



## **Psychological and Neuropsychiatric Long-Term Effects of COVID-19**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## **ABSTRACT**

Viruses are abundant, and several have been found to infect the CNS, resulting in neuropsychiatric disorders affecting the cognitive, emotional, behavioural, and perceptual domains. As the pandemic of the disease now known as COVID-19 has progressed, the psychological ramifications of the sickness have become more widely recognized. The present COVID-19 pandemic could have psychological effects for numerous causes. Certain situations, such as pervasive anxiety, social isolation, stress in health-care employees and other social workers, unemployment, and

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financial troubles, may make both infected and non-infected people vulnerable. Furthermore, psychological distress was found to be adversely linked with suggested health behaviours to reduce infection risk and favourably associated with non-recommended behaviours in quarantine conditions. The purpose of this research is to review the available information about the psychological and neuropsychiatric long-term effects of COVID-19. According to the existing literature, the COVID-19 pandemic has a significant negative influence on mental health, particularly in older persons with and without dementia. Viral infection, as well as the social isolation that follows in order to prevent it from spreading, has a variety of neuropsychiatric repercussions. To clarify such impacts and assess the long-term ramifications for the mental health of older persons, as well as explore alternative mitigating techniques, larger and more robustly designed research studies are needed.

*Keywords: COVID-19 pandemic; viral infection; psychological; neuropsychiatric; long-term effects.*

## 1. INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in December 2019 [1]. There are cumulative 280 million confirmed active cases and 5.8 million deaths as of December 2021[2]. The international community is concentrating its efforts on lowering virus transmission as well as death. Despite the high mortality rate, the vast majority of patients survive coronavirus disease 2019 (COVID-19); nonetheless, any systemic sequelae remain unknown and could pose a further worldwide public health concern. Pulmonary fibrosis, cardiovascular damage and neurological impairment are amongst the potential sequelae of COVID-19 in survivors [3]. Viruses are abundant, and several have been found to infect the CNS, resulting in neuropsychiatric disorders affecting the cognitive, emotional, behavioural, and perceptual domains [4]. Coronaviruses have also been detected in the brains of people who have had seizures, encephalitis, or encephalomyelitis, as well as in their cerebrospinal fluid [5,6].

As the pandemic of the disease now known as COVID-19 has progressed, the psychological ramifications of the sickness have become more widely recognized. The present COVID-19 pandemic could have psychological effects for numerous causes. Some of these factors are related to the pandemic's broader social impact and the government's response, which includes physical separation and quarantine [7,8]. Certain situations, such as pervasive anxiety, social isolation, stress in health-care employees and other workers, unemployment and financial troubles, may make both infected and non-infected people vulnerable. Other symptoms, such as anxiety over the course of their sickness,

stigma, and amnesia or traumatic memories of severe illness, may be unique to those infected with the virus [9,10]. In older persons and those with dementia, delirium is the most common acute neuropsychiatric symptom of covid-19 [11]. Delirium is linked to poorer outcomes and is more common in patients requiring intensive care, with one-third of patients reporting cognitive and behavioural problems after discharge [12].

The worldwide economy has been harmed by the protracted lockdown, imposed quarantine and social isolation, the sheltering of immunocompromised and older people, and the growth in unemployment, with the pandemic now constituting the greatest serious threat to persons and property. Furthermore, psychological distress was found to be adversely linked with suggested health behaviours to reduce infection risk and favourably associated with non-recommended behaviours in quarantine conditions [13]. COVID-19-related themes have also been found to be incorporated into the delusional system of people with long-term mental health difficulties, with nearly one-third (31%) of patients hospitalized to a mental hospital during the COVID-19 period displaying psychotic symptoms with COVID-19-related themes [14].

People's physical and mental health have been damaged by the abrupt and extreme changes brought on by the Coronavirus Disease 19 (COVID-19) pandemic. Social isolation and loneliness have a negative impact on individuals and especially older persons' mental health and may contribute to cognitive decline. The purpose of this research is to review the available information about the psychological and neuropsychiatric long-term effects of COVID-19.

## 2. METHODOLOGY

This study is based on a comprehensive literature search conducted on December 27, 2021, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the psychological and neuropsychiatric long-term effects of COVID-19. There were no restrictions on date, language, participant age, or type of publication.

## 3. DISCUSSION

In the acute phase, neurologic symptoms such as headache, nausea, vomiting, and disorientation, as well as hyposmia/hypogeusia and musculoskeletal symptoms, are usually mild and temporary. In a case series from Wuhan, 36 percent of patients admitted to the hospital for SARS-CoV-2 infection had neurological symptoms, the majority of which were mild symptoms like dizziness and headache, though these symptoms could be manifestations of systemic illness rather than a specific neurological syndrome. As part of their condition, several patients developed acute cerebrovascular disease or reduced awareness [15].

