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Overview of COVID-19 Infection Manifestation in Neuropsychiatry Aspect

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A B S T R A C T

At the end of 2019, the coronavirus infection pandemic shocked the world. This virus began with reports of infections in the Wuhan area, China. The death rate from COVID-19 infection can reach 3%; however, the mortality rate in critically ill patients with COVID-19 infection is much higher, reaching 61.5%. This study was aimed to summarize the neuropsychiatric impact and neuropathological mechanisms of COVID-19 infection. The primary manifestation of COVID-19 infection is respiratory tract infection. Coronavirus can penetrate the central nervous system and cerebrospinal fluid in less than a week. Histopathological examination of the brain of the deceased COVID-19-19 showed the potential for SARS-CoV-2 to infect the central nervous system (CNS). Neuroinflammation can also damage blood brain barrier. Several patients treated with COVID-19-19 infection exhibited confusion and agitation without respiratory symptoms or other signs of infection. The COVID-19 pandemic not only directly impacts infected individuals but has also caused a new wave of psychological stress in society.

1. Introduction

At the end of 2019, the coronavirus infection pandemic shocked the world. This virus began with reports of infections in Wuhan, China.[1,2] This coronavirus infection has a genome similarity of 75-80% with SARS-CoV-1 and 50% with MERS-Cov, so this virus is called SARS-CoV-2. In addition, SARS-CoV-1 uses the same receptors as SARS-CoV-2 when it enters the human body (angiotensin-converting enzyme-2). Differentiated with MERS-CoV virus enters via dipeptidyl peptidase4 (DP4).[3,4]

The death rate from COVID-19 infection can reach 3%; however, the mortality rate in critically ill patients with COVID-19 infection is much higher, reaching 61.5%. Individuals infected with COVID-19 range from no symptoms to severe manifestations such as severe pneumonia and acute respiratory distress syndrome (ARDS), which can cause death. The primary manifestation of COVID-19 infection is respiratory tract infection. This is related to transmission. COVID-19 is a respiratory infection that is transmitted mainly through respiratory droplets. The main transmission routes are close contact with people with the virus, especially when coughing, sneezing, and medical interventions in the respiratory tract, such as intubation, tracheobronchial aspiration, and mechanical ventilation. The SARS-CoV-2 molecule has been isolated from the blood, saliva, tears, conjunctival fluid, and feces of patients, so there is a possibility of transmission of infection by this route as well.[5]

The initial symptoms of COVID-19 infection in the respiratory tract are influenza, with fever, cough, dyspnea, and malaise/myalgia.[6,7] However, it is now known that COVID-19 infection can also involve other organs, including gastrointestinal symptoms, multiorgan failure (liver, kidney, heart), and neurological manifestations. There are increasing reports of neurological and neuropsychiatric symptoms. The symptoms may be non-specific, such as: as a somatoform disorder including muscle pain, dizziness, headache, anxiety, sleep disturbances, depression, fatigue, anger/stress, loneliness, stigmatization; or specific central nervous system (CNS) disorders, including stroke, seizures, encephalitis, ataxia, and myelitis; peripheral nervous system (PNS) disorders including loss of smell and taste (anosmia/hyposmia and ageusia/dysgeusia), Guillain-Barre syndrome and Miller Fisher syndrome; or psychiatric and neuropsychiatric disorders including major depressive disorder, bipolar, obsessive-compulsive disorder, and posttraumatic stress disorder. This study aimed to summarize the neuropsychiatric impact and neuropathological mechanisms of COVID-19 infection.

Neuropathology in COVID-19 infection

A study showed that SARS CoV-2 remained in aerosol for up to 3 hours. The infection period may begin shortly before the onset of symptoms and last 7-12 days in moderate conditions and up to two weeks in severe cases of COVID-19. First, the virus enters the host cell, replicates, accumulates, and is released extracellularly to the target cell. This directly causes damage and destruction of parenchymal cells, such as alveolar epithelial cells. At the same time, many pathogen-associated molecular patterns (PAMP) and damage-associated molecular pattern (DAMP) molecules are released to stimulate the innate immune response, induce inflammatory cell infiltration, and release many cytokines, chemokines, proteases, and free radicals causing acute respiratory disorder and sepsis.[8,9]

Many reports indicate the neuroinvasive potential of infection with the SARS-CoV-2.[9-11] Coronavirus can penetrate the central nervous system and cerebrospinal fluid in less than a week. Histopathological examination of the brain of the deceased COVID-19 showed the potential for SARS-CoV-2 to infect the central nervous system (CNS). Neuro-inflammation can also damage the blood-brain barrier.

