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Letter to the editor

Vitamin D deficiency and inactivated SARS-CoV-2 vaccines

Vaccines are a critical tool in the battle against COVID-19. An amazing article regarding the effects of 2 inactivated SARS-CoV-2 vaccines in symptomatic COVID-19 patients, and stated that the vaccine efficacy was around 72~78% in the United Arab Emirates and Bahrain [1]. The efficacy of the BNT162b2 and mRNA-1273 vaccine reached 94~95%, which was performed primarily in the United States. Although inactivated whole-virus vaccines may induce more types of antiviral antibodies than mRNA vaccines, the level of neutralizing antibodies was lower, resulting in a comparatively lower protective effect. The relationship between vaccine immunogenicity and protection showed that serum neutralizing antibody level is highly predictive of immune protection from symptomatic SARS-CoV-2 infection [2]. However, the study location and the associated environmental factors, such as vitamin D adequacy, should be considered

Vitamin D deficiency (VDD) occurs all over the world, predominantly in the Middle East, China, Mongolia, and India. In these areas, the mean serum 25(OH)D level is lower and the percentage of VDD is higher than those in Europe or America [3]. Vitamin D deficiency is prevalent among COVID-19 patients. Vitamin D exerts immunomodulatory effects both on innate and adaptive immune responses. It enhances the synthesis of anti-microbial peptides, promotes autophagy and increases the production of lysosomal degradation enzymes within macrophages. For adaptive immunity, vitamin D improves CD4+ T lymphocytes, suppresses T helper 17 lymphocytes and promotes the production of virus-specific antibodies by activating T-dependent B lymphocytes. In addition, vitamin D attenuates the cytokine storm, increases the bioavailability and expression of ACE2, inhibits renin expression and enhance type 1 interferon anti-viral replication. All of above mechanisms might contribute to the beneficial effects of vitamin D on COVID-19 [4].

In a systematic review and meta-analysis study, a very uncertain evidence was found for a cause-effect relationship of vitamin D status with various COVID-19-related health outcomes. The current use of high doses of vitamin D in COVID-19 patients is also lack of solid evidence [5]. However, it is unclear whether VDD will influence immune responses to inactivated SARS-CoV-2 vaccination. Therefore, we assume that the comparatively low vaccine effectiveness of inactivated SARS-CoV-2 vaccines is due, at least in part, to low levels of vitamin D in the geographic area (Middle East region) of the study. Whether vitamin D supplementation in the VDD population will mitigate this disadvantage

and improve the efficacy of vaccination merits further investigation.

Declaration of competing interests

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this article.

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Author contribution statement

All authors contributed to the writing of this letter. All authors read and approved the final manuscript for publication.

References

- [1] Al Kaabi N, Zhang Y, Xia S, Yang Y, Al Qahtani MM, Abdulrazzaq N, et al. Effect of 2 inactivated SARS-CoV-2 vaccines on symptomatic COVID-19 infection in adults: a randomized clinical trial. *JAMA* 2021;326:35–45.
- [2] Khoury DS, Cromer D, Reynaldi A, Schlub TE, Wheatley AK, Juno JA, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nat Med* 2021;27:1205–11.
- [3] van Schoor N, Lips P. Global overview of vitamin D status. *Endocrinol Metab Clin North Am* 2017;46:845–70.
- [4] Peng MY, Liu WC, Zheng JQ, Lu CL, Hou YC, Zheng CM, et al. Immunological aspects of SARS-CoV-2 infection and the putative beneficial role of vitamin-D. *Int J Mol Sci* 2021;22.
- [5] Bassatne A, Basbous M, Chakhtoura M, El Zein O, Rahme M, El-Hajj Fuleihan G. The link between COVID-19 and Vitamin D (VIVID): a systematic review and meta-analysis. *Metab* 2021;119:154753.

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