Editorial

Neurologic disorders and COVID-19

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SARS-CoV-2 with its wide range of disease severity ranging from asymptomatic carriers to severe respiratory compromise and death, is still with us. High rates of infection and subsequent long-term sequelae have raised significant concerns, particularly for those with underlying medical illnesses, who may be more severely affected. This includes not only those treated with immunosuppressive therapies for their neurologic disorders (e.g., myasthenia gravis or multiple sclerosis [MS]) but also those with significant functional disability from their disease and elderly patients with a history of cerebrovascular disease, Parkinson disease and dementia. As neurologic disorders are common, the effect of SARS-CoV-2 on patients with neurologic illnesses poses a substantial public health risk. Prioritizing this population is critical when considering the risks and benefits of vaccination.

The approval of vaccines for emergency use results in the potential to significantly reduce the incidence of symptomatic disease in these vulnerable populations. However, the rapidity of approval, and history of prior vaccination regimens resulting in neurologic and other complications, creates concern surrounding widespread vaccination.

The potential for neurologic complications is a concern, particularly for those who already have neurologic disorders. Neurologic complications have been reported in 30%-60% of patients with COVID-19 and typically fall into 3 broad categories: those that are caused acutely by the virus' systemic effects on the body itself, those that result from direct invasion of the nervous system, and those with long-term sequelae after an individual has recovered from the acute illness. Although there is no clear evidence at present that those with pre-existing neurologic illness are at higher risk of infection or neurologic complications, the question of whether individuals with neuromuscular or bulbar weakness may be more vulnerable to neurologic sequelae will require careful study.

Prevalence data on acute neurologic effects of COVID-19 are limited. In an article published in JAMA Neurology detailing 214 COVID-19-positive patients hospitalized in Wuhan, China, headache and dizziness were the most commonly reported neurologic complaints and seen early after symptom onset. These early symptoms contrast with the encephalopathy seen days to weeks into the hospital course of patients with severe disease. Encephalitis has been reported, mainly in a series of case reports[1], although imaging and CSF profiles have been nonspecifically abnormal or nonrevealing[3].

Evidence is largely lacking for direct CNS invasion of SARS-CoV-2 as a primary cause of neurologic sequelae. Several studies have detected low viral loads in brain tissue using quantitative real-time polymerase chain reaction (qRTPCR), but the clinical significance of these findings is uncertain. For instance, a recent autopsy study of 41 consecutive patients who died of SARS-CoV-2 infection found low to very low viral RNA levels in some of the brains by qRTPCR, but viral proteins were not detected, and the level of detectable RNA did not correlate with histopathologic alterations[4]. Other studies have not been able to detect viral RNA or protein in the brain. The virus does infect the sustenacular cells of the nasal mucosa, causing inflammation that causes loss of smell and headache. Similar systemic inflammatory effects of the virus might cause altered mental status in patients either directly or through an inflammatory cascade leading to cardiac or respiratory compromise with hypoxia or thrombosis. CNS effects have also been hypothesized to be caused by damage to vascular endothelium or blood-brain barrier breakdown. There have been case reports suggesting increased risk of large vessel occlusion and ischemic stroke associated with infection in the young[5]. It is also possible that the virus triggers underlying neurologic disease through immunomodulation as there have been case reports of acute inflammatory demyelinating polyneuropathy (AIDP), acute myoclonus, acute cerebellitis with ataxia, encephalitis, and status epilepticus occurring as para- or post-in-fectious phenomena. **In this issue there are two case reports one of a sciatic neuropathy following severe COVID-19 and the other of vaccine induced thrombo-cytopenia and cerebral venous thrombosis with extensive intracerebral haemorrhage**.

Long-term sequelae have been reported following previous viral epidemics; however, clear evidence linking specific complications to prior viral infection remains somewhat controversial and does not appear related to a single mechanism of action. The 1918 H1N1 pandemic's association with postencephalitic parkinsonism (PEP) and Zika virus-induced congenital Zika syndrome are examples. PEP is associated with encephalitis lethargica (von Economo encephalitis). Although encephalitis

lethargica has been associated with the H1N1 epidemic, this association has been challenged. Unlike the putative post-infectious autoimmune etiology of PEP, Zika syndrome is in large part the direct result of acute infectious injury to developing brain. Any report of long-term neurologic sequelae of COVID-19 will require careful analysis to demonstrate the validity of the association. Reports of long-term neurologic sequelae after recovery from COVID-19 have begun to be reported, and thus far include dysautonomia, chronic fatigue, and cognitive impairment[6]. with time it will be possible to fully characterize these issues and estimate their incidence. Patient registries will be crucial for determining whether SARS-CoV-2 infection, like other viral infections, will be associated with increased incidence of psychiatric disease, dementia, thrombosis, or demyelination later in life. **It is to the credit of the ASN that we already have such a registry where all Neurologists feed in their patient data on COVID-19 and vaccine related complications.**

Some literature supports the indirect effect of viral infections on those with neurologic disorders. Along with potentially triggering disease, there is an increased risk of mortality in patients with pre-existing neuromuscular illness who contracted influenza or pneumococcal pneumonia due to worsening respiratory status. Exacerbations of symptoms are commonly associated with infections, with infection accounting for almost half of patients presenting with myasthenia gravis flares. Viral infections are a common cause of transient worsening of existing symptoms in people with MS, and increased disability has been identified as a risk factor for severe COVID-19 in patients with MS. Viral illnesses can be a predisposing factor for delirium in patients with dementia or mild cognitive impairment, leading to poor prognosis. In addition, those on immunomodulating therapy are at risk for more severe, recurrent, and persistent infection.

COVID-19 has had profound effects on our health care system. The pandemic has been linked to decreased hospitalizations for those with ischemic stroke and other neurologic illnesses[7], resulting in poor access to care and increased burden of undiagnosed and untreated ischemic disease. **During the peak of the epidemic ASN members joined hands with the Sri Lanka Medical Association and Ceylon College of Physicians in the frontline. A high dependency unit was started for COVID patients in the Neurology Institute under the supervision of Neurologists. The ASN using their funds donated a transportable ventilator worth around two million rupees to the MICU of the National Hospital. Our members participated in educational programmes online for the public and healthcare staff.**

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