

Vitamin D and COVID-19 - What do the current recommendations say?

Pathmanathan S¹, Karuppiah D²

¹Diabetes and Endocrinology unit, National Hospital of Sri Lanka. ²Diabetes and Endocrinology unit, Teaching Hospital Batticaloa.

Correspondence email: psivatharshya@gmail.com

 <https://orcid.org/0000-0002-2510-3642>

COVID-19 pandemic remains a major public health threat in most countries. The causative agent is SARS-CoV-2 virus, a zoonotic virus, which lead to acute respiratory distress syndrome and result in mortality in COVID-19 patients. Ever since the discovery of the first case in the Wuhan city in China in late December 2019, both developed and developing nations are struggling to bring this pandemic under control. Currently we are facing an imminent risk of a third wave which is already in force in some countries. Development of an effective vaccine has helped to reduce the number of active cases; nevertheless it has failed to curb the disease completely. ^(1,2)

Vitamin D is a fat-soluble vitamin produced from 7-dehydrocholesterol due to the action of UVB radiation and subsequently converted to 25 hydroxy vitamin D3 (25(OH)D3) in the liver and then to the active form calcitriol, (1, 25(OH)D) in the kidneys or other organs.^{3,4} In addition to being involved in bone metabolism, facilitating the absorption of calcium and phosphorus from the intestinal tract, the role of vitamin D in the immune system has also been recognized. Vitamin D reduces the risk of microbial infections by stimulating innate cellular immunity, through the induction of

antimicrobial peptides, such as cathelicidins, IL-37 and defensins. It also inhibits the cytokine storm, reducing the production of pro-inflammatory cytokines such as IFN γ and TNF α . Finally, it modulates the adaptive immune response, suppressing the T-helper cells-1 response and promoting cytokines production by T-helper cells -2. This effect requires a sufficient serum level of 25(OH) D3 being crucial for macrophages to activate it into calcitriol, which activates the remaining cascade. Nevertheless it is not easy to fully understand the complex mechanism of vitamin D-mediated effects on immunity and studies are ongoing which could shed some more light in the future^(5,6,7,8).

It is challenging to conduct evidence-based medicine in cases such as the COVID-19 pandemic. Therefore specialized bodies like The European Centre for Disease Prevention and Control encouraged health care professionals to take actions that are logical in their own right, based on previously known findings in related fields. In the initial part of the pandemic, there were no data on the effects of vitamin D in SARS-CoV-2 infection. Considering the studies on the role of vitamin D in the prevention of acute respiratory infections, it was natural to ask the question of whether supplementation of



This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited (CC BY 4.0)

vitamin D can be used as a potentially interesting treatment for the prevention of severe acute respiratory syndrome in SARS-CoV-2 infections thereby reducing morbidity and mortality in COVID-19 high-risk patients.^(9,10,11)

Retrospective studies conducted in early 2020 reported significant association between vitamin D deficiency and poor clinical outcome of the COVID-19 cases. These studies reported that deficiency was highest in the most severe COVID-19 cases and some studies reported that after adjusting with confounding factor, a significant association was observed between vitamin D levels and disease severity, patients' mortality, CRP levels and increased lymphocyte percentage. Further, vitamin D sufficiency was also associated with lower risk of unconsciousness and hypoxia.^(12,13,14)

Similarly, few studies have highlighted that high doses of vitamin D may be given to COVID-19 patients especially with confirmed deficiency and also associated with co morbidities such as obese, elderly, dark skin texture and those living in higher latitudes. Therefore, several authors have emphasized the prophylactic use of vitamin D in the COVID-19 management.^(13,14,15)

But several more recent studies in many different regions worldwide on Vitamin D supplementation in COVID-19 patients have produced relatively inconsistent results. This could be due to different patient characteristics and study design across the studies.^(14,15,16)

Indeed, several randomized control trials are currently underway to investigate the impact of vitamin D supplementation on patients with COVID -19 infection. The results of these studies will be accessible in near future

and will provide valuable information such as to what extent vitamin D supplementation will benefit the patients with COVID -19 infections.^(13,14,15,16)

Until these results are available there are certain recommendations which could be adapted with regards to vitamin D supplementation in patients with COVID -19 infections.

