



## Review Article

## The sequel to COVID-19: the antithesis to life

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## Abstract

The pandemic of COVID-19 has afflicted every individual and has initiated a cascade of directly or indirectly involved events in precipitating mental health issues. The human species is a wanderer and hunter-gatherer by nature, and physical social distancing and nationwide lockdown have confined an individual to physical isolation. The present review article was conceived to address psychosocial and other issues and their aetiology related to the current pandemic of COVID-19. The elderly age group has most suffered the wrath of SARS-CoV-2, and social isolation as a preventive measure may further induce mental health issues. Animal model studies have demonstrated an inappropriate interacting endogenous neurotransmitter milieu of dopamine, serotonin, glutamate, and opioids, induced by social isolation that could probably lead to observable phenomena of deviant psychosocial behavior. Conflicting and manipulated information related to COVID-19 on social media has also been recognized as a global threat. Psychological stress during the current pandemic in frontline health care workers, migrant workers, children, and adolescents is also a serious concern. Mental health issues in the current situation could also be induced by being quarantined, uncertainty in business, jobs, economy, hampered academic activities, increased screen time on social media, and domestic violence incidences. The gravity of mental health issues associated with the pandemic of COVID-19 should be identified at the earliest. Mental health organization dedicated to current and future pandemics should be established along with Government policies addressing psychological issues to prevent and treat mental health issues need to be developed.

**Keywords:** Psychosocial, Mental Health, COVID-19, Social Isolation, Quarantine, Infodemic

## Background

The pandemic of COVID-19 that began from Wuhan, a city of Hubei province of China, spread like wildfire across every corner of the world with cumulative cases surpassing 23 million and what makes the situation more worrisome is the mortality due to COVID-19 that amounts to 800 906 deaths as of 23 August 2020 worldwide, threatening the very existence of mankind [1]. The current pandemic has afflicted every individual and sector directly or indirectly, and one aspect that has not been addressed appropriately till now is its psychosocial and other consequences that have begun to manifest in some or the other ways. The governments across many countries worldwide imposed lockdown to curb the community spread of COVID-19, considering its menacing fangs of infectivity.

Moreover, practices such as wearing masks, social distancing have also been extensively promoted. The human species is a wanderer and hunter-gatherer by nature, and physical social distancing and the nationwide lockdown has confined an individual to physical isolation and left no choice other than being connected virtually. The world has already witnessed mental health issues pertaining to such kinds of pandemics and their aftermaths [2,3]. The available literature on previous incidences of outbreaks indicates the occurrence of several mental health issues such as irritability, anxiety, depression, insomnia, anger, loneliness, and even suicidal tendencies [4-8]. Evaluating the community's mental health status in such pandemics needs special attention in the Indian context where social gatherings such as marriages, religious festivals, etc. are frequent and spread across the year [9]. Hence, challenges associated with the curbing of community spread of COVID-19 were consequentially increased. Research has shown that around 2/5 of the population is already subjected to anxiety and depression as a consequence of nationwide lockdowns against COVID-19 [10]. The present review article was conceived with

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the aim of addressing psychosocial and other issues and their aetiology related to the current pandemic of COVID-19. Mental health needs to be stressed during such critical times with the implementation of better government strategies and policies to deal with its psychological consequences.

The pandemic of COVID-19 has initiated a cascade of directly or indirectly involved events in precipitating mental health issues. The list of events is long that includes social isolation, overburdened health care workers, fear and stigma of COVID-19, uncertainty about the economy, fear of losing jobs and loss in business, increased screen time, especially in children and adolescents, misinformation circulating about the pandemic, increased domestic violence and other myriad inconceivable issues as of this date.

### Social isolation in elderly individuals

Social deprivation in an individual's life can have serious mental health consequences. The ongoing pandemic of COVID-19 has compelled the society to remain in social isolation, with a silver lining of being connected virtually through online platforms. Hawkey and Cacioppo (2010) had stressed the importance of the feeling of being socially connected in an individual's life, and lack of this feeling can have deleterious effects on physical and mental health [11]. The elderly age group, in particular, needs special mention, as it has been reported to be the most vulnerable group to have suffered the wrath of SARS-CoV-2 [12,13]. The current situation has drastically impaired the physical, social connectivity, an essential component of innate human needs [14]. The resulting loneliness from social isolation can lead to a greater risk of morbidity and mortality among elderly individuals [15-19]. At this age, individuals are already vulnerable to loneliness, which could be due to any illnesses, death of a spouse, or lack of friends [20]. The social distancing advisory by the government, specially targeted to protect elderly individuals from COVID-19, adds on to already existing loneliness, consequently increasing the risk of mental health issues [21].

