology	Not available	Anti-coronavirus monoclonal antibodies. Additionally, using "whole-genome CRISPR based screening capabilities to identify the host receptor for Wuhan coronavirus"	Preclinical	Pang <i>et al.</i> 2020 [52].
Chinese Centre for Disease Control and Prevention (CDC)	At least 1 mo for development, 2–3 y before availability for use	Not available Inactivated virus vaccine (postulated, not verified)	Preclinical; virus successfully isolated, currently selecting strain	Pang <i>et al.</i> 2020 [52].
Shanghai East Hospital (Tongji University)-Stermirna Therapeutics	<40 d for manufacture of vaccine samples	mRNA technology	Preclinical	Pang <i>et al.</i> 2020 [52].
Johnson and Johnson	1 y to market	Adenovirus—vectored technology used for Ebola vaccine (and Zika and HIV vaccine candidates)	Preclinical	Pang <i>et al.</i> 2020 [52].
University of Hong Kong	Months for animal testing, At least 1 y for clinical trials on humans	Modified nasal spray influenza vaccine (with surface antigen of coronavirus) prevents both influenza and corona virus	Preclinical; vaccine developed	Pang <i>et al.</i> 2020 [52].
University of Saskatchewan (VIDO-InterVac)	Target for animal testing in 6–8 w, human trials in at least a year	Not available	Preclinical	Pang <i>et al.</i> 2020 [52].
GeoVax—BravoVax	Not available	Modified Vaccina Ankara—Virus Like Particles (MVA-VLP) vaccine platform	Preclinical	Pang <i>et al.</i> 2020 [52].
Clover Biopharmaceuticals	Not available	Highly purified recombinant 2019-nCoV S protein subunit-trimer vaccine (S-Trimer), produced using Trimer-Tag© technology	Preclinical	Pang <i>et al.</i> 2020 [52].
CureVac	Not available	mRNA technology	Preclinical	Pang <i>et al.</i> 2020 [52].
Texas Children's Hospital Center for Vaccine Development at Baylor College of Medicine	Not available	Not available	Not available	Pang <i>et al.</i> 2020 [52].
Codagenix	Not available	Not available	Not available	Pang <i>et al.</i> 2020 [52].

Detection and diagnosis

After the outbreak of COVID-19 in Wuhan(China), WHO has recommended that samples should be taken from suspects of SARS-CoV-2 of respiratory tract specimens like bronchoalveolar lavage

fluid, pharyngeal and nasal swabs which are subjected to nucleic acid amplification diagnostic test, RT-PCR assay and specific method to identify patients with respiratory pathogens/infection [45]. To detect the infected cases of covid-19, molecular-based approaches (Nucleic acid test) are important. Other techniques like serological



antibody test are also used, which takes shorter time to detect the infection [46, 47]. RT-PCR and next-generation sequencing techniques are used to check for the presence of SARS-CoV-2 in the specimens of respiratory tract, which are time consuming but far more sensitive and efficient. Sequencing of genome is performed to design primers and probes that are specific to detect SARS-CoV-2. Viral RNA extract of COVID-19 is used as positive control in all assays. In real time RT-PCR assay primers and probes that specifically target gene of SARS-CoV-2 is used. For SARS-CoV-2 identification, open reading frames (ORF 1a and 1b), RNA-dependent RNA polymerase gene (RdRp), envelope (E), and nucleocapsid(N) are key sequences for diagnose [17].

Advancements in therapeutics treating Covid-19

One must accept with anguish that there is no specific treatment option found to treat COVID-19 till date [5, 48]. All the therapeutics now used to treat COVID-19 were once used to treat similar viruses named SARS-CoV or MERS-CoV, the outbreaks reported in 2003 and 2012, respectively [49]. Although they possess an array of working mechanisms, these drugs are not 'specifically' designed for the said infection [48]. Medical professionals are using these drugs either separately or in combination for specific duration. In the following sections, we have briefly discussed about the ongoing therapeutics for covid-19.

The first and important step that comes into light in case of viral or any infectious disease is to be away from the infected person or patients termed as social distancing. covid-19 is highly infectious and can enter the host through aerosols, just like tuberculosis [50, 51]. Therefore, it becomes essential to maintain adequate isolation to control the viral transmission. Care should be taken that even mild symptoms should be reported to medical professionals, so that further transmission can be prevented from confirmed patients. The medical treatment involves usage of pharmacotherapy, immunotherapy, cell therapy and vaccines [52-54]. Tables 1-4 briefly depict the details of all the therapeutics currently being used.

Apart from pharmacotherapy and other modes of treating covid-19, there is no available vaccine against the pandemic. Though it takes significant time to develop vaccines many of the firms and institutions have joined hands for the development of vaccines against COVID-19 [52, 53]. They are working around the globe to ensure that they explore every part of the virus characteristics. It should be taken care that cross-contaminations of other vaccines can occur, and the effect may be even worse than covid-19 [59].

Preventive and control measures

Every health malady outbreak results in the initiation of preventive measures at different levels inside a region, apart from the medications. Following these preventive measures would help in saving lives, hence would maintain the population levels at constant rate [50]. In case of COVID-19, as no specific medications are available, prevention would be the best opportunity to survive against this global pandemic [50]. The preventive measures can be followed in 3 levels including personal level, community level and population level. Laws should be made to facilitate the strict implementation of preventive measures at every level.

Role of individuals in the prevention of covid-19

The transmission of COVID-19 occurs through the exchange of aerosols when a healthy individual receives them from a sick person [60]. As it belongs to the category of severe acute respiratory syndrome (SARS), the highest viral content is possessed by the sputum and upper airway secretions [60]. The virus can even remain for days on the surface and can result in further complications [10]. Thus, it becomes important to wear a fluid resistant (Type-IIR) personal protective equipment (PPE) masks to avoid the entry of the aerosols and to maintain at-least a two-metre limit on contact. These masks should be used by both patients and healthcare professionals to avoid further spreading of the virus [61]. FFP2, FF3 and N95 are the types of high filtering masks that are usually referred to use against droplets. The WHO recommends the use of undamaged FFP2/3 and N95 masks for up to 4 h, as it is a median healthcare tolerance time for healthcare workers [51]. It is also recommended that regular washing of hands

should be done with soap, disinfectant or sanitizer with minimum 60% alcohol in it. Touching of nose, mouth and eyes should be avoided with unwashed hands [48].

Apart from protecting the body from the external aspects, it also becomes vital to maintain the health from internal side. It is reported that the western diet mainly comprises of saturated fatty acids, refined carbohydrates and fats, leads to the chronic activation of innate immune system and attenuation of the adaptive immune system [62]. It activates macrophages, neutrophils and dendritic cells, thus triggering activation of pro-inflammatory mediators. Also, consumption of high fat diet leads to B and T lymphocyte inactivation, macrophage infiltration to lungs which in turn leads to lung or possible neuro-inflammatory conditions [62]. On the other hand, obese people with a habit of high consumption of fats showed less response to COVID-19 vaccines [62]. In sum, it is important to consider the effects of our daily food and lifestyle on the susceptibility to COVID-19 infection. Therefore, it is recommended that individuals must shift their diet plans to high amounts of fiber, unsaturated fats, antioxidants and whole grains from eating unhealthy refined carbohydrates and saturated fatty acids [62].

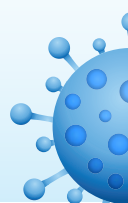
In addition to this, one must look after the safety protocols in clinics and hospitals. Room ventilation is believed to clear most of the viral aerosols (63%). After 2 exchanges, the viral load reduces in to 14% and after 5th exchange, <1%, which becomes an optimum environment for the patients [51]. Thus, it also becomes important to maintain regular room ventilation protocols. Apart from ventilation, it also becomes essential to maintain protocols to avoid cross-infection, through the only available way, that is PPE. Avoidance of patients, staff or visitors exposed to the virus, repeated handwashing, isolation of patients, cleaning the equipment regularly and proper disposal of PPE can help in the effective prevention of covid-19 transmission [48, 51].

Role of society in the prevention of covid-19

Along with personal efforts to stay away from the pandemic, efforts from other two levels, i.e., community and population are also essential. In the middle of the pandemic without availability of proper and specific therapeutic options, social distancing and quarantine prove efficient options to control the further spreading of the disease [63]. Social distancing refers to the maintenance of safe distance from individuals during interactions in public places like utility stores, hotels, theatres etc [64]. While quarantine can be defined as the restriction on infected persons in an isolated place from the public [63]. It is one of the most misunderstood and feared methods of controlling covid-19, because it may affect both infected and non-infected individuals with psychological, economical, and emotional complications such as post-traumatic stress disorder, depression, insomnia, mood swings etc [65]. From the economical point of view, quarantine reduces the productivity, hence minimalizes the economic growth [66]. According one study, the restrictions on travelling and traffic significantly reduced the transmission of the virus. Another study showed that quarantine strategies are more effective than traffic restrictions. According to them, it is estimated to reduce the number of cases by 89.7% [50]. Similarly, the idea of city lockdown was proved to be effective when a study reported 72% drop in the number of infected people. They also suggested that, postponing lockdown would worsen the situation by 5 times [50]. Owing to these factors, it becomes clear that quarantine can be the best self-preventive method that can be practiced at community and national level.

Contribution of pharmacy and healthline services

Being in the front line against the pandemic, a lot can be expected from the pharmacy and healthline services. Preventive and control measures can be at their best with the combination of quarantine and activity of healthline services [67]. The pharmacists can develop guidance for providing pharmacy services, where researchers across the globe, epidemiologists and clinicians can share their views and studies on the virus' characters and controlling methods [68]. This hub can result in the development of preventive and control methods. Also, on the other hand, pharmacists can put forward their formulary manuals and medicine news. Through this approach,



dosage, uses, ingredients and precautions about covid-19 therapeutics can be made available for the public [68]. Conducting drug-based research and evaluation of the drugs can also help the nation to look forward to developing new ways to fight the pandemic [68]. Establishment of digital platforms to create awareness about the pharmacotherapeutic approaches can help the people to overcome their misbeliefs and confusions about the pandemic and its treatment. This system can be the best method in situations like city lockdown and quarantine [68].

With respect to the healthline services, doctors and medical staff should provide their best service to treat the infected as well as to create awareness, among others [69]. Specialists and trained staff are the two most important necessities in battling covid-19. Providing individual care, enough time, facilities to patients can result in quick recovery from the disease [69]. Along with this, opening medical helplines, telecommunication for remote areas to provide information about available treatment information and preventive measures would be helpful [68]. It would be better if mobile health services get into the front, edifying as well as providing medical assistance. This would be considered as a better option in conditions like lock-down. Fig. 5 depicts the role of pharmacy and healthline in the prevention of covid-19.

Essentialities in research and development

Owing to the considerable impact of ongoing covid-19 pandemic on health security and global economy, one of the major problems raised was inadequate diagnostic and medical equipment, including test kits, face masks, sanitizers and therapeutic drugs [69]. It has now become necessary for scientists to standardize and develop the diagnostic test strips and enzyme linked immunosorbent assay (ELISA) kits as additional procurement [70]. Computational biological tools and bio-informatics analysis of covid-19 can be the resourceful keys to develop the molecular imaging of structural proteins and possible mutations [70]. The detection of possible reservoir and carriers of the virus can be done with serological surveys of suspected animals. This would surely help in the controlling the pandemic [70]. On the other hand, it is still essential to consider factors like temperature, UV, humidity, behaviour of aerosols and biophysical evaluation of all these factors for the effective study of covid-19, thus finding a pavement for its permanent cure [70].

CONCLUSION

The covid-19 pandemic has been the most dreadful disease in the history so far, accounting for loss of millions of lives. It has also resulted in the complete halt of importing and exporting essential things across the worlds, thus has impaired the global economy. The similarity of the virus with the already known viruses is considered because of the therapies working on it. Compared to the other viruses from the same family, it appears that covid-19 has been evolved to withstand all those therapeutics once effective against MERS-CoV and SARS-CoV-1. The ongoing therapeutics are used as a combination to reduce the viral load in patients, as no specific drug is available and many of them are yet to clear the clinical trials, including vaccines.

Though it possesses symptoms like pneumonia, it is lethal and highly contagious. Thus, it becomes utmost important to maintain the social distancing through lockdown. As no specific drug available, it is better to avoid the exposure by maintaining social distancing. Every citizen of the country must play his/her role in the prevention and control of the pandemic. It is recommended that both lock-down would result in significant decrease of mortality rate. The pharmacy and healthcare services are already doing their best to fight the pandemic. To boost up the efforts, one health approach is recommended. Along with the good practices, effective treatment, development of quick and precise diagnosing kits, ample production and distribution of PPE can reduce the effect of the pandemic significantly.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

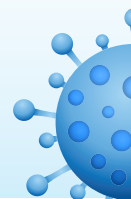
CONFLICT OF INTERESTS

Declared none

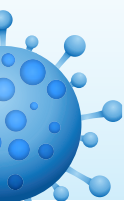
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Original Research Article

Knowledge, attitude, and practices towards COVID-19 among ayurvedic practitioners of Karnataka, India: a cross-sectional survey

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ABSTRACT

Background: COVID-19 is a highly infectious disease which was first identified in Wuhan, China and was subsequently declared as pandemic by WHO. As it is rapidly spreading and taken lives of millions, various countries have adopted unprecedented measures and treatment modalities. Since India has historical roots of Ayurveda, Ayurvedic system of medicine was consider to boost the immunity and also to prevent the infection. Hence the knowledge, attitude and practice of an Ayurvedic practitioner plays a major role in health system, which further helps to know the preparedness among them. With this context this study was conducted to assess knowledge, attitude and practice among them towards COVID-19.

Methods: Online cross sectional study was done among Ayurvedic practitioners of Karnataka. Google form was sent through social media to collect data and analysed using SPSS 25.

Results: The mean age among the participants was 30.5±9.1 years. Majority were females (54.3%), and 59.1% are currently practicing Ayurveda. Mean knowledge score was 10.5±1.9, thus 86.6% of the participants had good knowledge. 70.1% agreed for the fact that Ayurveda should be considered as a mainstream medicine whereas 88.2% were in opinion that Ayurveda should be considered as complementary therapy along with conventional treatment. Statistical association was seen between education and knowledge.

Conclusions: Good knowledge towards COVID-19 was seen among 86.6% and majority of them want Ayurveda to be considered as complementary medicine but before that evidence based treatment protocol needs to be developed to support claims regarding treatment/prevention of COVID-19.

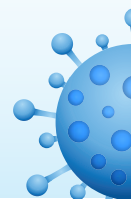
Keywords: Attitude, Ayurveda, Ayurvedic practitioners, COVID-19, Knowledge, Practice

INTRODUCTION

Corona viruses may cause illness in animals or humans. Several coronaviruses are known to cause respiratory infections ranging from the common cold to more severe diseases such as Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS) in humans. Novel corona virus (COVID-19) is an emerging respiratory tract infectious disease caused by the coronavirus subtype SARS-CoV-2 infection which

was first detected in Wuhan, China, in December 2019 which has wreaked havoc worldwide.

COVID-19 was declared as global pandemic by the world health organization (WHO) which is presently engulfing almost all the countries affecting over 12,844,410 people and has caused 5,67,657 deaths as of 12th July 2020.¹ India had 850,358 active cases and 536,231 discharged/cured cases with 22,687 deaths as on 12th July 2020.² It is expected that the number will grow in future.



Therefore, all possible preventive action should be taken to control the spread of the infection. Once the individual develops the infection it is equally important to treat him with the proper medication so that further transmission can be prevented.

Currently, there is no specific antiviral treatment and preventive vaccine. Therefore, the guidelines are recommended to decline the spread of infection and respond to the challenges during the epidemic. In terms of symptoms, the WHO reported that more than 80% of COVID-19 patients showed mild symptoms and recovered without any medical intervention, approximately 20% of infected cases had a severe illness such as shortness of breath, septic shock and multi-organ failure, and it has been reported that an estimated 2% of cases can be fatal. The risk of increased severity was noticed in the elderly and with underlying chronic diseases. The best prevention is to avoid being exposed to COVID-19. This is done by washing hands with soap and water, and using face masks, isolating confirmed and suspected cases. Some previous studies showed that HCWs had a lack of knowledge and attitude toward MERS CoV, and SARS.³

Healthcare workers (HCWs) are at the frontline of COVID-19 pandemic response and are exposed to dangers like pathogen exposure, long working hours, psychological distress, fatigue, occupational burnout and stigma, and physical violence. A poor understanding of the disease among HCWs can result in delayed identification and treatment leading to rapid spread of infections.⁴

Although allopathic system of medicine is being used for treating the infection, there is no specific medicine for COVID-19 as of now. Trails have been going on Ayurvedic system of medicine for immunity boosting, prevention and cure of disease. Just like China included Traditional Chinese Medicine (TCM) in the treatment protocol of coronavirus, India is also looking forward to incorporate its ancient medicine in the battle against the pandemic.

Ministry of AYUSH releases the recommendations, which emphasis on Ayurveda's immunity boosting measures for self-care during COVID 19 crisis. Some of the measures include, drinking hot water throughout the day, daily practice of yogasana, pranayama and meditation for at least 30 minutes, using certain spices like haldi (turmeric), jeera (cumin), dhaniya (coriander) and lahsun (garlic) during cooking. Immunity promoting measures includes eating chyavanprash, drinking golden milk (turmeric powder in milk), herbal tea or decoction (kadha) made from tulsi (basil), dalchini (cinnamon), kalimirsch (black pepper), shunti (dry ginger) and munakka (raisin). During dry cough/sore throat, steam inhalation with fresh pudina (mint) leaves or ajwain (caraway seeds) is advised.⁵

With the changing scenario, the Ayurvedic fraternity is also looking forward for its active involvement in the fight against the COVID menace and their current awareness about the disease, along with the attitude and relevant practices are of great importance. With the less evidence on their knowledge about the corona virus, this study was taken up among Ayurvedic practitioners in Karnataka, India.

Objectives

To assess the knowledge, attitude and practice towards COVID-19 among Ayurvedic practitioners of Karnataka, India; and to find out the association between socio-demographic factors and Knowledge score among Ayurvedic practitioners of Karnataka, India.

METHODS

Online cross-sectional survey was conducted among Ayurvedic practitioners of Karnataka, India. Study was conducted for a period of 2 months (May to June 2020). Data was collected through Google form which had 2 parts. First part consisted questions related to socio-demographic profile and second part consisted question related to KAP. This online questionnaire contained a total of 32 questions among which 13 for assessing Knowledge, 10 for assessing attitudes and remaining 9 for assessing practice.

Assuming the prevalence of knowledge about COVID-19 to be 50% as it's a new disease, sample size was calculated. Considering knowledge to be 50% with 95% confidence level and 10% relative precision, minimum sample size to be studied was calculated using sample size formula of single proportion to be 100.

As more responses were obtained than the required sample size, all the 127 responses were included. Data was analyzed using SPSS version 25 (Licensed to JSS AHER). Results were expressed as percentage, mean, and standard deviation. Chi-square was applied and Statistically significance was considered at $P < 0.05$.

Inclusion and exclusion criteria

Participants who were studying Ayurveda and/or practicing Ayurvedic system of medicine and who had access to the social media platform like WhatsApp, Facebook and Email were included in study and those who did not give consent and had no access to the social media platform were excluded. Later Google form was sent to them through social media platform. Further they were asked to share among their colleagues and friends who belongs to the Ayurveda fraternity.

Knowledge scoring

Scoring was done only for knowledge based questions as attitude and practice questions were subjective and



perspective based. For each correct answer 1 mark was assigned and a mean value was calculated. Participants who scored more than mean value were considered to have good knowledge and who scored less than mean value was considered to have poor knowledge.

RESULTS

The mean age among the participants was 30.5 ± 9.1 years. Majority were in the age group of 20-30 years (69.3%), followed by 31-40 years (20.5%), >50 years (6.3%), and 41-50 years (3.9%). 54.3% of the participants were females and 45.7% were males. 77.2% were either studying or completed bachelor of Ayurvedic medicine and surgery (BAMS) and 22.8% were either doing or complete post-graduation. 59.1% were practicing Ayurveda, 18.1% were studying under-graduation, 12.6% were pursuing post-graduation in Ayurveda and 10.2% were working as professors (Table 1).

In the present study, mean knowledge score was 10.5 ± 1.9 , thus 86.6% of the participants had good knowledge where as 13.4% had poor knowledge about COVID-19. Clinical symptoms of the COVID-19 were known to 97.6% of the participants and 92.9% knew about the incubation period. The severity of the disease is more likely among elderly, those with chronic illnesses and obese individuals according to 87.4% of the participants and 92.1% were agreed that the virus spreads via respiratory droplets of the infected individuals. Only 58.3% of the participants knew that antibiotics aren't the first line of treatment, 52.8% disagreed that influenza

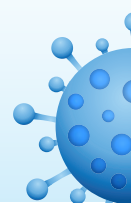
vaccine offers protection against the disease and 93.7% believed that currently there is no effective cure for COVID-19 but early symptomatic and supportive treatment is beneficial in recovery. 96.1% knew that isolation and treatment of the infected with the virus are effective ways to control the spread of the virus, 98.4% of the participants knew that the contacts should immediately self-quarantine themselves in a proper place and in general the quarantine duration is 14 days, 66.1% believed that Ayurvedic measure to strengthen immunity should be considered amidst the pandemic.

Table 1: Distribution of participants based on Socio-demographic details.

Variables	Frequency (n=127)	Percent
Age (in years)	20-30	69.3
	31-40	20.5
	41-50	3.9
	>50	6.3
Gender	Female	54.3
	Male	45.7
Education	BAMS	77.2
	MD/MS in Ayurveda	22.8
Occupation	Practicing Ayurveda	59.1
	PG student	18.1
	UG student	12.6

Table 2: Distribution of participants based on the knowledge regarding coronavirus.

Knowledge questions	Frequency	Percentage
The main clinical symptoms of COVID-19 are fever, cold, sore throat, dry cough, and myalgia		
False	3	2.4
True	124	97.6
The incubation period ranges between 2-14 days		
False	4	3.1
True	118	92.9
I don't know	5	3.9
Not all persons with COVID-19 will develop to severe cases. Only those who are elderly, have chronic illnesses, and are obese are more likely to be severe cases.		
False	13	10.2
True	111	87.4
I don't know	3	2.4
The COVID-19 virus spreads via respiratory droplets of infected individuals		
False	9	7.1
True	117	92.1
I don't know	1	0.8
Antibiotics are the first line of treatment		
False	74	58.3
True	41	32.3
I don't know	12	9.4
Influenza vaccine also gives protection from COVID-19		
False	67	52.8
True	35	27.6
I don't know	25	19.7



Knowledge questions	Frequency	Percentage
There currently is no effective cure for COVID-19, but early symptomatic and supportive treatment can help most patients recover from the infection		
False	4	3.1
True	119	93.7
I don't know	4	3.1
Isolation and treatment of people who are infected with the COVID-19 virus are effective ways to reduce the spread of the virus.		
False	4	3.1
True	122	96.1
I don't know	1	0.8
People who had contact with an infected COVID-19 patient should immediately self-quarantine in a proper place. In general, the quarantine period is 14 days.		
False	1	0.8
True	125	98.4
I don't know	1	0.8
Ayurvedic protocol to build immunity in the midst of the coronavirus pandemic is useless		
False	84	66.1
True	34	26.8
I don't know	9	7.1
Impaired Agni can make one more prone for COVID-19?		
False	19	15.0
True	87	68.5
I don't know	21	16.5
Immuno-modulators (rasayana) is a must in all individuals with chronic illnesses to improve immunity against COVID-19		
False	12	9.4
True	107	84.3
I don't know	8	6.3
If one is taking precautions as per the Ayurvedic protocol there is no need to follow respiratory etiquettes		
False	88	69.3
True	32	25.2
I don't know	7	5.5

Table 3: Distribution of participants based on the attitude regarding coronavirus.

