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Immunology

# VITAMIN-D LEVELS: NANO SOLDIERS AGAINST nCOVID-19 MEGA BATTLES

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**ABSTRACT** Presently the world is battling a deadly pandemic without any effective licenced drugs or biologics to vanquish SARS-CoV-2. The experience of managing the past viral aetiological outbreaks has been extrapolated to nCOVID-19, yet its effectiveness is uncertain. This connotation invokes a potential insight to focus upon those elements and etiquettes which are an integral part of our life and expound for nCOVID-19 treatment. This further impels us to consider our food as a time-tested medicine. In a study, a decrease in Vitamin-D levels accounted for the bovine coronavirus infection in calves. Interestingly it paves the way for exploring the role of Vitamin-D as an accessible 'magic bullet' against nCOVID-19. Currently, its metabolism and immunomodulatory characterization are well-established. In fact, the studies have described an inverse relationship between Vitamin-D level and respiratory infections. This further substantiates for understanding its shielding effect against nCOVID-19. Few researchers have recommended dosage of Vitamin-D intake among adult and high-risk individuals including front-liners. However, the enforcement of this potent nutritional ergogenic calls for dose rationalisation with due effectivity and safety based on large randomized controlled trials. This short review highlights the important scientific link between Vitamin D levels and susceptibility to COVID-19 in patients.

**KEYWORDS :** Coronavirus; nCOVID-19; vitamin D; magic bullet; immunomodulator

**BACKGROUND:**

A second wave of coronavirus (CoV) infections has swept the world and brought it to its knees. The world is witnessing the tight grip of the deadly pandemic caused by the newly identified strain of Coronavirus (SARS- CoV-2/nCOVID-19).[1] Currently, no specific drugs or biologics are available against nCOVID-19. However, the evidence from past viral outbreaks (SARS-CoV-1, MERS-CoV, EBOV and Influenza) have been extrapolated to combat SARS-CoV-2; yet the efficacy remains uncertain.[2] It was found that a decrease in vitamin D in calves accounted as the prime cause of bovine coronavirus infection previously. This leads to plausible insight for exploring and understanding the role of vitamin D against SARS-CoV-2 in order to optimize it as a potent nutritional ergogenic for the same. Vitamin D is a steroid hormone (also called sunshine-hormone) synthesized endogenously from UV-B radiation to the skin or as exogenous supplements from an animal source or fortified food. The complex synthesis and its metabolism is well established. It confers essential benefits in bone and muscle health, helps in immune functioning by defying inflammation and prevents respiratory infection.[1] Various studies and researches provide us with evidence of immunogenic and anti-microbial properties of Vitamin-D.[3] Vitamin D deficiency is seen in those who get limited exposure to sunlight or inadequate intake of vitamin D. The high-risk group also includes individuals with chronic lung disease, obesity and those who are physically inactive. Studies have shown an inverse relationship between Vitamin D level and respiratory infection. In this short review, we provide an insight into how Vitamin D can act as an immune shield in respiratory infections like nCOVID-19 and substantiate for supplementary benefits for the front line warriors, high-risk population and general adult population.

**Description:**

**Mechanism For Regulation Of Immunity In Viral Infections By Vitamin D Levels**

Vitamin D (Vit D) is a fat-soluble vitamin that plays major role in calcium homeostasis. It is synthesized endogenously in the skin when exposed to Ultraviolet-B (UV-B) radiations in sunlight. 1,25-dihydroxy vitamin D [1,25-(OH)2 D] is the active form of Vit D.[4] Our body's innate and adaptive immune system provides protection against viral infections and aids in regulating cytokine levels in young and elderly populations, respectively. Vit D has been widely implicated in enhancing the immune response and suppressing the cytokine storm. It's deficiency has been linked to increased susceptibility to viral infections.[5]

Immune cells have been known to express vitamin D receptors (VDR) and various immune cells (monocytes, dendritic cells, macrophages, B cells and T cells) are capable of converting 25-hydroxy Vit D (25OHD) into active form 1,25-(OH)2 D. This permits local regulation of the 1,25-(OH)2 D at the site of inflammation.[6] Binding of 1,25-(OH)2 D to the VDR leads to translocation of the complex into the cell nucleus where it modifies the expression of hundreds of genes, including those for cytokine production. The complex also induces the production of antimicrobial peptides including cathelicidin and defensins. A study by Zhao et al[7] showed reduction in the replication of rotavirus both in vitro and in vivo by administration of Vit D at dose of 5000 IU/kg. Induction of cytokine storm is reduced by Vit D. The innate immune system generates both pro-inflammatory and anti-inflammatory cytokines in patients suffering from nCOVID-19. Vit D can decrease the production of T helper cell type 1 (Th1) cytokines such as interferon-γ and tumor necrosis factor-α (TNF-α). Also, expression of pro-inflammatory cytokines by macrophages is reduced and anti-inflammatory cytokines is increased by Vit D administration. Binding to dipeptidyl peptidase-4 receptor (DPP-4/CD26) is one of the molecular virulence mechanisms employed by nCOVID-19.

