

Review Article:

Title: Effect of COVID–19 on Mental Health: The perspectives

Sabreena Shafi Sheikh¹, Karan Singh^{1*}, Sonam Bhatia², Saurabh Dahiya³, Anwar Hussain Ansari⁴

¹Department of Pharmacy, Lingayas University, Faridabad, Haryana-121002, India

²Regional centre for Biotechnology, Faridabad, Haryana-121001, India

³Department of Pharmaceutical Chemistry, Delhi Pharmaceutical Sciences and Research University, Delhi-110017, India

⁴Department of Cardiology, Safdarjung Hospital, Ansari Nagar, New Delhi-110029, India

*Author of correspondence: E-mail: dr.karan@lingayasvidhyapeeth.edu.in

Abstract

The year 2020 saw the emergence of a novel, highly contagious, coronavirus disease (COVID-19) that originated in the Wuhan province of China and spread across the globe. This led to a worldwide pandemic. The World Health Organisation (WHO), within a month of cases being detected, declared the illness as a “public health emergency of international concern”. COVID-19 caused by SARS-CoV-2 not only affected the public health resulting in neurological manifestations (headache, dizziness, or cerebrovascular symptoms), but also initiated a plethora of mental health issues like anxiety, depression and suicidal tendencies. Having spread to over 200 countries, this virus has been a dire cause of concern for primarily two reasons: the threat they possess to the physiological and psychosocial health of the individuals; and the fear, anxiety and panic that has arisen as a result of the pandemic. Most nations, including India, underwent a complete lockdown with stringent norms of social distancing, self-isolation, and quarantine (for infected patients). As the nation tried to manage the situation, guidelines were set up for all its citizens by providing personal protective equipment (PPE), instilling practices like wearing a protective mask, gloves and frequent sanitisation in order to curb the spread of disease and safeguard public health. This review discusses the influence of COVID-19 on the mental health of the general population, focusing on the adolescent, pregnant and elderly; its proposed mechanism of action, and possible strategic interventions to protect the people, offer supportive measures to enhance quality of life, and prevent the spread.

1. Introduction

The year 2020 commenced with a disconcerting revelation that a global pandemic had brought the world to a startling halt. The Coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus had crippled the public health, economy and the daily lives of billions. Originating in Wuhan, China it took around a month to be declared as a 'public health emergency of international concern' and thereafter less than two months to erupt into a pandemic owing to its high spread, morbidity, mortality and infectiousness (1). With more than three million affected and around 1.5 lakh succumbing to this outbreak, the countries had locked down national and international borders to contain it as per the WHO Situation Report, as on 17 April 2020. WHO has also published the Emergency Global Supply Chain System (COVID-19) catalogue, which lists all medical devices, including personal protective equipment, medical equipment, medical consumables, single use devices, laboratory and test-related devices. According to the latest WHO epidemiological update of September, 2020, over 32.7 million COVID-19 cases and 991 000 deaths have been reported to WHO.

The evolution of COVID-19 remains unpredictable and this unpredictability is exacerbated by the heterogeneity of health systems worldwide and difficulties obtaining accurate infection and immunity numbers. In view of the magnitude of the pandemic, most countries adopted lockdown as a containment strategy (2).

It is known that psychological factors play an important role in adherence to public health measures (such as vaccination) and in how people cope with the threat of infection and consequent losses (3). These are clearly crucial issues to consider in the management of any infectious disease, including COVID-19. Psychological reactions to pandemics include maladaptive behaviours, emotional distress and defensive responses (3).

People with pre-existing mental health and substance use disorders will be at increased risk of infection with COVID-19, increased risk of having problems accessing testing and treatment and increased risk of negative physical and psychological effects stemming from the pandemic (4).

The reduced regular activity and exercise due to a fear of infection as well as negative symptoms further compromise patients' physical health and immunity. Moreover, the psychiatric inpatient unit is a perfect breeding ground for the virus. Therefore, patients with

serious mental illnesses are very vulnerable, both environmentally and physically, to infectious diseases (5).

The clinical manifestations of COVID-19 are characterized by fever, cough, dyspnea, and bilateral infiltrates on chest imaging (6). After infection, the majority of individuals show moderate symptoms whereas approximately, 20% of the infected patients show severe illness of respiratory failure, septic shock (6), gastrointestinal complications (6,7), myalgias, lymphopenia, and parenchymal lung abnormalities (8). The severity of symptoms and death causing ability of the virus are highly dependent on underlying diseases such as cancer, hypertension, and cardiopulmonary diseases (6, 9).