Attitude	Frequency	Percentage
Do you have the confidence that India can win the battle against the COVID-19 virus?		
No	13	10.2
Not sure	14	11.0
Yes	100	78.7
Do you think Ayurveda should also be considered as a mainstream medicine in the treatment of nCOVID-19?		
No	24	18.9
Not sure	14	11.0
Yes	89	70.1
Ayurveda should be used as a complementary therapy along with conventional medicine for COVID-19		
No	10	7.9
Not sure	5	3.9
Yes	112	88.2
Do you think drugs like haridra (<i>Curcuma longa</i>), guduchi (<i>Tinospora cordifolia</i>), shunti (<i>Zingiber officinale</i>), pippali (<i>Piper longum</i>) prevent COVID-19?		
I don't know	5	3.9
No	10	7.9
Yes	112	88.2
Do you think Ayurveda can treat COVID-19?		
I don't know	26	20.5
No	17	13.4
Yes	84	66.1



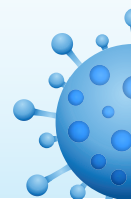
Attitude	Frequency	Percentage
Do you think following healthy diet, exercise regimen, adequate sleep reduces the risk of COVID-19?		
No	12	9.4
Not sure	10	7.9
Yes	105	82.7
In case there is an effective vaccine against COVID-19 would you take it and recommend it to others?		
No	8	6.3
Not sure	12	9.4
Yes	107	84.3
Do you think pratimarsha nasya is effective against COVID-19?		
No	14	11.0
Not sure	35	27.6
Yes	78	61.4
Strict action must be taken against persons/agencies involved in dissemination of misleading information regarding AYUSH drugs and services in relation to COVID-19		
No	4	3.1
Not sure	1	.8
Yes	122	96.1
I find tele-medicine to be helpful during this crisis		
No	18	14.2
Not sure	27	21.3
Yes	82	64.6

Table 4: Distribution of participants based on the practice regarding coronavirus.

Practice	Frequency	Percentage
In recent days, have you gone to any crowded place?		
No	102	80.3
Yes	25	19.7
In recent days, have you worn a mask when leaving home?		
No	7	5.5
Yes	120	94.5
Do you wash your hands with soap often?		
No	2	1.6
Yes	125	98.4
Do you use any ayurvedic soap/gel/powder to sanitize your hands?		
No	51	40.2
Yes	76	59.8
Do you use alcohol based hand sanitizer?		
No	8	6.3
Yes	119	93.7
Do you observe social distancing in your clinic/ hospital/casual interactions?		
No	6	4.7
Yes	121	95.3
Are you currently on any specific Ayurvedic regimen/treatment to protect yourself from COVID-19		
No	54	42.5
Yes	73	57.5
In case a patient with COVID related symptoms approaches you what would you suggest?		
Explain the risk to the patient/attenders and refer to COVID hospital	102	80.3
Refer to other general clinic/hospital	12	9.4
Symptomatic Ayurvedic treatment	13	10.2

Among the participants, 68.5% agreed that impaired Agni can make one more prone to the COVID-19, 84.3% believed rasayana (immuno-modulators) must be taken by all those who are chronically ill in order to improve their

immunity and 69.3% of the participants agree even though anyone is following Ayurvedic regimen for protection against the disease, respiratory etiquettes should also be considered (Table 2).



78.7% of the participants had positive attitude that India can win against the COVID-19. 70.1% think that Ayurveda should be considered as a mainstream medicine in the treatment of COVID-19 whereas 88.2% were of the opinion that Ayurveda should be considered as complementary therapy along with conventional treatment. Nearly 88% of the participants thought that drugs like haridra (*Curcuma longa*), guduchi (*Tinospora cordifolia*), shunti (*Zingiber officinale*), pippali (*Piper longum*) prevent COVID-19. 66.1% believe that Ayurveda can treat the COVID-19 and 82.7% of them thought that a healthy lifestyle which includes diet, exercise, adequate sleep reduces the risk of developing the disease. Once there is an effective vaccine 84.3% of the participants would get themselves vaccinated and also recommend it to others and 61.4% of the participants thought that pratimarsha nasya (nasal application) can be effective against the disease. 96.1% demand strict action against persons/agencies involved in disseminating misleading information regarding AYUSH drugs and services in relation with the COVID-19 and 64.6% have found tele-medicine to be helpful during this crisis (Table 3).

In our study, 29.1% of the respondents recommended ashwagandha, 17.3% vasa, 14.1% haridra, 10.2% amalaki and 7.8% guduchi, maricha, shunti along many other herbal formulations were recommended by the respondents in the view of preventing COVID-19.

In our study, 80.3% avoided going to crowded places, 94.5% wore masks while leaving their houses, and 98.4% had practice of washing hands with soap. Nearly 60% of participants were using Ayurvedic soap/gel/powder to sanitize their hands and 93.7% uses alcohol based hand sanitizer. 95.3% of the practitioners followed social distancing norms in their clinics/hospitals and even during their casual interactions. 57.5% of the participants are currently on specific Ayurvedic regimen/treatment to protect them from COVID-19 and 80.3% are explaining the risk if they are having COVID-19 related symptoms and referring them to COVID hospital (Table 4).

Table 5: Association between socio-demographic factors and knowledge.

Socio-demographic factors		Knowledge		P value
		Good (%)	Poor (%)	
Education	BAMS	81 (82.7)	17 (17.3)	0.016
	MD/MS in Ayurveda	29 (100%)	0	
Occupation	Practicing Ayurveda	77 (87.5)	11 (12.5)	0.057
	PG student	16 (100)	0	
	UG student	17 (73.9)	6 (26.1)	

All of those who are studying or completed MD/MS in Ayurveda had good knowledge and 82.7% of those who studying or completed BAMS are found to have good knowledge. This shows there is a statistically significant association between education qualification and

knowledge at p value 0.0016. Even though there is no statistical association (0.057) between occupation and knowledge, those who practicing Ayurveda and studying post-graduation are having more good knowledge when compared to under-graduation (Table 5).

DISCUSSION

The mean age among the participants was 30.5±9.1 years. Majority were females (54.3%), 77.2% were either studying or completed their under graduation and 59.1% are currently practicing Ayurveda.

Mean knowledge score in our study was 10.5±1.9, thus 86.6% of the participants had good knowledge. The findings were similar to a study conducted by Saqlain et al in Pakistan and Nepal et al in Nepal, among healthcare workers, where 93.2% and 82.15% of the participants had good knowledge scores towards COVID-19 respectively.^{6,7} Similarly a study conducted by Zhou et al among healthcare workers in Henan, China showed that 89% of HCWs had sufficient knowledge, about 85% of them feared self-infection with the virus, and 89.7% followed correct practices regarding COVID-19.⁸ The good knowledge among the participants is directly related to the education qualification of the study participants.

More than 97% of the participants in our study knew about clinical symptoms of COVID-19. This result is in par with result of the conducted by Saqlain et al among healthcare workers where 98.7% knew about common symptoms of COVID-19.⁶ The incubation period was known by 92.9% in the present study whereas 96.38% participants knew about incubation period in the study by Saqlain et al.⁶

As reported by Saqlain et al 78.99% of the respondents knew the severity of the disease is more likely in patients with other comorbidities which is in accordance with our findings where 87.4% respondents knew it whereas in the same study, 17.87% believed antibiotics to be the first line of treatment and in our study 32.3% agreed that antibiotics are the first line of treatment.⁶ This difference in the result is due to participation of different fraternity of health care professionals.

In the present study, 96.1% of the respondents strongly agreed that COVID patients should be kept in isolated and treated for COVID-19 and is the effective ways to reduce the spread. 98.4% of the participants knew that the contacts should immediately self-quarantine themselves in a proper place and in general the quarantine duration is 14 days. This results shows the awareness among our participants.

In this study, 66.1% believed that Ayurvedic measure to strengthen immunity should be considered amidst the pandemic, 68.5% agreed that impaired Agni can make one more prone to the COVID-19 and 84.3% of the participants believe rasayana must be taken by all those



who are chronically ill in order to improve their immunity against the disease. From these results we can see that, more than half of the participants agreed and recommended Ayurveda for strengthening and boosting the immunity against the infection.

Among 127 Ayurvedic practitioners, 88.2% were of the opinion to consider Ayurveda as complementary therapy along with conventional treatment. Nearly 88% of the participants thought that drugs like haridra (*Curcuma longa*), guduchi (*Tinospora cordifolia*), shunti (*Zingiber officinale*), pippali (*Piper longum*) prevent COVID-19, 61.4% of them thought pratimarsha nasya (nasal application) can be effective against the disease and 29.1% of the respondents recommended ashwagandha, 17.3% vasa, 14.1% haridra, 10.2% amalaki and 7.8% guduchi, maricha, shunti along other herbal formulations in the view of preventing COVID-19.

In the present study, all of those who are studying or completed MD/MS in Ayurveda had good knowledge and 82.7% of those who studying or completed BAMS were found to have good knowledge. This shows a statistically highly significant association between education qualification and knowledge at p value 0.0016.

Limitations of the study were most of the attitude and practice questions were subjective; and study cannot be generalized to all the Ayurvedic practitioners.

CONCLUSION

Good knowledge towards COVID-19 was seen among 86.6% of the Ayurvedic practitioners. Majority of them want Ayurveda to be either considered as complementary medicine or mainstream of medicine for COVID-19, but before that evidence-based treatment protocol needs to be developed to support claims regarding treatment/prevention of COVID-19

Measures regarding training of AYUSH doctors regarding infection prevention should be taken as it will be helpful in control of infectious diseases, their appropriate management and also boosts the confidence of these doctors.

Recommendations

As our study lacks complete representativeness due to its online nature of study thus more studies are warranted to

investigate the KAP towards COVID-19 among Ayurvedic practitioners.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Original Research Article

Pregnant women's knowledge and practice of preventive measures against COVID-19: a study from Mysore city, Karnataka, India

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ABSTRACT

Background: The presently ongoing COVID-19 pandemic has not spared any segment of society including pregnant women. It is absolutely essential that pregnant mothers and their caregivers be fully aware of accurate facts about COVID-19. Objective of this study was to assess the knowledge and practice of preventive measures against COVID-19 infection among pregnant women of Mysore City.

Methods: This was a cross sectional study, conducted among pregnant women attending prenatal care at a tertiary care centre. Data was collected using a validated questionnaire administered via google form to consenting pregnant women. The variables assessed were knowledge about aetiology, mode of spread and preventive measures to protect against COVID-19. Data was also collected on socio-demographic characteristics, which included age, parity, marital status, residence, occupation, participant's education, husband's education.

Results: Out of the 93 responders, majority 71 (76.3%) were in the age group 20-30 years. 17 (18.3%) were in the 30-40 years age group. Regarding number of children 41 (44.1%) had one child 16 (17.2%) had 2 children and 32 (34.3%) were primigravida. With respect to educational status 70 (75.26%) were having graduate degree. 19 (20.4%) were non graduates, but had completed high school. Educational level of the husbands of the respondents was along similar lines with 62 (66.66%) having completed graduation, and 28 (30.1%) had completed high school. 91(97.8%) respondents were correct in identifying virus as the cause of COVID-19. 88 (94.6%) rightly chose mode of spread by sneezing or cough. 1 (0.1%) respondent wrongly indicated that injections were the mode of spread. Main symptoms cough and fever were correctly identified by 80 (86%) respondents. The practice of preventive medicine was low with respect to all aspects of COVID prevention. Only 27 (29.7%) were following frequent handwashing recommendation. Only 26 (28.6%) were following staying indoors advise. 28 (30.8%) of the respondents were wearing masks. However, 82 (90.1%) were following at least one of the preventive measures.

Conclusions: The knowledge levels of pregnant women were satisfactory However this was not translated into practice by majority of the respondents.

Keywords: COVID-19, Infection, Knowledge, Pandemic, Practice, Pregnant mothers

INTRODUCTION

The presently ongoing COVID-19 pandemic has not spared any segment of society including pregnant

women. The immune-suppressive pregnancy state can lead to varied fetomaternal effects.¹ Health care professionals should themselves be aware of the many aspects of this new disease and they should disseminate



proper information to all sections of society.² It is essential that pregnant mothers and their caregivers be fully aware of accurate facts about COVID-19.

The World Health Organization (WHO) has recommended several preventive measures to arrest the disease and to prevent complications.³ All over the nation these measures have been actively implemented by governmental agencies. Health education about COVID measures are also going on continuously since the outbreak began.

Pregnancy being a state of special vulnerability to various infections including COVID, needs extra attention both by caregivers and medical professionals. COVID related basic knowledge and preventive measures should be adequately known to the pregnant mother. There are very few studies in this aspect from India. Hence, this study was undertaken to assess the knowledge of the pregnant mothers in relation to the causation, mode of transmission and preventive measures of COVID-19 infection and practice with respect to preventive measures adopted.

Objective of this study was to assess the knowledge and practice of preventive measures against COVID-19 among pregnant women of Mysore.

METHODS

This was a cross sectional study done for a period of three months. Pregnant women attending JSS Hospital, a tertiary care teaching hospital at Mysuru, South India were included. All mothers consenting for the study were included and there was no specific exclusion criteria. A validated questionnaire was administered using google forms. The questions evaluated knowledge and practice based on WHO recommendations on preventive measures against COVID-19.⁴ Socio-demographic variables assessed age, parity, marital status, area of residence, occupation, participant's level of education, husband's level of education.

Question of frequent hand washing with soap and water or using alcohol-based hand sanitizers; maintaining at least 1 meter distance from others; avoiding touching eyes, nose, and mouth with hands; covering mouth and nose while coughing or sneezing; wearing a face mask in public; and Staying indoors were used to assess the preventive measures practiced.

Statistical analysis

Statistical analysis was performed using SPSS version 23 (Licensed to the institution). Descriptive statistics like frequency, percentages, mean, standard deviation were calculated. Inferential statistics like Chi-square analysis was used to find the statistical association between the socio-demographic variables and Knowledge. P-value <0.05 was considered statistically significant.

RESULTS

There were 93 responders. Majority 71 (76.3%) were in the age group 20-30 years.

A total 17 (18.3%) were in the 30-40 years age group.

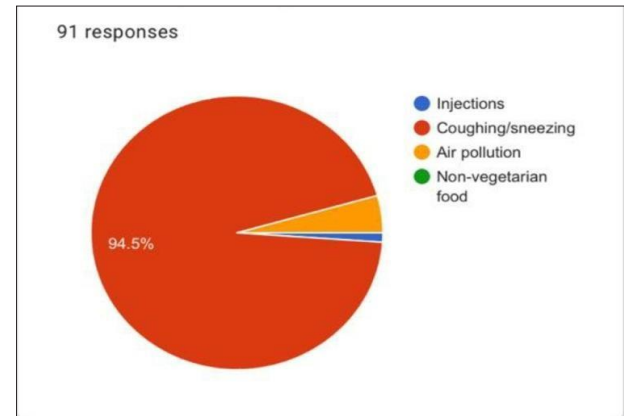


Figure 1: Responses to the question COVID is spread by ?

Mean age of the study participants was 28.6 (± 6.9). With respect to number of children, 41 (44.1%) had one child, 16 (17.2%) had 2 children. 32 (34.3%) were primigravida. 75.3% belonged to urban area and 24.7% belonged to rural area. 46.2% were employed and 53.8% of participants were employed skilled or unskilled work.

3.2% were illiterates and 26.8% had either completed under graduation/post-graduation, w.r.t education of their husbands, 34.4% hadn't completed graduation, 37.6% completed graduation and 28% had completed post-graduation. 88 (94.6%) rightly chose mode of spread of COVID-19 to be by sneezing/ cough. 1 (1%) respondent wrongly indicated that injections were the mode of spread (Figure 1).

Main symptoms of COVID infection as cough and fever were correctly identified by 80 (86%) of the respondents. Related to practice, only 27 (29.7%) followed frequent washing recommendations. 26 (28.6%) were following stayed indoors during pandemic and 28 (30.8%) of the respondents wore mask as required according to the guidelines. However, 82 (90.1%) followed at least one of the preventive measures.

There was an association between level of education and practice of preventive measures with respect to COVID. However, there was no association between age, occupation and any other socio-demographic variables with practice of COVID-19 and practice of preventive measures with respect to COVID (Table 1).

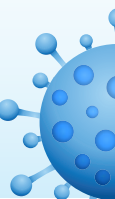


Table 1: Association of education with practice of adopting preventive measures.

Variables	Practice of preventive measures			Total	Chi-square value	P value
	Practiced only some of the preventive measures according to guidelines	Practiced almost all the preventive measures according to guidelines	Practiced all the preventive measures according to guidelines			
Level of education						
Illiterate	1	2	0	3	21.8	0.010
Primary education	5	0	7	12		
Secondary education	9	0	4	13		
Pre-university	8	1	31	40		
Under graduation	0	0	5	5		
Post graduation	2	2	16	20		

DISCUSSION

Knowledge is power in all areas of human enterprise. In the task of corona virus infection prevention and care, the public need to know fully and accurately about this new viral disease. On the other hand, misleading and incorrect information can be spread over social media which can cause wrong actions to be taken.

Pregnancy is a physiological state that predisposes women to viral respiratory infections. Due to the physiological changes in the immune and cardiopulmonary systems, pregnant women are more likely to develop severe illness after infection with respiratory viruses. In 2009, pregnant women accounted for 1% of patients infected with influenza A subtype H1N1 virus, but they accounted for 5% of all H1N1-related deaths.⁵

Present evidence suggests that pregnant women are at not at greater risk of becoming seriously ill than other non-pregnant adults if they contact corona virus. Majority of pregnant women experience only mild or moderate flu-like symptoms. Cough, fever, shortness of breath, headache and loss or change to your sense of smell or taste are other relevant symptoms.⁶

Over and above the impact of COVID-19 infection on a pregnant woman, there are concerns relating to the potential effect on fetal and neonatal outcome; poor practices of preventive measures among pregnant women would put these women at high risk of infection, which could worsen the country's maternal morbidity and mortality profile.²

Therefore, pregnant women require special attention in relation to education about prevention, mode of diagnosis, and methods in management.⁷ Several precautions needed be taken to minimize the risk of contracting and transmitting COVID-19 should be known to this category of the population.

In the study by John Bosco from Nigeria high parity rural residence, low educational attainment, were the factors associated with poor practice of preventive measures.⁷

However, in this study most of the study participants had adequate knowledge of the preventive measures, the level of practice of these measures were grossly adequate. This is surprising since population in Mysore with high literacy and economic status. Also, study hospital being private sector general hospital, the class of patients were expected to be following the various advisories scrupulously.

This higher knowledge levels could be because the Karnataka government had embarked on an aggressive media campaign to educate the populace on preventive measures to curtail person-to-person transmission of the virus for the last two months. The poor practice could be because this study was done in the early months of COVID onset in Mysore. People were yet to really grasp the seriousness of the situation. Also, availability of masks was a problem at that time.

The measures by govt and media and medical colleges are to be continued. Electronic media has a great role. Identifying leaders who can deliver the knowledge is important.

The strengths of this study are that this was a simple google based survey. It was easy for the investigator since the questionnaire could be accessed by the respondents on their smart phones. All the respondents need to do was to choose their option and click to select. Due to this method of collecting data adequate number of respondent's recruitment was possible. Some of the respondents voluntarily forwarded the links to other pregnant women.

The weaknesses of this study are the small number of respondents. Studies involving larger sample size would



have been better. Also, authors did not collect information from respondents about their knowledge about breast feeding in COVID positive mothers, their awareness about the type of diet to be followed by COVID positive pregnant women. Questions about vertical transmission were also not included.

There is a need to institute more measures to improve practice of these preventive measures among pregnant women. The review by Nolan et al made it clear that pregnant women like to receive emotionally demanding or intellectually complex information from a health-care professional in person.⁸

Media both private and public, medical colleges, have a role more aggressive methods would likely encourage women to practice these preventive measures to halt the spread of the virus.

CONCLUSION

The knowledge levels of pregnant women in Mysore city was found to be adequate. However, this was not translated into practice by majority of the respondents and the practice of preventive methods against COVID-19 virus was highly inadequate. Further large studies are required to get a fuller picture

Meanwhile education of pregnant women regarding all aspects of COVID virus infection is all the more imperative in view of the epidemic presently showing no signs of abating.

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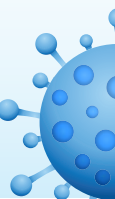
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Assessment of Clinical Pharmacists' Assistance for Patients With Established Cardiovascular Diseases During the COVID-19 Pandemic: Insights From Southern India

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Objectives: We aimed to assess the clinical pharmacist-initiated telephone-based patient education and self-management support for patients with cardiovascular disease during the nationwide lockdown during COVID-19 pandemic.

Methods: A prospective single-center telephone-based cross-sectional study was conducted among patients at the Cardiology Department and its speciality clinic at a 1,800-bed tertiary care hospital in Southern India. A validated 8-item clinical pharmacist aided on-call questionnaire with two Domains was administered during and after lockdown (15 March and 8 June 2020). Clinical pharmacist-provided educational assistance on self-management practices were in accordance with the guidelines of Indian Council of Medical Research (ICMR) and World Health Organization. Comparisons was performed using sign test and association of responses were analyzed using the Goodman and Kruskal's gamma test. All the tests were two-tailed, $p < 0.05$ was considered to be statistically significant.

Results: Of the 1,080 patients, 907 consented with a response rate of (83.9%) and 574 (96.36%) patients were analyzed post-intervention. Majority of the patients were male (54.7%) and had Acute Coronary Syndrome [NSTEMI (42.10%), STEMI (33.92%) and Unstable Angina (9.86)]. The majority of subjects had at least two co-morbid conditions [(Type II Diabetes (48.33%), Hypertension (50.11%)] and were rural population (82.5%) as self-employed (43.1%) with a middle-class economy (31.6%). In the Domain-1 of checklist the awareness toward complications caused by COVID-19 in cardiovascular diseases ($Z = -19.698$, $p = 0.000$) and the importance of universal safety precautions enhanced after clinical pharmacist assistance [$(Z = -8.603$, $p = 0.000)$ and ($Z = -21.795$, $p = 0.000$)]. In Domain-II of checklist there was a significant improvement in patients awareness toward fatal complications caused by COVID-19 ($Z = -20.543$, $p = 0.000$), maintenance of self-hygiene ($Z = -19.287$, $p = 0.000$), practice of universal safety precautions ($Z = -16.912$, $p = 0.000$) and self-isolation ($Z = -19.545$, $p = 0.000$). The results of our study population varied from baseline evaluation (41.7%, $n = 907$) to post-intervention (95%, $n = 574$) based on Literacy, employment status and economic status.

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Conclusions: The proactive role of clinical pharmacists in providing instructional services in collaboration with cardiologist during the pandemic circumstances increased patients understanding and mitigated infection exposure among patients, health care professionals and also assuring the continuity of care in patients with established cardiovascular diseases.

Keywords: COVID-19, cardiovascular diseases, clinical pharmacist, SARS-CoV- 2, corona virus 19

INTRODUCTION

In the last two decades, clustering and incidence of severe acute respiratory infections are one of the major threats to public health. Coronavirus disease (COVID-19) was first recorded in Wuhan, China, by the end of December 2019. Since then, COVID-19 has rapidly spread around the world. The COVID-19 was declared as a global pandemic on 11th March 2020 by the World Health Organization. COVID-19 has a major impact on public health and has a direct or indirect impact on social and economic activities. The exponential increase in the number of patients with COVID-19 in the past 6 months has overwhelmed health-care systems across the world. This is due to an inadequate understanding of the dynamic interplay of shifting epidemiology, publicity, pandemic prevention strategies, risk identification, and public health behavior (1). Cardiovascular disease is common comorbidity observed in patients infected with SARS or MERS (10 and 30% prevalence, respectively) (2). Currently, there is no promising evidence from randomized clinical trials (RCTs) that any potential therapy improves outcomes in patients with either suspected or confirmed COVID-19. Neither clinical trial data is supporting any prophylactic therapy.