Researchers have tried to identify the brain areas related to emotion processing and socialization, and the effects of prolonged social isolation on normal brain functioning [need further elucidation]. Various animal model studies have tried to address this question in entirety. Amygdala has been identified as a seat of social functioning in an individual [22]. Kanai et al. [23] assessed the amygdala's grey matter volume and found a correlation between physical and online social networking and the volume of the amygdala's grey matter. Prolonged social deprivation induces stress that culminates in hippocampal injury due to raised glucocorticoid levels and blood pressure [24-27]. Social isolation has also been recognized as an important risk factor for cognitive dysfunction, such as Alzheimer's disease, where this risk was doubled in lonely individuals [28]. Even an acute social isolation period could cause long-term memory dysfunction, as was evident from mice studies [29].

Various neurotransmitter system dysfunctions have also been demonstrated in experimental studies underlying social isolation in rodents [30-32]. The neurotransmitters dopamine and the serotonin were found to increase in the brain's prefrontal region in experimental mice study, which could underly abnormal behavior due to social isolation [33]. Serotonin has also been implicated in inducing aggression and

depression in a socially isolated animal model [34]. Glutamate levels are also elevated in socially isolated rats, where glutamate-induced excitotoxicity has been demonstrated, subsequently causing dysfunction of receptors and neuronal injury [35, 36]. The resultant brain injury could be attributed to the increased glutamatergic transmission through activation of N-methyl-D-aspartate (NMDA) receptors [37, 38]. These receptors have been found to be involved in the pathophysiology of various mental disorders such as depression, anxiety, and schizophrenia [39-41]. Glutamate receptors have also been reduced under the effect of social isolation in the cortex and hippocampus [42,43]. Furthermore, NMDA receptors' increased binding capacity under social isolation stress in the frontal cortex has also been reported [44]. AMPA ( $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid) is another ionotropic glutamate receptor, whose upregulation and activation in the amygdala could induce anxiety and depression-like behaviors in socially isolated mice [45, 46].

Social isolation also affects the noradrenaline system, where elevated levels have been demonstrated in the rat model's hippocampus, cortex, and cerebellum [47]. It could also lead to aggression induced adrenaline stress response [48]. The opioidergic system is involved in animal studies socialization, which could also be disrupted by social isolation [49-51]. The cannabinoid receptor system is also a vital neuromodulator in the central nervous system, whose depression has been demonstrated to be affected by fear, stress [52, 53]. In a socially isolated mouse model, disruption of the cannabinoid system-induced depression-like picture has been reported [54]. Nitric oxide is another signaling molecule suggested to have a role in learning, memory, synaptic plasticity, stress, seizure susceptibility, pain modulation, and depression in various brain regions [55-58]. Its social isolation role is evident in the studies demonstrating an exhibition of altered modulation of NMDA receptors and nitrenergic system balance in cortico-limbic areas in socially isolated mice [59, 60]. Both systems have also been linked to higher seizure susceptibility in socially deprived rats [35]. Haj-Mirzaian et al. [61] reported that four weeks of juvenile social isolation stress in mice could induce depression and anxiety-like pictures associated with increased hypothalamic responsiveness–pituitary–adrenal (HPA) axis, interleukin-1 $\beta$  upregulation. They increased the production of NO in the prefrontal cortex and hippocampus regions [61]. In conclusion, an inappropriate interacting endogenous neurotransmitter milieu of dopamine, serotonin, glutamate, and opioids could probably lead to observable phenomena of deviant psychosocial behavior that could plausibly have a deleterious effect on neuroeconomics of an individual with dysfunctional decision making distributed across and over time.

### The "Infodemic" alongside Pandemic

The current pandemic of SARS-CoV-2 is accompanied by an "Infodemic" of misinformation and myths are driven due to the consequential response of fear, stigma, and blame-game. The World Health Organization (WHO) has also raised concern about this deluge of conflicting and manipulated information on social media, that poses a global public health threat [62, 63]. The consequences of such an Infodemic could be appreciated by the misinformation spread during the outbreak of Ebola in

the Democratic Republic of Congo in 2019, which stirred violent behavior, lack of trust, and episodes of targeted attacks against health care workers [64]. Reports of similar incidences have surfaced in the news from India and other parts of the world, where health care workers engaged in COVID-19 sample collection and management were assaulted or abused [65-68]. Such kind of behavior, if not tackled timely by releasing correct information and appropriate Government intervention, could impede the efforts being made to manage and curb the spread of COVID-19. Misinformation could also be associated with the stigmatization of people with or suspected of having COVID-19, where such persons may not report the actual status of illness, and subsequently contribute to community spread of the disease [69,70]. Several incidences have been reported from many countries, where due to misinformation, people have suffered serious consequences, such as drinking methanol to cure COVID-19, which led to hospitalization, blindness, or deaths [71-74]. The government must take appropriate measures to track and prevent the spread of misinformation, rumors, stigma, and conspiracy theories on social media platforms, as it can lead to severe implications on people and the community [75].

