

COVID-19 and Dementia

Annals of Neurosciences

1–4

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DOI: 10.1177/09727531211009420

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Abstract

The World Health Organization has declared the COVID-19 outbreak a pandemic. The causative agent for COVID-19 is an RNA virus of the Coronaviridae family. In addition to the respiratory and other complications, a significant proportion of COVID-19 patients show neurological manifestations. Dementia is a neurocognitive disorder, the prevalence of which is projected to increase in the coming decades. This review provides an overview of the effects of COVID-19 on dementia patients.

Keywords

Coronavirus, severe acute respiratory syndrome coronavirus 2, COVID-19, SARS-CoV-2, dementia

Received 5 December 2020; accepted 23 February 2021

Introduction

The world is reeling with coronavirus disease-2019 (COVID-19). The causative agent for this disease is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It started with an outbreak of pneumonia of unknown etiology in Wuhan, Hubei Province of China, in December 2019. The coronavirus outbreak has turned into a pandemic. So far, this virus has infected more than 161 million individuals and caused more than 3.3 million deaths across different countries (see <https://coronavirus.jhu.edu/map.html>). The COVID-19 pandemic has burdened the healthcare system. It has negatively affected the world economy also.

SARS-CoV-2 is a positive-strand RNA virus and is a highly infectious agent requiring unprecedented measures to reduce transmission. It is primarily transmitted by sneezing and coughing. Measures including physical distancing, wearing of face masks, and hand hygiene are important to limit the spread of the virus in the population. The virus can cause a wide range of symptoms including fever, sore throat, dry cough, shortness of breath, and diarrhea.¹ A large portion of infected individuals remain asymptomatic, while others show mild, moderate, or severe symptoms. Higher mortality has been observed in patients with comorbid conditions including hypertension, diabetes, and cancer. Determination of the genetic sequence has allowed the development of diagnostic tests utilizing reverse-transcriptase polymerase chain reaction to detect the virus in the infected individuals.

This virus has generated enormous interest in the general public, clinicians, as well as basic science investigators. Researchers are trying to understand the biology of the virus as well as develop newer diagnostic tools and potential therapeutic measures. Major efforts are directed toward the development of vaccines against the virus. The scientific interest in the virus is evident from the fact that a PubMed search with the keyword “COVID-19” results in more than 133 thousand articles. In addition to respiratory complications, neurological symptoms have also been observed in a significant proportion of individuals infected with the virus. The dementia patients appear to be adversely affected by COVID-19. This review provides an overview of the effects of COVID-19 on dementia patients, and the potential effects of COVID-19 on the development of neurodegenerative diseases including dementia.

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COVID-19 and Dementia

The entry of SARS-CoV-2 in the cells is mediated by a glycoprotein, the spike protein, that protrudes out of the virus envelop. The S1 subunit of the spike protein binds to the receptor on the host cell, and the S2 subunit helps in the fusion of the virus with the cell membrane.² The virus uses angiotensin-converting enzyme-2 (ACE-2) as a receptor to enter the cells.³ Studies have examined the expression of ACE-2 in different organs. Li and colleagues analyzed the datasets from The Cancer Genome Atlas program and the Genotype-Tissue Expression project and found expression of ACE-2 in several organs including the brain.⁴ The presence of SARS-CoV-2 in the brain has not been conclusively established. While some studies did not find evidence of the virus,^{5,6} other studies have detected it in the cerebrospinal fluid of COVID-19 patients.^{7,8} It is unclear how the virus may reach the brain. Many patients show cytokine "storm" which may compromise the blood brain barrier and facilitate the "virus" entry into the brain. Olfactory pathway may be involved in virus entry to the brain and the hypothalamus could also serve as an entry route.

Dementia is a progressive decline in cognitive abilities which interferes with daily activities. Dementia is devastating with respect to not only the affected person but also the caregivers. The prevalence of dementia cases is projected to increase in the coming years, which is likely to put tremendous burden on the healthcare system and society. Alzheimer's disease (AD) accounts for majority of the cases. Other dementia conditions include vascular dementia, frontotemporal dementia (FTD), and Lewy body dementia.

Pulmonary complications are well recognized in COVID-19 patients. In addition, impairment of the sense of smell and taste has also been widely reported in these patients. It has been reported that about 30% of COVID-19 patients requiring hospitalization develop neurological manifestations including dizziness, impairment in consciousness, seizure, stroke, olfactory and gustatory dysfunctions, encephalitis, and headache.^{3,9} In addition to the acute effects, it is important to understand the potential long-term consequences of COVID-19 on neurological functions.