The pre-existing cardiovascular disease seems to be linked with worse outcomes and increased risk of death in patients with COVID-19. Patients requiring intensive treatment had a significantly higher prevalence of chronic health conditions such as diabetes, cardiovascular and cerebrovascular disease (3). Moreover, COVID-19 itself can cause induce myocardial injury, arrhythmia, acute coronary syndrome and venous thromboembolism (4). Providing clinical care for patients with chronic cardiovascular disease and other comorbidities during pandemic times is challenging. Telehealth is an ideal platform to deliver clinical care during disasters and pandemics. Telemedicine negated the risk of COVID-19 exposure or transmission (5). In India, providing healthcare is a challenge, telemedicine ensures the safety of patients and health workers, especially when there is a risk of infection (6). India's digital health policy advocates the use of digital tools and focuses significantly on the use of telemedicine services, particularly at the grassroots level in the health and wellness Centers, where a mid-level provider/health worker can connect patients to doctors through technology platforms to provide timely and best possible care (7).

Citizens can make informed choices, defend themselves and comply with prescribed practices by focusing on what can be done during COVID-19 and when adequate resources are accessible, easily understood and communicated via reliable

and accessible networks (8). Therefore, through collaboration between clinical pharmacist and cardiologist, we aimed to provide educational assistance regarding self-management practices in patients with existing cardiovascular diseases to mitigate exposure to COVID-19 infection.

METHODS

Study Design and Participants

A prospective single-center telephone-based cross-sectional study was conducted among patients at the Cardiology Department and its speciality clinic at a 1,800-bed tertiary care hospital in Southern India serving 37 specialities. A validated 8-item clinical pharmacist aided on-call questionnaire with two Domains (**Table 1**) was administered during and after lockdown (15 March and 8 June 2020). Majority of the participants with acute coronary syndrome were the subset population of an ongoing clinical study and are currently being followed up. Clinical pharmacist-provided educational assistance on self-management practices was in accordance with the guidelines of Indian Council of Medical Research (ICMR) and World Health Organization.

Reliability and Validity of the Questionnaire

Initially, the questionnaire was validated by selected faculty and research team using facial and content validation methods to ensure readability. To assess overall reliability, the internal consistency of individual items in each questionnaire domain was examined by the researchers. The questionnaire consists of two domains and eight questions pertaining to awareness and knowledge of subjects toward COVID-19. Each question consists of two responses which was scored as Yes is 1 and No is 2. The score for the questionnaire range between 8 and 16, for the purpose of identifying the status of awareness and knowledge, participants are divided into high knowledge (8–12) and low knowledge (13–16) categories that has been derived by cumulative score. Finally, the survey questionnaire was administered to patients by a clinical pharmacist to facilitate better understanding. Higher score (>12) for the questionnaire indicates that patients have lack of awareness and knowledge which indicates the need for educational assistance. This telemedicine questionnaire of clinical pharmacists to assess awareness and knowledge regarding COVID-19 for patients with established cardiovascular diseases was self-developed with scoring, there are no references identified to cite this conjecture.



TABLE 1 | 8-item telemedicine questionnaire checklist of clinical pharmacists to assess awareness and knowledge regarding COVID-19 for patients with established cardiovascular diseases.

S no	Questions	Response	Score
Domain-I: Assessment of awareness			
1	Are you aware of the spread and impact of Novel corona virus 2019?	YES	1
		NO	2
2	Are you aware of the complications caused by Novel corona virus among patients with cardiovascular diseases?	YES	1
		NO	2
3	Are you aware of your present and past medical history	YES	1
		NO	2
4	Are you aware of the importance of universal safety precautions to prevent getting infected from Novel corona virus?	YES	1
		NO	2
Domain-II: Assessment of knowledge			
5	Do u know that Novel corona virus cause (SARS-nCoV-19) life threatening fatal complications among patients with cardiovascular complications and other co-morbid conditions?	YES	1
		NO	2
6	Do you know that self-isolation and maintenance of hygiene can aid in preventing infection from Novel corona virus cause (SARS-CoV-2)?	YES	1
		NO	2
7	Do you know how to follow universal safety precautions to prevent getting infected from Novel corona virus?	YES	1
		NO	2
8	Do you know that self-quarantine is a procedure followed by people who are at risk during epidemic?	YES	1
		NO	2

The following questions in the domain-I and II are related to assess awareness and knowledge toward COVID-19 or SARS nCov-II infection in patients with established cardiovascular diseases by a clinical pharmacist through telephone.

This questionnaire is copyrighted and can be used as a tool for patients with established cardiovascular diseases without any changes and other clinical groups (can be modified accordingly) to assess awareness and knowledge about COVID-19 or SARS nCov-II infection.

The score for this questionnaire range between 8 and 16, participants are divided into high knowledge (8–12 score) and low knowledge (9–12) categories that has been derived by cumulative scores. Higher score (>12) for this questionnaire indicates that patients have lack of Awareness and Knowledge which indicates the need for educational assistance.

Sampling Method

This study followed a non-probability sampling method among the target population (subjects with established cardiovascular diseases at a tertiary care hospital).

Outcome

The primary outcome of the study is to identify the impact of the clinical pharmacist-initiated educational guidance on COVID-19 pandemic among patients with established cardiovascular disease. The secondary outcome is to ensure continuity of care and compliance with the prescribed drugs.

Statistical Analysis

Data were entered in MS Office Excel 2019 and analyzed using the IBM SPSS Statistics Version 25. Continuous variables were presented as mean \pm standard deviation (SD). Categorical variables were presented as absolute numbers and percentages. Comparisons between baseline and post assistance scores among the individuals were performed using sign test, Association of Responses with socio-demographic variables were analyzed using the Goodman and Kruskal's gamma test. All tests were two-tailed, $p < 0.05$ was considered to be statistically significant.

RESULTS

Of the 1,080 patients contacted by telephone, the response rate at the baseline was 907 (83.9%) and 574 (63.28%) post-intervention. The majority (54.7%) of the study population were male and had at least two co-morbid conditions (44.56%) in the age group (61–80 years) (Table 2). The patients in the study had Acute Coronary Syndrome [NSTEMI (42.10%), STEMI (33.92%) and UA (9.86%)] followed by associated comorbidities as described in Table 3. The questionnaire developed was administered during and after nationwide lockdown. In the Domain-1 the patients were aware of the spread of COVID-19 ($p = 0.000$) and their current condition ($p = 0.000$). However, majority of them were not aware of the complications caused by COVID-19 among patients with cardiovascular diseases ($Z = -19.698$, $p = 0.000$) and the importance of universal safety precautions, their awareness enhanced after clinical pharmacist assistance [(Yes = 85.01 vs. 98.08%, No = 14.99 vs. 1.92%, $Z = -8.603$, $p = 0.000$) and (Yes = 11.84 vs. 94.94%, No = 88.15 vs. 5.05%, $Z = -21.795$, $p = 0.000$)]. In Domain-II regarding knowledge aspect majority of the patient's knowledge improved regarding fatal complications caused by COVID 19 (Yes = 22.12 vs. 95.98%, No = 77.87 vs. 4.01%, $Z = -20.543$, $p = 0.000$), the process of self-isolation, maintenance of self-hygiene (Yes



TABLE 2 | Descriptive Summary of Demographics (N = 574).

S. no.	Parameter	Summary [#]
		(N = 574)
1.	Age (in years)	
	21–40	30 (5.32%)
	41–60	254 (44.34%)
	61–80	257 (44.56%)
	81–100	33 (5.76%)
2.	Gender	
	Male	314 (54.7%)
	Female	260 (45.23%)
3.	Literacy	
	Below high school	206 (36%)
	High school & above	287 (50%)
	Graduate & above	81 (14%)
4.	Economic status	
	Lower class	62 (10.7%)
	Upper-low class	254 (44.1%)
	Middle class	181 (31.6%)
	Upper class	77 (13.6%)
5.	Employment status	
	Salaried	111 (19.4%)
	Self-employed	248 (43.1%)
	Homemaker	215 (37.5%)
6.	Marital status	
	Married	530 (92.2%)
	Divorced/Widowed	51 (8.8%)
7.	Location	
	Urban	100 (17.5%)
	Rural	473 (82.5%)
8.	Smoking habit	
	Smokers	123 (21.5%)
	Non-smokers	450 (78.5%)
9.	Alcoholism	
	Occasional	153 (26.7%)
	Chronic	78 (13.5%)
	Non-alcoholics	401 (69.8%)
10.	Time spent on call per patient	22.54 ± 11.23 min ^a

[#] Data represented as number (proportion), ^adata represented as Mean ± SD, SD: Standard Deviation.

= 33.97 vs. 99.12%, No = 66.02 vs. 0.88%, $Z = -19.287$, $p = 0.000$), the importance of universal safety precaution (Yes = 44.94 vs. 94.94%, No = 55.06 vs. 5.06%, $Z = -16.912$, $p = 0.000$) and regarding self-quarantine (Yes = 25.08 vs. 91.98%, No = 74.91 vs. 8.02%, $Z = -19.545$, $p = 0.000$) depicted in **Table 4**. The individual responses of the patients for every question at baseline was evaluated to correlate the association of sociodemographic variables with awareness and knowledge which demonstrated that the responses of the patients varied based on Literacy, employment status and economic status as represented in **Table 5**.

DISCUSSION

Pandemics and epidemics are a widespread problem then and now as COVID-19. During such periods, people in the community face several challenges. Lack of awareness and consciousness often leads to an uneasy attitude which could adversely affect the patients with established cardiovascular complications. Different stakeholders in their respective countries are working together to “flatten the curve” by joint

TABLE 3 | Clinical parameters.

S. no.	Parameter	Summary [#]
		(N = 574)
1.	Acute coronary syndrome (ACS)	UA 57 (9.86%) NSTEMI 242 (42.10%) STEMI 195 (33.92%)
2.	Venous thromboembolism (VTE)	DVT 48 (8.4%) PE 33 (5.8%)
3.	T2DM	277 (48.33%)
4.	HTN	288 (50.11%)
5.	Kidney disease	72 (12.56%)
6.	T2DM + HTN	292 (50.86%)
7.	COPD	211 (36.73%)
8.	Depression	22 (3.8%)
9.	Atrial fibrillation	17 (2.9%)

T2DM, Type 2 Diabetes Mellitus; HTN, Hypertension; COPD, Chronic obstructive pulmonary disease; UA, Unstable angina; NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST-Elevation Myocardial Infarction.

[#] Data represented as number (proportion).

prevention initiatives led by the WHO. With a practically sufficient global lockdown, Pharmacists appear to be the first contact point for meeting the health requirements of the public (8).

We studied the role of clinical pharmacists' assistance for patients with established cardiovascular diseases during the COVID-19. The principal findings in our study at initial assessment were (1) Most of the patients were aware of their medical condition (CVD and comorbidities), (2) Most of the patients were aware of SARS-CoV-2 (COVID-19) infection, (3) majority of the patients were unaware of fatal complications caused by COVID-19 and association of COVID severity with CVD and comorbidities, (4) most of them were unaware of the importance of universal safety precautions, (5) majority of them don't know that self-quarantine is a procedure followed by people who are at risk during the epidemic.

Pharmacists continue to play their role in promoting continuity of pharmaceutical care, as well as supporting governments for disseminating information on precautions related to COVID-19 spread (13). Pharmacists are an integral part of health care performing exceptional roles in past pandemics and health crises, with some, such as Ebola and Zika, posing global health security risks (9). In this study after assessing the awareness and knowledge we provided educational assistance which helped our patients to gain (1) knowledge regarding fatal complications caused by COVID 19, (2) the process of self-isolation, (3) maintenance of self-hygiene, (4) the importance of universal safety precaution and (5) regarding self-quarantine practice. The Chinese Centre for Disease Control and Prevention recently published the largest COVID-19 case series in mainland China; the overall fatality rate was 2.3% (1,023 deaths among 44,672 confirmed cases), but the mortality rate in



TABLE 4 | Comparison of on call checklist responses before and after the clinical pharmacist assistance/intervention.

S No	Questions	Baseline responses	Post assistance/intervention responses			Z-value	P-value
			Yes	No	Total		
Domain-I:							
Q1	Are you aware of the spread and impact of Novel corona virus 2019?	Yes	487	0	487	−8.603	0.000
		No	76	11	87		
		Total	563	11	574		
Q2	Are you aware of the complications caused by Novel corona virus among patients with cardiovascular diseases?	Yes	109	0	109	−19.698	0.000*
		No	390	75	465		
		Total	499	75	574		
Q3	Are you aware of your present and past medical history?	Yes	563	0	563	−	1.000
		No	0	11	11		
		Total	563	11	574		
Q4	Are you aware of the importance of universal safety precautions to prevent getting infected from Novel corona virus?	Yes	68	0	68	−21.795	0.000*
		No	477	29	506		
		Total	545	29	574		
Domain-II:							
Q5	Are you aware of the importance of universal safety precautions to prevent getting infected from Novel corona virus?	Yes	127	0	127	−20.543	0.000*
		No	424	23	447		
		Total	551	23	574		
Q6	Do u know that Novel corona virus cause (SARS-nCoV-19) life threatening fatal complications among patients with cardiovascular complications and other co-morbid conditions?	Yes	195	0	195	−19.287	0.000*
		No	374	5	379		
		Total	569	5	574		
Q7	Do you know how to follow universal safety precautions to prevent getting infected from Novel corona virus?	Yes	257	0	257	−16.912	0.000*
		No	288	29	317		
		Total	545	29	574		
Q8	Do you know that self-quarantine is a procedure followed by people who are at risk during epidemic?	Yes	144	0	144	−19.545	0.000*
		No	384	46	430		
		Total	528	46	574		

*Statistically significant p-value (2-tailed, < 0.05) has been obtained by performing Sign test.

patients with underlying CVD reached 10.5% (10). However, these results emphasize the potential risk of fatality in our patients with established cardiovascular disease and provide evidence regarding the need for intensive treatment on the infection (11).

The other measure which has been mentioned a lot in recent weeks is hand hygiene. The World Health Organization (WHO) regards handwashing with soap and water and friction with hydroalcoholic gel as the most effective measures for the prevention of infections and antimicrobial resistance (12). Research in major public universities following the H1N1 influenza pandemic reported inadequate compliance with preventive measures, such as residence at home when the virus is ill to prevent transmission in 2009 linked to the results of this study (14). Researchers can work with public agencies/health departments to set up information and awareness centers through participatory groups that may have significant population effects. Our

study helped to implement preventive measures, such as isolation, quarantine and community confinement, early identification of cases, social assistance and the provision of patient-specific instructions.

As a consequence of COVID-19, the need for social distancing forced us to use all the resources in our toolbox, and telehealth is one of them that accelerated its adoption globally (15). Telehealth strategies should be encouraged with a view to increasing access and providing care to the patients with chronic diseases to promote continuity of their care which made us adapt the new normal practices. We need to make a conscious effort to avoid any possible worsening of the digital divide, and the government needs to take that responsibility in this case (16).

What was wonderful about it was during this pandemic when our patients are generally considered to be at greater risk of having more severe COVID-19 disease and when they have been asked to stay at home, through virtual



TABLE 5 | Association of baseline responses with socio-demographic variables among study participants.

Question	Response	Literacy						Employment status				Economic status				p-value	
		Gamma			p-value	Gamma			p-value	Gamma			p-value				
		1	2	3		1	2	3		1	2	3		4			
Q1	Yes	138	270	79	-0.776	0.000*	83	230	177	-0.043	0.693	55	223	153	56	0.252	0.008*
	No	68	17	2			28	18	38			7	31	28	21		
Q2	Yes	13	70	26	-0.532	0.000*	20	49	40	0.000	0.999	35	208	157	66	-0.329	0.000*
	No	193	217	55			91	199	175			27	46	24	11		
Q3	Yes	198	285	80	-0.556	0.055*	99	233	197	-0.042	0.761	46	246	175	70	-0.310	0.047*
	No	8	2	1			12	15	18			16	8	6	7		
Q4	Yes	4	32	32	-0.767	0.000*	26	20	22	0.266	0.021*	38	227	171	70	-0.465	0.000*
	No	202	255	49			85	228	193			24	27	10	7		
Q5	Yes	21	70	36	-0.520	0.000*	32	41	54	-0.008	0.925	44	38	26	19	0.336	0.000*
	No	185	217	45			79	207	161			18	216	155	58		
Q6	Yes	51	102	42	-0.323	0.000*	24	74	97	-0.337	0.000*	29	101	106	41	-0.196	0.003*
	No	155	185	39			87	174	118			33	153	75	36		
Q7	Yes	67	175	15	-0.076	0.275	47	113	97	-0.025	0.720	26	77	102	52	-0.379	0.000*
	No	137	113	67			64	135	118			36	177	79	25		
Q8	Yes	48	82	14	0.014	0.864	22	63	59	-0.114	0.157	19	53	54	7	0.094	0.222
	No	158	205	67			89	185	156			43	201	127	70		

*Statistically significant p-value has been derived from application of Goodman and Kruskal's gamma test.

Literacy: 1: Below high school, 2: High school & above, 3: Graduate & above. Employment: 1: Salaried, 2: Self-employed, 3: Homemaker. Economic status: 1: Lower class, 2: Upper-Low class, 3: Middle class, 4: Upper class.



visits, we are still able to maintain their continuity of care, evaluate their COVID-19 awareness and knowledge, and provide instructional assistance and mitigate their exposure to infection. Overall, the results reflect what might develop into a new standard of future health care, particularly during contagious outbreaks (17). In this difficult time, hopelessness is the mother of acceptance, virtual practices have become a new normal. But hopefully, as we emerge from this pandemic, the telemedicine infrastructure will remain and benefit those in need.

Strengths and Limitations

During the times of stretched clinical resources due to COVID-19, our research results helped to add new ways to reduce COVID-19 spread in patients with established cardiovascular diseases. Although our study is a single-center study involving a clinical pharmacist, despite its limitations, the results in our study suggest that the extended role of the clinical pharmacist may also be beneficial to other clinical groups. In addition, more awareness amongst the study patients could also be attributed to govt initiated awareness programmes on COVID-19 (18). The results of this study may not be generalizable beyond India due to differences in clinical pharmacist practice worldwide.

CONCLUSIONS

The clinical pharmacist may, however, play a pro-active role in promoting patient-specific treatment decisions by serving as a resource for physicians and other health care professionals to mitigate adverse events caused by SARS nCoV-2 infection in

patients with established cardiovascular disease. The enhanced role of clinical pharmacists in providing instructional services should mitigate infection transmission during the COVID-19 pandemic.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary materials, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The institutional ethics committee has approved this study and participants have been informed of the purpose of the study before participating and voluntary consent is obtained virtually. All procedures performed in this study involving human participants were consistent with the Declaration of Helsinki 1964 and its subsequent amendments or comparable ethical standards.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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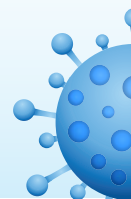
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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Knowledge, attitude, and practices toward COVID-19 among the college students in a southern city of Karnataka

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Abstract:

BACKGROUND: The new coronavirus disease COVID-19 has been spreading from Wuhan city to other cities in China and worldwide since December 2019. It was declared a pandemic by the World Health Organization on March 11, 2020. To guarantee the final success, people's adherence to the control measures is essential, which is greatly influenced by their knowledge, attitude, and practices toward COVID-19. Hence, the study was taken up to assess the knowledge, attitude, and practices among law college students.

MATERIALS AND METHODS: A cross-sectional study was conducted in Mysore in March 2020 among the students of Law College. Students who were not interested in taking up the study were not included in the study. A total of 256 study participants were included in the study. Data were collected using a pretested and self-administered questionnaire about knowledge-, attitude-, and practice-based questions on COVID-19. Data were entered in Microsoft Excel and were analyzed using SPSS V.23.

RESULTS: Among 256 study participants, 130 were female (50.8%) and 126 were male (49.2%). The main sources of information for the study participants are online newspapers/channels ($n = 70$) and social media ($n = 55$). The median score of knowledge, attitude, and practices is 5, 4, and 8, respectively. A comparison of the scholastic year with knowledge scores was found to be statistically significant at a $P < 0.05$.

CONCLUSION: The knowledge and attitude scores were low, but it was found that the study participants were following appropriate practices regarding COVID-19.

Keywords:

Attitude, COVID-19, knowledge, pandemic, practices

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Introduction

The new coronavirus disease COVID-19 has been spreading from Wuhan city to other cities in China and worldwide since December 2019.^[1] COVID-19 is a highly infectious and emerging respiratory disease; its main clinical symptoms are fever, dry cough, fatigue, myalgia, and dyspnea.^[2]

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It was declared a pandemic by the World Health Organization (WHO) on March 11, 2020. As of April 4, 2020, 976,249 cases have been confirmed globally, 2650 confirmed cases in India, and 128 cases in Karnataka with 3 dead and 12 cured of the disease.^[3,4]

The COVID-19 affects different people in different ways.^[5] Most infected people will develop mild-to-moderate symptoms

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and recover without requiring special treatment.^[5] The primary means of spreading the disease is through respiratory droplets.^[5] Individuals who have underlying medical conditions and those aged over 60 years have a higher risk of developing severe illness and death.^[5] There is no evidence that current medications can prevent or cure the disease although a few western, traditional, or home remedies can provide comfort and relief of symptoms of COVID-19.^[6] To date, COVID-19 cannot be prevented with a vaccine or treated with appropriate antiviral drugs.^[6] However, care should be taken to relieve symptoms for those affected. Most patients recover by supportive treatment.^[6]

Students are powerful agents of change.^[7] Any crisis presents an opportunity to help them understand, cultivate compassion, and create a safer and compassionate community.^[7] Creating awareness can encourage students to become advocates for disease prevention and control at home and in their community by communicating with others about how to prevent the spread of viruses.^[7] Simple steps can prevent infection and slow the transmission of COVID-19.^[5] They are as follows: wash your hands regularly with soap and water, or clean them with alcohol-based hand rub; maintain at least 1-m distance between you and people coughing or sneezing; avoid touching your face; cover your mouth and nose when coughing or sneezing with a tissue which should be discarded immediately; stay home if you feel unwell; refrain from smoking and other activities that weaken the lungs; practice physical distancing by avoiding unnecessary travel; and staying away from large groups of people.^[5]

As was shown in China and some other countries, COVID-19 outbreaks can be contained and prevent transmission.^[6] Unfortunately, new outbreaks can emerge rapidly.^[6] To guarantee the final success, people's adherence to the control measures is essential, which is greatly influenced by their knowledge, attitude, and practices toward COVID-19. Hence, the study was taken up to assess the knowledge, attitude, and practices among the law college students.

Materials and Methods

A cross-sectional study was conducted in Mysore in March 2020 among the students of Law College. Law College was selected arbitrarily. Using consecutive sampling technique, students who were present and provided informed consent on the day of the study were included in the study. Around 256 study participants took part in the study. Students who were not interested in taking up the study were excluded.

Data were collected using a pretested and self-administered questionnaire about knowledge-,

attitude-, and practice-based questions on COVID-19. The questionnaire was developed using the information from the WHO;^[8] before being used, it was tested for internal consistency among 20 students from the same law college.

