

The association of COVID-19 and catatonia in the ICU-recognition, management, and the role of electroconvulsive therapy

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ABSTRACT

Background: Catatonia has been an established neuropsychiatric syndrome for decades. It has been reported to occur in approximately 10% of patients with acute psychiatric illness. There are not many current data depicting a definite association between COVID-19 and catatonia, especially in the intensive care unit (ICU), and more research is needed in this area. Although a variety of neuropsychiatric manifestations have been reported, to our knowledge COVID-19 has a limited association thus far with catatonia. With the increased prevalence of psychiatric illness during the pandemic, it is hypothesized that catatonia will also have increased rates moving forward. We aim to review the association between COVID-19 and catatonia.

Methods: A thorough literature review was conducted focusing on studies which reported any association or non-association between COVID-19 and catatonia. It is our hypothesis that with an increase prevalence in mental health pathology, there has been a simultaneous increase in cases of catatonia.

Conclusion: Catatonia can be a life-threatening syndrome which can complicate management of various psychiatric as well as medical conditions. Hence, it is critical to evaluate and address the association between catatonia and COVID-19, which continues to impact communities and burden healthcare systems worldwide. Early recognition and interventions with life-saving procedures, such as electroconvulsive therapy, are necessary to reduce the long-term impact of catatonia.

Keywords: Catatonia, COVID-19, neuropsychiatric syndrome, pandemic, electroconvulsive therapy

BACKGROUND

COVID-19 AND CATATONIA - THE ASSOCIATION

Globally, governments and health care professionals are alarmingly aware of the physical effects and clinical presentation of coronavirus disease 2019 (COVID-19) and are taking preventive measures to keep citizens safe. The SARS-CoV-2 pandemic has had a serious impact on the mental states of individuals despite adequate social and physical restrictions. The

introduction of the omicron variant has further limited any progress made in the management of this disease.

Psychiatric manifestations like delirium are not unique to the current pandemic and were also noted in previous outbreaks of the Coronaviridae family, such as SARS and MERS (Middle Eastern Respiratory Syndrome), both during the acute infectious phase and after a variable period following the viral infection.¹ The studies conducted in the past have reported increased levels of antibodies against human coronavirus strains in patients presenting with psychotic symptoms as compared to non-psychotic controls.² Although depression, anxiety, and trauma are commonly observed in patients during the COVID-19 pandemic, catatonia is an infrequently observed neuropsychiatric finding in many cases, independent of past psychiatric history.³

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Catatonia is a psychomotor syndrome characterized by prominent motor, behavioral, and affective abnormalities. It is attributed not only to psychiatric conditions, such as depression and schizophrenia, but also occurs secondary to general medical conditions or toxic syndromes.⁴ Up to 20% of catatonia is caused by medical illness, and it has also been associated with other viral pandemics in the 19th and 20th centuries.⁵ Encephalitis lethargica, characterized by profound lethargy and abnormal movements, was used to describe catatonic symptoms that followed infection with influenza in the pandemic of 1918.⁶ Also, there is a recent refocus on the overlap of delirium and catatonia in medically ill populations, and evidence suggests that up to a third of critically ill patients meet the criteria for both delirium and catatonia, especially in intensive care units.⁷ This has led to an increase in psychiatric consultations to the ICU to evaluate and manage catatonia.

CATATONIA IN PATIENTS WITH COVID-19- A BIOPSYCHOSOCIAL PATHOGENESIS

Given the lack of robust observational data on COVID-19 associated catatonia, there is significant debate about its pathogenesis. It is unclear if these symptoms are attributable to viral infections or to the host response. There are various proposed pathophysiologic mechanisms, including direct CNS invasion of the virus, neuroinflammation secondary to systemic immune response, and hypoxic brain damage. The virus may enter the central nervous system from the nares through the cribriform plate or via hematogenous spread across the blood-brain barrier. The neurotropism of SARS-CoV-2 is theoretically conferred by the binding of glycoproteins on its surface to the angiotensin-converting enzyme 2, which is present in neurological tissue.^{8,9} Moreover, the changes in GABA-ergic and dopaminergic tracts in the cortico-basal-ganglia are also implicated in the causation of catatonia in COVID-19 patients.¹⁰ It is hypothesized that brainstem involvement of the virus may partially contribute to the acute respiratory failure of patients infected with COVID-19, but suspicion arises only after the neuropsychiatric manifestations are reported.¹¹

Furthermore, it is reported that the triggering effect of the pandemic crisis and the prevailing worldwide

uncertainty led to an increased incidence of psychiatric disorders. In addition, the limited access to mental health care in these psychiatric patients owing to lockdown constraints added to the increasing diagnosis of catatonia.