The infection has been reported to cause high mortalities in older people (10) and individuals with blood group A (11). Moreover, pregnant women with confirmed COVID-19 pneumonia can face adverse pregnancy and neonatal impacts (12).

Proposed mechanism:

Although the speculation is plenty, many researchers have tried to establish the probable mechanism of action of COVID-19 and its neurological as well as psychological effects on the human body.

The Central Nervous System is protected from viruses with its multilayer barriers and its immune response system. However, different viruses can affect the brain through a variety of mechanisms. Some proposed mechanisms by which the virus can cause infection include direct brain injury, hypoxic damage, upregulated angiotensin-converting enzyme 2 (ACE-2) receptors, and immune insufficiency, which can lead to toxic, infectious encephalopathy, viral encephalitis, and even acute cerebrovascular disease (10). The viruses have been found to cause direct brain injury through different mechanisms (14) including via blood circulation where the virus is released into the blood, causing an increase in the penetrability of the blood–brain barrier that leads to the virus entering the brain which causes encephalitis (15). Some viruses can also direct damage to the brain by involving the sensory or motor nerve endings (16).

It has been proposed that coronavirus causes its neurological symptoms via hypoxia. Since the virus primarily causes respiratory symptoms including shortness of breath and lack of oxygen in the lungs and consequent anaerobic metabolism in the brain, this can lead to brain injury displayed by brain swelling, interstitial edema, or cerebral vasodilation, etc. (17, 18).

Thus, hypoxia resulting from COVID-19 infection can result in neurological symptoms. COVID-19 also has the potential to cause hyper inflammation through cytokine storm syndrome (19).

Figure 1 below depicts the viral and host factors that influence the pathogenesis of SARS-CoV-2. Physical and biopsychosocial and psycho neuro immune effects impacted by the virus can be improved by a healthy lifestyle, exercise, a balanced diet, staying connected with family and loved ones using telecommunication or internet, and maintaining quality sleep (5).

The entry of virus inside the cellular receptor ACE2 (angiotensin-converting enzyme 2) is assisted by its spike proteins, which is followed by the entry of the virus genomic material (positive single stranded RNA) into the host cell. The virus genome contains two overlapping polyproteins (pp1a and pp1ab) which are cleaved into 16-non-structural proteins by the Mpro a “3C-like protease”, belonging to the proteases class of hydrolytic enzymes, and translated into structural proteins and non-structural proteins. This is followed by virus assembly, and subsequently virions are then released from the infected cell through exocytosis. The Mpro can act as a potential target for structure-based drug discovery due to the lack of homologues in human hosts. Targeting this enzyme with a suitable protease, small molecule inhibitor holds immense potential to curb virus replication and transcription (87).

In this respect, it is important to consider that since the impact of COVID-19 on the mental health and associated issues is unprecedented and cannot be understated, the propensity for suicidal tendencies cannot be overlooked. The steps to curb the global pandemic, viz. social distancing, isolation and quarantine have spread a wave of panic and uncertainty among the citizens at large, affecting all strata of populations with a lack of discernment.

Therefore, to put it succinctly, enhancing the psychosocial resilience of an individual for building overall immunity against the virus is highly crucial.

2. COVID-19 management

Given a population of 1.3 billion, it is estimated that even with a low death rate, as many as two million people in India could die from COVID-19 (21).

It is now clear that COVID-19 presents two major health problems. The first problem is the illness caused by the virus itself, which is usually self-limiting but can be fatal, especially in the vulnerable, the elderly and people with underlying health conditions. The second problem is the anxiety and panic that the virus triggers in the minds of virtually everyone who hears

about it. Both problems present substantial challenges to psychiatry (22). It has been well established that people suffering from a mental illness are more prone to poorer health outcomes and have a lower life expectancy as compared to the general population. This means that those patients are less likely to adhere to the stringent guidelines or receive due treatment and are thereby more prone to getting affected by the virus. The COVID- 19 outbreak has not only crippled the resilience of society as a whole but also instilled fear in the minds of the global population.

