

## LETTER TO THE EDITOR

# COVID-19 and vitamin D—Is there a link and an opportunity for intervention?

 **Hrvoje Jakovac**

Department of Physiology and Immunology, Medical Faculty, University of Rijeka, Rijeka, Croatia

Submitted 6 April 2020; accepted in final form 7 April 2020

TO THE EDITOR: The recent outbreak and rapid spreading of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are a global threat and primary concern worldwide, with a still uncertain outcome. With the lack of effective therapy, chemoprevention, and vaccination, focusing on the immediate repurposing of existing drugs gives hope of curbing the pandemic. Here, I underline that so far there are no reports on the vitamin D status among affected persons. On the other hand, a large number of well-established data showed antiviral effects of vitamin D, which can interfere directly with viral replication, but also can act in an immunomodulatory and anti-inflammatory way (7). The latter effects could be crucial for their assumptive beneficial effects during SARS-CoV-2 infection, since it seems that SARS-CoV-2 initially uses immune evasion mechanisms, which in some patients is followed by immune hyperreaction and cytokine storm (1), as a common pathogenic mechanism of acute respiratory disease syndrome (ARDS) and systemic inflammatory response syndrome (SIRS) development, regardless of the etiological factor. In that sense, the protective effect of vitamin D has been reported in many conditions associated with pneumonia, cytokine hyperproduction, and ARDS (2, 8, 10), and vitamin D was recently proposed as a repurposed drug for influenza A H5N1 virus-induced lung injury (3). Additionally, some studies suggest the effectiveness of vitamin D as an adjuvant therapy along with antiretroviral agents in HIV-infected patients (5). Furthermore, vitamin D pretreatment was beneficial in animal models of ARDS, reducing lung permeability by modulation of renin-angiotensin system activity and ACE2 expression (9). The role of vitamin D in the context of viral infections is also supported by findings of certain vitamin D receptor gene (*VDR*) alleles that are associated with increased susceptibility to respiratory infections (6), as well as with the progression of HIV infection (4).

Owing to the lack of specific treatment and urgency to act, these findings could be tentatively extrapolated to SARS-CoV-2 infection, justifying the use of vitamin D as a possible adjuvant therapy. From the public health aspect, the recommendation of intensive supplementation as possible prophylaxis also could be considered. Given the good tolerability and safety of even high doses of vitamin D, this approach complies *primum non nocere* principle.

Investigations on vitamin D status and *VDR* polymorphisms of affected subjects could contribute to explain “unusual be-

havior” of SARS-CoV-2 spreading and a tremendous variety of COVID-19 clinical presentations and outcomes.

## DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author.

## AUTHOR CONTRIBUTIONS

H.J. drafted manuscript; edited and revised manuscript; approved final version of manuscript.

## REFERENCES

1. Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, Tan KS, Wang DY, Yan Y. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status. *Mil Med Res* 7: 11, 2020. doi:10.1186/s40779-020-00240-0.
2. Hong M, Xiong T, Huang J, Wu Y, Lin L, Zhang Z, Huang L, Gao D, Wang H, Kang C, Gao Q, Yang X, Yang N, Hao L. Association of vitamin D supplementation with respiratory tract infection in infants. *Matern Child Nutr* 5: e12987, 2020. doi:10.1111/mcn.12987.
3. Huang F, Zhang C, Liu Q, Zhao Y, Zhang Y, Qin Y, Li X, Li C, Zhou C, Jin N, Jiang C. Identification of amitriptyline HCl, flavin adenine dinucleotide, azacitidine and calcitriol as repurposing drugs for influenza A H5N1 virus-induced lung injury. *PLoS Pathog* 16: e1008341, 2020. doi:10.1371/journal.ppat.1008341.
4. Jiménez-Sousa MA, Jiménez JL, Fernández-Rodríguez A, Brochado-Kith O, Bellón JM, Gutierrez F, Díez C, Bernal-Morell E, Viciano P, Muñoz-Fernández MA, Resino S. *VDR* rs2228570 polymorphism is related to non-progression to AIDS in antiretroviral therapy naïve HIV-infected patients. *J Clin Med* 8: E311, 2019. doi:10.3390/jcm8030311.
5. Jiménez-Sousa MÁ, Martínez I, Medrano LM, Fernández-Rodríguez A, Resino S. Vitamin D in human immunodeficiency virus infection: influence on immunity and disease. *Front Immunol* 9: 458, 2018. doi:10.3389/fimmu.2018.00458.
6. Jolliffe DA, Greiller CL, Mein CA, Hoti M, Bakhsoliani E, Telcian AG, Simpson A, Barnes NC, Curtin JA, Custovic A, Johnston SL, Griffiths CJ, Walton RT, Martineau AR. Vitamin D receptor genotype influences risk of upper respiratory infection. *Br J Nutr* 120: 891–900, 2018. doi:10.1017/S000711451800209X.
7. Teymoori-Rad M, Shokri F, Salimi V, Marashi SM. The interplay between vitamin D and viral infections. *Rev Med Virol* 29: e2032, 2019. doi:10.1002/rmv.2032.
8. Tsujino I, Ushikoshi-Nakayama R, Yamazaki T, Matsumoto N, Saito I. Pulmonary activation of vitamin D<sub>3</sub> and preventive effect against interstitial pneumonia. *J Clin Biochem Nutr* 65: 245–251, 2019. doi:10.3164/jcbr.19-48.
9. Xu J, Yang J, Chen J, Luo Q, Zhang Q, Zhang H. Vitamin D alleviates lipopolysaccharide-induced acute lung injury via regulation of the renin-angiotensin system. *Mol Med Rep* 16: 7432–7438, 2017. doi:10.3892/mmr.2017.7546.
10. Zhou YF, Luo BA, Qin LL. The association between vitamin D deficiency and community-acquired pneumonia: A meta-analysis of observational studies. *Medicine (Baltimore)* 98: e17252, 2019. doi:10.1097/MD.00000000000017252.

Correspondence: H. Jakovac (e-mail: hrvoje.jakovac@medri.uniri.hr).