SARS-CoV infection is also associated with ischemic stroke, polyneuropathy, and myopathy. The presence of symptoms of anosmia and ageusia as early symptoms of SARS-CoV-2 infection indicates the presence of symptoms of early invasion of the virus into the olfactory bulb. Experiments in mice have shown that SARS-CoV may enter the brain via the olfactory bulb and then spread to certain other parts of the brain, such as the thalamus and brainstem.[12]

Viruses can also enter the brain by infecting the endothelial cells that line the brain's blood vessels. The results of electron microscopy analysis of the frontal lobe identified SARS-CoV-2 virus particles in the endothelium and found transit of the virus to the neuropil. SARS-Cov-2 can enter the CNS using the perivascular space of the glymphatic system. Similarly, sensory fibers from the vagus nerve, which innervate the respiratory tract, may be present with other invasions.[13]

In studies conducted on patients infected with COVID-19, more than one-third showed neurologic symptoms in the acute phase of the disease, and about 34% showed brain abnormalities such as white matter hyperintensity and hypodensity micro bleeding, hemorrhage, and infarction.[13,14] Further evidence of SARS-CoV-2 neuro infection, edema, and neuronal degeneration was reported in post-mortem brain samples. A study showed that genome sequencing evaluation confirmed the presence of the virus in the cerebrospinal fluid. However, histopathological findings from autopsies of 18 consecutive patients with SARS infection -CoV-2 who died in a teaching hospital between April 14th and April 29th, 2020, showed hypoxic changes and did not

exhibit encephalitis or other virus-specific brain changes.[1,14]

Several mechanisms have tried to explain how the Sars cov 2 virus can affect the brain, including the host's response to infection. The occurrence of an exaggerated immune response is known as a cytokine storm. When a cytokine storm occurs, there will be excessive production of cytokines causing acute respiratory distress syndrome (ARDS) and multiple organ dysfunction syndrome (MODS), which leads to several diseases, especially from the CNS. Furthermore, evidence of neuroinflammation, both peripheral and central, was found. The effects of elevated cytokine levels affect not only inflammation and lung infection but also on the development of mental illness.[15]

However, research on this in neuro-immunological processes is lacking, as well as in psychiatric conditions such as mood and anxiety disorders. SARS-CoV-2 infection involves the carboxypeptidase, ACE-2, as a receptor for entry into alveolar epithelial cells. Downregulation of ACE-2 expression may not only play an essential role in the pathogenesis of SARS-CoV-2 but may provide an association between SARS-CoV-2-induced susceptibility to stress conditions. Indeed, the downregulation of ACE-2 expression in mice has increased sympathetic activity and decreased tryptophan uptake. This may decrease brain 5-hydroxytryptamine (5-HT; serotonin) levels, thereby increasing susceptibility to stressful conditions. In addition, hypothalamic ACE-2 receptors suppress anxiety-related behaviors and the synthesis of corticotrophin-releasing hormone (CRH), an important hormone involved in physiological stress responses.[12,13]

Therefore, the expression of ACE-2 in various human tissues, including the brain, suggests that brain infection from SARS-CoV-2 can result in profound central nervous system (CNS) symptoms, leading to these individuals experiencing psychiatric disorders, disease progression, in addition to aggravating the inflammatory immune effects associated with SARS-CoV-2 infection. So far, recent meta-analyses have supported the continuation of ACE-modulating drugs in SARS-CoV-2 positive patients.[9]

Neuropsychiatric manifestations of COVID-19

Several studies reported a high incidence of acute psychiatric symptoms in COVID-19 patients; about 35% showed symptoms of anxiety and depression.[13-15] Studies conducted on patients with SARS-CoV-2 showed higher manifestations of symptoms of depression, anxiety, and post-traumatic stress disorder (PTSD) when compared to non-COVID-19 controls. Several admitted patients exhibited confusion and agitation without any respiratory symptoms or other signs of infection.

