COVID-19 and neurologic Complications in Elderly patients

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Abstract

The COVID-19 pandemic continues to prevail as a catastrophic wave infecting over 111 million people globally, claiming 2. 4 million lives to date. Aged individuals are particularly vulnerable to this disease due to their fraility, immune dysfunction, and higher rates of medical comorbidities, among other causes. Apart from the primary respiratory illness, this virus is known to cause multi-organ dysfunction including renal, cardiac, and neurologic injuries, particularly in the critically-ill cohorts. Elderly patients 65 years of age or older are known to have more severe systemic disease and higher rates of neurologic complications. Treatment of neurologic dysfunction of COVID-19 is based on existing practice standards of specific neurologic condition in conjunction with systemic treatment of the viral illness. The physical, emotional, psychologic, and financial implications of COVID-19 pandemic have been severe. Long-term data are still needed to understand the lasting effects of this devastating pandemic.

Introduction

Over the course of one year, the novel SARS-CoV-2 virus has wreaked havoc globally accounting for over 111 million documented infections with a vast toll of death and disability. Although the proportion of severe cases is likely to depend on the study population and epidemiological behavior of the infection in each country or geographic region, current evidence suggests that older individuals and those with compromised immune systems are more likely to develop severe forms of COVID-19 (1,2).

Elderly patients 65 years of age or older are known to have more severe systemic disease and higher rates of neurologic complications. Morbidity and mortality is very high in the elderly population with 6–930 times higher likelihood of death compared to younger cohorts, with the highest risk in elderly patients ≥85 years and especially those with medical comorbidities such as hypertension, diabetes, heart disease, and underlying respiratory illness. Commonly reported neurologic dysfunctions of COVID-19 include headache, fatigue, dizziness, and confusion. Elderly patients may manifest atypical presentations like fall or postural instability (3). Other important neurologic dysfunctions in the elderly include cerebrovascular diseases, cognitive impairment, and neuropsychiatric illnesses (4). Elderly patients with preexisting neurologic diseases are susceptibility to severe COVID-19 infection and higher rates of mortality.

Material and methods

This is a systematic review of the studies regarding the neurologic complications in elderly patients related to Covid-19. The research included four databases (PubMed; medRxiv; COVID-19 Living Evidence database; European PMC)

Results

Many countries that have endured severe effects of the pandemic have also experienced highest morbidity and mortality in the elderly population, particularly those with underlying comorbidities (5). In fact, Italy has one of the world's oldest population, with 23% of people ≥65 years, which is likely the reason for Italy's high case fatality rate (7.2%) compared to other countries (6). In the United States (U.S.), although infection is most prevalent in the 18–29 age group (23%), elderly patients ≥65 years are 5–13 times more likely to be hospitalized and have 9–630 times higher likelihood of death; with the highest

rate of hospitalization and death among patients ≥85 years of age (7). Per the National Vital Statistics System data on the demographic and geographic trends of COVID-19 in the U.S between May 1 and August 31, 78.2% of deaths occurred predominantly in men (53.3%) aged ≥65 years (8). Neurologic dysfunctions of COVID-19 are also more common in the elderly population (9), and the presence of neurologic dysfunction has been identified as an independent predictor of mortality in hospitalized COVID-19 patients (10). As neurologic complications are often associated with disease severity and mortality, characterization of neurologic dysfunction and accurate prognostication is crucial. Here we briefly discuss common neurologic dysfunctions of COVID-19 in the elderly, possible determinants of disease severity in this age group, outcomes, and treatment.

Neurologic Associations and Complications in Aged COVID-19 Patients

The most commonly reported symptoms of COVID-19 are fever, dry cough, fatigue, and dyspnea (11). Elderly patients are likely to present with atypical symptoms such as falls, postural instability, or delirium. The pulmonary manifestations of COVID-19 drive most hospitalizations worldwide, more commonly in patients ≥65 years and those with comorbidities like diabetes and hypertension (12). Critically-ill COVID-19 patients frequently develop multi-organ dysfunction including arrhythmias, myocardial injury, heart failure, arterial and venous thrombosis, disseminated intravascular coagulation (DIC), dysregulated immune response, and neurologic complications (13). Preexisting vascular disease is known to predispose individuals to severe COVID-19 infection, with aged individuals being more susceptible to more severe courses (14).

Acute stroke is another commonly reported neurologic complication of COVID-19, particularly in the elderly population. Li et al. reported a 5% risk of ischemic stroke and a 0.5% risk of cerebral hemorrhage in 221 patients with COVID-19 infection from Wuhan, with the highest prevalence in aged individuals with underlying vascular and thrombotic risk factors such as hypertension, diabetes, and elevated plasma D-dimer levels (15). Recent systematic reviews report stroke incidence of 1–2% in COVID-19 patients, which is significantly higher than historical controls, including a cohort with seasonal influenza. Mortality among hospitalized COVID-19 patients with acute stroke is also extremely high. Reports have noted mortality rates of 31.5–34.4%, with highest impact in older patients. Elderly stroke survivors are also at increased risk of severe infection and suffer from higher mortality, likely related to their

underlying comorbidities and swallowing complications. A recent meta-analysis of 39 studies on COVID-19-associated stroke suggested a mean age of 63.4 ± 13.1 years with male predominance and clinical findings of elevated D-dimer, elevated fibrinogen, and the presence of antiphospholipid antibodies (16). Although many other neurologic and neuropsychiatric symptoms have been reported, focused reports on elderly is generally sparse.

Treatment and Treatment Response of Aged COVID-19 Patients:

As we approach one year since the World Health Organization's (WHO) initial declaration of the novel coronavirus pandemic, limited evidence-based therapies specific to COVID-19 are available with management primarily focused on treatment of associated complications and supportive care. Regarding management of neurologic complications of COVID-19, existing evidence-based therapies are used for specific neurologic conditions, in conjunction with systemic treatment with antivirals, corticosteroids, and immunomodulators, as appropriate.

