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MINI REVIEW

Alzheimer's disease in the era of COVID-19 pandemic: A mini review

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first detected in late 2019, Wuhan, China spread across the globe with a huge death toll and health complications. The coronavirus invades the nervous system and affects individuals suffering from neurological disorders like Alzheimer's disease (AD). Individuals homozygous for Apolipoprotein-E (Apoe) ε4 allele increase the risk for AD. Less expression of ACE2 is advantageous for AD individuals. Inability to adhere to rules pertaining to self-guarding such as physical distancing, wearing masks, and sanitizing hands from time to time increases the risks of infection. Social isolation deteriorates mental stability. Increased infection chance amongst caregivers is a tough challenge to look after the AD patients. In this review, we summarise the literature to highlight the current situation of AD-affected individuals in the COVID-19 pandemic, emphasizing the risk factors, lifestyle, and care for them.
Immense challenges are encountered by the old age people suffering from AD in the COVID-19 pandemic. Preferring home-based care and management for AD patients will reduce complications and promote well-being.

Keywords

Alzheimer's disease and related dementias, Angiotensin-converting enzyme 2, caregivers, dementia, elderly patient, severe acute respiratory syndrome coronavirus 2

Introduction

The novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first detected in late 2019; Wuhan, China, and WHO has declared COVID-19 as a pandemic on March 11, 2020. [1] Globally, as of December 15, 2021, there have been 270,791,973 confirmed cases of COVID-19, including 5,318,216 deaths, reported. [2] The outbreak started via a zoonotic spread from the seafood markets in Wuhan, China. It quickly engulfs approximately 200 countries by human-to-human transmission and through community spread. [3, 4] SARS-CoV-2 results in various symptoms, including fever, cough, and fatigue. [5] As SARS-CoV-2 infections increased dramatically, neurologic involvement surfaced. Reports are available for headache, dizziness, or a cerebrovascular event. [6, 7] Ageusia, anosmia was considered the initial symptoms of SARS-CoV-2 infection, which is a clear indication of neurological involvement. [8] The viral effect is not limited to taste and smell; it invades the nervous system and affects individuals suffering from neurological disorders like dementia. People with dementia pose a greater risk of infecting by COVID-19, are more likely to require hospitalization, and are prone to severity than others. [9]

According to WHO, more than 55 million people globally have dementia, and there are 10 million new cases every year. Dementia occurs due to various diseases and injuries that directly or indirectly affect the brain. AD is a neurodegenerative disorder, is the most common form of dementia with a significant contribution, 60-70% of all affected persons. [10] AD affects the memory and learning of the patients has become a growing concern. [11] AD patients showed severe changes in the protein profile of different brain regions, pointing towards neuronal damage amongst them. [12]

In this review, we summarize the literature to highlight the current scenario of the AD-affected individuals, giving importance to their risk factors, lifestyle, and care in the COVID-19 pandemic.

The role of APOE ε4 in COVID-19 infected AD individuals

Apolipoprotein E (ApoE) is a carrier for cholesterol which helps lipid transport and takes an active role in repairing brain damage. APOE polymorphic alleles are vital factors for AD. Individuals homozygous for APOE ε4 allele increases the risk for AD by 40% [13] and are more likely to be hospitalized due to the risk of COVID-19 compared to others with average APOE ε3/ε3 genotype. APOE ε4 is strongly related to the increased blood-brain barrier permeability which causes substantial CNS inflammation in retaliation to SARS-CoV-2 infection and possesses the capability of aggravating microglia-mediated neuroinflammation and subsequent neurodegeneration. [14]

Furthermore, APOE ε4 is also responsible for the increased cytokine production due to the inflammatory stimuli, which escalate the effects of inflammatory response related to COVID-19, leading to cytokine storm contributes to multi-organ failure, lung injury, and severe COVID-19 consequences, including mortality. [15] Disregard the pandemic, mortality from pneumonia is double in rate in individuals with dementia compared to the no suffers. [16]. There are contradictory findings that show AD patients who carried APOE ε4 had fewer chronic diseases. [17]