**Role Of Vitamin D Deficiency In nCovid-19 And Dose Recommendations**

Vit D deficiency is a global health problem common among all age groups. Negligible UV-B radiations reach the earth surface during winters at latitudes >40°. This increases the risk of Vit D deficiency during winter time. Epidemiological evidence suggests that during first month of winter, influenza infection is most common worldwide when Vit D levels are at their minimum.[8] Sufficient Vit D levels have shown to safeguard against influenza and respiratory syncytial virus (RSV) infections. Also, serum 25-hydroxy Vit D levels tend to drop with age. This is important with regard to nCOVID-19 as case fatality rates (CFRs) surge with age. Daneshkhah et al [9] showed that the age-specific case fatality rate (CFR) of nCOVID-19 was highest in Italy, Spain, France and India where, severe Vit D deficiency (mean 25OHD concentration <0.25 ng/L) is reported in comparison to other countries. In elderly population, over activation of adaptive immune system results from a shortage of memory B cells and aberrant innate immune response, which leads to cytokine storm as observed in nCOVID-19 patients. In another study, Lau et al [10] assessed 25OHD levels in twenty nCOVID-19 patients admitted in intesive care unit (ICU). 11 subjects had Vit D insufficiency (VID) and all patients below 75 years of age had VDI. Among these, 7 patients had <20 ng/mL and three had <10 ng/mL of 25OHD levels. This study demonstrated that VDI intensifies nCOVID-19 severity. As the severity of disease increased from mild to critical, serum 25OHD levels decreased from 31.2 ng/ml to 17.1 ng/ml and were statistically significant with clinical outcomes ($p<0.001$).

Above mentioned studies clearly indicate that having Vit D deficiency predisposes sensitive population (elderly and individuals with underlying health conditions) to an attack by it's own immune system and exacerbate the RTI by damaging the lung tissue. Therefore, in order to maintain an appropriate Vit D status and reduce the mortality, supplementation is needed to restore the Vit D levels reduced due to inadequate exposure to sunlight. Currently, The Institute of Medicine has placed the recommended dietary allowance, or RDA, for vitamin D at 600 international units (IU) per day for young adults and 800 IU per day for adults older than 70 years. [11] But this recommendation was issued in context with bone health. Based on observational studies, concentrations of at least 40-50 ng/mL are desired. Another study

reported that 38 ng/mL was suitable for reducing the risk of community acquired pneumonia. In order to achieve the above concentration range, dose of 2000-5000 IU/day of Vit D3 could be taken. The U.S. Institute of Medicine noted that for daily doses of < 10,000 IU/day no adverse effects have been reported for Vit D supplementation. However, the value for upper limit (UL) was corrected to 4000 IU/day based on all-cause mortality and chronic disease outcomes. [11] So, we recommend that keeping daily dose of Vit D below 4000 IU/ day could be beneficial in improving the immunity to combat nCOVID-19 infection more effectively.

## CONCLUSION:

The available literature beautifully enlightens us with the imperative role of diet and how these biochemical molecules boost up an individual's immunity; further rendering a shielding effect against infections. Dearth of treatment for nCOVID-19 leaves us with no choice but to take precautionary and prophylactic measures to stand a better chance to fight this pandemic. Hence, maintaining adequate Vit D levels is vital to prevent getting infected or to ward off the infection without mortality, in case it occurs. Clinical trials should be conducted in regard to n nCOVID-19 for assessing the effect of Vit D supplementation and determining the appropriate dose. We conclude that correlation exists between Vit D levels and nCOVID-19 susceptibility and Vit D could prove to be an essential element in our fight against nCOVID-19. Clinicians should thus advocate wisely in relation to the rapidly emerging views on nCOVID-19 treatment.

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## Author Contributions

The author was contributed to update all relevant information to formulate the design, drafted the manuscript review. The author gave final approval and agree to be accountable for all aspects of the work.

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