The survey instrument had 10 items to assess knowledge, 5 items for attitude, and 5 items to assess practices regarding COVID-19. The knowledge part of the questionnaire had questions regarding the organism causing the disease, how the disease is transmitted, who are at more risk of developing the disease, about usage of mask, antibiotics, vaccine, quarantine period, pet animals, package from China, and about the main source of information about COVID-19. The attitude section of the questionnaire had scenarios such as hoarding sanitary items, reporting to the doctor if had come in contact with a suspected person, preferring Ayurveda or other non-allopathic treatment, about isolation, and personal hygiene to assess the attitude of the students. The attitude section was measured using a 5-point Likert scale. Practice section had questions about the usage of hand sanitizer, maintaining cough hygiene, forwarding the social media messages without fact-checking, have they attended any mass gathering, and whether they follow the WHO or Ministry of Health and Family Welfare in any social media. Scores ranged from 1 to 10 for each knowledge, attitude, and practice section of the questionnaire. Personal information such as gender and the scholastic year was also collected.

Knowledge, attitude, practice scoring

For every correct answer, a score of 1 was given and score of 0 for every wrong answer, and the median score was calculated for knowledge, attitude, and practice. The participants who had score more than median were considered as good and less than score were considered poor.

Statistical analysis

Data were entered in Microsoft Excel and were analyzed using SPSS V.23. The analysis was done using descriptive statistics such as percentages, median, and interquartile range (IQR) and inferential statistics such as Mann-Whitney U-test for gender with knowledge, attitude, and practice scores, as well as Kruskal-Wallis test for the scholastic year with knowledge, attitude, and practice scores.

Results

Among 256 study participants, 130 were female (50.8%) and 126 were male (49.2%). 50 students (19.5%) are in their 1st year, 52 students (20.3%) in the 2nd year, 85 students (33.2%) in the 3rd year, and 69 students (27%) in their 4th year of law college. The



main sources of information for the study participants are online newspapers/channels ($n = 70$) and social media ($n = 55$) [Figure 1] (mixed responses were taken from the study participants).

Table 1 shows that the median score (IQR) of knowledge is 5 (4–6), attitude is 4 (2–5), and practice is 8 (6–8) regarding COVID-19. This shows that knowledge is good, attitude is poor, and practice is good regarding COVID- 19.

Comparison of gender and knowledge scores was done using the Mann–Whitney U-test; the median score for both males and females is 5 and the IQR is 4–5 and 4–6 for males and females, respectively. This was not statistically significant at a $P = 0.057$. Comparison of scholastic year and knowledge scores was done using the Kruskal–Wallis test; the median scores for the 1st, 2nd, 3rd, and 4th year is 5, 4, 5, and 5, respectively. The IQR for the 1st, 2nd, 3rd, and 4th year are 4–5.25, 3–5, 4–6, and 4–6, respectively. This was found to be statistically significant at a $P < 0.05$ [Table 2].

A comparison of gender and attitude scores was done using the Mann–Whitney U-test; this was found to be not statistically significant at a $P = 0.699$. Comparison of scholastic year and attitude scores was done using the Kruskal–Wallis test; this was found to be not statistically significant at a $P = 0.593$ [Table 3].

A comparison of gender and practice scores was done using the Mann–Whitney U-test; this was found to be not statistically significant at a $P = 0.447$. Comparison of scholastic year and practice scores were done using the Kruskal–Wallis test; this was found to be not statistically significant at a $P = 0.721$ [Table 4].

Discussion

The knowledge, attitude, and practices for a particular infectious illness can be influenced by various factors, namely, the severity of illness, the severity of its spread, and the fatality rate.^[9] COVID-19 is an emerging, rapidly

evolving situation; people need to know the coping strategy regarding the pandemic and should take necessary measures accordingly.^[10]

The median scores of knowledge, attitude, and practice regarding COVID-19 are low among the present study participants. The median score of knowledge about the disease among the study participants 5 out of 10 with an IQR of 4–6. The scores of attitude were lower among the study participants with a median score of 4 and the IQR of 2–5.

Table 1: Distribution of knowledge, attitude, and practice scores of study participants

	Median	Interquartile range
Knowledge	5	4-6
Attitude	4	2-5
Practices	8	6-8

Table 2: Comparison of gender and scholastic year with knowledge scores

Variables	Median	IQR	P
Gender			
Male	5	4-5	0.057
Female	5	4-6	
Scholastic year			
1 st year	5	4-5.25	0.004*
2 nd year	4	3-5	
3 rd year	5	4-6	
4 th year	5	4-6	

*P value is found to be significant at <0.05 . IQR=Interquartile range

Table 3: Comparison of gender and scholastic year with attitude scores

Variables	Median	IQR	P
Gender			
Male	4	2-5	0.699
Female	4	2-5	
Scholastic year			
1 st year	3	2-5	0.593
2 nd year	4	2-5	
3 rd year	4	2-5	
4 th year	4	2.5-5	

IQR=Interquartile range

Table 4: Comparison of gender and scholastic year with practice scores

Variables	Median	IQR	P
Gender			
Male	8	6-10	0.447
Female	8	6-8	
Scholastic year			
1 st year	8	6-10	0.721
2 nd year	8	6-8	
3 rd year	8	6-9	
4 th year	8	6-10	

IQR=Interquartile range

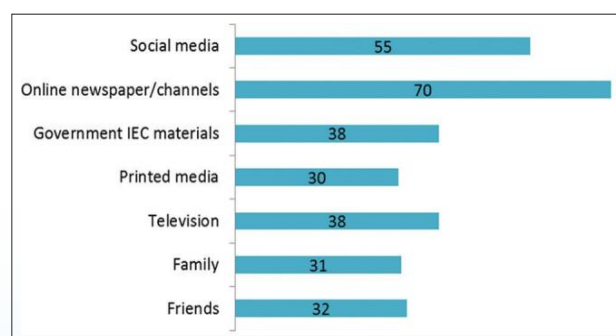


Figure 1: Main source of information regarding COVID-19 ($n = 256$)



An initial study from China by Zhong *et al.* analyzed the knowledge, attitude, and practice of the Chinese residents regarding COVID-19 through an online survey during the outbreak.^[2] Very good knowledge with 90% correct responses was observed in China in the study. Similarly, high level of good attitude and practice also was observed in the study.^[2] The higher prevalence and impact of the disease in China compared to that in India could be the reason for the major difference in the scores. Although health authorities and ministry have been consistently disseminating COVID-19 information even before the disease first appeared in India, there has also been a surge in false and inaccurate information. The overload of information may have caused confusion and difficulty in understanding the right information.

The sources of information for majority of the students were social media and online media. This has been responsible for dissemination of both right information and myths among public regarding the new viral disease. Same time, with this result, the online and social media platform can be utilized effectively for giving health education as well as preventing the misconception regarding prevention and control of disease.

Even though the scores of knowledge and attitude were low among college students, the practices were scored higher with a median of 8 and an IQR of 6–8. This is could be due to the fact that these practices were emphasized under hygiene and sanitation programs since decades to the people.

In the present study, the comparison of scholastic year and knowledge scores was done using Kruskal–Wallis test, which was found to be statistically significant at a $P < 0.05$. The similar results were found in a study done by Rugarabamu *et al.* among Tanzanian residents; overall, 84.4% of the participants had good knowledge which was significantly associated with education level ($P = 0.001$).^[11] The study also showed the significant association between gender and knowledge score, which is in contrast to the current study where the difference is statistically not significant.

Another study done in Malaysia by Azlan *et al.* showed that knowledge scores were significantly different across genders, age groups, regions, occupation groups, and income categories. Higher knowledge scores were obtained among female participants, those above the age of 50, people residing in Central Malaysia, and those in the higher income category.^[12]

The current study was conducted at a stage where the disease was not prevalent in India and only a few cases where tested positive among the people traveled from the affected area. The media coverage of the COVID-19

was also less, and the disease was not prevalent in the study area. Even, the government had not released much guidelines at the time of our study This could be a reason for the low scores in knowledge and attitude.

The strength of the study is that it was done in the early stage of the COVID-19 outbreak in India, especially in Karnataka. The results of the study can be used for implementing the preventive strategies at the earliest.

Conclusion

Although the knowledge and attitude scores were low, it was found that the study participants were following appropriate practices regarding COVID-19.

Recommendation

Public preparedness: Pandemic preparedness is the need of the hours in the current era of emerging and re-emerging diseases; therefore, emphasis needs to be given at adequate health education to the public at all sectors of the society.

Limitation

The disease being a new event, no much literature is available for a comparison of our study results, and since the study was done in a college, convenient sampling and sample size were used; hence, the results cannot be generalized.

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Conflicts of interest

There are no conflicts of interest.

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Knowledge, Attitude and Practice of Personal Safety Measures Adopted by Medical Practitioners during the Covid-19 Pandemic

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ABSTRACT

BACKGROUND

A novel coronavirus (now termed as SARS-CoV-2) was detected as the causative agent of severe pneumonia in Wuhan, Hubei Province, China, in December 2019. Declared by the World Health Organization (WHO) as a global pandemic in March 2020, it has created profound changes in global economy and healthcare systems. This study evaluates the knowledge and practice with regard to various personal safety measures used by the healthcare professionals.

METHODS

We conducted a questionnaire study after obtaining approval, from the Institutional ethical committee. An online survey was conducted using a preformatted questionnaire consisting of multiple-choice questions which assessed the knowledge and practices adopted by various healthcare professionals. The survey was done between 1st and 30th of June 2020 and a total of 536 responses was analysed.

RESULTS

58.4 % of the participants were females, 66 % of the healthcare workers worked at a private hospital / private medical college with 82.1 % being located in urban areas. Of the 536 respondents, 90.1 % practiced bathing immediately after returning home and 86.8 % sanitized their accessories. 86.9 % of the professionals used frequent sanitization with use of mask and gloves whereas only 12.3 % used full personal protective equipment. 58 % of females had used hydroxychloroquine as prophylaxis whereas only 41 % of males used it (statistically significant, $P = 0.005$). Healthcare workers in younger age group (23 - 40 years) were more likely to maintain distance with family members, and government doctors were significantly more likely to do so ($P < 0.001$) as compared to private practitioners.

CONCLUSIONS

With the medical professionals being at high risk for contracting the infection, the need to provide the healthcare professionals with adequate personal protective equipment is of utmost importance. There is also a need to maintain the well-being of the healthcare professionals as they are the weakest link in the chain.

KEY WORDS

Medical Practitioners, Personal Protective Equipment, Safety Measures

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BACKGROUND

In December 2019, a set of patients in the city of Wuhan, Hubei Province, China presented with severe pneumonia of unknown origin. Epidemiologically these were linked to a seafood market in the city. On January 7, 2020 the causative organism was identified to be a novel coronavirus now termed SARS-CoV-2.¹ In March 2020 the World Health Organization declared it a global pandemic.²

It is seen that during the outbreak of any new infectious disease, there are many unknown factors such as mode of disease transmission, risk factors, preventive measures and management options.³ There are various myths and rumours which increase the sense of panic not only among the lay people, but also among professionals. The spread of the novel coronavirus has created a similar situation because we are ill equipped, in terms of knowledge, supplies, infrastructure, and most important, not mentally prepared to deal with this crisis. The outbreak of this novel coronavirus has fundamentally changed the world and is rapidly changing the attitude of medical practitioners. The health workers have now switched to the norm of personal safety first followed by patient safety. This pandemic has also brought about huge changes in global economy and healthcare systems.⁴

In order to prevent transmission of disease from hospitals to the community, and to ensure smooth functioning of the health care system, it has become mandatory to ensure the safety of health care workers, who are at high risk due to close contact with patients. A similar situation was seen during the SARS-CoV-1 epidemic, where doctors and other health workers were highly infected, due to inadequate personal protection.⁵

The Covid-19 virus is transmitted either through close contact with an infected patient or by droplet spread.⁴ Hence, people who care for the infected patients are at the highest risk of getting affected. By the start of April 2020, over one million people had been confirmed.

Infected with SARS-CoV-2. Various guidelines have been enforced for the protection of health workers, including social distancing, hand hygiene, N95 masks, goggles, gloves, gowns, face shields, cover all's, precautions for aerosol generating procedures and frequent sanitization. The current guidelines from the World Health Organization regarding the use of various levels of personal protective equipment are based on the assumption that transmission occurs through droplets, either direct or indirect.⁶ Direct droplet spread occurs when respiratory particles greater than 5 microns in diameter are in contact with the mucosal surface of a recipient.

Indirect spread is said to occur when a fomite or an intermediate surface is touched by hand, and then contacts the mucosa.

Health care professionals should be educated on when to use which personal protective equipment (PPE), how to put on & take off, how to change them by themselves to prevent contamination and how to properly disinfect and discard this equipment. Health care institutions should have procedures and policies that describe the correct order of donning and doffing PPE in a safe manner.⁷

This study evaluates the knowledge and practice of the various personal safety measures used by medical practitioners to protect themselves from exposure to this pandemic.

METHODS

We conducted an online questionnaire survey regarding the knowledge and practice of personal safety measures used by medical practitioners during the Covid-19 pandemic. The institutional ethical committee approval was obtained. The survey was done between 1st - 30th of June 2020 and a total of 536 responses were analysed. We collected data using a preformatted questionnaire sent through e-mail or Google form and recorded all responses. The survey consisted of questions, with the help of which we assessed the knowledge of medical practitioners, and the various measures and practices adopted by them for their personal safety during the Covid-19 pandemic. All medical practitioners who agreed to participate in the study from the first to the thirtieth of June 2020 were enrolled in the study. We obtained 576 responses. The questionnaire was given as a pilot on 10 subjects to make sure that it was easy to understand and not time consuming. Based on the feedback obtained, it required no changes. The average time to complete the survey during the pilot was five minutes. The piloted subjects and the subjects who did not complete the questionnaire were excluded and the final number included for analysis was 536.

Statistical Analysis

The data was compiled and analysed using MS Excel and SPSS software version 25 at 5 % level of significance. The tools of statistics such as – descriptive statistics, chi-square test, some parametric / non-parametric tests were used for data analysis.

RESULTS

The demographic characteristics of our respondents are tabulated below.

	Age	Number	Percentage
	23 - 30	157	29.3
	30 - 40	172	32.1
	40 - 50	128	23.8
	50 - 60	54	10.1
	Above 60	25	4.7
Sex	Male	223	41.6
	Female	313	58.4
Family size	1 to 4 members	317	59.1
	5 to 8 members	206	38.4
	9 members and above	13	2.4
Place of work	Clinic	44	8.2
	Government hospital / government medical college	138	25.7
	Private hospital / private medical college	354	66.0
Area of work	Rural	27	5.0
	Semi urban / rural	69	12.9
	Urban	440	82.1
Department	Anaesthesia	43	8.0
	Laboratory medicine	17	3.2
	Medical specialty	192	35.8
Designation	Surgical specialty	284	53.0
	Consultant	379	70.7
	Intern	42	7.8
Experience group	Postgraduate	115	21.5
	0 to 10 years	253	47.2
	10 to 20 years	162	30.2
	20 to 30 years	82	15.3
	30 to 40 years	32	6.0
	40 years and above	7	1.3

Table 1. Demographic Characteristics

Fifty two percent of our respondents reported to have had encountered suspected Covid 19 patients. However, only 12.9 % were quarantined following such exposure. Five percent of the practitioners were forced to move out of their homes following suspected exposure, in order to minimise risk to their family members.

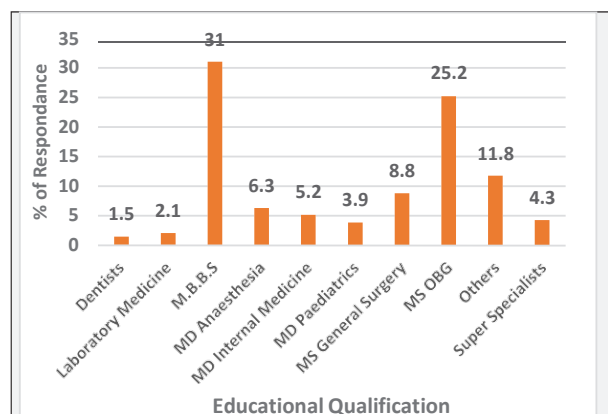


Figure 1. Classification of Respondents Based on Their Educational Qualification

Precautionary Measure Taken Before Consulting any Patient	Frequency	Percent
Sanitizing and full PPE	66	12.3
Sanitizing, mask and glove	466	86.9
Placing a mask / sanitizer outside the door for use by hospital staff and visitor	408	76.1
Taken hydroxychloroquine prophylaxis	199	37.1
Taken any online consultation / class because of Covid-19	164	30.6
Bathe immediately reaching home	483	90.1
Sanitize the accessories immediately reaching home	465	86.8
Maintain distance with family members when at home	251	46.8
Advised / administered hydroxychloroquine prophylaxis to family	128	23.9

Table 2. Precautionary Measures Taken by the Medical Professionals

Out of the 536 subjects, 86.9 % were using sanitization, mask and glove, while only 12.3 % were using full PPE as a precautionary measure during their working hours. Among the respondents who used full PPE along with sanitization, 43.9 % were from the surgical specialty, 39.4 % from medical specialty, 10.6 % were anaesthetists and 6.06 % belonged to laboratory medicine. Almost half the subjects (50.4 %) reported interference of PPE in the quality of work sometimes. Twenty seven percent of the subjects felt the interference of PPE with work frequently. Other forms of protection such as physical barriers were not widely used at the time of our data collection. There was no significant difference between male and female practitioners regarding the various personal safety measures. Similarly, on comparing the various age groups,

designation of practitioners, place of work and area of work; we found no significant difference in the use of personal safety measures. However, on comparing the different specialties, we found that dentists were significantly more inclined to use full PPE in their practice as compared to others (P value < 0.0001). Female practitioners were more likely to place sanitizers, masks at the entrance of their consulting rooms, as a measure for their own safety, although not statistically significant.

Regarding the use of hydroxychloroquine prophylaxis, 58 % of females had used it as compared to 41 % of males, which is statistically significant ($P = 0.005$). Practitioners in the age group of 23 - 30 and 30 - 40 years were significantly more likely to have taken hydroxychloroquine than older practitioners. However, those in older age group had administered prophylaxis more often to their family members, as compared to younger doctors. Similarly, physicians and general surgeons reported to have taken hydroxychloroquine along with their families significantly more than other specialists.

Those in the younger age group, between 23 - 40 years were more likely to maintain distance with their family members, especially physicians and paediatricians. Government doctors were significantly more likely to do so ($P < 0.001$) as compared to private practitioners. Incidence of exposure and post exposure measures were not part of our study. None of our respondents reported to have been infected by the SARS-CoV-2 virus, hence, post infection measures could not be evaluated. Further studies are required to evaluate the rates of infection of health workers in relation to the type of protective equipment they use.

DISCUSSION

The coronavirus disease 2019 (Covid-19) has become an international health crisis, and the global health care system was ill equipped to handle a crisis of such magnitude. The safety of healthcare workers has become the top priority, in order to prevent collapse of healthcare systems and also to prevent transmission of infection from health workers to the community. Medical practitioners are at the highest risk of infection because of frequent close contact with patients who are known or suspected to be infected. A similar situation was seen during the previous SARS-CoV-1 epidemic, where 20 % of the cases comprised of health care workers.⁸

Worldwide, over one million people were confirmed to be infected with SARS-CoV-2 by April 2020. Assuming that healthcare workers were infected at the same rate as in the SARS-CoV-1 epidemic, it would foretell the collapse of health care system, especially in developing countries.⁹

Specialty	Masks Only	Gloves Only	Mask + Face Shield	Mask + Gloves	Mask + Gloves + Face Shield	Mask + Gloves + Goggles	Mask + Gloves + Face Shield + PPE Suit	Total
Surgical	0	0	0	156 (61.9 %)	20 (7.9 %)	56 (22.2 %)	20 (7.9 %)	252
Medical	0	0	0	130 (78.8 %)	18 (10.9 %)	05 (3.03 %)	12 (7.27 %)	165
Anaesthesia	0	0	0	20 (55.5 %)	10 (15.8 %)	05 (13.8 %)	1 (27.7 %)	36
Lab medicine	0	0	0	08 (61.5 %)	5 (38.4 %)	0 (0)	0 (0)	13
Dental	0	0	0	05 (7.14 %)	45 (64.28 %)	15 (21.4 %)	05 (7.14 %)	70
								536

Table 3. Specialty Wise Distribution of Various Forms of Personal Protection during Patient Encounter

There has always been an acceptance that working in a healthcare setting carries a level of personal risk, however, it would seem unreasonable for a healthcare worker to carry out a healthcare activity if there was a high risk of death.⁸ Hence the need for personal protection of frontline warriors is of utmost importance to provide unconditional healthcare services.

Earlier in the pandemic, infection of healthcare workers was as high as 29 %, and this dramatically decreased thereafter due to PPE measures put in place to appropriately protect healthcare workers.¹⁰ Current personal protective equipment (PPE) and infection control guidelines from the World Health Organization are based on the assumption that the primary mechanism of transmission is direct and indirect droplet spread.¹¹

In the current crisis, health-care workers not only have to work harder and longer hours, they often do so in a context where the knowledge and understanding of the novel pathogen is still suboptimal. More than 50 % of the subjects in the current study reported interference of PPE in their quality of work. The use of PPE also interferes with vision, difficulty in operating or carrying out procedures. It not only hampers movement and interferes with skills, also, the regular donning and doffing of full PPE add to physical fatigue and psychological stress.

Aerosol generating procedures may lead to an increase in transmission rates among practitioners. However, the evidence is limited. Infections of health workers following the performance of aerosol generating procedures have been reported, but the exact timing and cause of transmission is unknown.¹² The risk is observed not only during the procedure, but during all periods of contact with the infected patient. Therefore, precautions, and proper PPE usage should be followed not only during procedural periods alone but increase this protection to all times of risk.¹³

While awaiting a vaccine, hygiene measures, social distancing and personal protective equipment are the only primary prophylaxis measures against SARS-CoV-2, but they have not been sufficient to protect our healthcare professionals.¹⁴ Some evidence of the in vitro efficacy of hydroxychloroquine against this virus is known, along with some clinical data that would support the study of this drug in the chemoprophylaxis of infection. However, there are still no data from controlled clinical trials in this regard.

In the aftermath of the current pandemic, the exact mode of transmission may still remain controversial as was the case with SARS-CoV-1 and influenza. Urgent further research is required to investigate SARS-CoV-2 transmission, risk factors and strategies to assure the safety of healthcare workers. In the interim, healthcare workers may choose to take a precautionary approach until robust evidence is available.

CONCLUSIONS

The medical work force is at high risk of exposure as well as increased viral load and although there is a need to balance limited supplies with staff and patient safety, this should not leave the healthcare professionals treating patients with inadequate PPE. Along with extrinsic organisational, infrastructural and procedural conditions, the intrinsic state

and well-being of the health-care worker must also be addressed in order for him or her not to be the weakest link.

Personal protection of frontline workers to provide unconditional healthcare services is of utmost importance in the current era as loss of even 1 doctor equals loss of services of almost 1000 patients.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

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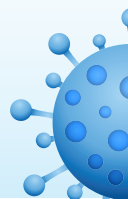
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Attitude of Medical Practitioners and Their Families Toward Handling of Suspected Covid-19 Patients in Mysore, India

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ABSTRACT

BACKGROUND

The novel corona virus 2019 has caused a great hue and cry, especially as the whole world has been caught unawares. We wanted to study the attitude of medical practitioners and their families toward the current situation and on their practice.

METHODS

We conducted an observational, cross sectional study in the form of an online survey with a questionnaire. All practitioners willing to participate in the study were included. A total of 567 responses were obtained, of which 536 were eligible to be included.

RESULTS

From the data analysed, 75 % felt that it was in the line of duty to handle Covid suspects. However, 84.5 % felt that they were putting self and their families at risk by doing so, and 74.4 % did not want to handle Covid suspects, because they did not belong to their speciality. The primary concern of 90 % of the respondents was the risk of exposure and quarantine. Occasional anxiety while going to work was seen in 53.7 % of the respondents. On surveying the attitude of family members, we found that 87.3 % of the parents and spouses feared for their safety, but at the same time felt they were doing their duty. While studying the attitude of children, 57.8 % of them felt that their parents were doing a noble job.

