

## Letter to the Editor

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# Potential role of vitamin D3 in preventing neurocognitive complications in COVID-19 survivors

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**To the Editor:**

Understanding about COVID-19 has evolved significantly over the past 2 years since its emergence as a lethal pandemic. Initially thought to be a disease of the respiratory system only, the disease was soon proved to be a multisystemic disease with brain involvement, no exception. A significant number of patients with COVID-19 infection manifest with neuropsychiatric complications.<sup>1</sup> These include asymptomatic and mildly symptomatic cases as well. The common neurocognitive deficits among the COVID-19 survivors are confusion, altered sensorium, and memory deficits, which may be seen during the COVID-19 infection to long after recovery from the infection.<sup>1,2</sup> Various factors (hypoxia, inflammation, immune activation, toxic damage, and neuro-invasiveness of the virus) due to the COVID-19 infection possibly attribute to brain damage and subsequent neurocognitive deficits, of which inflammatory/immune-mediated damage is a prominent one.<sup>3,4</sup> Evidence support inflammatory mediators like interleukin-6 (IL-6) as an essential moderator of neuropsychiatric complications among COVID-19 survivors in the long term.<sup>3</sup> Several inflammatory mediators, including IL-6, tumor necrosis factor-alpha (TNF- $\alpha$ ) and interleukin-1 beta (IL-1 $\beta$ ), are found to be elevated during COVID-19 infection, and their levels are very much increased during the cytokine storm that gives rise to severe form of COVID.<sup>4</sup> The inflammatory mediators (IL-6 and TNF- $\alpha$ ) cause microglial activation after crossing the blood–brain barrier, which stimulates the production of IL-1 $\beta$ .<sup>4</sup> The IL-1 $\beta$  has a propensity for the hippocampal neurons, and it disrupts the cognitive processing (long-term potentiation) at the hippocampus, which is responsible for the memory difficulties, impairment of attention.<sup>4</sup> Vitamin D3 is known to suppress the activity of these inflammatory mediators, and the level of vitamin D3 is found to be low in patients with COVID-19 infection.<sup>4</sup> Therefore, vitamin D3 deficiency can attribute to neurocognitive deficits in patients with COVID-19 infection. Monoclonal antibody tocilizumab blocks both anti-inflammatory and pro-inflammatory effects of IL-6.<sup>5</sup> Vitamin D lowers IL-6 production specifically, thus reducing pro-inflammatory effects, which is also proved in the treatment of Rheumatoid Arthritis.

Little is known about the course of the neurocognitive deficits associated with COVID-19 in the long run. Long-term sequel due to viral diseases exemplified by Subacute Sclerosing Pan-Encephalitis, Progressive Multifocal Leukoencephalopathy, HIV encephalopathy, and spongiform encephalopathies are well known. Neuropsychiatric manifestations in survivors of SARS and MERS have also been reported. These manifestations may directly affect the virus on the nervous system or may have immune-mediated pathogenesis.<sup>3</sup> Existing knowledge explains that neurodegeneration resulting in the death of neurons in the brain is mostly an irreversible phenomenon; thus, they persist, adversely affecting the individual's functioning and quality of life. Therefore, any preventive measure that prevents the hastening of neurodegeneration is likely to protect the neurocognitive functioning. Vitamin D deficiency is seen in severe cases, especially the at-risk immune-compromised patients. It can also affect the immune functions in COVID-19 patients. In this regard, positive health measures like exposure to sunlight (that helps in the synthesis of vitamin D), increasing diet rich in vitamin D, and supplementation of vitamin D may reduce the risk of cytokine storm and COVID severity. It may also reduce the risk of neurocognitive deficits in COVID-19 survivors. Monitoring and maintaining vitamin D levels and measures like prevention of hypoxia, judicious use of medications, and routine screening for the cognitive deficits during COVID-19 infection may help reduce the risk of development of neurocognitive deficits among COVID survivors.

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## References

1. Rogers JP, Chesney E, Oliver D, *et al.* Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. *Lancet Psychiatry*. 2020;7(7):611–627.
2. Gulick SA, Mandel S, Maitz EA, *et al.* Special report: cognitive screening after COVID-19. *Pract. Neurol.* <https://practicalneurology.com/articles/2021-may/special-report-cognitive-screening-after-covid-19/pdf>. Published May 2021. Accessed December 4, 2021.
3. Kappelmann N, Dantzer R, Khandaker GM. Interleukin-6 as potential mediator of long-term neuropsychiatric symptoms of COVID-19. *Psychoneuroendocrinology*. 2021;131:105295.
4. Alnefeesi Y, Siegel A, Lui LMW, *et al.* Impact of SARS-CoV-2 infection on cognitive function: a systematic review. *Front Psychiatry*. 2020;11:621773.
5. Silberstein M. COVID-19 and IL-6: why vitamin D (probably) helps but tocilizumab might not. *Eur J Pharmacol*. 2021;899:174031.