When one is responding to COVID-19 and is quarantined, mental predicaments become much harder. Even upon the release from quarantine, one might experience mixed feelings, including intense fear about his/her own and loved ones' health. Further, other symptoms such as sadness and irritation because a friend or loved one might have contracted COVID-19 can be frustrating. Other emotional and mental changes often result from the guilt of not being able to interact with other people, complete tasks, and take duties during the quarantine period. Furthermore, the financial and social burden of the issue adds to the mental health burden of the disease (23).

These are the following people at risk of psychological harm from social isolation during the COVID-19 pandemic (24)

People with pre-existing physical and mental health conditions (such as anxiety, depression, and obsessive-compulsive disorder)

Older people living alone or in institutions such as care homes and special needs facilities

Disabled individuals, especially those with learning and communication disabilities

People with recent bereavement, hospitalisation, or illness

Individuals infected with COVID-19 who are stigmatised in the community

Those subject to domestic violence, which is likely to be made worse during quarantine

People with drug and/or alcohol use disorders

Individuals with caretaking responsibilities, including childcare during extended school closures

People who are unemployed or those who have lost income during the pandemic

People living alone with limited social capital and support network

Individuals under mandatory quarantine and those in strict self - isolation due to serious physical health conditions (shielding)

Young people (due to closure of schools and colleges and sports and entertainment facilities)

Refugees, internally displaced people, and undocumented migrants

The major psychological symptoms among people include signs of anxiety, panic attacks, depression, and suicide (25, 26). To elaborate, the symptoms include persistent worrying or feeling overwhelmed by emotions; restlessness and irritability; sleep problems like insomnia or excessive sleeping; sweating, trembling, shortness of breath, or a sense of choking; and lack of interest, significant weight loss/gain, feelings of worthlessness or excessive guilt, and repeated thoughts of death or suicide (25, 26, 27).

3. Management of psychological issues

A long-time lockdown may lead to psychosocial difficulties for vulnerable population and consequently lead to stress, anxiety, frustration, boredom and depression and even suicidal idea and attempts. The Lancet Psychiatry (2020) also highlighted the mental health needs of vulnerable groups, including those with severe mental illness, learning difficulties and neurodevelopmental disorders, as well as socially excluded groups such as prisoners, the homeless and refugees.

Given the ability to avoid responsibilities along with reduced social and academic demands, it may have a positive impact on those with generalized anxiety, social anxiety, or agoraphobia. Conversely, there may be an immediate worsening of symptoms in those with obsessive-compulsive disorder, health-related anxieties, or posttraumatic conditions. A second possibility is that the ability to perceive potential negative impacts on anxiety is being mitigated by the fact that these clients are receiving therapy, something that is inherently protective (8).

This fits the general idea that avoidance used as a coping strategy may be effective in the short term but only increases anxiety in the long term (8).

Those who have children with developmental disabilities have been further challenged by having to manage the significant behavioral issues of their children with minimal supports (28).

Continued access to mental health services and supports across communities of need, whether in person or via electronic platforms, will be essential as society learns new ways to cope and adjust to life after COVID-19 (28).

Furthermore, specific populations like the elderly (29), the children (30) and the healthcare workers (31) might report different level of psychological distress. Experts point out the need to pay specific attention to other groups at risk of further distress that may need tailored interventions, such as people with pre-existing psychiatric conditions (32), pregnant women (33), persons in detention (34), international migrant workers (35), and international students (36).

COVID-19 is expected to have devastating mental health consequences in India through multiple pathways. Examples include lack of access to mental health resources (37, 38), stigma about the virus and mental illness (39, 40), widespread prevalence of untreated trauma and other psychiatric conditions (41), communal tensions (42), unemployment (43), police brutality (44), and starvation (45, 46). Therefore, adverse mental health consequences of the pandemic and lockdown are likely to be intensified among socially and economically disadvantaged groups that face poverty (47, 48) illiteracy (49), social exclusion (50, 51), and victimization (52, 53).

4. Consequences of COVID on general population

The mental health impact of COVID-19 on the general population, especially on those with pre-existing mental disorders, has been enormous. The lockdown has led to difficulties in terms of medication availability, access to health care, issues with transportation, and panic, adding to the number of relapses, especially in severe mental disorders like severe depression, schizophrenia, obsessive-compulsive spectrum disorders, and bi-polar disorders (54). Alcohol withdrawal disorders, including delirium tremens, have been on the rise after the initiation of the sudden lockdown (55).