#### **Psychological stress during the quarantine period**

People quarantined during previous outbreaks have reported a high level of mental stress [76]. The most common complaints include low mood followed by irritability and insomnia [77]. Other symptoms, such as emotional disturbance, [78] depression [76], post-traumatic stress symptoms [79], and anger [80], have also been reported. Health care workers were more susceptible to mental health issues than the general public during the quarantine period, with increased post-traumatic stress severity [79]. Even after three post quarantine years, the hospital staff reported high depressive symptoms [81]. It was also suggested that a quarantine period of more than ten days could lead to higher post-traumatic stress symptoms [76]. The Indian Government has released advisory from time to time on home and institutional quarantine, where more than ten days of quarantine for mild/pre-symptomatic/asymptomatic cases was recommended [82-85]. Although it was necessary to prevent the spread of infection, such preventive measures could create psychological stress in an individual and can have long term consequences affecting the individual and the entire public health system [4]. Hence, there is an urgent need to implement appropriate steps to address related mental health issues.

#### **Business and Economy**

The systemic lockdowns to curb the COVID-19 spread worldwide have significantly hit the economy, that also is a matter of great concern as it will consequently affect the business, entertainment, hotel sectors, and jobs. This pandemic has disrupted significant industry sectors, eventually leading to the closure of many business start-ups. Furthermore, the projected GDP growth is estimated low for the year 2020-12 [86]. This prevailing uncertainty of the economy will further escalate the anxiety and stress in people. There have been fewer incidences of such widespread pandemics, although available literature indicates subsequent low returns on assets [87]. The prevailing uncertainty and fear due to the current pandemic have made us realize that the world was completely unprepared

for such large-scale outbreaks. The loss to the economy will undoubtedly create psychological stress among people, leading to mental health issues.

#### **Psychological stress in migrant workers**

An important issue that needs attention has been of migration of daily wage laborers during the COVID-19 pandemic. This cohort of people was already at risk of psychological stress, as has been reported by Firdaus. They highlighted that mental health issues could pose a significant problem among single, illiterate daily wage laborers, migrant workers lacking appropriate housing, and sanitation [88]. The nation-wide lockdown has resulted in the loss of earnings and jobs, insecurities, and social isolation that is detrimental to the migrant population's mental health. This population was already vulnerable to risk-seeking behavior, as evidenced by the National Crime Records Bureau report, 2018, where 22.4% of suicides among daily wage earners were reported [89]. Another issue that confounded to the prevailing situation was the non-availability of transport to return home amid lockdown, in such a crisis of COVID-19 resulted in significant deaths of migrant workers in road accidents. [90] Such incidences might impact migrant workers' lives and mental health in the long term, possibly leading to high anxiety, depression, and suicidal tendencies. Consequently, social isolation, along with severely compromised available resources, confound further to the burning medical issue of COVID-19.

#### **Children and Adolescent Mental Health**

The COVID-19 seems to have spared the paediatric age group quantitatively, and a relatively milder presentation of the disease has been observed [13, 91]. However, the paediatric age group is more vulnerable to mental health disorders, owing to the confinement itself and an increased screen time due to excessive social media use and online teaching schedule. Additionally, misinformation, exposure to mass media coverage at an earlier age, fear, and stigma of COVID-19 might lead to mental distress in this age group [92-93]. This can be further aggravated by the quarantine of children diagnosed with or suspected of having COVID-19, leading to high levels of anxiety, stress, and even adjustment disorders [94]. At a younger age, such kind of social deprivation, separation from parents, and fear of unknown disease might have a long-lasting psychological impact on children and an even higher risk of developing post-traumatic stress disorder (PTSD) [4]. Previous studies have reported the development of PTSD in 30% of children after being quarantined amid health-related disasters [95].

#### **Education**

The current pandemic has affected various sectors of society directly or indirectly in unexpected ways, including education. The research has shown that students and healthcare professionals are the most vulnerable group developing anxiety, stress, and depression amid COVID-19 lockdown [96]. An unexpected shift in students' learning methods from traditional to virtual classroom teaching has created undue stress on students and teachers. Both have struggled while accessing these online platforms. Teachers might find it challenging to

deal with online teaching platforms and lack of resources efficiently.

In contrast, students might also experience difficulties accessing the online platforms and financial constraints, causing an inability to access the Internet and the unavailability of electronic tools, including the laptops, the phones, the computers, or even the radio and television. Moreover, the lack of adequate and effective interaction during sessions of teaching and knowledge dissemination has resulted in their subsequent pitfalls. However, both government and non-government organizations and educational technology companies are being made efforts to support the school system to make a smooth transition to the virtual world. This altogether has caused high anxiety among students amid the COVID-19 pandemic, together with poor economic conditions and hampered academic activities [97]. The uncertainty and fear of getting infected due to SARS-COV-2 have led to higher university students' anxiety [98].