At three months' time period after infection, the most common self-reported health difficulties among mild, moderate, and severe SARS-COV-2 survivors are mental health problems and social functioning issues [16]. Study findings of Nalleballe K. et.al. [17] revealed that 9086 (22.5%) of the total 40,469 COVID-19 patients displayed neuropsychiatric signs. Headaches accounted for 1501 (3.7%) of all neurologic symptoms, while sleep disturbances accounted for 1394(3.4%). Other symptoms included encephalopathy 937(2.3%), myalgia 821 (2.0%), pain 723 (1.8%), loss of taste and smell 477(1.2%), stroke and transient ischemic attack (TIA) 406 (1.0%), dizziness 379 (0.9%), extrapyramidal and movement disorders 277 (0.7%), seizures 258 (0.6%), polyneuropathy 247 (0.6%), and nerve root and plexus disorders 145(0.4%).

Frontline healthcare personnel, or those who directly provide care to the infected patient population, were more likely to report psychological symptoms, with nurses and women being the most affected [18]. Despite high infusion rates of sedative therapies and neuroleptics, a bicentre French study found that 84.3 percent of critically ill COVID-19 patents in the ICU had delirium, with 69.3 percent having hyperactive delirium. In patients with delirium and/or abnormal neurological examination, the duration of invasive mechanical ventilation was much longer than in patients with normal neurological examination and no delirium, and ICU length of stay was also significantly long [19].

According to the most recent UK surveillance report, altered mental state was reported in 31% of COVID-19 patients with 91 percent confirmed SARS-CoV-2 infection, with neuropsychiatric symptoms in 23/39 cases and new onset psychosis in all confirmed COVID-19 patients [20]. According to recent study in China, 35% of respondents expressed psychological discomfort, with 53.8% rating the pandemic's psychological impact as moderate or severe. Moderate to severe anxiety symptoms were recorded by 28.8%, while moderate to severe stress levels were indicated by 8.1% [21,22].

COVID-19's psychosocial effects are thus laying the groundwork for an unprecedented rise in the prevalence of anxiety and stress-related disorders, which can hasten the onset of a variety of other co-morbid psychiatric illnesses, including mood disorders (depression and bipolar disorder), schizophrenia, and substance abuse [23]. From pre-COVID to post-COVID, the prevalence of depression symptoms in the United States increased thrice [24]. The direct effects of viral infection (including brain infection), cerebrovascular disease, the degree of physiological compromise, the immunological response, medical interventions, social isolation, the psychological impact of a novel severe and potentially fatal illness, concerns about infecting others, and stigma are all likely factors in the psychiatric consequences of coronavirus infection. The immunological response to SARS-CoV-2 infection is intriguing, and there may be a hyperinflammatory state similar to that seen in hemophagocytic lymphohistiocytosis, in which C-reactive protein, ferritin, and interleukin-6 concentrations are elevated, albeit this condition is likely to be transient [25].

As many as 48% of confirmed COVID-19 inpatients have overt psychological symptoms (such as depression, anxiety, phobias, and even panic attacks), and frequently express regret, resentment, loneliness, helplessness, and irritation, with age (21–30 years) but not gender influencing anxiety and depression levels [26]. According to Méndez R et al. [27] cognitive complaints questionnaire, 24 percent of patients self-reported having some degree of impaired cognition (11.7 percent impaired memory function and 12.3 percent moderate or severe memory impairment), whereas 53.8% and 22.2% of patients had normal and optimal memory function, respectively. Patients with neurocognitive impairment and psychiatric morbidity were detected in 80 (46.8%) and 77 (45%), respectively. Semantic verbal fluency (32.7%) was the most impaired cognitive domain, followed by immediate verbal memory/learning (20.5%), working memory/executive function (12.3%), and delayed verbal memory (7.6%). Anxiety (35.1%) was the most common psychiatric illness, followed by depression (32.2%) and post-traumatic stress disorder (PTSD) (24.6%). The neuropsychiatric short- and long-term effects of SARS and MERS infection were documented by Rogers JP et.al [28]. Neuropsychiatric symptoms such as disorientation, depressed mood, anxiety, decreased memory, and sleeplessness were recorded in 27–41 percent of individuals during the acute illness, according to the researchers. Mania and psychosis caused by steroids have also been described.