Role of ACE2 in AD patients

Angiotensin-converting enzyme 2 (ACE2) is one of the critical factors for the resilience of AD patients to COVID-19. [18] Evidence suggests that the spike protein (S1) of SARS-CoV-2 interacts with the ACE2 receptor on the cell surface membrane to enter the cells. [19] Expression of ACE2 is relatively less in AD individuals. [20] Animal experimentations showed similar results of lower expressions. [21, 22] Studies are underway to investigate the cognitive impairment and activation of ACE2. [23] Shorter hospitalization was associated with diminished ACE2 receptors in COVID-19 patients suffering from AD. [18] However, it is still debatable regarding the alteration of ACE2 amongst the infected AD patients. [20]

Alzheimer's patients' life in COVID-19

COVID-19 pandemic strained the healthcare systems worldwide while simultaneously placing individuals with Alzheimer's disease and related dementias (ADRD) at a much higher risk of distress and suffering. [16]. Arising mental disruptions and psychiatric episodes among patients suffering from ADRD in this pandemic increased morbidity levels among these patients.

Multiple factors contributed to the increased risk of ADRD individuals on their cognitive and neuropsychiatric symptoms. [24] ADRD patients are usually unable to adhere to rules pertaining to self-guarding, especially when it comes to physical distancing. These individuals require assistance in their day-to-day activities where they rely on caretakers or social workers to aid them with the most basic routine. Their cognitive, behavioural, and physical conditions are further aggravated since visits from relatives and friends are less likely during the pandemic, which prevents them from engaging in social activities, physical exercises, or even receiving the necessary emotional and mental support. [25]

ADRD individuals also struggle to comply with safeguarding procedures such as wearing masks and sanitising hands from time to time. Removing masks, coming in contact with high-touch surfaces or even touching clinical staff violating the standard protocols are commonly seen in ADRD patients. Taking a nasopharyngeal swab for an RT-PCR or blood sampling is challenging for health care professionals since ADRD patients are constantly agitated and cognitively challenged to stay still or adhere to ground rules. All these complications have placed ADRD patients as a more susceptible group during the COVID-19 pandemic due to failure in compliance with infection control procedures. [16, 26] Approximately three-quarters of the

COVID-19 deaths were reported to derive from care homes due to the complications that arise from ADRD. [27] Older patients with dementia stay in care homes where proximity with each other in living rooms and dining rooms increases risks of infection. [26] In milder cases of dementia, unwillingness or inability to comply is observed in ADRD patients due to desolation and indifference. Those with a grievous form of dementia cannot comprehend, value, or recall most of the recommendations due to the gravity of their short-term memory loss and overall cognitive impairment. Behavioural and psychological symptoms (BPSD), such as intrusiveness, motor agitation, or wandering, may sabotage the attempts to maintain isolation. [16]

Professional caregivers may refrain from supervision of an ADRD patient infected with COVID-19, leaving them without proper care and treatment, further aggravating the disease and deteriorating the condition. At the same time, the setting in nursing care homes sometimes faces a shortage of PPE for staff, which worsens the situation. Other factors like lack of experience in the training and management of infection control also affect the patients. Private service care workers who travel to and from various facilities or homes to provide part-time nursing care to ADRD residents may contribute to the increasing likelihood of the spread of COVID-19 infection to colleagues and ADRD patients. [28]
In addition to being susceptible to COVID-19, older adults with dementia experience more serious viral-related symptoms than normal individuals. Moreover, age, obesity, cardiovascular disease, hypertension, and diabetes mellitus are common contributing risk factors between dementia, SARS-CoV-2 infection, and the illness's severity. [29] However, pre-existing brain pathology is the key factor of the increased risk of severe neurological complications from COVID-19. [30]

