Role of vitamin D deficiency and comorbidities in COVID-19

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Abstract

Recent manuscripts described the incidence of vitamin D hypovitaminosis in coronavirus disease 2019 (COVID-19) patients. Vitamin D deficiency is also common in patients with comorbidities that are associated with a poor COVID-19 prognosis. In this letter, we review the literature regarding the association of comorbidities, vitamin D deficiency, and COVID-19.

Key Words: COVID-19; SARS-CoV-2; Comorbidities; Vitamin D

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Core Tip: Vitamin D deficiency is a worldwide problem, and investigations on the benefits of regulating vitamin D levels and the immune response should be performed. Nevertheless, the association between low levels of vitamin D and coronavirus disease 2019 (COVID-19) needs to be further explored, especially investigations on the immune response to COVID-19 and COVID-19 vaccines in patients with and without comorbidities.

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We read with great interest the article entitled “Association between population vitamin D status and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) related serious-critical illness and deaths: An ecological integrative approach” recently published by Papadimitriou et al [1] in the World Journal of Virology [1]. This manuscript raised important questions and the authors performed an extensive analysis on vitamin D levels and COVID-19 incidence and severity in Europe, and the potential benefits of vitamin D supplementation to enhance the immune response to the SARS-CoV-2 [1]. In the light of these results, we humbly want to state a few points for consideration.

Severe coronavirus disease 2019 (COVID-19) patients present a systemic inflammatory response with a coagulation disorder, possibly evolving to death [2]. Several comorbidities have been identified as risk factors for poor disease prognosis, such as old age [3], co-infections [4], obesity and diabetes mellitus [5], severe asthma, alcohol drinking [6], chronic obstructive pulmonary disease [7], chronic liver disease [8], and cancer [9].

Vitamin D deficiency is associated with poor response to respiratory infections [10], and few reports have identified vitamin D deficiency in moderate and severe COVID-19 patients with conflicting results [1,11,12].

Vitamin D receptor is expressed in many immune cells, including monocytes, macrophages, dendritic cells, neutrophils, and lymphocytes [13-15]. Vitamin D increases the antimicrobial activity of monocytes and macrophages [16] and has anti-inflammatory effects due to the induction of T regulatory cells and reduction in the T helper-17 immune response and pro-inflammatory cytokine production [15].

Papadimitriou et al [1] performed an important investigation on the association of vitamin D deficiency and COVID-19 [1]. Vitamin D levels can be influenced by many factors such as sun exposure, genetics, supplementation, and comorbidities [17-20].

Vitamin D hypovitaminosis is associated with several comorbidities that are also related to poor COVID-19 prognoses such as old age [21], co-infections [18], obesity [22], diabetes mellitus [23], alcohol drinking, and smoking [24-26], uncontrolled asthma, but not controlled asthma, chronic obstructive pulmonary disease [25-28], cancer [29], and solid organ transplant recipient patients [30].

Besides comorbidities, vitamin D hypovitaminosis is associated with poor glycemic control [23], which is also associated with poor COVID-19 outcomes in diabetic and non-diabetic patients [31]. Cancer patients present low circulating levels of vitamin D [29] and experimental models have identified that vitamin D can modulate the disease development by regulating cell cycle and inflammatory response [32].

Vitamin D deficiency is a worldwide problem [33,34], and vitamin D supplementation has the potential to enhance the immune response to microorganisms [1]. Vitamin D supplementation has been investigated for the treatment and prevention of severe COVID-19, indicating a potential reduction in COVID-19 severity [35].

A recent investigation found that prophylactic vitamin D supplementation in elders improved the SARS-CoV-2 immune response [36], and another investigation identified that the treatment with vitamin D reduces COVID-19 severity [37]. Nevertheless, another report found no additional benefit in vitamin D supplementation during COVID-19 [38].

Low vitamin D levels also modulate the Renin-Angiotensin-System, which could increase the susceptibility to COVID-19 [39], since SARS-CoV-2 uses the angiotensin-converting enzyme 2 and Transmembrane Protease Serine 2 (TMPRSS2) to invade the host’s cells [40]. In addition, the lack of vitamin D is a risk factor for the development of autoimmune and neuropsychiatric disorders [41].

Lakkireddy et al [42] identified that increasing the serum levels of vitamin D to 80–100 ng/mL significantly reduced inflammatory biomarkers such as interleukin-6, C-reactive protein, and neutrophil-to-lymphocyte ratio during COVID-19, without side effects [42].

In addition, Papadimitriou et al [1] recommendation for vitamin D supplementation should also be considered in a broader context [1], outside the COVID-19 pandemic situation, due to the high incidence of vitamin D hypovitaminosis worldwide, the vast associations with other diseases, and the proposed doses do not require medical supervision [1].

COVID-19 vaccination is ongoing worldwide [43-45], since vitamin D can modulate the immune response to vaccines [46,47], investigations on the vaccines should consider evaluating vitamin D levels and the effects of supplementation on the immune response to vaccines.
In summary, vitamin D hypovitaminosis is associated with comorbidities that are known to affect COVID-19 severity and outcome. Further investigations should focus on patients with low vitamin D levels with and without comorbidities and supplementation trials to investigate the effects of vitamin D on the immune response to COVID-19 and COVID-19 vaccines.

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