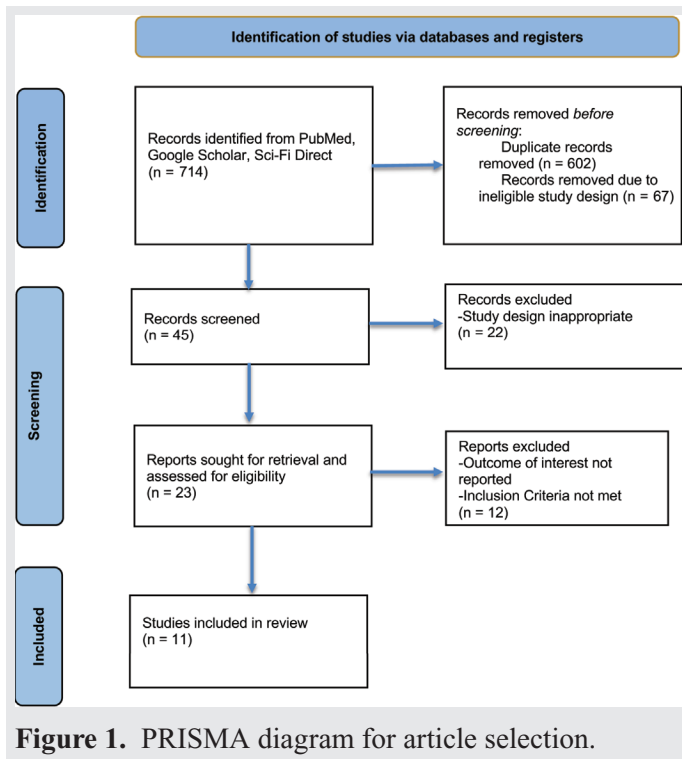
To date, there is significant information supporting an association between SARS-CoV-2 infections and neuropsychiatric complications.¹² However, detailed accounts of catatonic symptoms in COVID-19 disease are largely missing from the literature. In this present review, cases presenting with symptoms of anxiety, insomnia, and eventually catatonia are discussed.

METHODS

The authors conducted an extensive literature review to search for an association between COVID-19 and catatonia using the keywords “Catatonia,” “COVID-19,” and “Pandemic” on PubMed, Google Scholar, and ScienceDirect. Studies conducted on human species and published in the English language were included. The latest PRISMA guidelines were followed while screening and selecting the relevant articles for this review. The type of articles included in the final review included case reports, systemic reviews, case-control studies, and observational studies. The exclusion criteria were applied to unpublished articles, chapters from books, letters from editors, and commentaries. We also excluded articles that were duplicates and did not meet the outcome of interest. This process is displayed in a PRISMA diagram (Figure 1).

DISCUSSION

The global pandemic of SARS-CoV-2 is primarily known to involve the respiratory system; however, multiple cases have presented with various neuropsychological syndromes. Post infectious neuropsychiatric symptoms, including psychosis, delusions, catatonia, and affective disorders, have been reported since the 19th century.¹³ The association is especially strong for respiratory viruses, such as influenza, and is now reported in patients diagnosed with COVID-19 associated pneumonia.¹³ Although a variety of neuropsychiatric manifestations have been reported, COVID-19 association with catatonia is not yet fully established.



Gouse et al. first reported a correlation between the development of catatonic symptoms in COVID-19 patients and the concordant rise in serum pro-inflammatory markers.¹⁴ In general, there is also a co-occurrence of catatonic symptoms with non-viral inflammatory or autoimmune conditions and with biochemical inflammatory markers in the neuroleptic malignant syndrome.

Although most of the COVID-19 associated catatonic symptoms were observed in patients with underlying psychiatric disorders, there have been reports of this association even in the absence of any significant psychiatric history.¹⁵ Sarli et al. reported the case of a 59-year-old man with no prior psychiatric history who developed catatonia and showed severe depressive symptoms after experiencing financial struggles and quarantine isolation during the pandemic and nationwide lockdown.¹⁶ The timing of the neuropsychiatric manifestations is known to present at different intervals during the viral illness. In some cases, psychiatric symptoms were present during the acute phase of the illness, while in others, features of catatonia were reported weeks to months following recovery from illness.¹⁷ Zain et al. discussed a case

of delayed-onset psychosis two months following COVID-19 infection in a patient with no history of any psychiatric illness.¹⁷ The patient initially presented with agitation and aggressive behavior, gradually progressing to rigidity, echolalia, and loose associations during her course of hospitalization. Later, the family reported the presence of respiratory symptoms two months prior to her current hospitalization, confirmed as a COVID-19 infection with serum IgG levels. This suggests that the association between the illness and catatonia may not be recognized until late in the course of the infection.