Care of individuals with ADRD during pandemic

Patients suffering from or at the risk of ADRD usually require a caretaker throughout their life. The late stages of dementia require assistance throughout the day. This warrants the need for health care workers and caregivers. Apart from the day-to-day care of patients, physically present caretakers also play a key role in the treatment and prevention of dementia. Social activities are helpful to improve the cognitive function of patients, while loneliness and isolation from society pose a high risk in the development of ADRD and its symptoms. A study on loneliness and its risk on Alzheimer's disease suggested that 'loneliness is an important risk factor for all dementia' and reveals the importance of paying attention to reports of loneliness among the elderly. [31] However, due to the COVID-19 pandemic, the implementation of social distancing, clinical management of care for dementia patients, and providing physical assistance throughout the day to these patients have become more challenging. [32]

The sudden need for more health care workers on the frontline to battle COVID-19 and the fast spread of the virus may have led to a decrease in specialized health care workers in nursing homes and other related facilities. Many health workers and caregivers contacted COVID-19, leading to a reduction in staff, and sudden changes in these facilities posed a risk for ADRD patients. [33] These sudden changes and the disruption to social interaction led to deteriorating conditions in dementia patients and increased behavioral impairment such as agitation. The onset of symptoms such as delirium, depression, and sleep disturbances also increase. Cognitive exercises to improve their condition may not be carried out in these patients to prioritize the control of COVID-19. [32]

Since a lot of ADRD patients also fall into the 'substantial risk' category of COVID-19 due to their age, this could lead to further obstacles with respect to social isolation and decreased cognitive ability, as well as the challenges faced in providing health care to dementia patients who have contracted COVID-19. There is also a general fear and anxiety raised prominent issues such as refusing nursing homes or being reluctant to admit ADRD patients into their facility due to the fear of infecting other patients. The instance of caretakers refusing to continue care of dementia patients after a recent COVID-19 infection due to the fear of contracting or spreading the virus is a challenge. [34]
Additionally, the sudden shift in focus towards the Coronavirus pandemic may have given rise to insufficient funding to nursing homes and towards the care of ADRD patients.

Governments worldwide have applied multiple movement control restrictions on their people to control the spreading of the COVID-19 pandemic, which significantly impacted ADRD patients. Forced isolation has increased the number of psychiatric symptoms since the pandemic started. Most individuals reported stress, anxiety, and depression under the lockdown period. The situation became worse when lockdown periods were extended multiple times. Older ADRD patients suffered severe neuropsychiatric and behavioural disturbances during the lockdown. [15, 35] Neuropsychiatric symptoms and behavioural disturbances develop a progressing deterioration of the thinking process in older patients suffering from ADRD. Social isolation in nursing homes, operating with less staff, increases loneliness, boredom, and even greater agitation than non-sufferers. [36] Under increased aggression and agitation situations in ADRD patients suffering from behavioural disturbances, management, and daily care were challenging for the caretakers. [37, 38]

Elderly patients have a higher chance of being infected but a lower chance of recovering from the virus, which could lead to disease-related morbidity and mortality, including lung injuries, organ failure, and eventually death. The longer lockdown period is helpful to control the spread of infection, but it's the origin of developing neuropsychiatric symptoms and severe behavioural disturbance among ADRD patients. [15, 34, 35]

Conclusion

In this short span, we have provided an overview of the immense challenges encountered by the old-age people suffering from AD in the COVID-19 pandemic. Strategies like home-based care and management for AD-affected individuals might be useful. Optimizing the already existing facilities in nursing homes, hospitals may curb the spread of infections in AD patients. Countries heavily hit by the infection need more attention to reduce the complications and mortality and promote the well-being of older people with AD.

Abbreviations

Alzheimer's disease (AD), Alzheimer's disease and related dementias (ADRD), Apolipoprotein E (APOE), Apolipoprotein-E (Apoe) ε4, Behavioural and psychological symptoms (BPSD), Coronavirus disease (COVID-19), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

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Authors' contribution

a. Study planning: VT, TYS, JKD, FEM

b. Data collection/review of literature: VT, TYS, JKD, FEM, KWK

c. Manuscript writing: VT, TYS, JKD, FEM, KWK

d. Manuscript revision: VT, TYS, JKD, FEM, KWK

e. Final approval: VT, TYS, JKD, FEM, KWK

f. Agreement to be accountable for all aspects of the work: VT, TYS, JKD, FEM, KWK

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