The prolonged lockdown has further contributed to isolation, loneliness, boredom, and anger, all of which are risk factors for psychiatric disorders. Complex post-traumatic stress disorders and adjustment reactions can be chronic in such biological disasters and need to be interpreted in the varied sociocultural contexts of India (56).

It can be studied in different populations.

a. Adolescents

The importance of community involvement, awareness and behaviour change cannot be undermined in the current situation, especially for psychosocial issues due to COVID-19. Risk communication and community engagement is a critical component of the response to

COVID-19 (57). This crisis is not going to be controlled without community participation because ultimately control is based on individual behaviour.

The Government of India's Rashtriya Kishor Swasthya Karyakram (National Adolescent Health Programme) can play a pivotal role in social and behavioural change and enhance adolescent resilience against mental health challenges posed by the pandemic.

b. Elderly

COVID-19 has been postulated to be less fatal than its earlier congeners like Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), caused by the same family of viruses. However, the SARS-CoV-2 is much more contagious with an increased human-human transmission (58).

It has been observed that the severity and fatality of COVID-19 is directly related to age and immune-compromised states, as 15 percent of the first wave of deaths in China were aged above 60 years. According to Chinese Centre for Disease Control and Prevention, the mortality rate in age group 60-69 years is 3.6 percent which can reach up to 18 percent at 80 years and above (59). Similar data has been reported from the worst affected countries like South Korea, Iran, Spain, Italy and the United States (60).

Elderly patients above the age of 55 years had 3 times the mortality as well as increased hospitalization, delayed clinical recovery, increased pulmonary involvement, faster disease progression, and comorbidities of diabetes, hypertension, history of cerebro-vascular accident (CVA) and chronic obstructive pulmonary disease (COPD). The need for mechanical ventilation and oxygen therapy were double in them and their blood showed decreased lymphocytes, C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR): all of which are markers of inflammatory response to the virus (61). Adding to this, social isolation, loneliness, neglect, depression and anxiety are the comorbid factors that can make the lives of the elderly debilitating.

Iatrogenic infections, poor mobility of the patient and polypharmacy are the further concerns among the geriatric population. Being institutionalised, they can be exposed to poor hygienic conditions, overcrowding and a lack of supervision. Further, it is advisable that all elective surgeries (like hernia, cataract, knee-replacement, etc.) should be avoided as far as possible.

Most seniors are not comfortable with smart phones or the media language, hence the precautions for a pandemic need to be explained to them in their own simple terms. Cognitive impairment and problems like wandering, irritability and psychotic symptoms can worsen the

panic and make it difficult for them to follow the precautions of distancing and hand hygiene. Furthermore, people with mental health disorders (including elderly) are more vulnerable and are prone to exacerbations during such a crisis. Discrimination and lack of health-care utilization are other factors contributing to their poor care during the COVID-19 outbreak (62).

Lessons learnt from earlier pandemics like SARS have proved that regular telephonic counselling sessions (better than physical access), healthy contact with family, relevant and updated information, caring for the general medical and psychological needs and respecting their personal space and dignity are important components of mental health care in the elderly (63). Although they are not familiar with the digital technology, in this time and age, connecting through mobile applications is an effective way of making the elderly population self-sufficient. They need to be updated about the COVID-19 situation and the necessary measures in a relevant manner. Vivid data and unnecessary statistics are better avoided. Digital technology can enhance well-being and improve social connectedness by improving social support and engagement in activities (64, 65).

Banskota et al., 2020, proposed 13 smartphone applications for older adults to use daily while in isolation during the COVID-19 pandemic (Table 1).

Mobile Technologies can address loneliness and isolation, which have been associated with higher risks of depression and cardiovascular risk factors in older adults (67, 68).

It suggested that apps fulfil an unmet need and could help older adults maintain physical and mental health, independence, address disabilities, and some financial security. Most importantly, these applications encourage and allow for a less imprisoning and isolating experience for older adults during this crisis (66).

c. **Pregnancy**

As this is a new infection, little is known about COVID-19, particularly related to its effect on pregnant women and infants, and there is currently no definitive evidence-based guidance specific to pregnant women regarding the evaluation or management of COVID-19 (figure 2).

