Overview of Covid-19 Infection Manifestation in Neuropsychiatry Aspect

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ABSTRACT

At the end of 2019 the world was shocked by the corona virus infection pandemic. 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 infection is much higher, reaching 61.5%. The main manifestation of covid infection is respiratory tract infection. Corona virus can penetrate 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 BBB (Blood Brain Barrier). A number of patients treated with Covid 19 infection exhibited symptoms of confusion and agitation in the absence of respiratory symptoms or other signs of infection. A recent survey in China showed that 35% of respondents reported psychological distress while 53.8% rated the psychological impact of the pandemic as moderate or severe. The existence of the Covid pandemic not only has a direct impact on infected individuals but has also caused a new wave of psychological stress in society. This study attempts to summarize the neuropsychiatric impact and neuropathological mechanisms of Covid 19 infection.

Introduction

At the end of 2019 the world was shocked by the corona virus infection pandemic. This virus began with reports of infections in the Wuhan area, China. This corona virus occurred in early 2019 so it was named the corona virus disease 19 (Covid 19). This corona virus infection has a genome similarity of 75-80% with Sars Cov 1 and 50% with Mers Cov so that this virus is called Sars-CoV 2. In addition, Sars Cov uses the same receptors as SARS Cov 2 when it enters the human body (angiotensin-converting enzyme 2/ACE2). Differentiated with MERS-CoV virus enters via dipeptidyl peptidase4 (DP4).

The death rate from COVID-19 infection can reach 3%; however, the mortality rate in critically ill patients with Covid infection is much higher, reaching 61.5%. Individuals infected with Covid range from no symptoms to severe manifestations in the form of severe pneumonia and acute respiratory distress syndrome (ARDS) which can cause death. The main manifestation of covid 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 routes of transmission are close contact with people who have 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.

The initial symptoms of COVID-19 infection in the respiratory tract are influenza, with fever, cough, dyspnea, and malaise/myalgia. 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.4

**Method**

The research method used in this journal is a journal review the researcher searched for studies published between 1st January 2016 and 1st August 2021, using the following database: PubMed. The following keywords were applied in the database during the literature search: “Neuropathology” OR “neuropsychiatric” AND “Covid 19”. The research was limited to human studies published in the English language. The researcher then reviewed articles by combining the obtained journals.

**Neuropathology in Covid-19 infection**

An experiment showed that SARS CoV-2 remained in aerosol for up to 3 hours. The period of infection 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. (2) First, the virus enters the host cell, where it replicates, accumulates and is released extracellularly to the target cell, and this directly causes damage and destruction of parenchymal cells such as alveolar epithelial cells. At the same time, a large number of molecular pattern-associated pathogens (PAMP) and molecular pattern-associated damage (DAMP) molecules are released to stimulate the innate immune response, induce inflammatory cell infiltration, release a large number of cytokines, chemokines, proteases and free radicals, causing ARDS, sepsis and MODS.1

Many reports indicate the neuroinvasive potential of infection with the SARS-CoV-2. Corona virus can penetrate the CNS (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 BBB (Blood Brain Barrier).5

Sars Cov infection is also associated with ischemic stroke, polyneuropathy and myopathy. The presence of symptoms of anosmia and agueusia as early symptoms of Sars Cov 2 infection indicates the presence of symptoms of early invasion of 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.3

Viruses can also enter the brain by infecting the endothelial cells that line the blood vessels of the brain. 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 lymphatic system. Furthermore, the virus can invade the brain via other nerves, such as the trigeminal nerve, which projects nociceptive terminals into the nasal cavity. Similarly, sensory fibers from the vagus nerve, which innervate the respiratory tract, may be present with other infections.6

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 as well as microbleeding, hemorrhage and infarction.7 Further evidence of SARS-CoV-2 neuroinfection, edema and neuronal degeneration were reported in post-mortem brain samples, while in the case of encephalitis genome sequencing 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 14 and April 29, 2020 showed hypoxic changes and did not exhibit encephalitis or other virus-specific brain changes.8
Several mechanisms have tried to explain how the Sars cov 2 virus can affect the brain, including the host response to infection. The occurrence of an exaggerated immune response 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 lead to a number of diseases. Other complications, 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.

The renin-angiotensin system (RAS) plays an important role although 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 important role in the pathogenesis of SARS-CoV-2 but may provide an association between SARS-CoV-2-induced susceptibility to stress conditions. Indeed, downregulation of ACE-2 expression in mice has been shown to increase sympathetic activity and decrease tryptophan uptake which may lead to decreased 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 corticotropin-releasing hormone (CRH), an important hormone involved in physiological stress responses.

Therefore, the expression of ACE-2 in various human tissues including the brain, suggests that brain infection from SARS-CoV-2 can result in serious central nervous system (CNS) symptoms, leading to these individuals experiencing psychiatric disorders. Disease progression, in addition to aggravating the immune inflammatory 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, with Song and colleagues suggesting that blocking the CNS of the ACE-2 receptor with antibodies prevents neuroinfection.

**Neuropsychiatric manifestations of Covid-19**

Several studies reported a high incidence of acute psychiatric symptoms in Covid-19 patients, there were about 35% of patients showing symptoms of anxiety and depression. 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 controls. A number of admitted patients exhibited symptoms of confusion and agitation without any respiratory symptoms or other signs of infection.

The most commonly reported psychiatric deficits are depression and/or anxiety. That anxiety and/or 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 3 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. Presence of a previous psychiatric history or past traumatic event 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.

A recent survey in China showed that 35% of respondents reported psychological distress while 53.8% rated the psychological impact of the pandemic as moderate or severe. Therefore, it is very important to determine the effect of psychological stress on the general population as well as individuals with COVID-19 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. Short-term memory deficits, generalized memory loss, specific impairments in attention, memory, language, and praxis abilities, verbal coding and fluency and dementia diagnosis ICD-10.7

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 pandemic. Children are prohibited from doing activities outside, including going to school. School closures result in changes in sleeping patterns, eating patterns and making activities monotonous. Children are a group that is vulnerable to violence and child abuse.10

Conclusion

Psychosocial effects of COVID-19 lay the groundwork for an unprecedented increase in the prevalence of psychiatric disorders, which in turn could accelerate the development of a number of other comorbidities.

References