- Vitamin D is safe and vitamin D at a dose of 1000–2000 IU per day is enough to keep the immune system healthy.
- No mega-doses are needed which may only lead to increased risk for adverse events.
- If possible, patients can be tested for vitamin D levels in serum and supplements should only be provided to those below 50 nmol L⁻¹. This will protect the bone and be enough to enhance respiratory immunity against severe respiratory tract infections. This will help you to only supplement individuals that need extra vitamin D and avoid unnecessary costs.
- If Vitamin D levels cannot be performed, high risk groups such as dark skin, the elderly, patients with chronic diseases and obese patients should have first priority for supplementation.

Because a protective effect of vitamin D supplementation remains uncertain at present, taking vitamin D supplements should nevertheless not discourage the public from adhering to routine protective measures such as social distancing and wearing of face masks.

References

1. Fisher D, Heymann D. Q&A: the novel coronavirus outbreak causing COVID-19. *BMC Med* 2020;**18**:57.
2. Umakanthan S, Sahu P, Ranade AV, et al. Origin, transmission, diagnosis and management of coronavirus disease 2019 (COVID-19). *Postgrad Med J*. 2020;**96**:753–758.
3. Holick MF. Vitamin D deficiency. *N Engl J Med* 2007; **357**: 266–81.
4. Sahota O. Understanding vitamin D deficiency. *Age Ageing*. 2014;**43**(5):589. doi: 10.1093/ageing/afu104.
5. Hewison M. Antibacterial effects of vitamin D. *Nat Rev Endocrinol* 2011; **7**: 337–45.
6. Martineau AR, Jolliffe DA, Hooper RL et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ* 2017; **356**: i6583.
7. Daneshkhah A, Agrawal V, Eshein A et al (2020) The possible role of vitamin D in suppressing cytokine storm and associated mortality in COVID-19 patients, medRxiv preprint. 10.1101/2020.04.08.20058578
8. Autier P., Mullie P., Macacu A., Dragomir M., Boniol M., Coppens K., Pizot C., Boniol M. Effect of vitamin D supplementation on non-skeletal disorders: a systematic review of meta-analyses and randomised trials. *Lancet Diabetes Endocrinol*. 2017;**5**:986–1004. doi: 10.1016/S2213-8587(17)30357-1.
9. Bilezikian JP, Bikle D, Hewison M, Lazaretti-Castro M, Formenti AM, Gupta A, Madhavan MV, Nair N, Babalyan V, Hutchings N, Napoli N, Accili D, Binkley N, Landry DW, endocrinology: vitamin D and COVID-19. *Eur J Endocrinol*. 2020;**183**(5):R133–r147. doi: 10.1530/eje-20-0665.
10. Mohan M, Cherian JJ, Sharma A. Exploring links between vitamin D deficiency and COVID-19. *PLoS Pathog*. 2020;**16**(9):e1008874. Published 2020 Sep 18. doi:10.1371/journal.ppat.1008874
11. Trovas G, Tournis S. Vitamin D and COVID-19. *Hormones (Athens)*. 2021;**20**(1):207-208. doi:10.1007/s42000-020-00231-9
12. Hastie CE, Mackay DF, Ho F, et al. Vitamin D concentrations and COVID-19 infection in UK Biobank. *Diabetes Metab Syndr*. 2020;**14**(4):561–565. doi:10.1016/j.dsx.2020.04.050
13. Meltzer DO, Best TJ, Zhang H, Vokes T, Arora V, Solway J. Association of vitamin D status and other clinical characteristics with COVID-19 test results. *JAMA Netw Open*. 2020;**3**(9):e2019722. doi: 10.1001/jamanetworkopen.2020.19722.
14. Isaia G, Medico E. Associations between hypovitaminosis D and COVID-19: a narrative review. *Ageing Clin Exp Res*. 2020;**32**(9):1879–1881. doi: 10.1007/s40520-020-01650-9.
15. Mercola J, Grant WB, Wagner CL. Evidence Regarding Vitamin D and Risk of COVID-19 and Its Severity. *Nutrients*. 2020;**12**(11):3361. Published 2020 Oct 31. doi:10.3390/nu12113361
16. Kumar R, Rathi H, Haq A, Wimalawansa SJ, Sharma A. Putative roles of vitamin D in modulating immune response and immunopathology associated with COVID-19. *Virus Res*. 2021;292:198235. doi:10.1016/j.virusres.2020.19823