CONCLUSIONS

The majority of practitioners are not trained to handle the current crisis. Fear and anxiety because of lack of knowledge, poor attitude and lack of guidelines may lead to increased stress levels and reluctance to handle suspect Covid-19 patients.

KEY WORDS

Covid 19, Stress, Attitude of Health Workers

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BACKGROUND

During the outbreak of any new infectious disease, there are always many grey areas regarding the risk factors, mode of spread, prevention and treatment.¹ Also, rumours and myths create more panic among professionals and public alike, and they can significantly alter people's attitude towards the disease. We are witnessing a similar situation with the emergence and spread of 2019 novel coronavirus. Medical practitioners are ill equipped, in terms of knowledge, supplies, infrastructure, and most importantly, not mentally prepared to deal with this crisis. There is a sudden increase in the workload, they are forced to isolate themselves and are discriminated by laymen who once considered them next to God. These factors commonly lead to physical exhaustion, fear, emotional disturbances and sleep disorders.²

The chances of them getting infected are much higher, as they have a higher risk of exposure, which in turn leads to the fear of transmission to their loved ones and children. More importantly, the conflict between professionalism and the fear for safety of self and family causes burnouts and physical and mental symptoms.³ Many physicians have been known to develop depression, anxiety or burnout after being involved in a pandemic like situation.⁴ Protecting the mental wellbeing and personal concerns of healthcare workers caring for people with Covid-19 has been identified as imperative for the long-term capacity of the health workforce.⁵ There is a clear need for immediate action to safeguard the personal concerns and welfare of the health care workforce.⁶

This study intended to evaluate the attitude of medical practitioners and their families toward the current scenario and its effect on their practice.

METHODS

We conducted an observational, cross sectional study from first to thirtieth of June 2020. After approval by our Institutional Ethical Committee of JSS Medical college & Hospital, we conducted an online survey using an online questionnaire. The questionnaire was sent through Google form and all the responses obtained were recorded. It aimed to assess the attitude of medical practitioners towards the novel corona virus 2019 disease, as well as their concerns for their family and vice versa. The survey consisted of multiple choice questions where we assessed the willingness of the health care providers to care for an infected patient, concerns regarding quarantine, and hydroxychloroquine prophylaxis. All the medical practitioners who agreed to participate were enrolled in the study. We obtained 567 responses. We piloted the questionnaire on 10 subjects to make sure that it was understandable and not burdensome in terms of time. No changes were necessary based on the feedback, and no surveys from the pilot were included in the analysis. The average time to complete the survey during the pilot was five minutes.

Statistical Analysis

1. The data was analysed using MS Excel and R - 3.5.1 software.

2. All the tests of significance were carried out at 5 % level of significance.
3. The statistical methods used were:
 - Descriptive Statistics – minimum, maximum, mean, median, variance, standard deviation, skewness, kurtosis, frequency tables and cross tables.
 - Diagrams – Simple Bar diagram, pie diagram, Percentage component bar diagram.
 - Inferential Statistics – Chi-square test for association.

RESULTS

A total of 567 people responded to our survey. Five hundred and thirty six entries were considered for data analysis, after excluding non-eligible personnel such as non-medicos, incomplete and irrelevant entries. Female respondents accounted for 58.4 % and 41.6 % were males. The mean age of our respondents was 37.5 years. Their average family size was 4.5, with 59 % having a family size of ≤ 4 members, and only 2.4 % with ≥ 9 members. On an average, 0.57 members were < 10 years of age, 3.19 between 10 and 60 years and 0.74 were > 60 years of age. Among 31 % of the respondents, they were the sole medical practitioners in their families, whereas among 62 % there were 1 or 2 more medical personnel in the family. The majority (82.1 %) of our study population was from the urban setup, 5 % from rural areas and the remaining were from semi urban areas. Doctors working in a private hospital or medical college formed 66 % of the study population, 25.8 % worked in a government hospital or medical college and 8.2 % worked in a clinic setup. Consultants (70.7 %) formed the major chunk of respondents, 21.5 % were post graduates and 7.8 % were interns. Almost 50 % had less than 10 years of experience. Doctors working in a government setup were significantly more likely to encounter suspected Covid-19 patients ($P < 0.0001$) than those working in private hospitals or clinics.

On defining the attitude of medical practitioners, 75 % felt that it was in the line of duty to handle COVID suspects. However, 84.5 % felt that they were putting self and family at risk by doing so, and 74.4 % did not want to handle Covid suspects, as it was not their speciality. Consultants were significantly more likely to agree that it was in the line of their duty to handle suspect Covid-19 patients (chi square value 9.478, P value 0.008), as compared to residents and interns. There was no significant difference with regard to gender, age, family size or area of practice and the attitude of doctors as to whether they ought to manage suspected Covid-19 patients. General practitioners were significantly more likely (P value 0.005) to agree to treat suspected Covid 19 patients as part of their duty, as compared to specialists and super specialists. Also, doctors in a teaching facility significantly encountered and managed suspected patients as part of their routine work. Their experience and speciality had no significant effect ($P = 0.21$, chi-square value 10.816) on their attitude towards managing suspect Covid-19 patients.

The primary concern of 90 % of the respondents was the risk of exposure and quarantine. Female doctors significantly feared ($P = 0.026$) the risk of quarantine. On comparing the age groups, those between 30 and 40 years of age, and doctors above 60 years of age were more worried about getting quarantined.



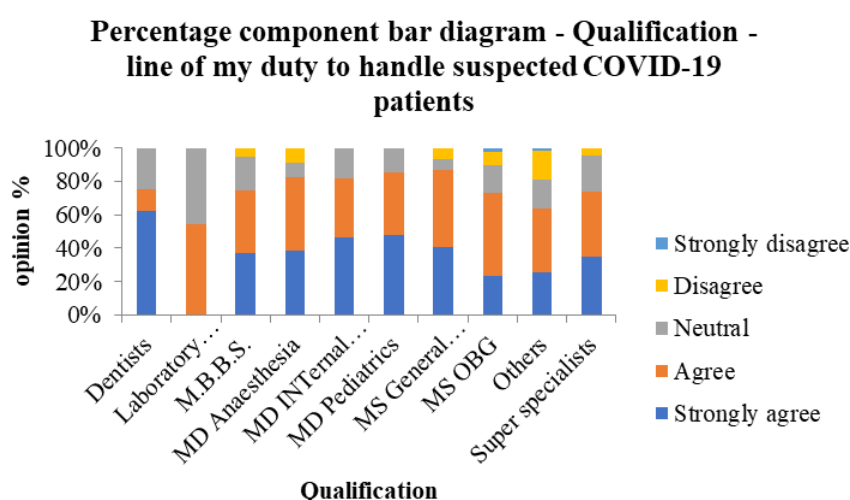


Figure 1. Qualification of Medical Practitioners Vs Willingness to Handle Suspect Covid 19 Patients

Age Group		Stress / Isolated from Family Because of COVID-19					Total
		Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree	
20 to 30 years	Count	39	49	41	20	8	157
	% of Total	7.3 %	9.1 %	7.6 %	3.7 %	1.5 %	29.3%
30 to 40 years	Count	36	60	43	26	7	172
	% of Total	6.7 %	11.2 %	8.0 %	4.9 %	1.3 %	32.1%
40 to 50 years	Count	18	37	33	32	8	128

Table 1. Age Group Vs Feeling Stressed or Isolated from Family

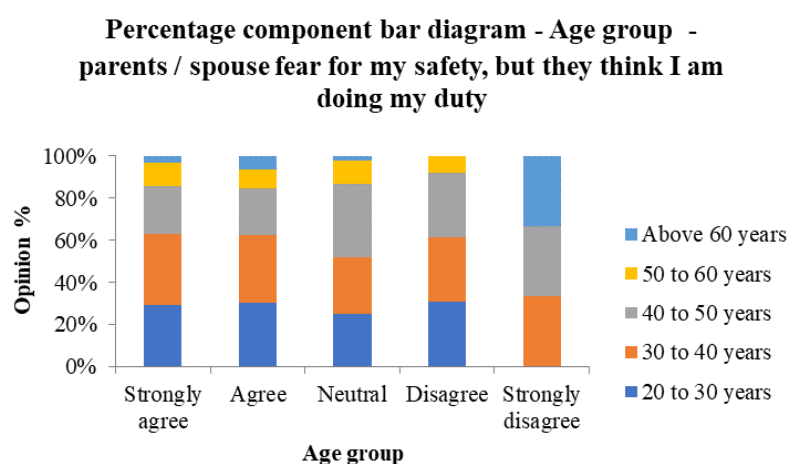


Figure 2. Attitude of Parents / Spouse Towards Practitioner's Duty

Dentists, gynaecologists and super specialists had the greatest fears regarding exposure and quarantine, although not statistically significant. Interns had greater concerns as compared to residents and consultants. Majority (74.4 %) of the practitioners were afraid that they would be infected, if they were quarantined; and among 91 %, the major concern was regarding the well-being of their families.

Occasional anxiety while going to work was seen in 53.7 % of the respondents. Females significantly reported to being nervous or anxious while going to work, as compared to males. Majority of practitioners above the age of 60 years, never had any anxiety issues. Smaller the family size, greater the anxiety levels were reported. There was no significant difference

among the anxiety levels of doctors from different specialities, however those in surgical specialities, had higher anxiety levels. Those working in rural areas reported significantly lower stress and anxiety levels.

Fifty one percent of the respondents admitted to feeling stressed or isolated from family members due to the fear of infecting them. Majority of them were > 40 years of age (76.7 %). Government doctors reported stress significantly more than those in private setup ($P = 0.0003$) irrespective of the speciality. 50 – 60 % of doctors were feeling stressed or isolated from family.

Irrespective of gender, age, family size, place of work, department and designation, a vast majority of doctors



strongly agreed that they were exposing their families to the risk of infection by handling these patients. However, only 37.1 % had taken hydroxychloroquine prophylaxis, and 23.9 % had administered it to family members also. There was a significant difference among the specialists who had taken HCQ prophylaxis.

None of the dentists in our study had taken it, whereas up to 55 - 60 % of physicians, surgeons and paediatricians had taken hydroxychloroquine. Similarly only 0.6 % of interns had taken hydroxychloroquine as compared to 30 % of consultants ($P < 0.0001$).

Regarding the attitude of family members, 87.3 % of the parents and spouses feared for their safety, but felt that they were doing their duty. On studying the attitude of children, 57.8 % of them felt that their parents were doing a noble job. However, 41.6 % of the family members preferred that the respondents stayed home, as it meant keeping safe. Occasional discrimination by lay people was reported by 33.4 % of children and family members, as they belonged to a doctor's family. General practitioners significantly ($P = 0.03$) reported to being discriminated against.

Similarly doctors in the age group of 20 - 40 years significantly ($P = 0.035$) reported to being discriminated against.

There was no association between gender or age group and the fear of parents or spouse for the safety of the doctors. Majority of them (30 - 40 %) strongly agreed that they were putting themselves and their families at risk. Similarly we found no variation in the fear factor of family members with regard to place or area of work, designation, age or years of experience. 20 % of interns said that their families preferred them to stay at home, as compared to 12 % of residents, and < 10 % of consultants.

On comparing specialities, almost 80 % of dentists and 70 % of laboratory medicine doctors felt that their families preferred them to stay home, as compared to < 40 % of other specialities.

Majority (50 - 60 %) of the children agreed that their parents were doing a noble job. However, children of doctors who were less than 40 years of age were more likely to disagree, especially the children of resident doctors. More than 50 % of their children were neutral or disagreed that their parents were doing a noble job. On comparing the thoughts of children of consultants, especially those > 40 years of age, around 45 % of children agreed.

DISCUSSION

Covid-19 is an emerging, and rapidly evolving health challenge all over the globe. It has had a profound impact, probably the most serious public health threat since the 1918 H1N1 influenza pandemic. The impact of the disease is beyond mortality, and morbidity has become apparent since the outbreak of the pandemic. Healthcare systems and workers all over the world are ill prepared to handle a crisis of such huge magnitude. Adequate manpower and resources are not available in many areas. Furthermore, there is the fear of contracting the infection by the healthcare workers themselves.

Our study highlights the attitude of medical practitioners in various setups, and their willingness to put themselves and

their families at risk of exposure and quarantine. We found that almost 75 % felt that it was their duty to treat Covid 19 suspects, however they were unwilling to do so, if it was not in line with their specialisation. Similarly, Olum et al. studied the attitude of 581 health care workers in Uganda, and reported that that about four - fifth of the respondents had poor attitude towards Covid-19 and up to 60 % of health workers admitted to having avoided patients with symptoms suggestive of Covid 19, probably due to lack of proper protective equipment, and also inadequate knowledge about managing such patients. Therefore the health workers should be provided with continued professional education in order to improve their knowledge and attitude towards patients.⁷

Huynh Giao et al. conducted a cross sectional study in a district hospital in Vietnam to assess the knowledge and attitude of health workers. They reported that 82 % were worried about infection due to exposure, and 79 % were worried regarding infection of family members. Nearly 97 % were worried about isolation, but were willing to accept institutional isolation if infected.⁸ We found that 74 % of practitioners in our study feared the risk of infection and quarantine, whereas 91 % were afraid of the well-being of their families.

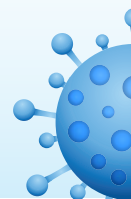
Increased workload, isolation and discrimination commonly resulted in physical exhaustion, anxiety, emotional disturbances and sleep disorders.² They studied 1563 health workers, and found that 50.7 % of the participants had symptoms suggestive of depression, 44.7 % anxiety and 36.1 % had some form of sleep disturbances. Such heightened levels of depression and anxiety had been reported in other health workers such as ambulance personnel and paramedics.³

The fear of transmitting the infection to their loved ones and children is also a major contributing factor to stress and depression. Further, there is a mental conflict between professionalism and concern for personal and family safety which can cause both physical and emotional burnout.^{3,12}

Services to provide counselling and psychiatric screening for anxiety, depression and suicidal tendencies for practitioners who are dealing with infected patients are scarce.⁴ The World Health Organization has predicted that many physicians may develop post-traumatic stress disorder, depression or burnout after the cessation of the pandemic.⁴

The issue that needs to be addressed is: What are the obligations of medical personnel to the society, and vice versa, what the society should do for these frontline warriors? There are guidelines which suggest that, although there is a professional obligation, it is not absolutely necessary for health workers to treat infected patients while putting themselves at risk.⁹

The American Medical Association Code of Ethics states that "Because of their commitment to care for the sick and injured, individual physicians have an obligation to provide urgent medical care during disasters. This holds good even in the face of greater than usual risks to their own safety, health or life. The physician workforce, however, is not an unlimited resource; therefore, when participating in disaster responses, physicians should balance immediate benefits to individual patients with ability to care for patients in the future."¹⁰ It is also true that physicians should be provided with adequate



safety measures, proper equipment, and adequate compensation for those infected in the line of duty.

CONCLUSIONS

The majority of medical practitioners felt ill equipped to handle the current crisis. The fear factor and anxiety due to lack of knowledge, negative attitude and lack of well framed guidelines could be few reasons for the increased stress levels and reluctance to handle suspect Covid-19 patients. Probably, with additional educational interventions and campaigns, they might be in a stronger and more confident position to handle such situations; as good knowledge has a higher probability of positive attitudes.¹¹

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

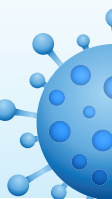
Financial or other competing interests: None.

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12. Miscellaneous

SI No	Title	SDG IMPACT
98	COVID 19 in ayurvedic perspective, B Venkataiah., V Kirthana., Dr Narayana Murthy M.R., International Journal of Health & Allied Sciences, 9, 91-96	Goal 3: Good health and wellbeing
99	Legislation to combat Covid-19: Indian Scenario, Dr Chandrakanth H.V., Dr Smitha Rani, Medico-Legal Journal, 0025-8172	Peace, Justice and strong institutions Goal 3: Good health and wellbeing
100	Combating the COVID-19 pandemic in a resource-constrained setting: Insights from initial response in India, Mohan Bairwa, Praveen Kulkarni, BMJ Global Health, 5	Goal 3: Good health and wellbeing
101	Cause of Death Certification in COVID-19 Deaths, Chandrakanth Hungund Veeranna, Smitha Rani, Indian Journal of Critical Care Medicine, 24, 863-867	Goal 16: Peace, Justice and strong institutions



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COVID 19 in ayurvedic perspective

V Kirthana, B Venkataiah¹, M R Narayana Murthy

Abstract:

The age-old science of Ayurveda has many secrets hidden within. The coronavirus disease is a novel disease, as indicated by its nomenclature also. The plural medical system approach is being implemented to combat the disease. There are many references in the ayurvedic textbooks/classics/Samhitas about janapadodwamsa or epidemics in the age of gods and the management of such epidemics or janapadodwamsa can also be evidenced in the classics of Ayurveda. The principles of Ayurveda can be applied for both preventive and curative aspects of disease. The practical knowledge and the knowledge about the stage of the disease are essential to bridge the ayurvedic principles with the preventive and curative aspects of the disease. The efficiency of ayurvedic drugs is known by practice. However, new drugs can be formulated with a combination of drugs. The search for new drugs and new preventive practices in an integrated approach is what the approach is to be to tackle the novel virus. In this regard, the current paper aims to bridge the preventive aspects of COVID 19 with respect to various stages of disease in ayurvedic aspect.

Keywords:

Ayurveda, COVID 19, health, prevention, public

Introduction

(Acharya Charaka in his treatise Charaka samhita, Vimana sthana 3:6 quotes about JANAPADODWAMSA or EPIDEMICS.)

The conversation between Atreya and Agnivesha, which is documented as Charaka samhita, a standard treatise in the Ayurveda science quotes that all though there are dissimilarities between every individual, there are certain factors which are similar among all. They are AIR, WATER, DESHA (Place of living), KALA (time/season). Vitiating among any of these factors manifests diseases having similar symptoms, which ultimately may lead to the destruction of country. Such manifested disease leading to destruction in mass is termed as "JANAPADODWAMSA or EPIDEMIC."

The history of such an epidemic outbreak dates back to 3000 BC, where an epidemic

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wiped out a whole village in China. The archaeological site is now called "Hamin Mangha." The latest being CORONA VIRUS PANDEMIC, named later as COVID-19 or NOVEL CORONA VIRUS DISEASE or nCoV, which began in December 2019 in a Hubei province of China called as Wuhan city.

The virus has affected 206 countries causing 40,777 confirmed deaths and 827,419 confirmed cases globally (as on April 1, 2020).^[1] The situation is no less bad in India with 1764 active Cases, 150 Cured/Discharged, 50 deaths and 1 migrated case as on April 2, 2020.^[2]

The World Health Organization (WHO) declared it as a pandemic on March 11, 2020.^[1]

This pandemic has the following symptoms:^[3]

1. Fever– Usually high grade
2. Cough– Nonproductive/dry
3. Shortness of breath
4. Running nose

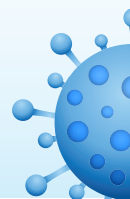
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5. Gastrointestinal disturbance– Diarrhea/nausea
6. Headache.

The symptoms get exhibited within 2–14 days of exposure to virus.^[3]

Acharya Charaka, in his treatise has widely explained the etiology, signs/symptoms, and treatment protocol for aagantuja jwara.

(Charaka samhita. Chikitsa sthana. 3:4)

Acharaya Charaka has mentioned that Jwara is that which causes distress to Deha (Body), Indriya (Sense organs), manas (Mental faculty), that which disease which produces greater discomfort among all diseases and that which takes a lot of Bali is termed as Jwara and that is explained by Acharyas initially owing to its importance in its destructive capacity.

Mentioning various types of Jwara's, he also mentioned about Aagantuja jwara, that which is caused by external/foreign bodies or Germs.

The Current Pandemic Can Be Grouped Under Aagantuja Jwara

Ayurveda categorizes diseases and treatment in terms of Doshas vitiated (Dushyas), Prakriti of the individual (Body constitution), Adhishthana of disease (Target organ of disease).

However, the treatment of a disease includes much more aspects like Roga marga (Pathway of disease), Kala (Time/Season of disease manifested).

Trying to understand COVID 19 in Ayurveda perspective:

Doshas Involved– Vata, Pitta

Since the disease produces dryness (Dry Cough) and shortness of breath, it can be considered that vitiation of Vata dosha is present.

The presence of high-grade fever annotates vitiation of pitta dosha.

Roga Marga– Abhyantara

Since the disease involves phupusa (lungs), the pathway of the disease can be considered as internal.

Adhishtana– Phupusa

The target organ for the disease manifestation is phupusa or lungs.

Type of Vyadhi– Agantuja Jwara

That which is caused by Virus (Foreign body).

Kala– Time of Vyadhi– In Indian Context– Summer

Most of the cases started by the end of February and the beginning of March, i.e., end of Shishira ritu and beginning of Vasantha ritu.

The period was Ritusandhi, i.e., junction period of two ritus, where it is said that the time is apt for the occurrence of any disease as the immunity of individuals would have reduced.

Transmission– Droplet

Ayurveda way of treatment

The treatment aspect of Ayurveda can be understood in three categories–

1. Ahara
2. Vihara
3. Aushada.
 - a. Abhyantara
 - b. Bahya.

Aushada– Abhyantara aushadi

Acharya Charaka in his treatise, has explained that Tikta rasa aushadi should be given during Jwara kala.

(Bitter taste dominant medications)

Accordingly, considering the prakriti of the individual, roga and rogi bala, kala and adhishthana of roga the treatment of different type of jwara is to be decided.

Since the COVID is vatapittaja vyadhi,

- i. Kirata– Swertia chirata– Gentianaceae:

The anti-pyretic activity of kirata is documented by RL Singh, Pankaj singh, Anju agarwal that both the crude and purified extracts significantly inhibited cell proliferation and induced apoptosis. It may cure infectious diseases, tonsillitis, bronchitis, pneumonia, whooping cough, acute enteritis, gastritis, urethritis, nephritis, tuberculosis, gall bladder infection, influenza and high blood pressure. Besides, the anti-helminthic, hypoglycemic and antipyretic antifungal and antibacterial properties there are amarogentin (most bitter compound), swerchirin, swertiamarin and other active principles of the herb.^[4] The plant also has hypoglycaemic property and hence should be administered carefully

A study by Bhargava *et al.* reported the anti-pyretic activity of kirata by studying Antipyretic Potential of Swertia chirata Buch Ham. Root Extract. They



reported that the antipyretic effect of the extract was comparable to that of paracetamol (150 mg kg⁻¹ body weight, p. o.), a standard antipyretic agent.^[5]

(ii) Amrita– *Tinospora cordifolia*– Menispermaceae

The antipyretic activity of amrita is very well known and documented. However, its anti-pyretic activity is studied by Upadhyaya *et al.* reported that traditionally *T. cordifolia* is known for its jwarahara activity (antipyretic activity). The water-soluble fraction of 95% ethanolic extract of *T. cordifolia* plant has shown significant antipyretic activity. In another experimental study, antipyretic effects have been reported in the hexane-and chloroform-soluble portions of *T. cordifolia* stems. Various studies show remarkable anti-infective and antipyretic properties of *T. cordifolia*. Pre-treatment with *T. cordifolia* was shown to impart protection against mortality induced by intra-abdominal sepsis following coecal ligation in rats and significantly reduced mortality from induced by *Escherichia coli* –induced peritonitis in mice^[6]

A study by Neha rawat and Rakesh Roushan reported that Guduchi is highly rich in anti-oxidants. It also has anti-pyretic, anti-viral, and wound healing properties.^[7]

(iii) Katu rohini– *Picrorhiza kurroa*–Plantaginaceae

A study by Masood *et al.* documented that the plant is considered as an important medicinal plant which is mostly used in the traditional medicinal system for asthma, jaundice, fever, malaria, snake bite, and liver disorders. Different pharmacological activities of *P. kurroa* include anti-microbial, anti-oxidant, anti-bacterial, anti-mutagenic, cardio-protective, hepato-protective, anti-malarial, anti-diabetic, anti-inflammatory, anti-cancer, anti-ulcer, and nephro-protective activities were recorded from this plant^[8]

A study by Krupashree *et al.* reported that the study demonstrates antioxidant and protective effects of *Picrorhiza kurroa* against oxidative damage of macromolecules such as DNA, protein, and lipids.^[9]

(iv) Musta– *Cyperus rotundus*– Cyperaceae

A review by Nagarajan *et al.* suggested that both *Aconitum heterophyllum* and *Cyperus rotundus* are reported to possess anti-inflammatory, antipyretic, antibacterial and antidiarrheal properties, while anti-inflammatory and antibacterial activities are attributed to *C. scariosus*.^[10]

(v) Vasa– *Adathoda vasica*– Acanthaceae

A potential drug with highly used in Kasa (Cough), Swasa (Respiratory distress/Asthma/Bronchitis) is reviewed by Ankit Gupta and P. K. Prajapati and reported that Highly significant ($P < 0.001$) results on Shwasakashtata (Difficulty in respiration) were found in all the test drug groups except in Vasa Ghrita, which was only significant ($P < 0.05$). The effect on Kasa (Cough) was also highly significant ($P < 0.001$)

in all groups, whereas it was insignificant (>0.10) in the Vasa Ghrita (Medicated ghee prepared with Vasa) group.^[11]

(vi) Usage of Ginger, Turmeric, Long pepper, Clove, Garlic, Cumin, Coriander, Cinnamon, Basil leaves (Tulsi) in excess either along with food or alone

(vii) Ushna jalapana (Frequent intake of hotwater)– Can be added with Mint leaves and Coriander leaves, Fennel, Ajwain.

