The Importance of Vitamin D3 in COVID-19 Patients

Nasser, F. A1*, Younis, L. A1, Abidreda, Kh. H1, Alyasiri, I1

1. College of Pharmacy, Jabir ibn Hayyan Medical University, Najaf, Iraq

*Corresponding Author: fadhil.abass@jmu.edu.iq

Abstract

Outbreaks of a respiratory ailment in Wuhan, China, known as the coronavirus 2 (COVID-19), began in late December 2019. Since then several advises have been made to boost immune system to fight more efficient with this infection. Previously published studies showed that vitamin D3 (Vit D3) level is low in COVID-19 patients. One of the most important factors in COVID-19 severity would be the inflammatory response. It is well documented that the inflammatory cytokine storm increases the severity of COVID-19. Cytokine storm results from dysregulation of the innate immune system with an outpouring of proinflammatory cytokines and chemokines, leading to abnormal activation of the adaptive immune pathway. It has been approved that the Vit D3 has immunomodulatory functions and plays an anti-inflammatory role, particularly in viral infections. Therefore, current study was designed to investigate the possible role of Vit D3 deficiency in the COVID-19 patients' innate immunity. This study included 180 participants as follows: group A consisted of 60 COVID-19 positive patients with normal level of Vit D3, group B consisted of 60 COVID-19 positive patients with Vit D3 deficiency, and group C consisted of 60 COVID-19 positive patients that had received Vit D3 therapy. The results showed that the rate of hospitalization in group B (41.3%) was significantly increased compared with group A (12.5%). In this regards Vit D3 therapy lead to significant increase in the level of Vit D3 and the patients who received Vit D3 were recovered from Hospital 5 days in average sooner than group B. Therefore, consumption of Vit D3 as a daily supplement would be a reasonable suggestion for these days of COVID-19 pandemic to increase the power of immunity of the body.

Keywords: Coronavirus (COVID-19), Health, Risks and Vitamin D3

1. Introduction

In December 2019, the World Health Organization (WHO) cataloged coronavirus disease 2019 (COVID-19) as "novel coronavirus-induced pneumonia" after the virus spread swiftly following its first appearance in Wuhan, China. The International Viral Classification Commission designated the new coronavirus as the cause of severe acute respiratory syndrome on the same day (SARS-CoV-2). Recent history has seen the
occurrence of severe respiratory sickness associated to a coronavirus, such as COVID-19, multiple times. COVID-19, SARS, and MERS are all coronavirus-based respiratory illnesses that have been discovered in the last two decades. We know that coronaviruses are viruses that are surrounded by a capsid and have a single-stranded RNA genome (26e32 kb) (1). It has also been shown that patients with COVID-19 infection have normal or decreased leukocyte counts, radiographic signs and symptoms such as pneumonia, as well as clinical signs and symptoms like fever, nonproductive cough, dyspnea, myalgia, and fatigue (2). This resembles the signs and symptoms associated with SARS-CoV and MERS-CoV infections. Although we don't know exactly how the pathophysiology of COVID-19 works, we can still gain useful insights into SARS-CoV-2 infections by looking at how similar MERS-CoV is to SARS-CoV, because we can use this information to better detect COVID-19. Previous published study conducted by De Wit, Van Doremalen (2) showed that Corona virus S protein, a critical factor in virus entrance, infects host cells. SARS-envelope CoV's spike glycoprotein has a strong cellular receptor, which is ACE2, and it's the reason why the virus is able to spread. SARS-CoV and MERS-CoV infection stops the IFN-I pathway in infected mice, which protects them against viral infection, but infection prevents IFN-I (IFN-a and IFN-b) from activating (3). Human health studies have established that human body levels of Vit D3, calcium levels, and bone metabolism are connected to the immune system (4). Vit D3 levels affect how the adaptive immune system, such as T-cell activation and dendritic cell maturation, works. Vit D3 is also responsible for skin's natural antibacterial defense and helps in various other ways as well (5). It's already been mentioned how the interaction between Vit D3, calcium levels, and bone metabolism are linked. Experts are currently trying to understand the association between Vit D3 levels and the immune system's ability to fight off illness. A study found that Vit D3 insufficiency was linked to higher rates of illness and death, and was particularly evident in older people (6).