MANAGEMENT OF COVID-19 ASSOCIATED CATATONIA AND THE CONTROVERSY SURROUNDING BENZODIAZEPINES

A significant problem in treating catatonic patients infected with COVID-19 has been weighing the pros and cons of administering benzodiazepines, since benzodiazepines can worsen the respiratory function in an already critically ill patient secondary to COVID-19 infection. However, benzodiazepines have been one of the most effective available treatments for catatonia. Patients admitted to the ICU and undergoing mechanical ventilation have compromised respiratory function that predisposes them to respiratory suppression secondary to benzodiazepine use. Kwon et al. reported a case of a middle-aged woman with a history of bipolar and schizoaffective disorder who died of massive pulmonary embolism secondary to catatonic immobility. Since the patient was hospitalized for COVID-19, the decision was made to delay the lorazepam challenge due to the potential risk of worsening lung function and developing hypoxemic respiratory failure. Although it is difficult to be certain, if proper diagnosis and treatment had been started earlier, it is possible her terminal event of the pulmonary embolism might have been avoided.¹⁸ Furthermore, the concurrent existence of delirium in hospitalized patients also limits the use of benzodiazepines in those cases since these drugs can lead to paradoxical agitation.¹⁹

SHOULD ECT BE MORE WIDELY AVAILABLE?

Since benzodiazepines is associated with decreased risk auditory dry and can contribute to the development of delirium, electroconvulsive therapy (ECT) is

alternative treatment consideration in patients with catatonia coexisting with COVID-19.²⁰ Electroconvulsive therapy has a particularly robust effect in both adults and children for the treatment of catatonia in patients with autism or intellectual disability and can be safely administered to the medically ill patients with minimal to no contraindications.²¹ The use of maintenance of ECT (M-ECT), defined as ECT continued beyond the index course, is often necessary and safe and may prevent relapse in catatonia, which can be associated with severe sequelae, such as hyperthermia, autonomic instability, electrolyte imbalances, and death.^{22,23} However, the fluctuations in the medical condition of the patient during the course of the viral disease often hinders the timely initiation and spacing of ECT sessions. With the emergence of COVID-19, however, this already under-identified condition and a poorly served patient group may have become further marginalized due to institutional regulations limiting access to ECT. During the pandemic, isolation requirements, procedure limitations, need to reduce non-emergent procedures, and the risk of aerosolization related to ECT have limited access to this effective and potentially lifesaving procedure. Despite these challenges, neuropsychiatric symptoms observed in infectious diseases emphasize the need for ECT to remain a non-elective procedure during future global pandemics.²⁴

THE ROLE OF AMANTADINE AND MEMANTINE

Amantadine, a drug that blocks viral replication at earlier stages and is used for the treatment of influenza, has also been proposed to be effective in the treatment of COVID-19. Moreover, amantadine has been approved as a corrective medication for involuntary movement disorders, like neuroleptism and Parkinson's disease. Since benzodiazepines would be relatively contraindicated due to respiratory suppression, and electroconvulsive therapy can aerosolize virus particles, other safer alternatives like amantadine and memantine could be used for treating catatonia in patients with COVID-19 pneumonia.²⁵ Also, these drugs do not have any deleterious effects on co-existing delirium.

Separate from the COVID-19 infection, the inadvertent usage of high dose corticosteroids for treating patients has added to the psychiatric manifestations

of the disease.²⁶ Moreover, hyponatremia has also developed in COVID-19 infections and could contribute to the development of psychotic symptoms. Coexisting electrolyte abnormalities in patients with COVID-19 has led to misdiagnosis of catatonia.²⁷

In many cases, catatonia is recognized after it is too late and serious sequelae have occurred; these include dehydration, aspiration, pressure ulcers, pulmonary emboli, and progression to malignant features. One of the most dangerous consequences may be iatrogenic; this occurs when clinicians prescribe dopamine antagonists and inadvertently provoke the malignant form of catatonia known as the neuroleptic malignant syndrome.²⁸

CONCLUSIONS

The COVID-19 pandemic has had a significant impact on psychological and physical health. The association of COVID-19 and catatonia has been highlighted in numerous studies but requires more research. Catatonia superimposed on COVID-19 infection can be debilitating and possibly pose a threat to meaningful long-term recovery. Lessons learnt from the pandemic in the treatment of this association include the need for early diagnosis and intervention and possibly easier access to well-established neuromodulation techniques, such as ECT.

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