

SHOULD YOUNG COVID-19 PATIENTS BE SUPPLEMENTED WITH VITAMIN D?

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ABSTRACT

It is well known that vitamin D's general immunomodulatory actions are helpful in viral infections and that a shortage is linked to a more serious prognosis for Covid-19. In this systematic review, we examined the existing literature on evidence as to whether there is also link between vitamin D range levels in pediatric population and the outcome of the Covid-19 infection. We looked for studies that measured vitamin D blood concentrations and examined the effects of vitamin D supplementation in young infected patients. Vitamin D may decrease the risk of respiratory infections in a number of ways through its interactions with numerous cells, including by decreasing viral survival and replication, reducing the cytokine storm, raising angiotensin-converting enzyme 2 concentrations (ACE2) while not damaging the endothelial integrity. The incidence or severity of Covid-19 is linked with blood 25-hydroxyvitamin D concentrations, according to many observational studies. However experimental verification is still needed. Given their safety and broad therapeutic window, vitamin D supplements seem to be an effective way for individuals and doctors to prevent or treat Covid-19. Nonetheless, the outcomes of significant vitamin D randomized controlled trials are further needed.

Keywords: 25-hydroxyvitamin D; Covid-19; vitamin D

Introduction

As sun exposure is a prerequisite for vitamin D synthesis, the Covid-19 pandemic's limits on sun exposure may have had an impact on vitamin D levels across the world. This review sought to determine studies conducted on the 25 Hydroxyvitamin D levels of healthy kids and teenagers throughout the pandemic so far (1). Overtime, many viral infections have been linked to vitamin D, and this connection has been well-documented. In recent research, the significance of vitamin D in Covid 19 infection was emphasized. In the current investigation, we are putting forward the hypothesis that 25(OH) D insufficiency would have a connection to the severity of the infection rate in the pediatric population.

Individual immune systems are involved substantially in the susceptibility and pathogenesis of viral infections. These systems are influenced by a number of circumstances. Vitamin D has been shown to be crucial in adjusting both the innate and adaptive immune systems. When being exposed to UVB radiation, provitamin D3 (7-dehydrocholesterol) in the skin transforms into previtamin D3 (2). The liver receives the previtamin D3 and hydroxylates it at the 25th carbon atom. Vitamin D3's active metabolite 1,25(OH) undergoes a second hydroxylation at C-1 in the kidneys. Moreover, macrophages, monocytes, B lymphocytes, and T lymphocytes have all been shown to 1-hydroxylate vitamin D3. Lack of vitamin D is connected to an increase in contracting a variety of viruses, including the Epstein-Barr virus, Hepatitis B,

Human Respiratory Syncytial Virus, Human Immunodeficiency Virus, and influenza. Yet, it is unclear how vitamin D may contribute to SARS-CoV-2 infection (3).

Several studies have shown that vitamin D could potentially have a protecting effect against SARS-CoV-2 infection and associated clinical severity via immune system modulation (4-6). Recently, an original study research from India found children with vitamin D insufficiency had the poorest morbidity outcome (7).

Methods

The effectiveness of 25(OH)D supplementation, to counter the Covid-19 infection, morbidity, and mortality was examined in a broad analysis of existing studies. The search was conducted on 10th of March 2023 via PubMed database. In this review some selected articles that authors found to be relevant are presented in order to highlight if there is a connection between the levels of vitamin D and the severity of the Covid-19 infection in children. Particular attention was paid to studies that showed that vitamin D deficiency might increase the severity of the illness development.

Discussions

A fat-soluble vitamin with the common name “calciferol”, vitamin D may be obtained in dietary supplements, such as milk formulas added with vitamin D, and other foods where it is naturally present (egg yolk, beef liver). Ergocalciferol and cholecalciferol, the two main forms of vitamin D, are both readily absorbed in the small intestine. Absorption occurs as a result of both passive diffusion and a mechanism involving intestinal membrane transporter proteins (8).

