

Vitamin D deficiency's Association with COVID-19 Prevention and Treatment

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Abstract

The SARS-CoV-2 has been creating havoc around the world for almost fourteen months and is as problematic as ever. Up to this day, more than 82.5 million people are infected and 1.8

million killed. Despite its destructive force, there is currently no vaccine or treatment plan that can be widely used by the entire world at a relatively low cost. Remdesivir five-day treatment cost more than 3122 Canadian dollars and is inaccessible to civilians in third-world countries. Vaccines have the same issue as remdesivir-lack of inaccessibility and high cost. Therefore, a short-term cheap relief treatment that most civilians around the world can have access to has to be implemented. Vitamin D has become a possible option as statistics and researches have shown a strong correlation between vitamin D level and infection rate and severity of COVID-19. This paper will discuss the relationship between vitamin D and COVID-19 through 1)Function of vitamin D, 2)Population affected by vitamin D deficiency, 3)Vitamin D deficiency aggravating symptoms of COVID-19, 4)A statistical analysis over 4131 patients on their COVID-19 test results and vitamin D level, and finally 5) A discussion on vitamin D deficiency leading to an increase in COVID-19 infection rate. (1, 2, 3)

Keywords: COVID-19, COVID-19 treatment, Vitamin D deficiency, SARS-CoV-2

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1. Introduction

The first case of the COVID-19 disease appeared in Wuhan, China in December 2019, while its sole cause, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first identified in January of the following year. This disease has led to a massive outbreak, first in China, then around the world and was declared by the World Health Organization as a global pandemic in March 2020. Up to this date, the COVID-19 disease has caused the

death of 1.73 million people while infecting over 78.6 million people worldwide. All of these make SARS-CoV-2 one of the most dangerous and harmful coronavirus. (1,2)

Currently, multiple vaccines are being developed in multiple nations, such as China and the United States. However, they are still largely unavailable and very expensive to average civilians from third world countries, such as Algeria and Syria. One other type of treatment method proven useful when patients contract SARS-CoV-2 is the Remdesivir drug, which would cost \$3 210 for people with personal insurance. The cost of such drugs made it unaffordable to many individuals. Another type of treatment is a combination treatment consisting of two monoclonal antibodies: casirivimab and imdevimab. Unfortunately, this treatment is still in the clinical trial and is only issued to specific groups of patients, including moderate COVID-19 patients older than twelve years old and weighs more than 88 pounds and patients older than sixty-five years old and is likely to develop severe COVID-19 symptoms. As a result, it is crucial to develop a treatment method that is affordable and accessible to the general public. (3,5)

The SARS-CoV-2 has the ability to spread to anyone in all age groups and gender in the form of airborne particles. Of all these patients, older adults with age over sixty-five, people with chronic disease, people with a weakened immune system, and obese people with a BMI (Body Mass Index) of 40 or higher are at high risk of developing severe symptoms. Most of these people are prone to vitamin D deficiency as their exposure to the sun is less than an average adult. This shows a strong connection between vitamin D deficiency and developing a severe symptom after infecting SARS-CoV-2.(6,7) I have done a search on Google Scholar, Nature, the Government of Canada website, the World Health Organization, et Cetra with the keywords: COVID-19, SARS-CoV-2, Vitamin D treatment, treatment methods, and COVID-19 prevention. Therefore, this research paper will explain the role of vitamin D in COVID-19 treatment.

2. Vitamin D And Its Functions

Currently, there are two main types of Vitamin D that humans consume. First, vitamin D3, or also known as cholecalciferol, is produced by the UVB radiation hitting the 7-dehydrocholesterol in the skin, while the second Vitamin, vitamin D2 or also known as ergocalciferol, is largely artificial. These two types of vitamin D are very similar to each other as they can both be added to food and be consumed in the diet, and they serve the exact purpose. However, the structure of ergocalciferol and cholecalciferol are different from each other.