The Federation of Obstetric and Gynaecological Societies of India in their recommendations suggest that for delivery, intubation and resuscitation, and during surgery for a suspected or

confirmed COVID-19 positive patient the following should be used: disposable surgical cap, medical protective mask (N95), work uniform, disposable surgical gown, disposable latex gloves and full-face respiratory protective device or powered air-purifying respirator.

For those wishing to breast-feed, precautions should be taken to limit the viral spread to the baby by observing strict hand hygiene before touching the baby. A face mask should be worn while breast-feeding. With regards to expressing breast milk, women should use a dedicated breast pump and ensure appropriate cleaning after each use (69, 70). When a mother with COVID-19 is too sick to care for the newborn, the neonate can be managed separately and can be fed freshly expressed breast milk, with no need to pasteurize it, as human milk is not believed to be a vehicle of COVID-19 transmission (70).

With regard to COVID-19, the limited data currently available do not indicate that pregnant individuals are at an increased risk of infection or severe morbidity (e.g., need for intensive care unit [ICU] admission or mortality) compared with non-pregnant individuals in the general population. An intense inflammatory response has been reported as one of the key features of severe COVID-19 (71), and as there is relative immunosuppression in pregnancy this may partly explain why many pregnant women do not develop severe respiratory symptoms (72). However, pregnant patients with comorbidities may be at increased risk for severe illness consistent with the general population with similar comorbidities (73).

Subsequently, Chen et al. (74) observed similar results in confirmed COVID-19 patients, showing that the most common symptoms in 112 women with available data were fever (75%), cough (73%) and lymphopenia (44%) (74). These figures have been similar in other studies (74, 75)

d. Health workers

It can be anticipated that health and social care professionals will be at particular risk of psychological symptoms, especially if they work in public health, primary care, emergency services, emergency departments and intensive or critical care. The World Health Organization has formally recognized this risk to healthcare workers, (75) so more needs to be done to manage anxiety and stress in this group and, in the longer term, help prevent burnout, depression and post-traumatic stress disorder.

The government should give special attention to systematic psychological health care which is required by health-care staff and patients, and systematic psychological self-care must be

given a high priority in coping with the detrimental impacts of COVID-19 and social distancing (76).

5. Psychological support during the pandemic

The current outbreak of COVID-19 is heavily impacting the mental health globally. Despite all resources employed to counteract the spreading of the virus, additional global strategies are needed to handle the related mental health issues (77). This outbreak is leading to additional health problems such as stress, anxiety, depressive symptoms, insomnia, denial, anger and fear globally (77). To protect people and prevent the spread, it is critical that public mental health paradigms and measures are used (78).

The Ministry of Home Affairs invoked the lockdown in India under Section 6 of the Disaster Management Act, and the guidelines were published by the Home Secretary under Section 10 of the same as reported by NDTV news channel (79). In the event of this lockdown, a wave swept over the country. Panic gave way to mass hysteria, sporadic violence, and non-compliance to the lockdown as misinformation was rampant through increased social media consumption and penetration (80).

The worst affected social group during the current lockdown are the laborers and their families, and more particularly migrants who had left their homes for seeking odd jobs at various places, both urban and rural in industries, services, construction and even in agriculture. New policies by Government to run special trains, monetary aids to migrants and poor and relief camps are appreciable and need to be monitored so that the benefits could reach to afflicted populations (87).

The immunocompromised migrants are more prone to co-infections too caused by deadly pathogens owing to quorum sensing mediated virulence (92, 93, 94). Hence, we need more vigilant approach which can also take care of immense problems face by laborers and people of vulnerable group. The rational drug design approach to identify new anti-Coronavirus drugs is an excellent strategy to screen drugs/natural/synthetic compounds against this deadly pathogen (95, 96, 97).

According to the Lancet, 2020, although the lockdown in India has managed to flatten the epidemic curve the withdrawal strategy has to be slow, deliberate and well-calibrated. The governments need to step up to protect their populations and people in a non-threatening, non-panicky manner to ensure safety of all individuals (81).

