Series of Clinical and Medical Case Reports and Reviews

Review Article

The Role of Vitamin D in COVID-19: A Review Study

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Received: 01 November 2022
Accepted: 05 December 2022
Published: 15 December 2022

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is defined as the virus causing the present coronavirus disease outbreak (COVID-19) that has been initially discovered in Wuhan, China after complaints of severe pneumonia. The impact of vitamin D on complications and treatment of COVID-19, as well as its potential role in lowering the incidence of COVID-19, has been the subject of much investigation. The correlation between COVID-19 infections and vitamin D will be demonstrated in the presented work.

Keywords: SARS-CoV-2, vitamin D, COVID-19

Abbreviations: SARS: severe acute respiratory syndrome, SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, ARDS: acute respiratory distress syndrome

1. Introduction

The WHO first identified COVID-19 in China in December 2019 and declared it a pandemic on March 11, 2020 [1]. The family of viruses known as coronaviruses (CoVs) is responsible for intestinal and respiratory disorders in both people and animals [2]. The advent of the SARS epidemic in China between the years 2002 and 2003 and the Middle East Respiratory Syndrome (MERS) in the Arabian Peninsula in the year 2012 demonstrate that they can potentially result in severe disease. They typically give people moderate cold. The globe was combating a new coronavirus since December 2019. The virus causing the present COVID-19 which has been discovered initially in Wuhan, China after reports of significant pneumonia is known as SARS-CoV-2 [3, 4]. With regard to COVID-19, there is no proven treatment at this time. Thus, prompt patient isolation, early diagnosis, and protective circumstances for stopping the infection were critical components in the management of COVID-19 patients. Treatment for COVID-19 was often supportive and included respiratory and nutritional assistance [5]. Even though almost all people with COVID-19 are asymptomatic or only experience minor signs, a few individuals might experience fatal clinical syndromes like ARDS (acute respiratory distress syndrome), pneumonia, microvascular thrombosis, myocarditis, and cytokine storm [6]. Single-strand positive-sense RNA from the genome of SARS-CoV-2 is contained within a membrane envelope with a mean diameter of 75 nm–150 nm. Coronaviruses have a crown-like shape (corona is *Latin* for garland or crown) due to the glycoprotein spikes covering the envelope. The SARS-CoV-2 genome is around 30 K nucleotides long. This virus shares over 85% of its homology with the SARS-CoV [7].

The effect of vitamin D in the management and side effects of COVID-19, as well as its potential role in lowering the incidence of COVID-19, have been the subject of much investigation. Through stimulating the release of cathelicidin and defensin proteins in macrophages and monocytes, vitamin D has antiviral action and prevents viral replication [8, 9]. The presented study will demonstrate how vitamin D affects COVID-19 infections and its role in preventing them.

1.1 Vitamin D as an immune response regulator

Another well-known role of vitamin D is immunomodulation [10]. Through the generation of numerous antimicrobial peptides (defensins, cathelicidins, and IL-37), it supports innate immunity. As demonstrated in **Figure 1**, vitamin D also influences adaptive immunity by regulating the key proinflammatory cytokines (like TNF-alpha, IL6, and interferon-gamma) and the response mediated by Th1 cells. In case of vitamin D insufficiency, this

regulation is anticipated to be less effective, yet it may be restored with proper supplementation [11].

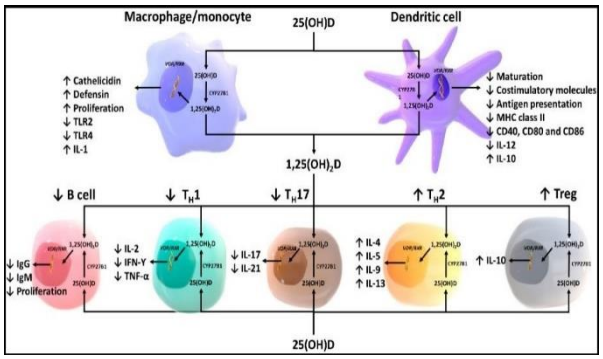

Figure 1: Schematic representation of vitamin D and its metabolites and action of 1,25-dihydroxyvitamin D on the innate and adaptive immune system [12].