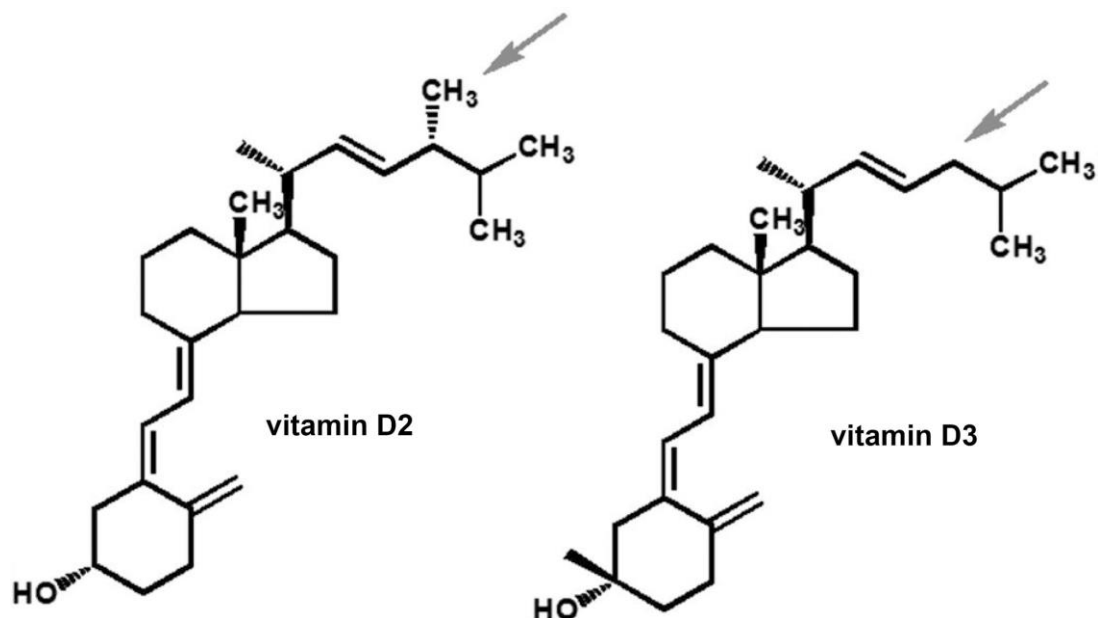


Figure 1: Diagram of a molecule of vitamin D2 and a molecule of vitamin D3 This diagram shows the molecule of vitamin D2 and vitamin D3, respectively. As seen on the diagram, the difference between the two molecules is that vitamin D2 has an additional methyl group (CH₃) located at the site of the arrow. (8)

Vitamin D2 and vitamin D3 have to be biologically activated by going through two hydroxylation reactions in the liver before it can be used by the body. The first reaction is arbitrated by 25-hydroxylase (CYP2R1) and produces 25-hydroxyvitamin D (25 OH-D) which is only used for the purpose of diagnosing. The 25OH-D then goes into the second hydroxylation reaction in the kidney and produces the final functional calcitriol (1,25-dihydroxyvitamin D). The level of vitamin D in an individual's body can be easily found by measuring the concentration of 25 OH-D concentration in the blood plasma(8)

Calcitriol is used in the human body to regulate calcium and phosphate levels, but they have also been found to serve the purpose of maturing immune cells.

Vitamin D has been found to provide antiviral and antibacterial protection against many diseases that cause respiratory tract infections, such as tuberculosis, Epstein Barr virus, and influenza, through physical barriers and improving immune systems. Severe respiratory tract infections will increase the level CYP27B1 in the respiratory epithelial cells, which would convert into the calcitriol through the hydroxylation reaction. This increase in calcitriol will induce the secretion of cathelicidin. Cathelicidin is a family of polypeptides in the lysosomes of macrophages and polymorphonuclear leukocytes; it serves a crucial role in the fight against bacteria and viruses. The reason being that cathelicidin has been found to engage and enhance white blood cells (Neutrophils, T cells, and monocytes) in the infected area. As stated in the previous paragraph, both vitamin D2 and D3 have the ability to produce calcitriol through the two hydroxylation reactions in the liver and in the kidney, which means that the amount of cathelicidin will also increase as the level of vitamin D in the body increases. This discovery suggests that vitamin D may be involved in the fight against ARDS(Acute respiratory disease syndrome) and heart failures. (17)