Aushada– Bahya– Urdhwagata shodana

i. Nasya– Medicated Nasal drops can be instilled into both the nostrils every day and night. Since the pathway of disease is upper respiratory track, Nasya can be beneficial to combat the disease and to keep the channel clear for breathing

ii. Kavala graha– Keeping the medicated oil or kashaya (decoction) in the mouth for some time until the eyes starts watering

This keeps the oral cavity clean, strengthens the gums, and, most importantly, clears the mucus plugs if adhered in the channel.

iii. Gandusha– Gargling

The procedure helps to clear the sinuses and keeps the channel patent

iv. Swedana– Sudation

Frequent inhalation of steam with addition of bronchodilating drugs like Vasa (*Adathoda vasica*), Bharangi (*Clerodendrum serratum*) depending on roga and rogi bala.

The procedure helps to clear the airways and aids smooth respiration.

v. Dhupana– Fumigation

Fumigating the house and surroundings periodically with drugs like guggulu (*Commiphora mukul*), Nimba (*Azadirachta indica*), Vacha (*Acorus calamus*) The efficiency and mode of action of dhoopana drugs are documented by Shrestha *et al.* in their work Dhoopana Karma: A review through Brihatrayi^[12]

A study by Tillu *et al.* further noted the medical benefits of both bahya and abhyantara chikitsa. He further states that immunomodulators such as Ashwagandha, Guduchi, Yashtimadhu, Shatavari, and Amalaki can be provided to diseased persons to enhance their immunity. They further recommend clinical research of the same.^[13]

Vihara

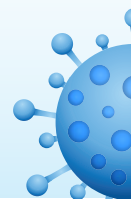
i. Avoid unnecessary gathering

ii. Maintain distance from each other

iii. Maintain isolation

iv. Avoid sleeping during the daytime

v. Avoid excessive physical activity including excessive walking or jogging Among individuals under observation, to combat mental stress and anxiety.



- Application of lukewarm oil on anterior fontanelle is known to reduce anxiety
- Shirodhara– A panchakarma procedure is known to reduce mental stress and anxiety can be performed
- A good sleep.

Yogasana can be practiced for positive health:

1. Pranayama– Particularly bastrika and kapalabhaati can be performed for 10 min each
2. Asanas like– Bhujangasana, Vajrasana, and Padaangushtasana, can be performed for respiratory wellness.

Ritusandhi

Ritusandhi refers to the junction of two ritus. It is said that the disease during this period occurs because of change in kala i.e., shifting one one ritu to another (the last 15 days of previous ritus and initial 15 days of successive ritu) and that the human body fails to adjust for such changes. Hence to combat the disease during this period, the achara (regime) and ahara (diet) during this period should gradually change from the previous ritu to successive ritu.

In the current scenario, since the COVID outbreak in India started in ritusandhi kala, the diet and regime should be followed carefully.

The diet and regime of both Shishira and Vasantha ritu should be followed.

Shishira Ritu

Mid-January to mid-March (approximately) is considered as *Shishira Ritu* (winter). During this season, the environment remains cold. The strength of the person becomes less, deposition of the *Kapha Dosha* and digestive capacity remains in a higher state. Foods having *Amla* (sour) as the predominant taste are preferred. Cereals and pulses, wheat/gram flour products, new rice, corn, are advised. Ginger, Garlic, *Pippali* (fruits of *Piper longum*), Sugarcane products, Turmeric, Clove, Cinnamon, Cumin are to be taken in more quantity.

Vasantha Ritu

The approximate time is from mid-March to mid-May. Strength of the person remains in a medium degree, vitiation of *Kapha Dosha* occurs and *Agni* remains in Manda state.

One should take easily digestible foods. Among cereals, old barley, wheat, rice are preferred. Among pulses, lentil, Mugda, and others, can be taken. Food items tasting Tikta

(bitter), Katu (pungent), and Kashaya (astringent) are to be taken.

A study by Ravi Philip Rajkumar has identified a potential psychoneuroimmuno modulator mechanism for the interventions suggested by the government. He has stated that "A potential psychoneuroimmune mechanism was identified for five of the proposed methods, via neurobiological mechanisms such as modulation of monoamine function, stress axis response and autonomic activity, as well as reduction of anxiety, depression and perceived stress in human subjects."^[14]

Ayurveda and Public Health

Acharya Sushruta has depicted different modes of communicable disease transmission while explaining the treatment model for Kushta roga (type of skin disease) in his classical treatise *Sushruta Samhita*.

He says through excess of all forms of contact (*Prasanga*), physical contact (*Gatrasamsparsat*) , expelled air (*Nihsvasat*), eating with others in the same plate (*Saha bhojanata*), sharing a bed (*Sahashayyanat*), using clothes, garlands or ornaments of infected individuals (*Vastra malaanuepanat*) infectious diseases spread from person to person.

Owing to the reference and evidencing the current scenario, it can be said that role of Ayurveda in maintaining Public Health is highly influential.

The very aim of Ayurveda is treating the diseased and Protecting the health of the healthy

(Charaka samhita. Sutra sthana. 30:26)

i.e., Protecting the health of healthy and reducing the ailment of diseased.

The aim of Ayurveda and Public health seems to be in line with each other.

Integrating the age-old practice of Ayurveda with modern problems provides a better alternative for the problems.

The Ayurvedic practice is not just for those who are diseased but also for those who are healthy to protect their health status. The iceberg phenomenon can be understood with Shatkriya Kalas of the Ayurvedic concept.

Ayurveda explains the stages of disease in 6 stages, i.e.,

1. *Sanchaya*– *Stage of accumulation*– This is the first stage of any disease where the doshas (Responsible for disease formation) are increased in their own site.



This can be analyzed with the aversion toward food or activities or a feeling of uneasiness before the onset of Vyadhi (Disease-CoVID 19)

2. *Prakopa– Stage of provocation*– With the advancement in disease, the increased doshas tends to leave its site of origin and tries to move to other site. The stage of vyadhi (Disease– CoVID 19) when doshas start producing respiratory symptoms
3. *Prasara– Stage of propogation*– The doshas having a tendency to leave their site of origin to site of disease expression (Target organ) will start moving from their site of origin. This is the stage of when all the symptoms of vyadhi (CoVID 19) starts exhibiting (cough, gastro-intestinal disturbances, Fever, Running nose, Myalgia)
4. *Sthanasamsraya– Stage of localization*– The vitiated doshas starts localizing in such areas which are prone to respective disease. The virus producing CoVID 19 is prone to producing respiratory symptoms and the target organ is lungs. This stage can be considered as the premonitory stage of the disease. Once the infection has occurred the above stages may occur simultaneously depending on the severity of infection and susceptibility of the individual
5. *Vyakta– Stage of manifestation*– The doshas localized in the target organs starts exhibiting the symptoms. This is the visible stage of the disease. The vyadhi (CoVID 19) is exhibited with all the signs and symptoms in its full form
6. *Bheda– Stage of complication*– The dosha vitiation will be completed by fifth stage. If the treatment is not available at disease manifested stage, then the disease may further aggravate to produce complications. The vyadhi (CoVID 19) may produce renal complications and pneumonia leading to death of the individual.

It is up to the stage of sthanasamsraya (Stage of localization) the disease is not clear in its manifestation and can be compared to the iceberg hidden in the water. The stages after sthanasamsraya are perceivable to eyes and are being treated.

The concept of prevention can be applied at each level of kriyakala.

The primordial prevention can be applied at stage 1 and stage 2:

The act of social distancing and preventing unnecessary movement within or outside the unaffected countries.

The primary prevention can be applied at stage 3 and stage 4:

Prophylactic medications can be started in such countries where the disease has started a slow raise. Health education to all classes of people is the need of

the hour. Bursting the myths and wrong messages being spread in the community should be stopped and should be replaced with correct information. Providing adequate specific protection measures like supply of masks, hand sanitizers to those who are in need.

The secondary prevention can be applied at stage 4 and stage 5:

The countries which have already developed clusters of diseases with community transmission should accelerate the process of disease detection and adequate treatment for the same. The disease should be identified at stage 4 in order to prevent the community spread. The people should be educated to the extent such that the chain of infection is broken by their non-participation in the epidemiological triad.

The tertiary prevention can be applied at stage 6:

The people who are at the verge of losing life due to CoVID 19 are to be given supportive care to prevent to aid the process of respiration.

A study by Sanjeev Rastogi, Deep Narayan Pandey, Ram Harsh Singh suggested disease stage-wise categorization of patients into unexposed asymptomatic, exposed symptomatic, with mild symptoms and with moderate-to-severe symptoms and treatment protocol to be assigned depending on the disease stage.^[15]

Conclusion

COVID 19, a new strain of virus causing mortality all over the world, can be prevented with appropriate food intake, hygiene, and social distancing.

The stage of the disease in the community needs to be decided, and the administration of medicine can be done by ascertaining the roga bala and rogi bala.

Prophylactic measures can be applied by administering anti-pyretic drugs like Amrita, Kirata inappropriate and required form and dosage. Intake of Ginger, Garlic, Cumin, Coriander, Cinnamon, Clove, and Turmeric in excess quantity for its prevention.

Distancing one from the affected individuals is the key. Respiratory and personal hygiene is to be followed in order to protect oneself from the disease.

Following the recovery, the individuals should not resort to daily routine activities until the individual regains strength and his agni bala (digestive capacity) is normal.

Ayurveda not only aims to heal the diseased but also to protect the health of the healthy individuals; hence, the



measures applied for the treatment of disease should also be followed by healthy individuals to prevent the disease occurrence.

"PREVENTION IS BETTER THAN CURE"

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Conflicts of interest


There are no conflicts of interest.

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Legislation to combat Covid-19: Indian Scenario

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The Covid-19 pandemic has required prominent new laws to be passed across the globe. India did not formulate new legislation as it was able to use sections 2 and 2A of the Epidemic Diseases Act 1897 to control the spread of the disease. This 123-year-old (Colonial era) Act was passed to curb the spread of the then prevalent bubonic plague; it gives the government powers to curtail the disease spread and designates penalties for violating the regulations and confers legal protection on the officers who implement its provisions.¹

The Act is regulatory in nature. It emphasises the powers of the government but is silent on the rights of the citizens. It is silent on the scientific steps that the government needs to take to prevent the spread of the disease.²

The Indian government also resorted to using the provisions of the Disaster Management Act 2005, to impose a nationwide lockdown for over two months which started on 25 March 2020. India considered Covid-19 as a disaster, which the Act defines as “a catastrophe, mishap, calamity or grave occurrence in any area, arising from natural or man-made causes, or by accident or negligence”.³

The Oxford Covid-19 government response tracker, which follows and compares worldwide government responses to the pandemic, found that the Indian government's response to be the most stringent.⁴

There has been violence against healthcare workers who were perceived as carriers of the disease; this violence made it necessary to pass an ordinance to amend the Epidemic Diseases Act. By the said ordinance, whoever commits or abets violence against health care workers, are punishable with imprisonment ranging from 3 months to 5 years, and a penalty can be imposed ranging from Rs 50,000 to 2 lakhs. In a case of grievous injury, the punishment is more severe. It also imposes time-bound investigations in addition to compensation for injury or damage to property, to almost twice the fair market value.⁵

India is the second-most populous country and hence it is a Herculean task to contain the spread of the disease. The need for comprehensive legislation to deal with all the issues connected with Covid-19 has been expressed in certain quarters instead of ad-hoc rule making.

The initial measures taken by the Indian government were praised by the World Health Organization; however, only time will tell whether the right decisions were made.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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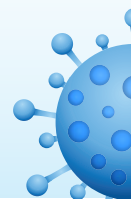
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Combating the COVID-19 pandemic in a resource-constrained setting: insights from initial response in India

GRID COVID-19 Study Group

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ABSTRACT

The low-and-middle-income country (LMIC) context is volatile, uncertain and resource-constrained. India, an LMIC, has put up a complex response to the COVID-19 pandemic. Using an analytic approach, we have described India's response to combat the pandemic during the initial months (from 17 January to 20 April 2020). India issued travel advisories and implemented graded international border controls between January and March 2020. By early March, cases started to surge. States scaled up movement restrictions. On 25 March, India went into a nationwide lockdown to ramp up preparedness. The lockdown uncovered contextual vulnerabilities and stimulated countermeasures. India leveraged existing legal frameworks, institutional mechanisms and administrative provisions to respond to the pandemic. Nevertheless, the cross-sectoral impact of the initial combat was intense and is potentially long-lasting. The country could have further benefited from evidence-based policy and planning attuned to local needs and vulnerabilities. Experience from India offers insights to nations, especially LMICs, on the need to have contextualised pandemic response plans.

INTRODUCTION

In the absence of a specific treatment or vaccine for a global crisis like the COVID-19 pandemic, combative interventions are time-sensitive and resource-intensive.^{1 2} About 85% of the world's population (6.4 of 7.6 billion, 2018) reside in low-and-middle-income countries (LMICs).³ Methods such as social distancing, personal protection, aggressive contact tracing and isolation, and mass movement restriction seem untenable in LMIC contexts given the socio-economic disparities and living conditions.⁴ Healthcare resources are scarce and surge capacity weak.⁵ Vulnerabilities (predominance of unstructured employment, limited employment security and health protection, inadequate health awareness and care access) remain high and underassessed.⁴

With a population of ~1.4 billion, India's response to COVID-19 directly affects 17.7% and 21.8% of the global and LMIC populations, respectively.³ This paper aims to provide

Summary box

- Low-and-middle-income countries (LMICs), where 85% of the world's population reside, need context-relevant approaches.
- We analysed India's (an LMIC) initial response to the pandemic (from 17 January to 20 April 2020).
- India's variegated epidemiological, sociopolitical and systemic vulnerabilities make its pandemic response complex.
- India could leverage pre-existing legislative provisions to adopt a collective combat, with states taking the lead with support from the union government; the pre-emptive stringent nationwide lockdown had benefits as well as uncovered vulnerabilities.
- Insights from India's initial response will help in response preparedness and planning for future pandemics, especially in the LMIC context.

a descriptive account of India's response to the pandemic in the initial months, that is, from 17 January (when it issued its first travel advisory for COVID-19) until 20 April (initiation of graded relaxation of the nationwide lockdown). We build the analysis on India's LMIC context.

COLLATION OF INFORMATION

Setting

India has a semifederal democratic governance system. The Constitution of India vests the responsibility of 'health' in its states, and that of preventing the spread of infectious diseases from one state to another concurrently with the Government of India (GoI) and the states.⁶

The GRID COVID-19 Study Group

Our group (n=55) has members located across 40 institutions in India (21 of 28 states and 3 of 8 union territories (UTs)). These include teaching faculty (n=47) and residents (n=3) in departments of community medicine in medical schools, full-time public health researchers (n=3), monitoring and evaluation expert (n=1),



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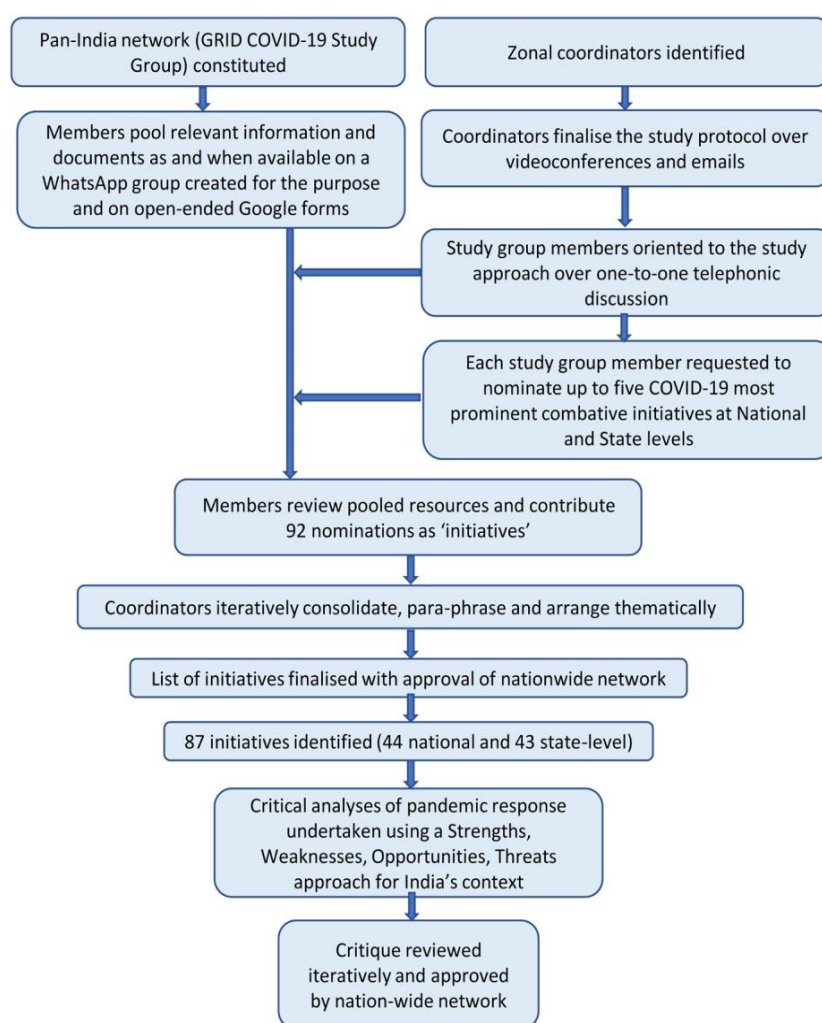


Figure 1 Study flow diagram. GRID, Generating Research Insights for Development.

and a pharmacoepidemiologist (n=1) in academic research organisations. The members were identified based on their engagement in COVID-19 pandemic containment in various capacities (as programme advisors, implementers, members of rapid response teams, researchers) in respective states/UTs and at the national level. The group kept track of COVID-19 developments in respective and neighbouring states and UTs.

Data sources

The group members pooled government communications (eg, public orders, circulars, advisories, guidelines, press releases, updates on official websites), guidance documents from stakeholder constituencies (eg, professional associations, local authorities), and excerpts from leading national and local newspapers (on open-ended Google Forms), social media resources ('MyGov Corona Newsdesk' on the Telegram app) and relevant reports by sharing them to a common group created on WhatsApp (a popular social media app used on mobile devices).

For data on cases (number of active cases, recovered/discharged, deceased and migrated, at the national and state level), we archived information from the Ministry of Health and Family Welfare (MOHFW; mohfw.gov.in) every day between 22:00 and 23:59 India standard time to capture updated statistics.

Quality check and archiving

A group of nine coordinators provided oversight. Two coordinators (ArM and SB) curated the repository by removing duplicate documents and verifying authenticity through triangulation from multiple sources, including government documents and websites. Data were archived chronologically according to date and with labels for easy retrieval.

Synthesis and analysis

We designed a timeline of key events related to the pandemic in India by sequencing major government circulars and interventions. Between 21 and 26 April, the group members reviewed the repository of resources



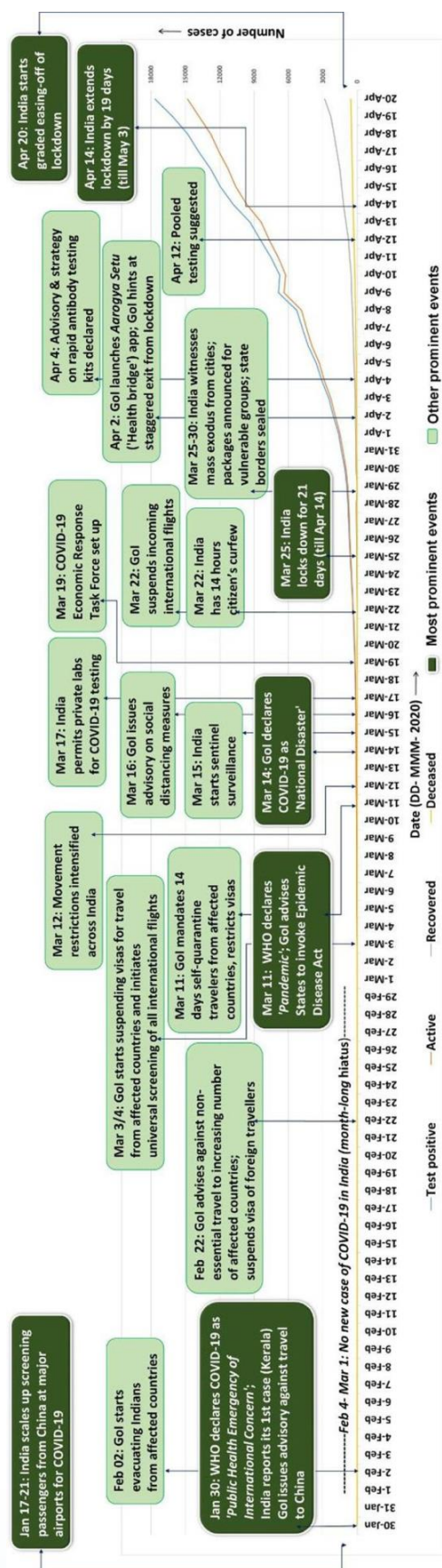


Figure 2 Timeline of major events in India in response to the COVID-19 pandemic. WHO, World Health Organization; GoI, Government of India.

pooled and submitted 92 nominations for the most prominent initiatives by GoI and respective states/UTs in response to the pandemic during the study period. The members provided the source reference (as available) for the nominations they made. We did not reject any nomination; the coordinators validated each of these by reviewing the reference provided, searching for additional information on the internet and contacting the contributing member for clarification, if needed. Two coordinators (ArM and SB) carefully examined each nomination for its content, free-listed the phrases, and moved similar phrases together through discussion and mutual agreement. If the same initiative had been nominated multiple times, it was clubbed together. The two coordinators placed the nominations under relevant themes according to the WHO 2018 updated checklist for pandemic influenza risk and impact management.⁷ They paraphrased the nominations for clarity and brevity in track changes mode to trace the edits. The coordinators (MB, PC, PK, BR, SS, AS, MKS) independently reviewed the paraphrasing and theme assignment and made edit suggestions as and where necessary. Subsequently, over sessions of video meetings, all the coordinators resolved the suggestions through discussion, review of references and consensus. The list was circulated back to the study group, and suggestions were addressed by reiterating the process before finalising for approval. Finally, 87 initiatives were identified, of which 44 were at the national and 43 at the state level. Critical analyses of the interventions and developments regarding combat of the pandemic in the initial months were done using a SWOT (strengths, weaknesses, opportunities and threats) framework through multiple rounds of feedback and editing to build consensus using the process described above. Figure 1 shows the flow diagram of the study.