1.2 Vitamin D and cardiovascular system in COVID-19

In addition to the myocardial injury and type 1 myocardial infarction, arrhythmias, acute cor pulmonale, acute coronary syndromes, cardiomyopathy, thrombotic problems, and cardiogenic shock, COVID-19 was linked to cardiovascular sequelae [13–15]. According to preclinical research, vitamin D might prevent atherosclerosis by preventing macrophages from becoming foam cells and by boosting cholesterol efflux [16]. In clinical and experimental tests of vitamin D insufficiency, the different cardiovascular risk factors that were linked to greater mortality from COVID-19 have been more evident as well. The risk factors that are related to vitamin D deficiency for CVD in COVID-19 are diabetes, hypertension, CKD, and obesity. Vitamin D deficiency might increase vascular resistance and vasoconstriction, upregulate the renin-angiotensin-aldosterone system (RAAS), and predispose to hypertension [17–30].

1.3 Vitamin D and pulmonary infections in COVID-19

A current meta-analysis that looked at a total of 1,787 patients who have pulmonary tuberculosis and the impact of supplementation with vitamin D on various outcomes showed a few benefits and came to the conclusion that the supplementation must be thought of as adjuvant therapy along with the antibiotics [31]. The correlation between viral infections and vitamin D was discovered as a result of seasonal variations in the levels of vitamin D and the corresponding rise in influenza. In contrast, except throughout pandemics, levels of serum vitamin D rise during summer and influenza almost disappears. Even in pandemics, cold months are when most people pass away [32]. Infections, particularly respiratory tract infections are linked to lower concentrations of vitamin D [33]. Because of its effects such as promoting T-lymphocyte chemotaxis and eliminating respiratory pathogens by triggering apoptosis and autophagy in the infected epithelium, vitamin D is crucial in preventing respiratory system infections [34]. According to reports, a few COVID-19 patients with severe symptoms had low T-lymphocyte count [35]. This result supports the idea that vitamin D could be helpful in treating COVID-19 because vitamin D supplementation raises the level of T-lymphocytes [36].

Considering the demonstrated role of vitamin D in many infectious respiratory tract disorders, it stands to a role that vitamin D could be involved as well in the infection of SARS-CoV-2. The enhanced production of Th1 pro-inflammatory cytokines (which lead to cytokine storm) is the mechanism through which SARS-CoV-2 causes damage to the tissue of the lung and causes acute respiratory failure to occur [37]. Vitamin D decreases cytokine storm by converting the pro-inflammatory Th1 and Th17 response to the anti-inflammatory Th2 and Treg response [38].

1.4 Mechanisms of vitamin D to reduce viral infections

Recent studies have shown a few of the mechanisms through which vitamin D lowers microbial infection incidence. Various pathways are used by vitamin D to lower risks of the viral infections and mortality. Three mechanisms are used by vitamin D to lower the risk of the common cold [39–43]:

1. adaptive immunity
2. cellular natural immunity
3. physical barrier

A recent study supported that vitamin D might help to reduce the incidence of COVID-19 mortality and infection. Maintaining cell junctions and gap junctions, boosting cellular immunity through the reduction of cytokine storm with an impact on the interferon γ and TNF, and regulating adaptive immunity through the suppression of T helper cell type 1 response and inducing T cells are a few examples of these. In HIV infection, supplementation with vitamin D has been reported to increase CD4 + T cell count as well [44].

Lymphopenia can be defined as one of the key signs of a severe infection with SARS-CoV-2 [45]. Vitamin D displayed activity in the tissue of the lung and had a protective effect on experimental interstitial pneumonitis in human cell lines as well as mice models [46]. Numerous in vitro researches had shown that vitamin D contributes significantly to the role of local "respiratory homeostasis," either through the stimulation of antimicrobial peptide expression or through directly preventing replication of the respiratory viruses [47]. Thus, heart failure and ARDS, which are symptoms of critically ill COVID-19 subjects can be caused by vitamin D inadequacy. Because of this, chronic CVD and reduced lung function might result from vitamin D deficiency promoting the renin-angiotensin system (RAS) [48]. People with these comorbidities make up a greater

proportion of the severe illness cases in COVID-19 [45].

2. Conclusion

Since higher blood levels of vitamin D have been associated with a decreased severity and risk of COVID-19, maintaining enough vitamin D blood levels by supplementations or sun exposure is advised for the general populace to be able to handle the pandemic.

3. Recommendation

Despite the fact that various work has demonstrated the immunomodulatory properties of vitamin D in addition to its important role in the preservation of immune homeostasis; well-designed randomized controlled trials have been considered necessary to clarify the plausible role of vitamin D in protective immune responses against the respiratory microbes and in the prevention of different types of acute infections of the respiratory tract.

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