To detect the levels of vitamin D in the body, serum 25(OH)D concentration is currently the most sensible blood analysis. This measures the vitamin D that is produced by the body, together with the one ingested from food and supplements. Plasmatic 25(OH)D has a life of 15 days, which some authors considered this to be long. Serum 25(OH)D concentrations are reported in both nanomoles per liter (nmol/L) and nanograms per milliliter (ng/mL).

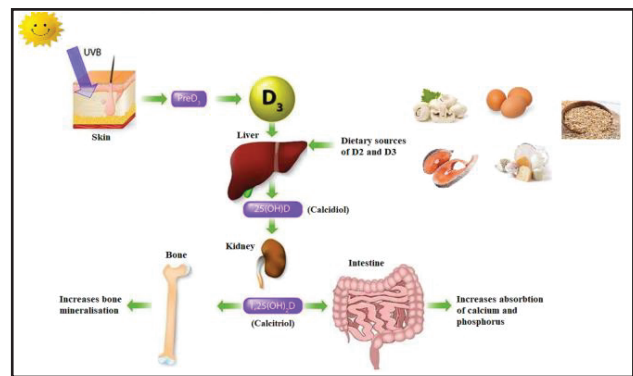


Figure 1: Author's adaptation of the vitamin's D metabolism (9)

One nmol/L equals 0.4 ng/mL, and 1 ng/mL equals 2.5 nmol/L (10). 25(OH)D exists in our body as 25(OH)D and as circulating 1,25(OH)2D. The latter is generally not used to measure the serum concentration of vitamin D because it has a short half-life. Serum levels of 25(OH)D are directly influenced by the parathyroid hormone (PTH), as well as calcium and phosphate. Only when the levels of vitamin D are critically low, that is when the 1,25(OH)2D levels usually decrease. In recent years, vitamin D testing has increased exponentially. The medical specialists are still debating whether the vitamin D deficiency has any relevance on the outcome of respiratory infections (8, 10).

To offer a better overview of the importance of vitamin D, Lordan offered a very good definition of what vitamin D deficiency is (8). According to him, vitamin D insufficiency is considered when 25-hydroxyvitamin D level falls below 21-29 ng/mL (50-75 nmol/L). At the same time, the vitamin D is considered to be deficient when the level is lower than 20 ng/mL (50 nmol/L). The authors further make his point by establishing that vitamin D deficiency is severe when the levels are lower than 10-12 ng/mL (25-30 nmol/L). At this point, the person is at risk of developing osteomalacia in adults and rickets in children.

To conclude, a range of 30-50 ng/mL (75-125 nmol/L) show sufficient concentration of 25(OH)D and this can prevent vitamin D deficiency and toxicity (8).

In addition to maintaining bone health and regulating blood calcium and phosphorus levels, vitamin D is also involved in division of cells, proliferation, apoptosis and so on. It is an

essential nutrient and hormone (11). It is also well known the immunomodulatory effect on innate and adaptive immunity, as well as on the synthesis of antimicrobial peptides (12).

An analysis of the vitamin D status of the world's population shows that more than 33% of people have vitamin D deficiency (below 20ng/ml), while over 50% have insufficient levels of 25 hydroxycholecalciferol (20–30ng/ml) (13).

A higher risk of acute respiratory tract infections has been related to low blood levels of vitamin D, or the “sunshine vitamin” (ARTIs). Otitis media, sinusitis (70% viral), acute pharyngitis, bronchitis (also 70% viral), influenza, and pneumonia are all examples of ARTIs (14). Moreover, acute respiratory tract infections account for about half of prescriptions for antibiotics for adults and nearly 75% of prescriptions for antibiotics for children (14). Almost 60% of youngsters in Romania suffer from respiratory tract disorders out of all ailments. According to the Ministry of Health's study, respiratory disorders were responsible for 22% of all fatalities in 2016. Over 29% of children in our nation lack adequate levels of vitamin D (15). Reduced circulating 25(OH)D concentrations have also been linked to Covid-19 severity and the risk of contacting the infection, according to reports (16). The outcome is more severe in some instances. Children may develop a multisystemic inflammatory syndrome (MIS-C) after the infection with SARS-CoV2 (17). Here, we have tried to demonstrate that vitamin D metabolism can be altered in airway diseases, which suggests that vitamin D insufficiency might develop as a result of pulmonary inflammation.