Several studies have examined the effects of COVID-19 on dementia patients. A study by Cagnin and colleagues¹⁰ evaluated the effects of quarantine on behavioral and other parameters in dementia patients in Italy. It was found that one month from the declaration of quarantine, AD patients showed more anxiety and depression. Worsening of hallucination and sleep disorder were associated with dementia with Lewy body, and wondering and change in appetite were associated with FTD. In addition, during the lockdown period in Spain, the neuropsychiatric symptoms such as apathy and anxiety worsened in AD patients and in individuals with mild cognitive impairment.¹¹ Another study found that about 26% of AD patients who were confined to their homes for about two months demonstrated

neuropsychiatric changes.¹² These patients also showed a worse performance on mini-mental state examination in comparison to the patients who did not show neuropsychiatric changes. In retirement homes in France, the AD patients showed a higher level of depression and anxiety during the virus crisis than before.¹³ These effects could be due to restrictions imposed including physical distancing to reduce the spread of the virus in society. An increase in the anxiety level in dementia patients has also been observed by Cohen and colleagues.¹⁴ Further, worsening of behavioral symptoms in dementia patients was observed after 8 weeks of quarantine period.¹⁵ During the pandemic situation, the caregivers of dementia patients are also facing difficulties in providing the required care. Cagnin and colleagues found that one month from the declaration of quarantine in Italy, more than 60% of caregivers of dementia patients reported stress-related symptoms.¹⁰ Further, the stress level of caregivers of dementia patients was found to be increased after 4 weeks of lockdown.¹⁴ Thus, being confined due to the virus crisis increases neuropsychiatric symptoms in dementia patients, and increases the stress levels in the caregivers.

As mentioned earlier, ACE-2 serves as the receptor for SARS-CoV-2 for entry into the cells. An increase in ACE-2 expression has been observed in the AD patient brain^{16,17} raising the possibility that AD patients may be more susceptible to developing severe COVID-19 symptoms. People with dementia are likely to have comorbid conditions and thus may develop a more severe form of COVID-19. In fact, dementia has been suggested to be a risk factor for hospitalization in COVID-19 patients.¹⁸ Further, dementia, especially in the late stage, increases mortality risk in these patients.¹⁹

Apolipoprotein E (ApoE) plays an important role in lipid metabolism and other processes.²⁰ ApoE4 allele is an established risk factor for the development of AD.²¹ In a Biobank community cohort in the UK, it was observed that the ApoE e4e4 allele increases the risk for severe COVID-19.²² Furthermore, the ApoE e4e4 allele is associated with higher mortality in COVID-19 patients.²³ Although these studies need to be extended to a larger population, they raise the possibility that AD patients may be more susceptible to adverse effects of SARS-CoV-2.

In a study conducted to examine postdischarge symptoms, a significant number of survivors reported impairment in memory about 100 days after hospitalization.²⁴ The severely affected COVID-19 patients show higher levels of cytokines.³ Considering that systemic inflammation could contribute to the development of neurodegenerative diseases, the COVID-19 survivors may be at higher risk for developing these conditions.⁹ Evidence of neuronal injury has been found in severe COVID-19 cases, and activation of glial cells has been found in moderate and severe COVID-19 patients.²⁵ Autopsy studies have shown neuronal loss in brain areas including hippocampus in the these patients.²⁶

In this pandemic situation, dementia patients need special attention as they may not be able to properly follow the preventive measures that help reduce the chances of infection, such as hand hygiene, wearing a face mask while in public places, and maintaining physical distancing. Some dementia patients do not use the facial mask properly or they even remove them. This necessitates constant reminders by the caregiver. The dementia patients may have difficulty in recognizing the early symptoms of COVID-19 and thus may not seek the required help in time.

People with dementia benefit from group activities, but during the pandemic, these group activities are not possible or are curtailed to a significant extent. The elderly individuals including those with dementia are advised to reduce their interaction with others. This may lead to the feeling of loneliness or even neglect, because those in the advanced stage of the disease will not be able to appreciate the importance of restrictive measures to control the spread of the virus.

Concluding Remarks

The full extent of neurological manifestations of COVID-19 is yet to be understood. There is an urgent need to develop effective strategies for the surveillance of, and the care for, neurological symptoms in COVID-19 survivors. Carefully planned longitudinal follow-up studies will help us understand whether COVID-19 is associated with a higher risk of developing neurodegenerative disorders including dementia. These studies will benefit from neuroimaging analyses along with cognitive assessment. In addition, basic science research is required to understand whether the virus affects the processes involved in the development of dementia and other neurological conditions. Dementia research has received considerable funding. Although the current pandemic demands allocation of resources for COVID-19 research to develop cures and vaccines (fortunately, some vaccines are already in use), the other conditions including dementia should not be neglected. Finally, the lessons learned from this pandemic would certainly help plan better to deal with similar situations in the future.

Acknowledgments

Research in the author's laboratory has been supported by the Department of Biotechnology, Council of Scientific and Industrial Research, and National Brain Research Centre. Funding of the Dementia Science Programme by the Department of Biotechnology is especially appreciated since it strengthened the author's interest in dementia.

Author Contribution

SKS contributed to this article.

Declaration of Conflicting Interest

The author declares that there is no conflict of interest.

Ethical Statement

No experiments were conducted by the author for this review article. Hence, ethical approval was not required.

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