



## Role of Vitamin D Supplementation in Prevention and Treatment of COVID-19

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Dear Editor,

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a primary concern among the nations worldwide as the virus is highly contagious. Hence, there is a pressing need to develop effective preventive and therapeutic strategies to combat this global public health problem.

COVID-19 infection is associated with the increased production of pro-inflammatory cytokines, increased risk of pneumonia, sepsis and acute respiratory distress syndrome. Accumulating evidence suggests that Vitamin D has antiviral, immunomodulatory and anti-inflammatory actions [1]. Therefore, I would like to underline the importance of Vitamin D levels in COVID-19 patients.

Calcitriol (1,25dihydroxycholecalciferol) which is the active form of vitamin D acts as an immune system modulator by providing effective physical barrier and strengthening both innate and adaptive immunity. It maintains epithelial barrier integrity by restoring tight

junctions, gap junctions, and adherens junctions [2]. In addition to this, Vitamin D enhances innate immunity by increasing the production of Antimicrobial Peptides such as cathelicidin (LL-37) in respiratory epithelial cells which has the ability to disrupt bacterial membranes via electrostatic interactions [3]. It also induces cellular immunity by increasing the production of anti-inflammatory cytokines and suppressing pro-inflammatory cytokines such as TNF-alpha and interferon-gamma. This prevents the generation of cytokine storm which is the underlying mechanism of acute respiratory distress syndrome. Moreover it also affects the adaptive immunity by decreasing the production of pro-inflammatory cytokines during both TH1 and TH2 response and suppresses the pro-inflammatory Th17 cells. In addition to this, it binds to the non-coding region of FoxP3 increasing the production of regulatory Treg cells and IL-10, thus reducing inflammation.

Studies suggest that Vitamin D has a potential role in protecting against viral respiratory infections especially against enveloped viruses. The immunoregulatory functions of vitamin D are mediated via enhancing the level of virus specific CD8 + T cells in respiratory viral infections such as Epstein Barr Virus and Influenza. Furthermore, it also boosts the macrophage maturation and oxidative burst capacity along with inhibiting autophagy which is associated with viral replication.

It is seen that the fatality rate of COVID-19 increases with latitude (5.2% in northern latitudes and 0.7% in southern latitudes) [4]. This can be attributed to less sunlight exposure in countries in northern latitudes predisposing them to higher prevalence of vitamin D deficiency. Furthermore, since vitamin D deficiency increases with age, older population is likely to suffer from severe ARDs due to SARS-CoV-2. It has been reported that while the case fatality rate (CFR) of COVID-19 is 1.4%, it is much

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higher in patients with pre-existing co morbidities such as Cardiovascular disease (13.2%), Diabetes (9.2%), Hypertension (8.4%), Respiratory disease (8.0) [5]. This can also be ascribed to the low vitamin D levels commonly associated with these disorders.

A meta-analysis of 25 randomized clinical trials has also suggested that regular oral vitamin D2/D3 intake (in doses up to 2000 IU/d) is protective against acute respiratory tract infection, especially in vitamin D deficient individuals [6]. Therefore, it seems logical to provide prophylactic supplementation and adjuvant therapy of vitamin D in order to boost the immune system and to prevent and reduce the severity of COVID-19 infection especially in older population with co-morbidities.

#### Compliance with Ethical Standards

**Conflict of interest** The authors declare that they have no potential conflict of interest.

**Human and Animal Rights** This letter did not include human participants or any animals.

**Informed Consent** As there were no participants then there is no question of informed consent.

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