From previous outbreaks of SARS-CoV-1 and MERS, as well as recent reports of neurological and neuropsychiatric difficulties following COVID-19, it is obvious that a high proportion of survivors will suffer from a variety of neuropsychiatric and cognitive consequences. These are likely to have a negative impact on their mental, physical, and cognitive health. As a result, their emotional, vocational, and financial situations would be affected. Some of these patients may have a full-blown neurological or psychiatric disorder, while others may only have moderate cognitive issues, raising their risk of dementia. COVID-19 appears to alter the cognitive domains of executive processes, attention, and memory, according to early indications. A rise in emotional disorders, anxiety, exhaustion, and PTSD is also a possibility [29-31].

Pandemics have harmed people's psyche and harmed society, and there is a sense of worry over people's psychology. Coronavirus is affecting people's lifestyles and has impacted how people work in several industries. Maladaptive behaviours, defence, and emotional reactions are some of the psychological variables that cause individuals to react directly in the face of a pandemic when they feel threatened. As a result, it is clear that the larger the outbreak, the greater the impact on people's general well-being [32].

Individuals with no previous history of neuropsychiatric diseases have also experienced psychotic symptoms as a result of SARS-CoV-2 infection. A UK monitoring research indicated that 43 percent of people who developed neuropsychiatric symptoms as a result of COVID-19 developed new onset psychosis [33]. Individuals who tested positive for SARS-CoV-2 despite having no upper respiratory symptoms have reported new onset psychotic symptoms, which have been linked to higher peripheral inflammatory markers (e.g., CRP) [34].

Individuals who had recently (within one year) been diagnosed with a mental disorder had a considerably elevated risk of SARS-CoV-2 infection in the United States, with an adjusted odds ratio more than seven for both depression and schizophrenia. Furthermore, persons with a recent diagnosis of a mental problem and SARS-CoV-2 infection had an 8.5 percent death rate and a 27.4 percent hospitalization rate, compared to 4.7 and 18.6 percent, respectively, among those with SARS-CoV-2 and no mental disorder [35].

Though the current health priority for COVID-19 management is limited to containment and pulmonary symptom management, the infection's potential acute and long-term neuropsychiatric consequences can increase morbidity and decrease quality of life. The novel coronavirus appears to be spreading across the nervous system, according to new research. Its most common neuropsychiatric consequences are delirium, encephalopathy, olfactory abnormalities, abrupt behavioural changes, headache, and cerebrovascular accidents. These are linked to an increase in peripheral immunological markers, infection severity, and the rate of case fatality [36].

At the peak of COVID19 pathology, psychotic abnormalities such as delusions, hallucinations, disorganized thought, speech, and behaviour may be associated with delirium; nevertheless, they may continue when delirium fades and the infection resolves. Sometimes, weeks or months after recovering from an infection, psychiatric signs appear without delirium or confusion, making the distinction between a main schizophrenia psychosis and a post-COVID19 psychosis more challenging. COVID19's psychotic aftermath necessitates an immediate critical assessment of its pathobiology in order to design an effective therapy strategy. Sleep problems, which are typically seen as COVID19 neuropsychiatric sequelae, have distinctive features such as difficulties falling asleep and dissatisfaction with sleep quality [37].

Evidence of a higher frequency of psychiatric manifestations with atypical characteristics in patients who recovered from COVID 19 infection raises the question of whether these disturbances are linked to the stress that comes with every systemic infection or to specific neurobiological changes associated with COVID 19. COVID19 pathogenesis is defined by a mix of systemic inflammation, hypoxia due to respiratory failure, and neuroinflammation (either due to viral neurotropism or in reaction to cytokine storm), all of which damage the brain and may cause or exacerbate mental and cognitive issues [38].

COVID-19 infections have expanded rapidly, putting a huge strain on healthcare systems around the world. In the current climate, the most important interventions are epidemiological measures to prevent infection, effective treatment of patients with severe illnesses to minimize mortality rates, and the development of diagnostic tests [39]. Furthermore, the COVID-19 outbreak's acute, medium, and long-term mental-health repercussions for patients, their families, medical professionals, and the general public should not be overlooked.

#### 4. CONCLUSION

The coronavirus disease (COVID-19) epidemic is a global public health emergency that poses a threat to psychological resilience. The existing studies have significant clinical ramifications, as well as implications for health policies aiming at preventing a wave of mental illness in the aftermath of the present pandemic. COVID-19

survivors should prioritize public health prevention, early detection, neurocognitive remediation, and treatment of mental symptoms, which may lead to an improvement in quality of life and daily functioning. According to the data, the COVID-19 pandemic has a significant negative influence on mental health, particularly in older persons with and without dementia. Viral infection, as well as the social isolation that follows in order to prevent it from spreading, has a variety of neuropsychiatric repercussions. To clarify such impacts and assess the long-term ramifications for the mental health of older persons, as well as explore alternative mitigating techniques, larger and more robustly designed research studies are needed.

#### CONSENT

It is not applicable.

#### ETHICAL APPROVAL

It is not applicable.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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