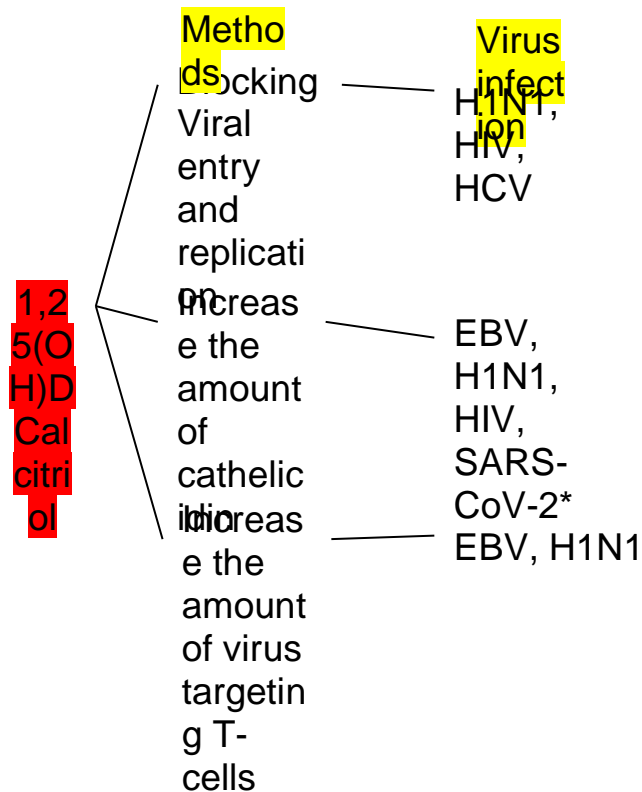


Figure 2: This diagram shows the different methods of protection that the 1, 25(OH)2D3 offers to the body when encountering different viral infections(EBV, H1N1, HIV, HCV). Some of the antiviral measures include blocking viral entry and replication, Increasing the amount of cathelicidin, and increase the amount of virus targeting T-Cells (17)

3. Vitamin D Deficiency in Relation with COVID-19

Vitamin D deficiency is very common in current society, covering almost half of the American population (41.6% of vitamin D prevalence rate in the U.S.). A study from Meltzer et al. shows that persons living in higher latitudes in the winter, nursing home residents, health care workers, and people with darker skin are more prone to vitamin D deficiency. In another epidemiological research done on the level of 25OH-D has shown that a significant number of healthy adults are found to be vitamin D deficient at the end of winter. This study result shows that even healthy adults are at large risk of vitamin D deficiency, let alone the four types of patients mentioned in the last paragraph of the introduction. Most of these survey populations have one thing in common: The lack of exposure to sunlight.

