



# Scientia Psychiatrica

Journal Homepage: [www.scientiapsychiatrica.com](http://www.scientiapsychiatrica.com)

eISSN (Online): 2715-9736

## Delirium in Covid-19 Patients: Literature Review

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### ARTICLE INFO

#### Keywords:

COVID-19  
Delirium  
Pandemic  
Coronavirus

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All authors have reviewed and approved the final version of the manuscript.

<https://doi.org/10.37275/scipsy.v3i4.52>

### ABSTRACT

Many countries throughout the world have experienced an extraordinary health crisis as a result of the coronavirus-2 infection (SARS-CoV-2). The coronavirus 2019 (COVID-19) is particularly concerning in older adults, for whom multimorbidity and vulnerability that underpins the risk of negative consequences following the illness. Individuals who are diagnosed with the coronavirus disease 2019 have breathing and digestive issues. The SARS-CoV-2 virus has the potential to affect central nervous system (CNS) which results in delirium and respiratory failure. Delirium is a severe brain dysfunction that can be potentially lethal and is characterized by inattention and mental changes that are fluctuating.

### 1. Introduction

The pandemic of coronavirus disease 19 (COVID-19) marks the first appearance of the highly contagious severe coronavirus 2 (SARS-CoV-2), which has lately been linked to major worldwide morbidity and mortality.<sup>1</sup> The SARS-CoV-2 virus is a zoonotic virus that is related to the coronavirus that caused Middle East Respiration Syndrome (MERS) and the Acute Respiratory Syndrome (SARS). Through human-to-human transmission, the COVID-19 spreads fast, mostly through breathing droplets, direct touch and fomites.<sup>2</sup> Individuals diagnosed with the coronavirus disease 2019 [COVID-19], also known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus, mostly have respiratory and intestinal

symptoms. Although many coronaviruses may have neuroinvasive properties, SARS-CoV-2 may also be able to infiltrate the central nervous system and cause neurological symptoms due to its similar viral structure and infection pathways.<sup>3</sup>

The presence of neurologic symptoms in individuals with moderate or severe coronavirus disease-19 (COVID-19) is becoming more common, either at diagnosis or during the course of the disease.<sup>4</sup> Many COVID-19 patients which admitted to the hospital may develop delirium, and given early insights into the virus's pathobiology, which indicates brain stem invasion, and also especially in the intensive care unit (ICU), the emerging treatments

used to treat these severely sick individuals, management prevention of delirium may be done extremely difficult.<sup>5</sup>

Delirium is one of the most frequent acute illnesses in hospitals, affecting around 25% of elderly patients.<sup>6</sup> Delirium which described as a disruption of consciousness or cognitive function with abrupt start and variable course, is well acknowledged as one of the most common outcomes of hospitalization in the elderly, even outside of the setting of the COVID-19 epidemic.<sup>4</sup> ICU Delirium defined as an acute central nervous system (CNS) condition that occurs in critically sick individuals. When considering COVID-19, keep in mind that delirium might be a prodromal indication of hypoxia or infection, both of which can lead to serious respiratory failure.<sup>7</sup> The objective of this review would be to identify problems associated with the development of delirium throughout the COVID-19 epidemic.

### **Symptoms of COVID-19**

Coronavirus illness (COVID-19) poses a significant new danger to our healthcare system, notably to the health of the elderly. As the epidemic has spread rapidly throughout the world, it has become obvious that the elderly are the most vulnerable to serious illnesses and fatalities.<sup>8</sup> COVID-19 generally manifests as fever, myalgia, tiredness, and dyspnea, as well as less frequent symptoms such as vomiting, nausea, diarrhea, headache, and abdominal discomfort.<sup>2</sup>

Aside from respiratory failure, mental and neurological problems must be monitored during SARS-CoV-2 infection.<sup>7</sup> There are numerous reasons why the present COVID-19 pandemic might have mental implications. Several of these factors are related to the pandemic's broader societal impact and the government's reaction, which includes physical separation and quarantine.<sup>9</sup> In the hospital care of COVID-19, respiratory isolation and limits on family visits are typical practices. Despite their necessity, policies that restrict patients' access to caregivers and

providers may raise the risk of delirium and delay diagnosis.<sup>10</sup>

In addition to the usual COVID-19 presentation, acute Brain dysfunction manifested in delirium could be a sign of SARS-CoV2 virus' neuroinvasive potential.<sup>2</sup> In a study of 214 COVID-19 diagnosed patients conducted by Mao et al., neurological symptoms emerged in 45 percent of very sick patients, which several symptoms indicating change of consciousness.<sup>7</sup>

