

Could Vitamin D Supplementation Help in Long COVID?

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Patients with long COVID-19 — where the effects of an initial COVID infection last more than 12 weeks — had lower levels of 25(OH) [vitamin D](#) than other patients who survived COVID-19, in a retrospective, case-matched study.

The lower levels of vitamin D in patients with long COVID were most notable in those with brain fog.

These findings, by Luigi di Filippo, MD, and colleagues, were [recently presented](#) at the European Congress of Endocrinology (ECE) in Istanbul, Turkey, and published in the *Journal of Clinical Endocrinology & Metabolism*.

"Our data suggest that vitamin D levels should be evaluated in COVID-19 patients after hospital discharge," write the researchers from San Raffaele Hospital, Milan, Italy.

"The role of vitamin D supplementation as a preventive strategy of COVID-19 sequelae should be tested in randomized controlled trials," they urge.

The researchers also stress that this was a controlled study in a homogeneous population, it included multiple signs and symptoms of long COVID, and it had a longer follow-up than most previous studies (6 vs 3 months).

"The highly controlled nature of our study helps us better understand the role of vitamin D deficiency in long COVID and establish that there is likely a link between vitamin D deficiency and long COVID," senior author Andrea Giustina, MD, said in a press release from the ECE.

"Our study shows that COVID-19 patients with low vitamin D levels are more likely to develop long COVID, but it is not yet known whether vitamin D supplements could improve the symptoms or reduce this risk altogether," he cautioned.

"If confirmed in large, interventional, randomized controlled trials, [our data suggest] that vitamin D supplementation could represent a possible preventive strategy in reducing the burden of COVID-19 sequelae," Giustina and colleagues summarize.

Reasonable to Test Vitamin D Levels, Consider Supplementation

Invited to comment, Amiel Dror, MD, PhD, who led a related [study](#) that showed that people with a vitamin D deficiency were more likely to have severe COVID-19, agreed.

"The novelty and significance of this [new] study lie in the fact that it expands on our current understanding of the interplay between vitamin D and COVID-19, taking it beyond the acute phase of the disease," Dror, from the Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel, told *Medscape Medical News* in an email.

"It's striking to see how vitamin D levels continue to influence patients' health even after recovery from the initial infection," he noted.

"The findings certainly add weight to the argument for conducting a randomized control trial (RCT)," he continued, which "would enable us to conclusively determine whether vitamin D supplementation can effectively reduce the risk or severity of long COVID."

"In the interim," Dror said, "given the safety profile of vitamin D and its broad health benefits, it could be reasonable to test for vitamin D levels in patients admitted with COVID-19. If levels are found to be low, supplementation could be considered."

"However, it's important to note that this should be done under medical supervision," he cautioned, "and further studies are needed to establish the optimal timing and dosage of supplementation."

"I anticipate that we'll see more RCTs [of this] in the future," he speculated.

Low Vitamin D and Risk of Long COVID

Long COVID is an emerging syndrome that affects 50% to 70% of COVID-19 survivors.

Low levels of vitamin D have been associated with increased likelihood of needing [mechanical ventilation](#) and worse survival in patients hospitalized with COVID-19, but the risk of long-COVID associated with vitamin D has not been known.

Researchers analyzed data from adults aged 18 and older hospitalized at San Raffaele Hospital with a confirmed diagnosis of COVID-19 and discharged during the first pandemic wave, from March to May 2020, and then seen 6-months later for follow-up.

Patients were excluded if they had been admitted to the intensive care unit during hospitalization or had missing medical data or blood samples available to determine (OH) vitamin D levels, at admission and the 6-month follow-up.

Long COVID-19 was defined based on the UK National Institute for Health and Care Excellence (NICE) guidelines as the concomitant presence of at least two or more of 17 signs and symptoms that were absent prior to the COVID-19 infection and could only be attributed to that acute disease.

Researchers identified 50 patients with long COVID at the 6-month follow-up and matched them with 50 patients without long COVID at that time point, based on age, sex, concomitant comorbidities, need for noninvasive mechanical ventilation, and week of evaluation.

Patients were a mean age of 61 years (range, 51-73) and 56% were men; 28% had been on a ventilator during hospitalization for COVID-19.

The most frequent signs and symptoms at 6 months in the patients with long COVID were asthenia (weakness, 38% of patients), dysgeusia (bad taste in the mouth, 34%), dyspnea (shortness of breath, 34%), and anosmia (loss of sense of smell, 24%).

Most symptoms were related to the cardiorespiratory system (42%), the feeling of well-being (42%), or the senses (36%), and fewer patients had symptoms related to neurocognitive impairment (headache or brain fog, 14%), or ear, nose, and throat (12%), or gastrointestinal system (4%).

Patients with long COVID had lower mean 25(OH) vitamin D levels than patients without long COVID (20.1 vs 23.2 ng/mL; $P = .03$). However, actual vitamin D deficiency levels were similar in both groups.

Two thirds of patients with low vitamin D levels at hospital admission still presented with low levels at the 6-month follow-up.

Vitamin D levels were significantly lower in patients with neurocognitive symptoms at follow-up ($n = 7$) than in those without such symptoms ($n = 93$) (14.6 vs 20.6 ng/mL; $P = .042$).

In patients with vitamin D deficiency (< 20 ng/mL) at admission and at follow-up ($n = 42$), those with long COVID ($n = 22$) had lower vitamin D levels at follow-up than those without long COVID ($n = 20$) (12.7 vs 15.2 ng/mL; $P = .041$).

And in multiple regression analyses, a lower 25(OH) vitamin D level at follow-up was the only variable that was significantly associated with long COVID ($P = .008$; odds ratio, 1.09; 95% CI, 1.01 - 1.16).

The findings "strongly reinforce the clinical usefulness of 25(OH) vitamin D evaluation as a possible modifiable pathophysiological factor underlying this emerging worldwide critical health issue," the researchers conclude.

The study was supported by Abiogen Pharma. One study author is an employee at Abiogen. Giustina has reported being a consultant for Abiogen and Takeda and receiving a research grant to his institution from Takeda. Di Filippo and the other authors have reported no relevant financial relationships.

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