

# Implications of Vitamin D Levels in COVID-19 Morbidity and Mortality

Nahal Emami Fard<sup>1</sup>, Niki Sadat Afjeh<sup>1</sup>, Paniz Poursharif<sup>2</sup>

1. McMaster University, Biology, Class of 2021

2. McMaster University, Life Sciences, Class of 2021

Received | 14 October 2020  
Accepted | 29 October 2020  
Published | 4 December 2020

## SUMMARY

Recent research shows relationships between optimal vitamin D levels and better outcomes in COVID-19. Vitamin D is a hormone required for healthy bones. When its levels in the blood drop below 25 nmol/L, one is vitamin D deficient. Insufficiency is when blood vitamin D levels are below 75 nmol/L. 70% of the US population are vitamin D deficient, while 30% are vitamin D insufficient. This study analyzes three articles revealing associations between vitamin D levels and risk of death and severe health complications from COVID-19 in adults. Maghbooli et al. (2020) reports that vitamin D sufficient patients had lower risks than deficient patients of severe COVID-19 complications. A study by Raharusun et al. (2020) finds that 98.9% of vitamin D deficient COVID-19 patients and 88% with vitamin D insufficiency died. Only 4% of sufficient individuals died. Meltzer et al. (2020) reports higher rates of COVID-19 in vitamin D deficient compared to sufficient groups. Vitamin D sufficiency may activate the immune system's antiviral response. Vitamin D binds to immune cells, stimulating the production of an antibacterial protein. More studies should examine vitamin D sufficiency as a potential mitigator in COVID-19 consequences.

## ABSTRACT

Vitamin D is a steroid hormone known for maintaining bone health. Vitamin D deficiency is a 25-hydroxyvitamin D (25(OH)D) serum concentration below 25 nmol/L. In contrast, vitamin D insufficiency occurs at levels below 75 nmol/L.<sup>1</sup> Vitamin D insufficiency and deficiency affect 70% and 30% of the US population, respectively.<sup>1</sup> Emerging evidence associates optimal vitamin D levels with better clinical outcomes in COVID-19.<sup>2</sup> This literature review analyzed three preliminary articles that explored associations between vitamin D levels, COVID-19 mortality, and risk of adverse clinical outcomes in adult hospitalized patients.<sup>3-5</sup> Google Scholar was used to find studies that diagnosed COVID-19 with reverse transcription (RT-PCR). In a cross-sectional analysis, Maghbooli et al. (2020) reported that vitamin D sufficient patients had a significantly lower chance (9.7%, n=77, p=0.01) of severe COVID-19 complications than deficient patients (32.8%, n=158, p=0.01).<sup>3</sup> This study is under review for diagnosis accuracy and sample size. A retrospective cohort study by Raharusun et al. (2020), which included active and expired cases (n=780), found that 98.9% (p<0.001) of vitamin D deficient COVID-19 patients and 88% (p<0.001) with insufficiency died, but only 4% of sufficient individuals died.<sup>5</sup> Lastly, a retroactive cohort study by Meltzer et al. (2020) reported higher rates of COVID-19 infection, 21.6% (95% CI, 14.0-29.2%), in vitamin D deficient groups (n=172), compared to 12.2% (95% CI, 8.5-15.4%) in sufficient groups (n=327).<sup>4</sup> The 25(OH)D levels were measured within one year of COVID-19 testing.<sup>4</sup> All studies controlled for age, sex, and comorbidities, while the first controlled for BMI and smoking, and the third controlled for race.<sup>3-5</sup> Vitamin D sufficiency may activate the innate and adaptive immune systems, leading to an antiviral response.<sup>6,7</sup> Receptor binding of vitamin D on neutrophils and macrophages stimulates cathelicidin expression, an antibacterial peptide.<sup>7</sup> Macrophage and T-regulatory cell quantities also increase.<sup>7</sup> These results reveal the need for randomized controlled studies of vitamin D sufficiency as a potential mitigator in COVID-19 outcomes.

**Keywords:** Vitamin D deficiency, vitamin D insufficiency, vitamin D sufficiency, COVID-19 mortality, COVID-19 morbidity

## ACKNOWLEDGEMENTS

There are no acknowledgements. The authors report no conflicts of interest.

## REFERENCES

- (1) Liu X, Baylin A, Levy PD. Vitamin D deficiency and insufficiency among US adults: prevalence, predictors and clinical implications. *Br J Nutr.* 2018;119(8):928–36.
- (2) Cashman KD, Dowling KG, Škrabáková Z, Gonzalez-Gross M, Valtueña J, De Henauw S, et al. Vitamin D deficiency in Europe: pandemic? *Am J Clin Nutr.* 2016;103(4):1033–44.
- (3) Maghbooli Z, Sahraian MA, Ebrahimi M, Pazoki M, Kafan S, Tabriz HM, et al. Vitamin D sufficiency, a serum 25-hydroxyvitamin D at least 30 ng/mL reduced risk for adverse clinical outcomes in patients with COVID-19 infection. *PLoS One.* 2020;15(9):e0239799.
- (4) 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
- (5) Raharusun, P. (2020). Patterns of COVID-19 Mortality and Vitamin D: An Indonesian Study. Available at SSRN 3585561.
- (6) Rhodes JM, Subramanian S, Laird E, Griffin G, Kenny RA. Perspective: Vitamin D deficiency and COVID-19 severity - plausibly linked by latitude, ethnicity, impacts on cytokines, ACE2 and thrombosis. *J Intern Med* [Internet]. 2020; Available from: <http://dx.doi.org/10.1111/joim.13149>
- (7) Siuka D, Pfeifer M, Pinter B. Vitamin D supplementation during the COVID-19 pandemic. *Mayo Clin Proc.* 2020;95(8):1804–5.

## ARTICLE INFORMATION

### Senior Editor

Stefano A. Biasi

### Reviewers and Section Editors

Caitlin Reintjes, Zoya Adeel

### Formatting and Illustrations

Youssef El-Sayes