The social and economic issues due to COVID-19 pandemic will result in mass unemployment, depleted social safety nets, homelessness, increase in gender-based violence, alcoholism, hunger, loan defaults and millions slipping into poverty. This post-COVID landscape will definitely lead to an increase in mental health issues such as chronic stress, anxiety, depression, alcohol dependence and self-harm (82). Providing social prescribing, on-line counselling, social distancing therapies, Telehealth counselling, use of remote general practice consultations to mitigate psychological harm during the COVID-19 pandemic (based on Calgary-Cambridge communication model) etc. are some of the possible interventions.

Primary care has unique strengths, including continuity of care, that lend themselves to alleviating psychological harm via evidence-based approaches including video consultations and social prescribing (83).

The cornerstones of mental health treatment remain the same as in the pre-pandemic period. Patients may need reassurance, appropriate safety-netting, and self-care advice, as from WHO. Decisions regarding mental health interventions for patients will depend on the severity of symptoms and screening results, pre-existing mental health conditions, available social resources, patient wishes, and the estimated risk of adverse health outcomes. As in typical practice, specialist advice or referral to mental health services may be required (31).

WHO advice for people in isolation (31):

Stay connected and maintain your social networks

Keep your daily routines or create new ones if circumstances change

During social distancing, stay connected to friends, family, and community members via telephone, email, social media, or video conference

During times of stress, pay attention to your own needs and feelings

Engage in healthy activities that you enjoy and find relaxing

Exercise regularly, keep regular sleep routines, and eat healthy food

A near constant stream of news reports can cause anyone to feel anxious or distressed. Seek information updates and practical guidance at specific times during the day from health professionals or reliable sources such as the WHO

Avoid listening to or following rumours that make you feel uncomfortable

Possible interventions that can be undertaken to deal with the pandemic (31):

This pandemic has been a wake-up call for the entire global population to act quickly. There have been guidelines aimed at enhancing resilience of vulnerable populations against mental health issues. A lot of interventions are being taken up by support groups, the government, non-governmental organisations, philanthropists, religious groups, etc. to help humanity as a whole.

Examples of online mental and physical health support during the pandemic (31):

World Health Organization. WHO Mental Health Gap Action Programme (mhGAP)

https://www.who.int/mental_health/mhgap/en/

Every Mind Matters.

<https://www.nhs.uk/oneyou/every-mind-matters/>—Provides simple tips and advice to start taking better care of your mental health

Big White Wall.

<https://www.bigwhitewall.com>—A safe community support for mental health NHS.

Breathing exercise for stress.

<https://www.nhs.uk/conditions/stress-anxiety-depression/ways-relieve-stress/>

NHS. Mindfulness.

<https://www.nhs.uk/conditions/stress-anxiety-depression/mindfulness/>

Mind. Relaxation: tips and exercises to help you relax.

<https://www.mind.org.uk/information-support/tips-for-everydayliving/relaxation/relaxation-tips/>

One You. Home workout videos.

<https://www.nhs.uk/oneyou/for-your-body/move-more/home-workout-videos/>

Imperial College London Primary Care. Brief physical activity guidance for older adults in isolation.

<https://imperialprimarycare.blogspot.com/2020/04/brief-physical-activity-guidance-to.html>

Current proposed treatments for COVID-19:

The drug discovery process from identifying a potential lead to successfully formulating and developing a pharmaceutical product or vaccine can take up to 10 - 15 years. Therefore, it is advisable to come up with other strategies to treat conditions which are debilitating and have no immediate cure such as the COVID-19. Either repurposing of drugs or identifying suitable

nutritional components from food sources can be effective ways of providing immunity and resilience to the general population.

FDA approved drugs include Hydroxychloroquine, Chloroquine, Ivermectin, Arbidol, Remdesvir, Cinanserin and more which have been already used to treat COVID-19 patients (88, 89), but these drugs have their own toxic and pharmacokinetic implications and their mechanism of action remains unclear. Further, vitamin B12 has been reported to interfere with RNA polymerase activity of SARS-CoV-2, which is a natural dietary supplement (90).

It is suggested that the daily consumption of red raspberry, black berry, pomegranate juice, and more importantly “black tea” (comparatively economical) might protect humans from the primary infection of COVID-19. The two compounds from black tea (TDG [theaflavin 3,3'-O-digallate] and TG [theaflavin 3-O-gallate]) two derivatives of theaflavin belonging to the anthocyanins flavanols sub-class, have been found to be active through *in silico* studies, which suggested that theaflavin derivatives can play a vital role in the treatment of COVID-19 as well (87). The dietary polyphenols in black tea and berries hold immense potential to bind with the substrate binding pocket of Mpro and Spike proteins. Compounds with highest docking scores sanguin-H-6 and theaflavin digallate, are well established vasodilators and hence can also be repurposed as treatments for COVID-19 (87).