Results

Is it well known that there is an important contribution of vitamin D when it comes to the immune system function, as well as its effects on the gut, kidneys, and bones, as well as controlling calcium and phosphorus balance. The useful functions of this vitamin in both acute and chronic disorders have become more essential as a result of this problem. As there are not too many research articles available that correlates vitamin D to the COVID-19, specially in the pediatric population, our research tried to add to

the existing literature. Some of our conclusions showed that this vitamin's levels in children are connected to tachycardia and tachypnea, gastrointestinal problems, and O₂ levels. Those young patients that had vitamin D levels within normal range had infections that were less severe, involved less often, and had less gastrointestinal symptoms.

According to a comparable research study conducted by Kalichuran et al., serum levels of vitamin D was different between the control group and the placebo group. Those in the control group with lower levels of vitamin got infected with Covid-19, as opposed to those in the placebo group whose levels were in the normal range (18). The literature also includes other investigations into vitamin D's significance in instances of Covid-19 infections. One in particular showed that, despite the vitamin's effects on the cytokine cells response, higher doses of 25(OH)D may be utilized in order to lessen the severe immune response (19). The activation of immune system induced by SARS-CoV2 infection leads to exaggerated cytokine production, which is referred to as a “cytokine storm” (20). In another study, the clinical indicators, laboratory data, and chest radiography findings were used to classify the severity of Covid-19 in children. The young patients were divided into five categories, according to the severity of the symptoms: asymptomatic, mild, moderate, severe, and critical (21). They demonstrated that patient levels of this vitamin were less when compared to those from the control group. Also, there has been identified a connection between high temperature and vitamin D. This being said, the temperature was higher in patients with lower levels of this vitamin compared to those patients whose vitamin D levels were considered to be normal. Overall, their findings suggested that the prevalence and severity of Covid-19 illness may be influenced by the vitamin D status of the pediatric population (22).

Overall, more study is needed to establish whether there is a relationship between vitamin D levels in kids, when it comes to influenza and colds. These studies revealed that this vitamin may be helpful. According to research by Zhu et al. on the impact of vitamin D in easing influenza symptoms, taking vitamin D supplements lowers

the chance of developing serious respiratory illnesses (23). In addition, Rondanell et al. shows that vitamin D may lessen cold symptoms by boosting adaptive immunity in several immune system components (24).

It was shown in the research on vitamin D's impact on illness that this vitamin significantly contributes to the efficient activation of innate immunity by modifying the immune system. When pathogenic lipopeptides stimulate toll-like receptors, the body responds by producing antimicrobial peptides (defensins and catalysidines).

The immune system relies heavily on regulatory T cells to recognize and eradicate viruses. According to a scientific research, vitamin D may reduce Covid-19 infection by triggering regulatory T cells. Patients with the Covid-19 infections often presented at the onset of the disease a poor systemic microcirculatory function. This can be explained by endothelial cells dysfunction produced of direct viral infection (17).

In the winter, the main sources of this vitamin are food and supplements as sunshine exposure is insufficient to generate vitamin D. According to recent research, children are more likely to be stuck at home as the pandemic spreads, and this confinement increases the frequency of kids with low vitamin D levels. These results highlight the significance of sunshine in children's naturally rising vitamin D levels.

Conclusions

Overall, the current review found that there is a very important correlation between normal or high vitamin D levels and the outcome of the SARS-Cov2 infection, This suggests that moderate vitamin D supplementation can improve immune function and that excessive intake should be avoided. The inability to reach patients throughout the study was one of the research's constraints, however this problem was resolved with careful preparation. Future clinical studies may assess the effectiveness of vitamin D on children recovering from coronavirus infection. Also, the current study was only completed at one center, while several centers might provide more reliable findings.

In the literature there is some evidence that blood vitamin D may be a biological factor influencing COVID-19 results.

Our conclusions support the fact that checking the plasmatic levels of vitamin D can help to reduce the severity of symptoms that patients show. Taking into consideration the lack of specific treatment for the Covid-19 infection, this can also help in prophylaxy of the disease.

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