INDIA'S INITIAL RESPONSE

Figure 2 presents a timeline of events, and box 1 provides a list of initiatives undertaken in the initial 3 months by the union, and states and UTs to combat the pandemic.

Preparing for an emergency

India reported the first three cases between 30 January and 2 February—all returnees from Hubei Province, China. After a hiatus through February, cases started increasing from early March. Starting mid-January (17–21 January) through mid-March, India issued advisories against non-essential international travel and suspended pre-existing visas in a graded manner at its ports of entry: air, sea and land.⁸ By mid-March, states/UTs had started prohibiting mass gatherings and levying curfew in selected areas. The public were advised to observe social distancing, hand hygiene and cough etiquettes, and to stay at home. On 22 March, GoI called for a voluntary citizens' curfew. The country went under a 21-day complete lockdown on 25 March (with just about 3.5 hours' notice on 24 March).⁹ The lockdown was extended thereafter.

Box 1 List of some of the prominent initiatives/interventions in India in response to the COVID-19 pandemic (based on WHO 2018 checklist for pandemic influenza risk and impact management)⁷

1. Preparing for an emergency.
 - 1.1. Planning coordination and resources.
 - ▶ Gol constituted 11 empowered groups and a coordination group for pandemic response.
 - ▶ States formed multidisciplinary taskforces and advisory panels.*
 - ▶ Gol solicited public and private donations for PM's National Relief Fund.
 - ▶ Gol launched the PM CARES Fund—individuals, PSUs and corporates contributed funds.
 - ▶ India proposed the creation of SAARC COVID-19 Emergency Fund to neighbouring nations.
 - 1.2. Legal and policy issues.
 - ▶ Epidemic Diseases Act, 1987 invoked—international travel suspended; states gained increased administrative power, started locking down before declaration of a nationwide lockdown.*
 - ▶ Disaster Management Act, 2005 invoked—Gol declared the pandemic as a 'national disaster', increased fund access to states and UTs; nationwide lockdown implemented from 25 March.
 - ▶ Section 144 of Criminal Procedure Code, 1973 activated prohibiting public assembly of ≥4 people.*
 - ▶ States drafted respective COVID-19 pandemic regulations.*
 - 1.3. Ethical issues.
 - ▶ ICMR released the national guidelines for ethics committees reviewing biomedical and health research during COVID-19 pandemic by second fortnight of April 2020.
 - 1.4. Risk communication and community engagement.
 - ▶ Religious leaders, celebrities and social influencers engaged in social mobilisation.
 - ▶ Caller tunes set in regional languages on prevention of SARS-CoV-2 and stigma.
 - ▶ MOHFW, states released information materials and daily updates on COVID-19 situation.
 - ▶ MOHFW created a central repository of SOPs, guidelines and resources developed by it.
 - ▶ MOHFW and state representatives conducted regular periodic press briefings; Press Information Bureau, Gol made media releases actively.
 - 1.5. Points of entry.
 - ▶ *Airports*: travel advisories issued against non-essential travel to high-risk countries (17 January); screening of passengers coming from high-risk countries scaled up (17 January); pre-existing visas suspended; universal screening initiated (4 March); mandatory 14-day quarantine on arrival (11 March); Indian citizens evacuated from affected countries.
 - ▶ *Sea ports*: in sync with International Health Regulations, 2005, the Ministry of Shipping issued advisories, quarantine and entry protocols (28 January).
 - ▶ *Land checkpoints*: immigration checkpoints with neighbouring countries shut down; cross-border passenger train and bus services, and border local markets suspended; those with influenza symptoms or travelling from afflicted countries quarantined.
 - 1.6. Travel restrictions.
 - ▶ International travel advisories issued against non-essential travel from January.
 - ▶ By mid-March, most pre-existing visas suspended.
 - ▶ International and domestic commercial flights prohibited.
 - ▶ During nationwide lockdown, passenger trains suspended, mass movement restricted, and interstate and interdistrict borders* sealed.
2. Surveillance, investigations and assessment.
 - 2.1. Laboratories.
 - ▶ Testing scaled out from NIV to 51 ICMR centres, with additional 50 collection centres (16 March).
 - ▶ Private labs roped in; existing facilities upgraded.
 - ▶ Sample collection kiosks and mobile COVID-19 testing vans set up.*
 - ▶ 'Made-in-India' coronavirus testing kits released to the market (end of March).
 - 2.2. Surveillance, outbreak investigation and monitoring.
 - ▶ ICMR centres checked random samples (symptomatic but without travel history to outbreak zones) for community transmission between 15 and 29 February (20 samples in total), and then from 16 March (each of the 51 centres tested 10 samples each week).
 - ▶ ICMR estimated proportion of COVID-19 cases based on SARI and ILI sentinel surveillance.
 - ▶ IDSP network leveraged for community-based surveillance.
 - ▶ Testing criteria revised as per need for information and evolution of the pandemic.
 - ▶ Private sector engaged for sentinel surveillance.
 - ▶ Over-the-counter sales of cold and influenza medications monitored.
 - ▶ Drones used for monitoring sanitisation, public movement and surveillance.*
 - ▶ Call data records used to track COVID-19 clusters and those returning from 'super-spreader' events.*
 - ▶ Citizens under home quarantine tracked with a tool, the 'COVID-19 Alerting Tracking System'.*
 - ▶ Mobile app released for reporting SARI by private providers.*
 - ▶ Cluster containment strategies adopted to assess and counter risk.
 - ▶ Village taskforce constituted to monitor and report COVID-19 cases and enforce lockdown.*
 - ▶ Civil society organisations helped in identifying hotspots and in mitigating stigma.*
 - ▶ Contact tracing and surveillance undertaken with engagement of community medicine experts and other personnel of medical colleges.*

Continued



Box 1 Continued

2.3. Risk and severity assessment.

- ▶ Fever and influenza clinics set up at health facilities for risk assessment and triage.
- ▶ Active and passive surveillance intensified to identify geographical hotspots and suspects.
- ▶ Front-line workers conducted home visits to identify and inform individuals with comorbidities.*
- ▶ Rapid response teams constituted at national and state levels.
- ▶ Aarogya Setu mobile app launched for risk communication and tracking.¹⁵
- ▶ Released plan for graded relaxation of lockdown from 20 April using colour zoning (based on case load and case doubling rates) for surveillance and cluster containment strategies.

3. Health services and clinical management.

3.1. Health services.

- ▶ *Health service continuity*: ~US\$2 billion emergency financial package for healthcare by Gol; free-of-cost testing and treatment for COVID-19 under the national universal health insurance scheme ('PM JAY'); patients with chronic diseases given medicine refill stock for 3 months in advance;* home delivery of 1 month's antituberculosis medicines*; amendment of telemedicine practice guidelines by Gol (24 March); attacks on HCWs engaged in COVID-19 response made promptly punishable under law*; PPE given to HCWs with a guidance plan on reuse*; rationing of HCWs engaged in COVID-19 care (stand-by staff, staff rotation).*
- ▶ *Facilities*: military hospitals engaged in preparing dedicated COVID-19 facilities, including ICUs; upgrading/modifying existing public hospitals and private hospitals as COVID-19 hospitals*; converting hotels, train coaches, sports stadiums, schools and so on into isolation/quarantine centres.*
- ▶ *Personnel*: additional healthcare personnel appointed on ad-hoc basis; release of advance/increased salaries for HCWs engaged in COVID-19 response*; deployment of medical and paramedical students in screening, contact tracing and other services*; more than thirty thousand doctors (including retired, armed forces, private doctors) volunteered in response to Gol request; volunteers deputed in service delivery to elderly, differently abled, children and transgenders*; teams engaged in community activities provided with non-contact thermal screeners, masks and gloves*; accident insurance for HCWs and front-line workers involved in COVID-19 response.*
- ▶ *Essential medicines, supplies and medical devices*: India's car makers helped to produce low-cost ventilators, masks and protective equipment; Gol with state government increased production and procurement of PPE, N95 masks and ventilators; Ministry of Textiles, MSMEs and workers' (eg, weavers) association increased production of masks; price of masks (two-ply/three-ply surgical masks, N95) and hand sanitisers capped by Essential Commodities Act, 1955; early delivery of medicines and medical equipment was incentivised*; military transport fleet engaged in logistics support; civil society organisations helped in delivery of public healthcare/hygiene services.*
- ▶ *Managing mortality*: MOHFW released guidelines on dead body management. Guidelines issued for relatives and crematoria staff involved in final rites.*

3.2. Clinical management.

- ▶ *Treatment and patient management*: stock appraisal of drugs, PPE, critical care infrastructure and demand forecasting*; SOPs by apex medical centres and disseminated (through webinars and website) on various aspects of patient management (triage, testing, admission, discharge and so on); hospitals conducted mock drills for emergency response for handling COVID-19 cases*; hydroxychloroquine endorsed for COVID-19 prophylaxis and treatment and declared as Schedule H1 drug, thus restricting its over-the-counter sale; influenza desk made mandatory at all health facilities*; online trainings offered to increase clinical management capacity among personnel.
- ▶ *Infection prevention and control*: administrative procedures eased for procuring PPE, masks and sanitisers; work distribution and PPE matched to work profile*; SOPs prepared for hospital infection prevention and control—institutions adapt/prepare SOPs as per local needs; crowd management in hospitals to minimise mixing of those with and without COVID-19 risk profile.

4. Preventing illness in the community.

4.1. Non-pharmaceutical countermeasures.

- ▶ *Personal interventions*: IEC initiatives for spreading awareness on social distancing, hand hygiene, cough etiquettes, movement restriction and stigma mitigation; incentive for self-registration and home quarantine for those returning from international travel; time-stamped route maps of each patient with COVID-19 released to the public (for general awareness)*; videos hosted on MOHFW website on making of masks at home, appropriate method for donning and removing them, and on hand hygiene; launch of self-assessment interactive apps for COVID-19*; governments posted guidance on preventive measures (dos and don'ts) on official web portals and in print and social media for wider dissemination.
- ▶ *Community interventions*: shutting down public places, for example, offices, schools, malls and so on; advisories for work-from-home and shelter-in-place; nationwide lockdown (from 25 March); release of prisoners to decongest jails*; waiving off school examinations*; wearing masks made mandatory during outings*; floor marking for social distancing in queues; hand sanitisers and thermal scanners at shop, residential society and office entrances.

5. Maintaining essential services and recovery.

5.1. Essential service continuity.

- ▶ Gol recommended states and UTs to use the State Disaster Response Fund for providing food and shelter to migrant workers during the lockdown period.
- ▶ Shrines volunteered to offer cooked meals and share costs incurred by government for surge.*
- ▶ RBI (India's central regulatory bank) took initiatives to expand liquidity.
- ▶ Gol announced US\$22.6 billion relief package for poor, rural and migrant population (Prime Minister's Poor Welfare Scheme; PM GKY).
- ▶ Increased share and subsidies on rations distributed through the public distribution system.
- ▶ Disbursement of advance/increased pensions for retirees, differently abled, widows and elderly.*
- ▶ Subsistence amounts given to construction workers.*

Continued



Box 1 Continued

- ▶ Doorstep delivery of daily essentials (eg, groceries, vegetables, medicines) during lockdown.*
- ▶ Movement restriction waivers provided for limited hours of the day to buy essentials.*
- ▶ Internet data purchase allowance for students to continue online classes.*
- ▶ Vigilance tightened against price inflation and hoarding/black marketing of general commodities.
- ▶ Mobile automated teller machines parked near residential apartments.*

5.2. Recovery.

- ▶ Helplines set up and online counselling sessions organised for mental health conditions.
- ▶ Relief camps and helpline numbers for stranded migrants with help from civil society organisations.
- ▶ RBI advises banks to offer 3-month moratorium on loan instalment payments by individuals.

6. Research and development.

- ▶ Indian firms initiate work on 'vaccine candidates', some along with international collaborations.
- ▶ Request for proposals on COVID-19-related research from major research councils and institutions.
- ▶ Major research labs engaged in diagnosis, vaccine development and disease prediction modelling.
- ▶ Biotechnology/bioengineering labs suggested low-cost ventilators and equipment for surge.
- ▶ Leading scientific journals in India worked towards coming up with special issues on COVID-19.
- ▶ Approval and market release of first Made-in-India COVID-19 testing kit (25 March).
- ▶ India joined WHO Solidarity Trial to develop therapy for COVID-19 (27 March).
- ▶ Private hospitals permitted to initiate trials with convalescent plasma therapy (19 April).
- ▶ ICMR constituted thematic taskforces for exploring research avenues.

*Initiative undertaken by some states/UTs.

Gol, Government of India; HCWs, healthcare workers; ICMR, Indian Council of Medical Research; ICU, intensive care unit; IDSP, Integrated Disease Surveillance Programme; IEC, Information, education and communication; ILI, Influenza-like illness; MOHFW, Ministry of Health and Family Welfare; MSMEs, micro small and medium enterprises; NIV, National Institute of Virology, Pune; PM, Prime Minister; PM CARES, Prime Minister Citizen Assistance and Relief in Emergency Situations; PM GKY, Pradhan Mantri Gareeb Kalyan Yojana; PM JAY, Pradhan Mantri Jan Arogya Yojana; PPE, personal protective equipment; PSUs, public sector undertakings; RBI, Reserve Bank of India; SAARC, South Asian Association for Regional Cooperation; SARI, severe acute respiratory infections; SOPs, standard operating procedures; UT, union territory.

Surveillance, investigation and assessment

Community-based surveillance activities were scaled up across India by end of March. The number of testing and collection centres was increased, testing criteria were extended, and private laboratories were engaged. On 4 April, free-of-cost testing and treatment for COVID-19 was mandated under the national universal health insurance scheme (Pradhan Mantri Jan Arogya Yojana), further expanding testing outreach.¹⁰ Geographical areas with higher number of cases were labelled as hotspots, and aggressive cluster containment strategies were adopted. Areas were earmarked as red (hotspots), yellow and green zones in descending order of case load; while stringent restrictions continued in the red zones, others were conditionally eased from 20 April.¹¹ Some states extended the lockdown without relaxation.

Health services and clinical management

The GoI and state governments scaled up provisions for institutional quarantine and isolation centres and COVID-19 hospitals (beds with oxygen and critical care services). Ventilators and personal protection equipment were consigned from vendors in the country and abroad. Training of personnel in the care of COVID-19 suspects and patients was undertaken aggressively. A series of guidelines and standard operating procedures were released by the MOHFW, GoI and the country's apex medical institutions (eg, All India Institute of Medical Sciences, New Delhi) and disseminated as webinars and video modules.^{12 13} Private providers and facilities were

identified and mobilised for institutional surge preparedness. Volunteering was solicited from healthcare professionals. Telemedicine guidelines were launched on 25 March to facilitate access to medical consultations.¹⁴ The Aarogya Setu (Health Bridge) app was launched on 2 April and made mandatory in offices and public places to enable dissemination of advisories, best practices and tracking.¹⁵

Preventing illness in the community

Non-pharmaceutical interventions were targeted at the individual and the community. These were mainly through public health communication and implementation of social distancing, movement restriction and wearing of mask in public places. The lockdown limited people's exposure to the virus.

Maintaining essential services and efforts for recovery from the pandemic

Consultations between the union and states prior to and during the lockdown were undertaken for stringent implementation of restrictions while minimising disruption of essential goods and services. The Ministry of Home Affairs, GoI issued guidelines on 24 and 25 March specifying the services that were exempt from the lockdown restrictions.⁹ In addition to health and police services, the list included regulated financial markets, and staff engaged in petroleum products, supply chain, cargo, customs, mining, forest, and social welfare department, and others.⁹ Interventions to mitigate hardship



Box 2 Perceived strengths, weaknesses, opportunities and threats in the Indian context during the initial months of combating the COVID-19 pandemic (definitions adapted from WHO documents)^{26 27}

Strengths: factors intrinsic to India that position it towards a strong performance against the COVID-19 pandemic.

- ▶ **Governance:** semifederal, democratic and decentralised governance; consultative decision-making processes (eg, taskforces); multiple channels of public communication; strong engagement with development partners.
- ▶ **Existing legislative mechanisms** (eg, the Epidemic Disease Act, 1897; the Indian Ports Act, 1908; the Drugs and Cosmetics Act, 1940; the Essential Services Maintenance Act, 1968; the Disaster Management Act, 2005): if invoked, these allow special administrative powers to the government.
- ▶ **Programmatic outreach:** allows targeted delivery of entitlements to the vulnerable (eg, the public distribution system for food security, zero-balance and minimal documentation bank accounts for direct cash transfer, social security schemes, commitment to universal health coverage and so on).

Weaknesses: factors intrinsic to India that impede performance and need change/investment.

- ▶ **Fragile and chronically underfunded health system:** poor infrastructure and tertiary care capacity; inconsistent supplies; data challenges (eg, quality, timeliness, adequacy); limited engagement of private sector; absent/inadequate health insurance cover.
- ▶ **'Missing millions'** (the homeless migrants, illegal immigrants, people in humanitarian crises, disaster-ravaged groups): although not adequately assessed, the numbers are substantial.
- ▶ **Limited institutional preparedness for managing pandemics:** India has managed recent infectious disease outbreaks, but protocols (eg, for public health emergency management protocols, public-private collaboration, research engagements) are in evolution.

Opportunities: prospects in the current COVID-19 context that could be exploited for effective combat of COVID-19.

- ▶ **A better understanding of SARS-CoV-2 and COVID-19:** scientific evidence on disease management, prevention and containment is increasingly available from January 2020.
- ▶ **Favourable age pyramid:** only ~8.5% of India are over 60 years of age, majority are under 30. A young population may have a lower risk of mortality from COVID-19 and help in faster economic recovery.
- ▶ **Indigenous capacity:** India's large pharma, research and development, and the information technology industry can contribute to global efforts (vaccine development, delivery, diplomacy).
- ▶ **Wide reach of telecommunications and social media:** makes risk communication faster and with outreach for public engagement.
- ▶ **Availability of deployable health human resources:** for example, community medicine and public health professionals for technical support, physicians from the Indian system of medicine for primary care coverage, huge network of community-based workers (especially in states with weaker health infrastructure) for outreach, and private laboratories, hospitals and organisations for service scale-out; expansion of tertiary healthcare institutions in recent times.

Threats: elements in broader environment that could endanger/inhibit progress in the combat of COVID-19.

- ▶ **Huge population size and LMIC context:** India's vast population, poor living and health access conditions, and heterogeneous epidemiological profile increase the risk of spike in COVID-19 cases and of overwhelming system capacity.
- ▶ **Economic stagnation:** growth of India's economy has been slower, of late—could limit fiscal space for aggressive countermeasures against the pandemic.
- ▶ **Limited surge capacity** for testing and institutional care (eg, critical care experts, infrastructure, access, space for isolation); inadequate supply of PPE.
- ▶ **Implementing prolonged restriction will impede** essential services, lead to loss of livelihoods (job profiles inconducive to working from home; farmers must protect the spring harvest) and cause adverse economic impact. The strategy for exit from lockdown is complex.
- ▶ **Sociobehavioural complexities:** risk of some people flouting preventive directives, stigmatisation, misinformation and rumour mongering, violence against healthcare workers and police, hoarding of essentials (PPE, medicines, sanitisers, groceries) and upsurge in psychosocial health issues (eg, depression, alcohol withdrawal, domestic violence).

LMIC, low-income and middle-income country; PPE, personal protective equipment.

among the poor and vulnerable were introduced by the GoI and state governments.¹⁶

INSIGHTS

Understanding the Indian context for pandemic response

India presents a mix of inherent strengths and weaknesses in combating the pandemic (box 2). Thereupon, the COVID-19 pandemic uncovers some perceivable opportunities and threats. An appreciation of these facets will help the reader understand the context and its influence on India's response.

Combating risk of importation of the virus

'Nobody can be fully prepared to a pandemic'.¹ India also could have benefited from even further pandemic response planning and preparedness. The country had its first case

on 30 January. Between January and early March, India focused almost exclusively on minimising the risk of importation. In hindsight, it seems that aggressive surge preparedness could also have been undertaken in the meanwhile (especially in February) given that the virus had originated from an immediate neighbouring country and that WHO had already declared it as a 'Public Health Emergency of International Concern' on 30 January.¹⁷ The graded border control approach using selective screening and travel restrictions in January to February, leading to universal screening, visa suspensions and mandatory quarantine in March, could not adequately counter the risk of importation. Moreover, relying on thermal scanning was not infallible as several cases were afebrile/asymptomatic. Cases started increasing rapidly in early March. Containment and surge efforts followed subsequently (around mid-March).

Box 3A Insights from India's initial response (17 January–20 April) to combat the COVID-19 pandemic: strengths in India's response

- ▶ *Conspicuous political commitment*: union and state governments and political parties mostly came together supporting one another during the crisis.
- ▶ *Visa restrictions*: India experienced limited importation from countries for which travel advisories were restrictive. India suspended most of its existing visas from 15 March.²⁸
- ▶ *Initial engagements*: stakeholder constituencies (governments, private sector (profit, non-profit), civil society, communities and individuals) were responsive to the COVID-19 scare despite the delay during the earliest months (January–February) and instituted preventive measures in support of one another.
- ▶ *Legislative frameworks enabled administrative leadership*: invocation of the Epidemic Diseases Act, 1897 (on 11 March) and the Disaster Management Act, 2005 (on 14 March) allowed further administrative power and fund access to GoI and state governments. Support for nationwide lockdown shows collective leadership from stakeholder constituencies.
- ▶ *Community-based surveillance*: in the absence of adequate testing resources, India scaled up its house-to-house mass surveillance and sensitisation efforts through syndromic approaches, leveraging existing integrated surveillance systems and its large network of front-line workers.
- ▶ *Programme outreach helped in targeting the entitlements*: pre-existing social welfare programmes, internet banking services and Jan Dhan bank accounts (zero-balance bank accounts for the poor) facilitated disbursement of entitlements to targeted beneficiaries with speed and minimal pilferage.²³
- ▶ *ICMR supported GoI* with setting up the network of labs for testing and serosurveillance, and by setting up thematic taskforces (to plan, implement and monitor guidelines). It also advised on treatment protocols based on upcoming local evidence.
- ▶ *States have the potential to innovate; the chance of success increases with prior experience in managing disasters and outbreaks*: while GoI facilitated the combat of the pandemic, states rapidly innovated, co-learned and co-adapted various innovations with local effectiveness. Examples include the following:
 - Aggressive community containment after an outbreak (Bhilwara model, Rajasthan).
 - Convergence in an urban setting (Vishakhapatnam in Andhra Pradesh).
 - Community-based surveillance with high coverage despite difficult mountainous terrain (the Himachal Pradesh experience of engaging front-line health workers, and the Jammu and Kashmir experience of leveraging technology).
 - The ethnic tribal communities in the North-East demonstrated how community vigilance and local systems of governance could coexist with formal epidemiological surveillance.
 - Odisha, one of the most resource-constrained and disaster-ravaged states in India, emerged as a 'first mover' in pandemic preparedness with its adeptness at managing natural disasters.
 - Kerala was able to 'bend the curve' (number recovered > number tested positive each day; Kerala model) through system-wide effort across a strong health system; the state has successfully combated the Nipah virus outbreak and a severe flood in the recent past.
- ▶ *Engagement of district administration with local medical colleges for patient care and surveillance guidance (in some districts)*: this helped in techno-administrative convergence with contextualisation and in the mobilisation of human resources.