### Psychological Stress in Health Care Workers

Health care workers (HCW) on the frontline, is the most vulnerable population in the current pandemic. Studies have reported and raised the concern of significant mental health disturbances such as depression, anxiety, and insomnia in health care workers engaged in COVID-19 management [99, 100]. The vulnerability of HCWs for depression, anxiety along with post-traumatic stress disorder was also observed during the previous outbreaks of the middle east respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS) [101-104]. The previous outbreak SARS has shown that healthcare providers involved in the management of SARS-affected patients were also prone to stigmatization associated with the disease [105]. Similar stigma has been associated with the pandemic of COVID-19, where reports of doctors' eviction from their homes and incidences of assault have been documented [106, 65]. The overburdened health care system, misinformation, psychological stress, and uncertainty of the current pandemic may lead to and add to mental health issues among healthcare workers.

Violence against women has also increased globally amid lockdown during this pandemic [107]. Previous studies have also indicated a rise in domestic violence cases during natural disasters [108]. Another concern related to COVID-19 is the increase in screen time during the lockdown, especially in children and adolescents. In present times of social isolation and deprivation with minimal physical contact stimulation and illogical infatuation with social media, it has seemingly made matters worse. There have also been reports of suicide attempts made by people experiencing substance withdrawal [109, 110]. Compliance with forced home quarantine is often being violated in India, unlike in other countries [111].

### Measures for combating psychosocial stress due to COVID-19

There is a need to understand the psychological impact of COVID-19. This will help people across all strata of the society to cope up with the challenges faced. This pandemic could be the much-needed wake-up call to the necessity of long-term changes to India's health system. The psychological stress, anxiety, fear, and helplessness associated with the current

pandemic of COVID-19 needs timely measures to improve society's mental health [112-114]. The disruption of the health care system, including mental health services, [at the time of need when psychological stress in the general population has increased], leaves people helpless [10, 115]. This could, in turn, precipitate incidences of panic, agitation, violence, and increased suicide rates and could be more damaging than the virus itself. The problem should be identified at the earliest, and timely measures targeting psychological issues can prevent crises in such a stressful situation [116].

The previous outbreak of SARS made us realized that psychiatrists could play a critical role in improving the overall health-care service utilization effectively [3]. They may offer a balanced perspective with adequate counselling sessions to provide awareness and mental health education as well as effective management of anxiety and apprehension. The government should intervene early and develop prevention and intervention models targeted at mental health disorders associated with the pandemic. The mental organization targeted at current and future pandemics should also be established [117]. COVID-19 has created mayhem and misery, but there are some positive aspects about lockdowns as well, such as a decrease in pollution level [118], a chance to reconnect with family members [119], and improved family relations and dynamics [120].

### Conclusion

The pandemic of COVID-19 has afflicted every individual and has initiated a cascade of directly or indirectly involved events in precipitating mental health issues. The psychosocial aspect of this pandemic should not be disregarded as it may culminate into various psychiatric disorders. This study presents the various underlying factors that need to be addressed urgently. Governments should intervene early and develop prevention and intervention models targeted at mental health disorders associated with the pandemic. Mental health organization dedicated to current and future pandemics should be established, especially targeting the vulnerable cohort of the society like pediatric, elderly, and frontline workers.

### Abbreviations

SARS-CoV-2: Severe Acute Respiratory Infection-Coronavirus-2; NMDA: N-methyl-D-aspartate; AMPA:  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazole Propionic Acid; HPA: Hypothalamic-Pituitary-Adrenal; WHO: World Health Organization; PTSD: Post-Traumatic Stress Disorder; HCW: Health Care Worker; MERS: Middle East Respiratory Syndrome.

### Declarations

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### Availability of data and materials

Data will be available by emailing bhupendra.kool9999@gmail.com

### Authors' contributions

BP is the principal investigator of this manuscript (Review), who designed the study and coordinated all aspects of the research, including all steps of the manuscript preparation. He is responsible for the study concept, design, writing, reviewing, editing, and approving the manuscript in its final form. SB, AJS, and AD contributed to the study design, analysis, and reviewed and approved the manuscript. SK, AT, JG and GR contributed to the interpretation of data, drafting the work, writing the manuscript and reviewed and approved the manuscript. All authors read and approved the final manuscript.

### Ethics approval and consent to participate

We conducted the research following the Declaration of Helsinki. However, Review Articles need no ethics committee approval.

### Consent for publication

Not applicable

### Competing interest

The authors declare that they have no competing interests.

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