The most commonly reported psychiatric deficits are depression and anxiety. Anxiety and depression were highest in patients recovering from severe COVID-19 and found a correlation between length of stay and levels of depression/anxiety. Previous psychiatric history and female gender were predictors of depression and anxiety. Symptoms of depression and anxiety normalized at one month of follow-up but were predictors of PTSD lasting longer, persistent depressive symptoms at three months of follow-up. Post-traumatic stress disorder (PTSD) can occur in approximately 6.5% to 42.8%. Men are considered more at risk of developing PTSD. Previous psychiatric history or past traumatic events increases the risk of PTSD, and symptoms of depression and anxiety during COVID-19 are predictors of PTSD. Some PTSD improved after treatment follow-up after 1-3 months, and other studies stated PTSD symptoms persisted after 3-month follow-up treatment.[14]

Therefore, it is imperative to determine the effect of psychological stress on the general population and individuals with COVID-19 and whether psychological stress has a biological component that may be relevant to the pathophysiological changes associated with SARS-CoV-2 infection. In addition to being at risk of causing neuropsychiatric symptoms, patients post-COVID-19 infection are at risk for

cognitive disorders whose incidence increases with increasing age of patients infected with COVID-19.[12]

The COVID-19 infection has also created many new psychosocial problems for children. Children are vulnerable to COVID-19 infection, but beyond that, children are also victims due to the restrictions on activities that occur during the COVID-19 pandemic. Children are prohibited from doing activities outside, including going to school. School closures result in changes in sleeping and eating patterns, making activities monotonous. Children are a group that is vulnerable to violence and child abuse.

2. Conclusion

The psychosocial effects of COVID-19 lay the groundwork for an unprecedented increase in the prevalence of psychiatric disorders, which could accelerate the development of many other comorbidities.

3. References

1. Tripathy S, Singh N, Singh A, Kar SK. COVID-19 and psychotic symptoms: The view from psychiatric immunology. Curr. Behav. Neurosci. Rep. 2021; 8: 172–8.
2. Robles R, Rodríguez E, Vega-Ramírez H, Álvarez-Icaza D, Madrigal E. Mental health problems among healthcare workers involved with the COVID-19 outbreak. Rev Bras Psiquiatr. 2021; 43: 494–503.
3. Desai S, Sheikh B, Belzie L. New-Onset Psychosis Following COVID-19 Infection. Cureus. 2021; 13: e17904.
4. Lam MH-B, Wing Y-K, Yu MWM, Leung C-M, Ma RCW. Mental morbidities and chronic fatigue in severe acute respiratory syndrome survivors: Long-term follow-up: Long-term follow-up. Arch. Intern. Med. 2009; 169: 2142–7.
5. Troyer EA, Kohn JN, Hong S. Are we facing a crashing wave of neuropsychiatric sequelae of COVID-19? Neuropsychiatric symptoms and potential immunologic mechanisms. Brain Behav. Immun. 2020; 87: 34–9.
6. Chacko M, Job A, Caston FIII, George P, Yacoub A, Cáceda R. COVID-19-Induced Psychosis and Suicidal Behavior: Case Report. SN Compr. Clin. Med. 2020; 2: 2391–5.
7. Banerjee D, Viswanath B. Neuropsychiatric manifestations of COVID-19 and possible pathogenic mechanisms: Insights from other coronaviruses. Asian J Psychiatry. 2020; 54: 102350
8. Pearce L, Davidson SM, Yellon DM. The cytokine storm of COVID-19: A spotlight on prevention and protection. Expert Opin Ther Targets. 2020; 24: 723–30.
9. Zhou F, Yu T, Du R, Fan G, Liu Y. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet. 2020; 395: 1054–62.
10. Isung J, Aeinehband S, Mobarrez F, Nordström P, Runeson B. High interleukin-6 and impulsivity: Determining the role of endophenotypes in attempted suicide. Transl Psychiatry. 2014; 4: e470.
11. Vega-Fernández JA, Suclupe-Campos DO, Aguilar-Gamboa FR. Neurological damage in SARS-CoV-2 infections. J Fac Hum Med. 2021; 21: 387–98.
12. Steardo LJr, Steardo L, Verkhratsky A. Psychiatric face of COVID-19. Transl Psychiatry. 2020; 10: 261.
13. Fiorillo A, Gorwood P. The consequences of the COVID-19 pandemic on mental health and implications for clinical practice. Eur Psychiatry. 2020; 63: e32.
14. Wilson JE, Mart MF, Cunningham C, Shehabi Y, Girard TD. Delirium. Nat Rev Dis. Primers. 2020; 6: 90.

15. Iqbal Y, Alabdulla M, Latoo J, Kumar R, Albrahim S. Mania and hypomania associated with COVID-19: A series of 15 cases seen by the consultation-liaison psychiatry service in Qatar. Qatar Med J. 2021; 2021: 65.