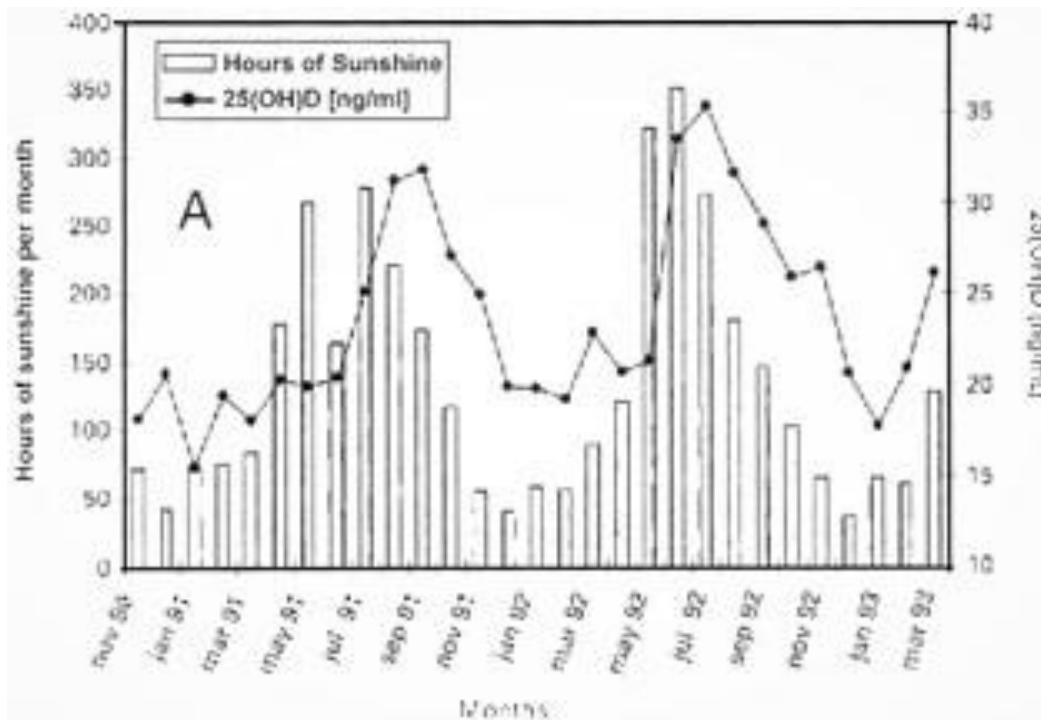


Figure Three: The relationship between the concentration of 25OH-D and hours of sunlight over two years and three months. (26)

Clinical data and research has shown that vitamin D has the ability to defend against respiratory tissue inflammation. SARS-CoV-2 has been found to target the patient’s immune system during infection, which will lead to hyperinflammation(Cytokine storm). The cytokine storm occurrence in the lung will often lead to acute respiratory disease syndrome and other complications due to its ability to cripple the body’s immune system. On the other hand, vitamin D has the ability to increase secretion of cathelicidin, which can enhance and encourage the immune system. A recent study was done by the doctors from Tyne Hospitals in Newcastle, North East London on the concentration of 25 OH-D in 134 patients (mainly of Caucasian origin) who are infected by the SARS-CoV-2. The results showed that eighty-one percent of the patients in ICU (Intensive Care Unit) have vitamin D deficiency (Patient is considered vitamin D deficient if their 25 OH-D concentration is smaller than 50 nmol/L), while only 60.9 percent of patients from the general ward have vitamin D deficiency. This data shows that vitamin D deficiency will worsen the symptoms of COVID-19. Therefore, it can be assumed that vitamin D, an antiviral and antibacterial substance to H1N1, Mycobacterium tuberculosis, HIV, etc. has the ability to reduce the severity of SARS-CoV-2 infection by limiting the ARDS and heart failures-the two main severe symptoms of COVID-19. (17)

A study has been conducted by Meltzer et al. on the relationship between COVID-19 test results and vitamin D level. The researchers have retrieved the data of 4314 patients from the University of Chicago Medicine (UCM) electronic health record during the time period of March 3rd to April 10, 2020. A patient is considered vitamin D deficient if his most recent 25(OH)D3 level within one year was lower than 20ng/mL; A patient is considered vitamin D sufficient if his most recent 25(OH)D3 level within one year was higher than 20ng/mL. Other characteristics are also considered in the study, including age, gender, sex, race, ethnicity,

employment status, median date since last vitamin D check, comorbidity, BMI(body mass index), and most recent vitamin D treatment.