Drug repurposing for COVID – 19 treatments:

A team of researchers in California led by Sumit Chanda employed a small-molecule drug library called ReFRAME (84), which was created in 2018 by Calibr, a non-profit drug discovery division of Scripps Research, La Jolla, CA. Initially, in collaboration with other researchers in Hong Kong, they shortlisted 300 possible COVID-19 drugs from a library of nearly 12000 compounds showing potential activity against SARS-CoV-2. Upon conducting tests, it was found that 21 of these existing drugs showed potential for repurposing to thwart the novel coronavirus. 13 of them were found effective at doses that likely could be safely given to people. The majority of these drugs have been tested in clinical trials for use in HIV, autoimmune diseases, osteoporosis, and other conditions (85, 86).

Further study showed that some of the most promising drugs on the list reduced the number of SARS-CoV-2 infected cells by 65 to 85 percent. The most potent of these was apilimod, a drug that has been evaluated in clinical trials for treating Crohn's disease, rheumatoid arthritis, and other autoimmune conditions. Apilimod is now being evaluated in the clinic for

its ability to prevent the progression of COVID-19. Another potential antiviral to emerge from the study is clofazimine, a 70-year old FDA-approved drug that is on the World Health Organization's list of essential medicines for the treatment of leprosy. Research showed that remdesivir, an anti-viral drug originally developed against Ebola virus and authorised by USFDA, could be considered as a positive control against the remaining shortlisted drugs (85).

Conclusion:

This comprehensive review has been a compilation of the exhaustive research and literature survey carried out by scientists globally. The impact of COVID-19 on the human psyche and its repercussions to the world at large can't be emphasised enough. This review has been drafted with the motto of providing a cohesive collation of material which offers an introduction to the disease, its effect on the public physical and mental health, the psychological issues associated with the pandemic, suggested interventions and possible treatment strategies that may be undertaken for diverse populations.

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Table 1. 13 smartphone apps for older adults to use daily while in isolation during the coronavirus disease 2019 pandemic (66).

Sr. no.	Application name	Developer	Function
1. Social networking apps	a. FaceTime b. Skype	Roberto Garcia, Apple engineer, Skype technologies	May be used on mobile devices and computers; allows for communication between Apple/Skype users via one-on-one or group phone or video calls
2. Medical apps	a. Teladoc b. Doctor on Demand c. K Health: Primary care	Teladoc K Health Inc. Phil McGraw, Adam Jackson	Connects with doctors (24x7), provides digital primary care, chronic care and psychological management, prescription management
3. Health and Fitness apps	a. Calm b. Headspace: meditation and sleep c. Yoga: down dog d. MyFitnessPal	Michael Acton Smith and Alex Tew Headspace Inc. Yogi Buddhi Co. Under Armour Inc.	For mindfulness and meditation to lower stress and improve sleep, relaxation, check calories and log exercise
4. Food and Drink apps	a. DoorDash- Food delivery b. Instacart	DoorDash Inc., Maplebear Inc.	Food delivery service. Allows users to order food from participating restaurants and cafes.
5. Apps for visual and hearing impairment	a. Be My Eyes- Helping the Blind b. Glide – live video messenger	Hans Jorgen, Glide	Connects blind and visually impaired people with sighted people who assist them with tasks.

