REVIEW ARTICLE
COVID-19 INDUCED CATATONIA: A REVIEW OF THIS RARE PHENOMENON

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Background: Catatonia is a psychomotor syndrome characterized by numerous clinical features, a few being stupors which is the most common sign, posturing, forced grasping, echopraxia, etc. There have been cases documented in the literature of Catatonia occurring with COVID-19. This article will focus on the complete and brief overview of catatonia observed in patients with COVID-19 infection. Methods: We outline the evidence of the pathophysiology of COVID-19 in the CNS system, the effect of the virus in inducing catatonia, and its outcome. The literature used in the article is mostly case reports from different parts of the world thus; we have generalized our review taking into consideration multiple factors. Results: In patients with COVID-19, neuropsychiatric manifestations are very commonly appreciated. Catatonia has been documented in many patients along with respiratory symptoms such as fever, shortness of breath, and cough. There are multiple etiologies associated with this presentation which have been discussed in detail in this article. In many patients, there was no history of any psychiatric illness. The timing of presenting with catatonic features was also different for different individuals. Conclusion: COVID-19 has been believed to contribute to the presentation of catatonia. There is no specific timeline between the onset of symptoms and the presence of COVID-19 infection. However, coronavirus can be responsible in a few ways for inducing catatonia in patients with or without any previous psychiatric illness. Therefore, COVID-19 should be considered as one of the major factors in this complex psychiatric disease, catatonia.

Keywords: COVID-19; Catatonia; Encephalitis; Benzodiazepine.

INTRODUCTION
Catatonia is a psychomotor syndrome characterized by numerous clinical features, a few being stupors which is the most common sign, posturing, forced grasping, echopraxia, etc. Catatonia can be further classified into two types, retarded and excited catatonia. While retarded catatonia affects mobility, excited catatonia is characterized by severe psychomotor agitation presenting with life-threatening complications like hyperthermia and autonomic dysfunction. Owing to its rapid and lethal presentation, exciting catatonia is also known as malignant or lethal catatonia.1,2

COVID-19 was identified in December 2019 in Wuhan, China and soon was declared to be a pandemic that is still challenging the world in many different ways. It is caused by the virus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and noted to spread from person to person. COVID-19 can present with a wide range of symptoms like fever, chills, shortness of breath, loss of taste and smell and can also progress to respiratory failure, multi-organ dysfunction, and death.3

There have been cases reports and case series documented in the literature of Catatonia occurring with COVID-19.4–6 This article aims at a detailed review of the catatonia induced by COVID-19 in affected patients, the course of the disease, and its potential outcome.

Pathogenesis:
As per recent studies, the SARS-Cov-2 virus is transmitted in humans via droplets of respiratory particles.7 On contact with the viral microbe, the virus gains entry into the lungs and attaches itself to the angiotensin-converting enzyme 2 (ACE2) receptors with the help of the S glycoprotein exhibited by the virus. The aids in the process of viral entry into the cells and dissemination of the disease.8 Even though the exact mechanism remains unclear a similar kind of mechanism is believed to be involved for catatonia induced by COVID-19. The ACE 2 expressed by the endothelium of the brain capillaries interact with the virus passage of COVID-19 into the brain by crossing the blood-brain barrier or direct spread through the ethmoid bone. The stagnant nature of the blood flow in the brain circulation may have also known to promote the above process further.9,10
Another proposed mechanism includes the involvement of Gamma-aminobutyric acid (GABA) and Dopamine pathways.\textsuperscript{11,12}

The cytokine storm induced by the COVID-19 infection leads to the release of proinflammatory cytokines. These proinflammatory cytokines once in the circulation significantly disrupts the GABA signals in the basal ganglia.\textsuperscript{13}

Moreover, the hypodopaminergic condition in the basal ganglia has been linked to correlation with the inflammatory mediators like interferon-alpha which can precipitate the manifestations of catatonia.\textsuperscript{14}

Although the above-mentioned mechanism is considered to be the potential mechanism behind COVID-19 inducing catatonia, further research is anticipated to interpret a more basic mechanism.

**Clinical Manifestation:**
Catatonia in general can present in retarded or exciting forms. While excited catatonia can manifest with severe psychomotor excitement, the retarded type as per the name demonstrates slowing of activity which can be demonstrated as mutism, staring, immobility, rigidity, and posture changes.\textsuperscript{1}

Previously documented literature hypothesizes that the ongoing inflammatory process and the anxiety may contribute to catatonia in the patients with COVID-19. Few cases documented and reported in the literature which presented mainly with anxiety and later progressed into catatonia.\textsuperscript{15–20}

Many of the patients had a significant history of psychiatric illness which may point towards the certainty that catatonia may be induced in patients with COVID-19 mainly due to the psychological component.\textsuperscript{21}

Patients have demonstrated different ranges of presenting symptoms. In some patients with COVID-19, there has been a progression of respiratory symptoms into neurological symptoms demonstrating signs of catatonia.\textsuperscript{22}

The cytokine surge and inflammatory response in patients with COVID-19 have also contributed to catatonia irrespective of any previous psychiatric history. Whereas in others, signs of catatonia developed after one to two months of recovering from COVID-19 infection.\textsuperscript{23} A delayed presentation of autoimmune encephalitis and malignant catatonia was noticed among few patients after recovery.\textsuperscript{24}

**Diagnosis and Treatment:**
Though the diagnosis of COVID-19 is based on RT-PCR and IgG antibodies, catatonia is diagnosed based on clinical manifestations and the resolution of symptoms on the administration of benzodiazepines, which remains the mainstay of the treatment for catatonia to date. Electro-convulsant therapy (ECT) is considered in patients who do not respond or have minimal response to benzodiazepines.\textsuperscript{25}

If a patient is presenting with simultaneous encephalitis, it is necessary to perform imaging, CSF studies, and EEG which shows slowing of the cerebral hemisphere and no seizure activity. In such cases, early intervention with high-dose steroids and plasmapheresis has shown rapid improvement.\textsuperscript{24}

**CONCLUSION**
Even though the pandemic is still affecting many parts of the world, it can be even more challenging for patients with psychiatric disorders. In a nutshell, this article highlights that catatonia has been documented in the vast majority of people irrespective of their psychiatric history and COVID-19 is also believed to be one of the contributing factors affecting multiple pathogeneses. The onset of catatonia however was different for different individuals. In some, it presented in conjunction with the respiratory symptoms, while in a few it was a late presentation. Patients can manifest with life-threatening excited catatonia or retarded catatonia.

Few have also presented with encephalopathies. The treatment, however, varied for different people. Benzodiazepines are the mainstay treatment in these patients but there have been reports of patients recovering without any medical intervention as well. Although we appreciate the efforts put into various reports and studies contributing to this topic, our idea behind this letter is to give a brief idea and an overall picture by compilation of various data available for the convenience of physicians, students, and readers. We present a concise and complete idea of our approach towards Covid-19 induced catatonia.

**REFERENCES**

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