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Letter to the Editor

Outcome of COVID-19 not only depends on a few but the entire spectrum of severe neurological complications

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We read with interest the article by Cervantes-Arslanian *et al.* about the prevalence, associated risk factors, and outcomes of serious neurologic manifestations (encephalopathy, stroke, seizure, and meningitis/encephalitis) among patients hospitalized for a SARS-CoV-2 infection ^[1]. Of 16225 COVID-19 patients enrolled in a registry with data about the entire hospitalisation, 2092 (12.9%) developed serious neurologic complications, such as encephalopathy (n=1656), stroke (n=331), seizure (n=243), and meningitis/encephalitis (n=73) ^[1]. Patients with severe neurological complications were older and suffered from more chronic diseases than those without ^[1]. Patients with severe neurological complications had more severe COVID-19, fewer ICU-free, hospital-free, ventilator-free days, and higher mortality than those without ^[1]. The study is appealing but raises concerns that need to be discussed.

It is not comprehensible why COVID-19 patients were only investigated for a small segment of the many neurological complications known to occur in association with the viral infection. We should be told why the study focused only on encephalopathy, stroke, seizure, and meningitis/encephalitis ^[1]. The spectrum of neuro-COVID is much broader and additionally includes conditions such as acute disseminated encephalomyelitis (ADEM), acute, hemorrhagic leucoencephalitis (AHLE), cerebral vasculitis, immune encephalitis, hypophysitis, cerebellitis, ventriculitis, intracerebral bleeding, subarachnoid bleeding, reversible, cerebral vasoconstriction syndrome (RCVS), posterior reversible encephalopathy syndrome (PRES), multiple sclerosis, neuromyelitis optica spectrum disorder, pontine myelinolysis, venous sinus thrombosis, Wernicke encephalopathy, pseudotumor cerebri, headache, impaired consciousness, delirium, transverse myelitis, and opsoclonus myoclonus syndrome (OMS) respectively opsoclonus myoclonus syndrome ataxia syndrome (OMAS) ^[2, 3]. Disease of the peripheral nervous system (PNS) triggered by a SARS-CoV-2 infection are Guillain-Barre syndrome, and its various subtypes, Parsonage-Turner syndrome, polyneuropathy, myasthenia, myasthenic syndrome, myositis, dermatomyositis, and rhabdomyolysis.

Encephalopathy is defined as neuropsychiatric deficit in the absence of any abnormality on cerebral MRI ^[4]. Since encephalopathy was the most common neurological disease on admission, we should be told if all 1656 patients with encephalopathy had truly undergone a cerebral MRI and had a normal result.

Since the latency between the positive SARS-CoV-2 PCR and admission was up to 21 days, we should be told if the many differentials of encephalopathy were truly excluded in all 1656 patients with SARS-CoV-2 associated encephalopathy. The most common of the differentials of SARS-CoV-2 associated encephalopathy include hepatic, Hashimoto, metabolic, infections, toxic, traumatic, and hypoxic-ischemic encephalopathy and non-convulsive status epilepticus.

Seizures can be a complication of a number of central nervous system (CNS) disorders. We should know how many of those with stroke or encephalitis also developed seizures. In other words, how many patients overlapped between these three groups? We disagree that the study had prospective design. Since data for evaluation were extracted from a registry database, the study obviously had a retrospective design.

Overall, the interesting review has some limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could enhance the study. The spectrum of severe neurological complications of COVID-19 is broad and should not be neglected in a study about the neurological complications of SARS-CoV-2 infections.

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