Previous research has found a link between COVID-19 neurological symptoms and disease severity. The majority of these studies either focused on impaired awareness or did not give a clear definition of delirium as their main exposure.<sup>10</sup>

### **SARS-CoV and nervous system**

Human coronaviruses are found to be neuroinvasive. SARS-CoV has been linked to myopathy, polyneuropathy, and major artery ischemic stroke, and postmortem investigations have shown SARS-CoV RNA in hypothalamic and cortical neurons.<sup>11</sup> SARS-CoV enters cells via the receptor known as angiotensin-converting enzyme 2 (ACE2) cellular receptor, which is found not only in type II pneumocytes and ciliated upper respiratory cells, which cause respiratory symptoms, as well as in the central nervous system (glial cells and neurons) and endothelial cells.<sup>3</sup> Massive storm of cytokine, damage of endothelial, hypoxemia, increased oxidative stress, and, most likely, direct infection of the Central Nervous System (CNS) by SARS-CoV-2 can promote the occurrence of encephalopathy, with delirious manifestations, particularly in elderly frail multimorbid subjects and those with a history of dementia.<sup>4</sup> Coronaviruses can induce direct brain injury after infecting the CNS by increasing demyelination, release of interleukin, and the permeability of the blood-brain barrier.<sup>10</sup>

## **Delirium in COVID-19**

Delirium in COVID-19 patients may be caused by direct invasion of CNS, activation of CNS inflammatory mediators, a subsequent impact of the failure of other organ system, an effect of sedative techniques, extended mechanical ventilation duration, or environmental variables such as social isolation.<sup>5</sup> The virus may enter the brain directly by intra-nasal access via olfactory neurons, which results an early symptom known as anosmia, or indirectly through breaching the blood-brain barrier via lymphatic dissemination or haematogenous.<sup>2</sup>

Delirium is seen as a "barometer" or "vital indicator" of serious disease in elderly people. As in case of COVID-19, older individuals frequently do not exhibit the usual febrile reaction, and many do not exhibit dyspnea even when hypoxia is present.<sup>8</sup> Early detection of delirium is essential in COVID-19 patients so it may be an early sign of increasing failure of respiratory, further failure of other organ, or viral transmission to the CNS, mediated by possible SARS-CoV2 neuroinvasive pathways.<sup>7</sup>

## **4. Discussion**

The etiology of COVID-19 delirium, as well as its long-term consequences, are most likely complex. Indirect causes such as hypoxia, pyrexia, metabolic abnormalities, dehydration, and medicines may all be important. Direct mechanisms, such as neuroinflammation and vascular damage, might potentially play a role.<sup>6</sup> Coronaviruses have been proven to be neuroinvasive, with the ability to infiltrate the central nervous system (CNS) via the olfactory nerve or even the blood circulation along neuronal pathways.<sup>10</sup>

Patients with proven and suspected infections may experience recurrent mental and neuropsychiatric symptoms for a variety of causes, including illness progression, bad medication reactions, social isolation, uncertainty, and physical discomfort.<sup>12</sup> SARS-CoV2 infection is usually accompanied with

COVID-19 delirium and/or neurological symptoms, resulting in prolonged sedation and mechanical ventilation and a significantly poorer prognosis.<sup>3</sup> Standard non-pharmacological approaches to treat or prevent delirium may be difficult in isolated conditions, and these circumstances may worsen delirium.<sup>5</sup>

## **5. Conclusion**

Delirium is an essential missing component when thinking about management and evaluation of patients with COVID-19. Delirium should be included as a presenting characteristic in guidelines, screening should be a standard of care, and non-pharmacological methods to delirium prevention and management should be used as early and frequently as feasible.<sup>8</sup> Neuroinflammatory pathways are known to have a role in the etiology of delirium, and they may hold the key to understanding delirium in the context of COVID-19<sup>10</sup> To offer persuasive evidence to patients, health-care providers, and policymakers, it is critical to gather continually updated data. Clinicians treating patients with COVID-19 must be aware of the potential of delirium and trained in how to treat it effectively.

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