Delirium management has long been a priority in the care of older adults. Multidisciplinary care focused on prevention of delirium using non-pharmacologic strategies, is the best practice (17). Non-pharmacologic interventions include patient-centered care with frequent re-orientation, regular visits from family and friends, optimization of hearing and vision by ensuring access to hearing aids and glasses, adequate hydration, adequate sleep, early mobilization, and minimization of unnecessary lines, tubes, polypharmacy, and precipitating medications. In centers with pandemic-related visitation restrictions, care teams can help meet the emotional needs by displaying family photos, facilitating the use of technology to connect patients with their families, and assessing patients' desire to access spiritual care. Early mobilization is the single intervention with the strongest evidence of decreasing the incidence and the length of delirium. Pre-COVID literature suggests that delirium can be prevented with appropriate in-hospital multimodal approach in about 30% of cases (Siddiqi et al., 2016). Regular clinical assessments for pain, agitation, and delirium with validated screening tools can help with early recognition and management (18). Patients on immunosuppressants and those with neuroinflammatory diseases like multiple sclerosis should continue treatment of their underlying illness while applying precautions to prevent viral spread and ensuring access to healthcare via teleneurology.

Discussion

Elderly patients with COVID-19 are susceptible to neurologic conditions like acute stroke, acute encephalopathy, neuropsychiatric manifestations, and complications related to underlying CND. Reports from heavily affected countries like China, Italy, and the U.S. have informed that elderly population suffer a high rate of COVID-19-associated mortality (19). As neurologic dysfunctions of COVID-19 lead to increased morbidity and mortality, systematic studies on acute and long-term implications of neurologic complications of COVID-19 are imperative.

One of the biggest concerns of the COVID-19 pandemic is the tendency to periodically overwhelm hospitals and medical centers at the local, regional, and national level. A finite supply of healthcare resources led healthcare leaders to craft directives that address scarce resource allocation. The Italian Society of Anesthesiology, Analgesia, Resuscitation, and Intensive Care published guidelines that informed care during the outbreak in Northern Italy in March-2020 (20). Although this policy was criticized for overreliance on chronologic age and resource prioritization for younger patients, it prompted a search for more equitable criterias. Numerous national and international societies have released policy recommendations to guide resource allocation which involves a few common themes. First, it is inappropriate to use chronological age alone as an exclusion criteria. Second, given the heterogeneity in the baseline health status of aged adults, use of objective measures such as the Clinical Frailty Scale or Sequential Organ Failure Assessment are thought to be valid and equitable alternatives in assessing potential benefit of therapeutic intervention. Third, implementation of protocols to prioritize advanced care planning is not only an integral component of patient-centered care but may also help in allocation of limited resources by promptly identifying patients who opt not to be intubated or resuscitated. In one study, only 2.9% of COVID-19 patients older than 80 years survived to hospital discharge after receiving cardiopulmonary resuscitation (Hayek et al., 2020). Hence early discussions regarding goals of care is important, particularly in patients with neurologic dysfunctions. Depending on the type and severity of the disease, neurologic conditions often hold a grave prognosis, reduce life expectancy, or are associated with difficult to control pain and depression. Additionally, caregivers of patients with neurologic conditions are known to have similar rates of distress and burnout as that of cancer patient caregivers (Kim and Schulz, 2008). In severely ill patients with persistent encephalopathy or coma requiring full time care, burden of disease is tremendous from clinical, social, and economic standpoint. Given the high burden of disease both on patients and caregivers, early goals of care discussions

become extremely important in patients with neurologic dysfunction. Lastly, healthcare systems need to work on facilitating access to in patient and outpatient palliative care and hospice services for COVID-19 patients.

Strained healthcare systems and rising healthcare costs are global problems predating the coronavirus pandemic. With the additional economic burden related to severe COVID-19 illness and the short and long-term disability associated with neurologic complications, the financial hit is likely to be staggering. For perspective, the estimated annual direct and indirect costs for ~795,000 strokes in the U.S. from 2014 to 2015 was $45.5 billion, while healthcare cost related to delirium alone was $164 billion in 2011 (21). Although the actual economic impact of COVID-19 and related neurologic complications is yet to be determined, it is likely to have profound financial implications for an extended period of time.

The scientific community is only beginning to evaluate the long-term effects of the pandemic. Robust long-term data are lacking, especially pertaining to neurologic complications. One of the first studies to focus on outcomes after hospitalization for COVID-19 found that 44% of Italian patients rated their quality of life as worse (≥10 point difference on a scale of 100) since contracting COVID-19. Though patients were assessed at a mean of 60.3 days since symptom onset, 87.4% reported at least one ongoing COVID-19-related symptom, particularly dyspnea and fatigue. Prolonged symptoms are also reported among those with mild COVID-19 infections. In a telephone survey of American adults with mild COVID-19 illness conducted 14–21 days after a positive PCR test, 47% of respondents aged ≥50 years reported ongoing symptoms (22). Data on COVID-19-associated neurologic conditions including inflammatory, vascular, autoimmune, and neurodegenerative diseases are urgently needed (23). Similarly, neuropsychiatric conditions related to social isolation are only just beginning to surface and are likely to have significant long-term implications.

Conclusion

In conclusion, COVID-19 has been a catastrophic pandemic, particularly for the elderly, who tend to suffer from neurologic complications as well as a very high rate of morbidity and mortality. The physical, emotional, psychological, and financial implications of this disease have been severe. Long-term data are still needed to understand the lasting complications of this devastating pandemic.

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