ICMR, Indian Council of Medical Research; GoI, Government of India.

Meanwhile, COVID-19 was declared a pandemic by WHO.¹⁷ Worsening situations internationally, such as in Italy, UK and Iran, added to India's anxiety.

Since mid-March, India has acted swiftly to stem the rising cases of COVID-19. Existing legislative provisions (prominently the Epidemic Diseases Act, 1897 and the Disaster Management Act, 2005) and semifederal governance structure provided due leverage. India thus mobilised resources and provided administrative flexibility to state governments to utilize the disaster funds, enabling contextual action. As a consequence, states could implement mass movement restrictions, access funds, mandate citizens into institutional quarantine and isolation, and regulate industries (implement work-from-home advisories). Alongside, GoI suspended visas and declared a nationwide lockdown.

Experience with 'pre-emptive' nationwide lockdown

The first phase of the lockdown (25 March–14 April) in India was unlike any other country in scale, timing and stringency. The lockdown gave India time for surge preparedness especially in testing capacity and institutional healthcare provisions.¹⁸ People also accepted and supported the stringent restrictions (pandemic

response may evoke strong support or protests in democratic settings). Prevention, containment, impact mitigation and recovery efforts gradually became concurrent. Administrative decision-making capacity was increasingly strengthened (up to subdistrict levels). To compensate for insufficient testing capacity, the country engaged its massive network of community-based workers and undertook aggressive community-based surveillance, contact tracing and cluster containment strategies.¹⁹ Official channels of communication to stakeholders gradually became structured and consistent, allaying spread of misinformation. Meanwhile, aggressive media coverage increased public awareness.

In the absence of robust epidemiological data and amidst predictions of rapid increase in COVID-19 cases, India locked down 'pre-emptively' and 'nation-wide' at extremely short notice. The lockdown slowed down the spread of infection: the case doubling time (7-day moving average) on 25 March was 3.4 days and on 19 April was 6.2 days; however, the number of cases kept increasing.²⁰ On 24 March, when India declared lockdown, it had 564 cases and 10 deaths; on 20 April, when graded relaxation



Box 3B Insights from India's initial response (17 January–20 April) to combat the COVID-19 pandemic: facets for further strengthening

Aspects specific to the COVID-19 pandemic.

- ▶ **Countering risk of importation:** India's graded checks at airports, sea ports and land borders (January–March 2020) varied in stringency, criteria and timing. Universal screening and mandatory quarantine at airport arrivals were initiated late (in March). Just 19% of air passengers arriving between 17 January and 23 March could be screened.²⁹ Some passengers dodged advisories (self-declaration of symptoms, mandatory self-quarantine).
- ▶ **Surge preparedness:** India had limited surge preparedness in February. Limited testing capacity (number and coverage), restrictive testing criteria and cautious engagement with private sector impeded initial 'test-isolate-treat' efforts. Frequent modification of criteria for testing, quarantine and isolation required repeated unlearning and relearning. States were able to ramp up quarantine and isolation facilities but were relatively under-resourced for beds with oxygen and critical care support.
- ▶ **Leveraging IT:** despite its huge IT capacity and potential to generate indigenous big data, India could not adequately leverage technology for surveillance or data analytics. The Aarogya Setu app (for tracking and public messaging) was criticised for gaps in data security.¹⁵
- ▶ **Data integration, reconciliation and access:** while the Indian Council of Medical Research and the Ministry of Health and Family Welfare released data summaries on a daily basis from late March, the two initially had mismatch and needed reconciliation. The National Centre for Disease Control could not publish its weekly outbreak reports (from routine influenza syndromic surveillance) since February 2020.³⁰ Validated multi-jurisdictional and sectoral information was unavailable and impeded research.
- ▶ **Preventing potential super-spreader events:** during the pandemic, outbreaks were linked to mass congregations that had been organised in violation of administrative restrictions. Contact tracing and isolation-quarantine activities had to be surged up impromptu and sustained thereafter but not all attendees could be traced back to the community.
- ▶ **Quality of quarantine and isolation facilities:** India's quarantine facilities were criticised for lack of civic amenities and hygiene and for overcrowding.³¹ Some people resisted/escaped institutional quarantine-isolation; family members were anxious.³²
- ▶ **Lockdown:** The 'pre-emptive' nationwide lockdown implicated fiscal 'sacrifice' and collateral impact (impaired routine health services, loss of livelihoods, massive reverse migration, mental health challenges). 'Cash injections' by the government to mitigate hardship were inevitable yet inadequate.
- ▶ **Managing the 'infodemic':** information overload (both correct and wrong), media attention, wide access to social media and deep penetration of tele-networks enabled fast dissemination. Alongside increasing awareness, public anxiety, stigmatisation and rumour mongering were also seen.

Aspects that go beyond the COVID-19 pandemic.

- ▶ **Building on experience:** India's initial response to COVID-19 reiterates gaps it witnessed during the 2009 H1N1 (swine influenza) pandemic, that is, screening limited to major airports, urban-centric approach, limited diagnostic centres, lack of intensive care capacity and access.³³ India needs proactive preparedness given recent outbreaks (eg, Nipah and Zika virus diseases, acute encephalitis syndrome). India's Influenza Pandemic Preparedness Plan is of 2009; the December 2019 version is awaited in the public domain.
- ▶ **Decision-making for public health action:** committees constituted initially for the pandemic were led by experts beyond epidemiology and public health disciplines. Decisions were inconsistently based on evidence. Having an exclusive public health cadre could have made processes more efficient.
- ▶ **Gaps in the health sector cannot be corrected rapidly:** India's health system has traditionally been underfunded year-on-year (allocation in 2019–2020 annual union budget ~1.4% of gross domestic product).

IT, information technology.

was allowed, there were 17 656 cases and 559 deaths.¹² By 20 April, cases had been identified in 31 of 36 states and UTs and in 402 of 718 districts.²¹ Twenty districts accounted for over half the cases and two-thirds deaths—these were among the most urbanised, affluent and industrialised districts in the country.²¹ States and UTs showed variegated epidemiological curves (online supplemental figure 1A and B).

Contextual opportunities, for example, a relatively young population, accruing global understanding of the virus and the disease, and capacity for generating indigenous research evidence, remained underutilised as India went into a very stringent lockdown. The lockdown uncovered vulnerabilities and triggered cascading effects across sectors and industries.²² The economy which was already ailing got further disrupted. The impact was highest at the 'base of the pyramid' (lowest socioeconomic strata) of the Indian society. People lost jobs and livelihood; reports of hardship, stress, anxiety and domestic violence came up. GoI and state governments rolled out initiatives

to mitigate hardship among the vulnerable using pre-existing institutional mechanisms and programmatic outreach (eg, validated bank accounts for direct benefit transfer, network of public distribution system for food security, and others).²³ They were assured of food and shelter. Nevertheless, the initiatives were inadequate to check reverse migration. Millions of workers migrated back home in the absence of any source of continued livelihood. The 'reverse migration' was frequently on foot and in overcrowded conveyances, thus threatening to push the virus deeper into rural India where pandemic preparedness was further weak.²⁴ Given its ramifications and potentially long-term impact (including that related to stigma), strategising exit from the lockdown and subsequent recovery of communities from the pandemic was challenging.

Critical analyses for practice and preparedness

Given the dynamicity of India's response, our current account may be non-exhaustive, but captures information



from across the country. Some of the approaches undertaken by India seemed to have worked out in favour, while some needed better planning. We have summarised the insights from India's response to the pandemic in the initial months in [box 3A and B](#).

CONCLUSION

Within the initial few months, India could mobilise collective leadership and action, and secure public cooperation to undertake stringent combative measures against the pandemic. Apart from isolated incidents, there was minimal public resistance to the stringent nationwide movement restriction norms. Experience from India suggests that the LMIC context could be volatile, ambiguous and uncertain, and hence engaging with the community and other stakeholders is a critical facilitator. It also highlights that LMICs have complex socioepidemiological ecosystems with refractory vulnerabilities that could compromise the sustainability and impact of stringent measures. Combative response to pandemics in such settings is likely to be improvisatory and broad-based (less precise) in the absence of a structured pandemic response plan. Stringent measures must be carefully weighed against alternatives and undertaken with concurrent mitigation and recovery initiatives. A contextualised and updated pandemic response plan with dynamic decision support systems could help in ensuring timely and structured response to national and international epidemiological triggers (scarce resources need efficient planning). Unfortunately, most LMICs either do not have a national plan for pandemic preparedness and risk management or have one that has not been updated recently.²⁵ COVID-19 pandemic combat strategies and experience vary worldwide. India is relatively better resourced as compared with other LMICs in several aspects, and hence some of the Indian experience may not be readily extrapolatable to other LMICs. Nevertheless, India shares several challenges and vulnerabilities typical of LMICs (eg, high population, resource constraints, socioeconomic milieu). Going forward, countries and especially LMICs (including India) will find the Indian experience variously relatable for planning response against the current and future pandemics, despite resource inconsistencies, while also appreciating that each country has its unique contextual strengths and weaknesses to account for and leverage.

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Cause of Death Certification in COVID-19 Deaths

Chandrakanth Hungund Veeranna¹, Smitha Rani²

ABSTRACT

Introduction: Appropriate cause of death reporting is vital in the pandemic circumstance for effective planning of the control measures. Accurate reporting and registration of the reason for death are crucial in planning of health programs in turn contributing for the national development.

Background: All births and deaths occurring across India should be mandatorily registered per the Registration of Births and Deaths Act passed in the year 1969. The act also requires the issuance of cause of death certificate by the doctor attending the departed during his last illness. Data obtained from the cause of death certificate provides cause-specific mortality profile, which is required to analyze the health trends of the population.

Review results: This article discusses the available guidelines on the appropriate documentation of cause of death in the confirmed or suspected coronavirus disease-2019 (COVID-19) infection resulting into death.

Conclusion: Proper certification of the cause of death leads to better epidemic surveillance. Scrutiny of the clinical sequences from the cause of death certificate is useful to prioritize the allocation of resources for critical care management and to augment our knowledge about underlying causes resulting in mortality from COVID-19.

Clinical significance: Dissemination of available guidelines on proper documentation of the cause of death in confirmed/suspected COVID-19 cases will reduce the errors in cause of death reporting.

Keywords: Cause of death, COVID-19, Medical certification of cause of death, Mortality statistics.

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BACKGROUND

The civil registration system in India aids in recording of births and deaths under a legislative policy, dating back to the British era. Central Births, Deaths and Marriages Registration Act was passed in the year 1886 which offered voluntary registration. The Registration of Births and Deaths (RBD) Act enforced in 1969 overcame the then prevalent varied provisions of law pertaining to births and deaths registration in India. It integrated the system of registration across the country making the registration process mandatory.¹ As per the RBD Act, information on the births and deaths occurring in a health facility and such other like institutions should be provided by the doctor in charge or a person authorized on his behalf.²

The act also requires that the medical practitioner has to issue a cause of death certificate if the deceased is attended by him during his terminal illness. The certificate should be issued without charging any fee. The certificate issued should be in the prescribed format, i.e., form no. 4 for institutional deaths and form 4 A for non-institutional deaths. The certificate should be sent to the registrar along with form no. 2 which is a death reporting form.³

The medical certification of cause of death (MCCD) scheme falls under the legal ambit of RBD Act and is implemented in all the medical institutions in the country, including government, private, and non-profit-making healthcare facilities.⁴

Data obtained from MCCD provides cause-specific mortality profile, which is required to analyze the health trends of the population. Precise reporting of causes of death has a key role in planning of health programs and national development. Appropriate cause of death reporting is exceptionally relevant in the situation of a pandemic for effective planning of the control measures.

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REVIEW RESULTS

Wuhan Municipal Health Commission, China, at Wuhan, Hubei province, first reported corona virus disease (COVID-19) in late 2019. The World Health Organization (WHO) declared the disease outbreak as a public health emergency of international concern on January 30, 2020. The disease was declared as a global pandemic on March 11, 2020.⁵

During such circumstances, mortality surveillance is a vital public health tool to evaluate the impact of the disease. Correct death certification is necessary to recognize the disease burden and its progression. Death certificate data can inform the public and policymakers on the progress of the COVID-19 pandemic and provide valuable information about who is dying, where they are from, and what were their associated medical conditions.⁶

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When COVID-19 is determined to be the cause for death, it must be stated on the death certificate to measure the effects of the pandemic accurately and aptly undertake public health response. Monitoring the emergence of COVID-19 and guiding public health response requires precise and timely reporting of death.⁷ Hence, the objective of this article is to discuss the available guidelines on the appropriate cause of death certification in confirmed or suspected COVID-19 infection leading to death. These guidelines are based on the guidance notified by Department of Health Research, Ministry of Health and Family Welfare, Govt. of India,⁸ which is in concurrence with international guidelines for certification and classification (coding) of COVID-19 as cause of death formulated by WHO.⁹

Medical Certification of Cause of Death Format

International statistical classification of diseases and related health problems (ICD) manual published by WHO contains a format for cause of death certification. It necessitates the certifying doctors to document the pathophysiological sequence of clinical conditions leading to death, their time interval, and other contributory causes.¹⁰

The format of the certificate prescribed in India (Annexure 1) conforms to the standard recommended by the WHO. Cause of death fragment in the certificate is divided into:

- Part I: It comprises the immediate cause of death which is entered in line (a) and antecedent causes needs to be filled in line (b) and (c)
- Part II: Other significant conditions contributing to death but not related to the diseases or conditions causing it are entered in part II.

Death often is an outcome of combined effect of two or more independent or related conditions. One condition may lead to another, which in turn can lead to a third condition. Wherever there is a sequence, the underlying cause of death is coded with ICD-10 codes and is considered for statistical purposes. The disease or injury that starts the train of morbid events and leads directly to death or the situations of the accident or violence which produces the fatal injury is labeled as underlying cause of death. The morbid conditions or injuries resulting from the underlying cause of death are called as antecedent and immediate cause.¹¹

Information under part I pertains to the underlying cause of death, antecedent cause of death, and immediate cause of death, written from below upward, clearly portraying the sequence of events ending with immediate cause written in line (a). The sequence gives the order of association between the events leading to death both with respect to time, etiological or pathological relationship. Properly recording the sequence helps to adopt suitable strategies to cut the chain of events at its most susceptible point and thus prevent death. The original format, approved by WHO, had only (a), (b) and (c) under part I. As per the recommendations of Forty-Third World Health Assembly 1990, an extra line (d) has been added below (c).¹²

The form must be filled by the attending doctor having first-hand knowledge regarding the clinical history. Parenthetical statements and abbreviations should not be used while reporting the cause of death. Single cause must be documented on each line of part I. The underlying cause of death has to be entered on the last line used in the part I. Immediate cause of death stated on line (a) can be a sole entry made in cause of death section, if that is the only condition leading to death. The immediate cause refers to the terminal disease, injury, or complication directly producing the

death. It does not refer to the mechanism of death or final event. Death mechanisms such as cardiac arrest or respiratory arrest must not be stated as the immediate cause of death, as it is a statement not clearly related to the disease process, and it just indicates to the fact of death.¹³

Cause of Death Certification in Deaths from COVID-19

Definition of Death Resulting From COVID-19

As per the guidelines issued by WHO, death due to COVID-19 is defined for surveillance purposes as, “a death resulting from a clinically compatible illness, in a probable or confirmed COVID-19 case, unless there is a clear alternative cause of death that cannot be related to COVID disease (e.g. trauma)”. There must not be a period of complete recovery from COVID-19 amid illness and death.⁹

Terminologies to be Used While Certifying the Cause of Death⁹

Since there are various types of coronaviruses, it is suggested that one should not use the term “coronavirus” instead of COVID-19. This aids in decreasing the ambiguity for the classification or coding and to screen these deaths correctly. Although COVID-19 (Corona virus disease-19) is an abbreviation, it is WHO specified and is acceptable term to be recorded as an underlying cause of death.

Completing MCCD Resulting From COVID-19⁸

COVID-19 is a viral infection, which can present as ‘influenza-like illness’ (ILI) or “Severe acute respiratory illness” (SARI). They are nonspecific to the disease itself, and hence they can be used in the sequence of the events but not an underlying cause of death.

COVID-19 is said to cause pneumonia/acute respiratory distress syndrome (ARDS)/cardiac injury/disseminated intravascular coagulation etc. which may result into death and maybe entered in line (a) or (b). COVID-19 is likely the underlying cause of death that results into ARDS or pneumonia in most of the cases of COVID-19 deaths (test positive and symptoms positive). In such scenarios, COVID-19 must be entered in the last line/lowest line of part I of MCCD form 4/4 A. Since acute respiratory failure is a mode of death, it should not be written in line a/b/c.

Patients may have other preexisting comorbid conditions, such as chronic obstructive pulmonary disease, asthma, chronic bronchitis, ischemic heart disease, cancer, and diabetes mellitus. These conditions increase the risk of developing respiratory infections and may lead to complications and severe disease in a COVID-19 positive individual. These conditions are not considered as the underlying cause of death, as they have directly not caused death due to COVID-19. A patient may have many comorbid conditions, but only those which contributed to death must be recorded in part II.

COVID-19 Case Definitions for Global Surveillance as Prescribed by WHO⁹

Confirmed case: “A confirmed case is a person with laboratory confirmation of infection with the COVID-19 virus, irrespective of clinical signs and symptoms.”

Suspected case: “A patient with acute respiratory illness (that is, fever and at least one sign or symptom of respiratory disease, for example, cough or shortness of breath) with no other etiology that fully explains the clinical presentation and a history of travel to or residence in a country, area, or territory that has reported

local transmission of COVID-19 disease during the 14 days prior to symptom onset.”

OR

- “A patient with any acute respiratory illness and who has been a contact of a confirmed or probable case of COVID-19 disease during the 14 days prior to the onset of symptoms.”

OR

- “A patient with severe acute respiratory infection (i.e., fever and at least one sign or symptom of respiratory disease, for example, cough or shortness of breath) and who requires hospitalization and who has no other etiology that fully explains the clinical presentation.”

Probable case: “A probable case is a suspected case for whom the report from laboratory testing for the COVID-19 virus is inconclusive.”

DISCUSSION

Examples of Certification

Example 1: A 40-year-old male was tested positive for COVID-19 two weeks back. He developed pneumonia 1 week later and suffered from respiratory distress for the last 3 days before his death.

For the abovementioned case scenario, the chain of events to be recorded in MCCD is given in Table 1.

Example 2: A 70-year-old female, who was a primary contact of a patient tested positive for COVID-19, presented with influenza-like illness of 4 days duration. She developed respiratory distress and died a day later. The test result of COVID-19 is not available. She has been suffering from type 2 diabetes mellitus for the past 10 years.

In the above case, conditions leading to death has to be mentioned in part I, and comorbidities to be reported in part II (Table 2).

Individuals with COVID-19 may die due to other diseases or accidents, such cases are not deaths resulting from COVID-19,

Table 1: Certification of cause of death for example 1

Cause of death		The interval between onset and death approx.
Part I		
Immediate cause	(a) Acute respiratory distress syndrome	3 days
Antecedent cause	(b) Pneumonia	7 days
	(c) COVID-19 (test positive)	14 days
Part II		

Table 2: Certification of cause of death for example 2

Cause of death		Interval between onset and death approx.
Part I		
Immediate cause	(a) Acute respiratory distress syndrome	1 day
Antecedent cause	(b) Influenza like illness	4 days
	(c) Suspected COVID-19	4 days
Part II		
	Diabetes mellitus	10 years

and they should not be certified as such. In such circumstances, if the certifier is convinced that the COVID-19 intensified the consequences of the accident, COVID-19 can be reported in part II as a contributory cause.

Manner of death in COVID-19 infection is frequently “natural,” as it is the disease that causes death. If an individual tested positive for COVID-19 commits suicide, the manner of death must be recorded as suicide / pending investigation if the medical autopsy is awaited.⁸

Most of the deaths from COVID-19 occur in a hospital setup, and in such cases, the place of death should be recorded as “Hospital.” Cases where death of the individuals occurs in their residence after being discharged from the hospital, the place of death must be noted as “House.”⁸

ICD-10 Coding of COVID-19

International classification of diseases (ICD) is the global health information standard for mortality and morbidity statistics. It is the foundation for the identification of health trends and statistics globally. It organizes data into standard groupings of diseases, allowing easy storage, retrieval, and interpretation of health information for evidence-based policy making. It also aids in sharing the health information and comparing it with the trends in other hospitals, regions, settings, and countries. The ICD-10 uses alphanumeric code with a letter in the first position and a number in the second, third, and fourth positions; the fourth character follows a decimal point. The code numbers can range from A00.0 to Z99.9. Codes U00-U49 is kept reserved for the provisional assignment of new diseases of uncertain etiology.¹⁴

ICD codes assigned for COVID-19 are:¹⁵

U07.1: COVID-19, virus identified.

U07.2: COVID-19, virus not identified.

- Clinically-epidemiologically diagnosed COVID-19
- Probable COVID-19
- Suspected COVID-19

Although both categories, U07.1 (COVID-19, virus identified) and U07.2 (COVID-19, virus not identified), are appropriate for cause of death coding, it is recognized that in most of the countries details pertaining to laboratory confirmation of the disease will not be stated on the death certificate. In the absence of this point, it is suggested for mortality purposes only to code COVID-19 provisionally to U07.1 unless it is specified as “probable” or “suspected.”

A manual credibility check is endorsed for certificates reporting COVID-19, particularly for those certificates, where COVID-19 is reported but not designated as the single underlying cause of death.⁹

CONCLUSION

Strengthening cause of death certification is required in most of the countries across the globe for better epidemic surveillance.¹⁶ Since COVID-19 death certificates have considerable influence on local and national responses toward the evaluation and management of the pandemic, additional effort is required by the certifying doctor while reporting the cause of death.

CLInICAL SIGNIFICANCE

Dissemination of available guidelines on proper documentation of the cause of death in confirmed/suspected COVID-19 cases will better equip the doctors to avoid errors in reporting.

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AnnEXURE 1

FORM NO. 4
(See Rule 7)
MEDICAL CERTIFICATION OF CAUSE OF DEATH
(Hospital in-patients. Not to be used for still births)
To be sent to Registrar along with Form No.2 (Death Report)

Name of the Hospital I hereby certify that the person whose particulars are given below died in the hospital in Ward No on at A.M./P.M.

NAME OF DECEASED				For use of Statistical Office
Sex	Age at Death			
	If 1 year or more, age in Years	If less than 1 year, age in Months	If less than one month, age in Days	If less than one day, age in Hours
1. Male				
2. Female				
CAUSE OF DEATH				Interval between on set & death approx.
<p>I</p> <p>Immediate cause (a) State the disease, injury or complication Due to (or as a consequences of) which caused death, not the mode of dying such as heart failure, asthenia, etc.</p> <p>Antecedent cause (b) Morbidity conditions, if any, giving rise to the above Cause, stating underlying conditions last Due to (or as a consequences of)</p> <p>(c)</p> <p>II</p> <p>Other significant conditions contributing to the death but not related to the disease or conditions causing it</p>				

Manner of Death

How did the injury occur ?

1. Natural 2. Accident 3. Suicide 4. Homicide
5. Pending investigation

If deceased was a female, was the death associated with pregnancy ? 1. Yes 2. No
If yes, was there a delivery ? 1. Yes 2. No

Name and signature of the Medical Attendant certifying the cause of death
Date of certification

SEE REVERSE FOR INSTRUCTIONS

(To be detached and handed over to the relative of the deceased)

Certified that Shri/Smt./Kum. S/W/D of Shri
..... R/O Was admitted to this
hospital on and expired on

Doctor
(Medical Supdt. & Name of Hospital)