Of the 4314 patients studied over the course of thirty-eight days, 3815 did not have their vitamin D level measured in the past year and 10 did not have a complete set of data to all the characteristics. As a result, only 489 patients are included in the final results.

Within the 489 patients:

-172 patients(35%) have vitamin D deficiency during the past year before the study was conducted; 317 patients(65%) do not have vitamin D deficiency.

-71 patients(15%) of the 489 total were tested positive for COVID-19.

-Of the 71 patients, 32 are vitamin D deficient, while 39 are vitamin D sufficient

Result from multivariable linear model for the same 489 patients:

-Patients who likely have vitamin D deficient have 21.6% chance of contracting the SARS-CoV-2 compared to the 12.2% of patients who likely are vitamin D sufficient.(22)

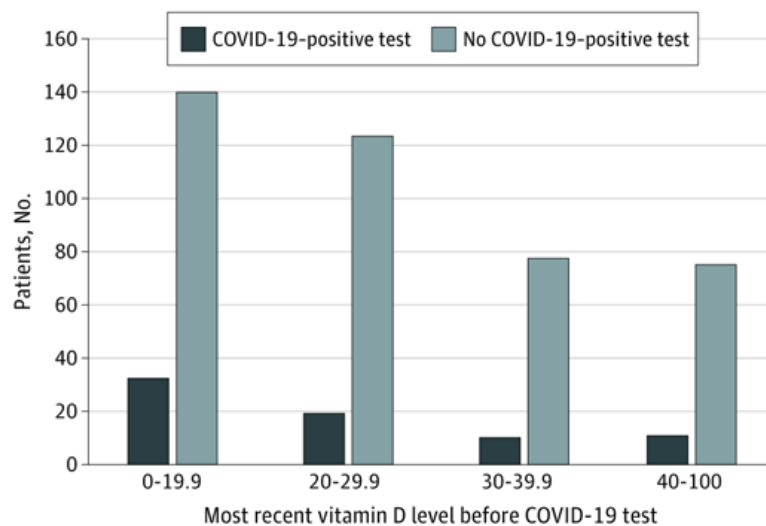


Figure Four: A double bar graph showing the number of COVID-19 positive tests on the level of vitamin D between one year and before 14 days of the COVID-19 test. The result shows that people with low vitamin D concentrations or with vitamin D deficiency are much more likely to contract SARS-CoV-2. (22)

5. Discussion and Conclusion

From the study conducted above, the multivariable analysis shows that people are much more likely to contract the SARS-CoV-2 if they are vitamin deficient. However, other variables could be affecting the final result in the multivariable analysis, which means that Vitamin D deficiency is not the sole factor to increasing probability of contracting SARS-CoV-2. It is only a statistical correlation.

Studies and statistics have shown that vitamin D has a significant connection with the COVID-19 disease. The reason being that vitamin D deficiency can worsen the symptoms of COVID-19 and increase the infection chance as well. The final product of vitamin D2 and

D3, calcitriol, have been found to have the ability to increase the secretion of cathelicidin, a polypeptide that can strengthen the immune system. There is a strong correlation that suggested vitamin D deficiency will increase the chance of contracting SARS-CoV-2. However, this correlation is based on analysis of statistics and data of COVID-19 infections. A detailed clinical research has to be hosted in order to confirm the correlation. (10)

Due to the exceedingly high cost and low availability of COVID-19 vaccine and other treatment methods. I recommend that each individual should be taking a considerable amount of vitamin D through food, vitamin D supplements, and increasing the exposure to sunlight. Regardless of which methods, it is crucial to be vitamin D sufficient to decrease the chance of infecting SARS-CoV-2 or improve/minimize the symptoms of SARS-CoV-2. Most importantly, increasing the daily intake of vitamin D is a cheap, easy method that the people from all nations and classes can use in the fight against COVID-19. However, vitamin D only serves as a temporary supporting role to the solution. A SARS-CoV-2-related vaccine is needed for a permanent and final solution to this global pandemic. (23)

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