Pathogenesis of SARS-CoV-2

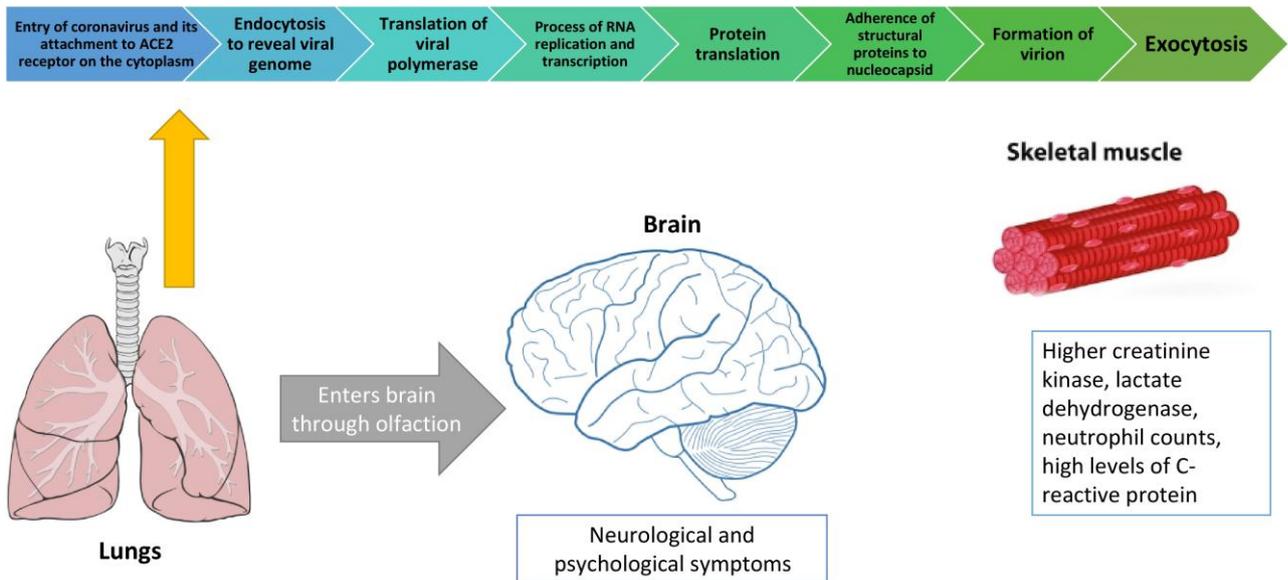


Figure 1: Putative mechanisms underlying neurobiological and psychological events of COVID-19 and their effect on mental health-related issues through psycho neuro immunity (adapted from Nami et al., 2020)

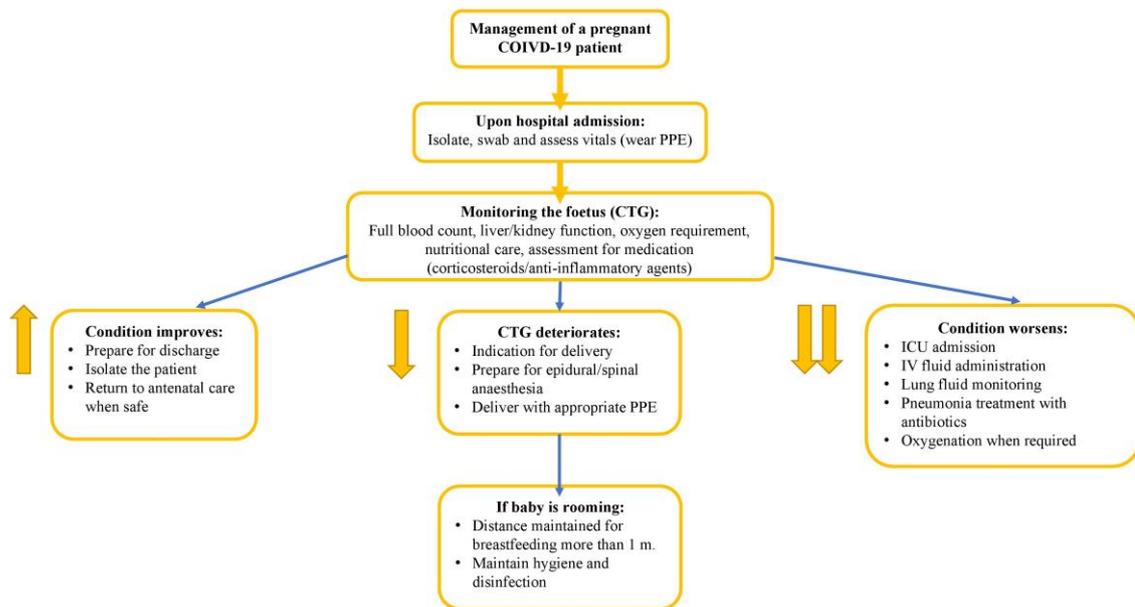


Figure 2: A brief overview of the management of a pregnant woman with COVID-19