Cytokine storm results from dysregulation of the innate immune system with an outpouring of proinflammatory cytokines and chemokines, leading to some degree of abnormal activation of the adaptive immune system. It has been approved that the Vit D3 has immunomodulatory functions and plays an anti-inflammatory role, particularly in viral infections. The anti-viral immunity could be induced by Vit D3. It is of prime importance nowadays considering the global COVID-19 pandemic. The anti-bacterial responses like stimulation of cathelicidin and β-Defensin 2 are also observed during an immune response to the viral attack thereby preventing the virus entry into host cells and its subsequent multiplication (7). Vitamin D3 is also responsible for inducing autophagy as a result of both anti-bacterial and anti-viral activity. This is also one of the ways for host cells of getting rid of viral load. Autophagy leads to the encapsulation of viral particles and degradation in lysosomes and creating a hostile anti-viral schematic event via antigen presentation and adaptive anti-viral responses (8-10).

In the past, antimicrobial peptides (AMPs) were used as natural antibiotics to eliminate bacteria, but today they have further applications. AMPs build chemical barriers on the skin's surface. It is believed that AMPs
activate and coordinate the innate and adaptive immune systems, which are responsible for providing our bodies with immunity (8-10).

There are two classes of powerful antimicrobial proteins in the body: cathelicidins which is produced in skin tissue and beta-defensins. When the subject is human cathelicidin, it's often referred to by one of its peptide variants (LL-37) or the name attributed to its precursor protein (hCAP18) (8-10).

Cathelicidin, an antimicrobial peptide and endogenous inflammatory mediators might be working together to produce certain proinflammatory effectors via various routes. Cathelicidin peptides are cell motility-inducing chemokine secretory peptides. They also play a role in stimulating innate immune responses alongside their direct antibacterial activity (8-10).

Neutrophils and neutrophil like cells are the cells of immune system which can generate cathelicidins, as well as skin cells. Several published studies have revealed that Vit D3 directly interacts with cathelicidin in keratinocytes (11, 12). The results of the previously published studies showed that oral Vit D3 supplementation boosts cathelicidin production and antimicrobial activity in keratinocytes when done in vitro, which confirms earlier findings of the same experiment done in the laboratory (11, 12).

Therefore, current study was designed to investigate the possible role of Vit D3 deficiency in the COVID-19 patients' innate immunity.

2. Materials and Methods

2.1. Study design

This study included 180 participants, the participants were divided into three groups as follows: group A (control) consisted of 60 COVID-19 positive patients with normal level of Vit D3, group B consisted of 60 patients with Vit D3 deficiency (Vit D3 deficiency was defined as a 25(OH) D level of <12 ng/mL (30 nmol/L)), and group C (Vit. D3) consisted of 60 patients that had received Vit D3 therapy at a dose of 5000 IU of Vit D3 (Devit-3 ampoule, Deva Company). Using CT scans and PCR estimations, it was found that patients had been infected with corona viruses.

2.2. Sample preparation

Samples were gathered following the agreed-upon timeline between April 2019 and April 2020. The tests were performed in the Najaf Health Department's Public Health Laboratory, which is located in the city. At the beginning of the experiment blood samples were taken and Vit D3 level was measured. The Cobas 6000 analyzer (Roche Diagnostics, Germany) was used to measure 25 (OH) D levels. The technique behind the Cobas 600 analyzer was chemiluminescent immunoassay. After the initiation of the experiment the blood samples were taken in 24 h intervals.

2.3. Exclusion criteria

Diabetes mellitus (chronic), renal problems, and liver abnormalities are all examples of medical conditions that prevent someone from participating in the study.
2.4. Statistical analyses

The statistical analysis was performed using SPSS. The findings were calculated using the mean and standard deviation (Mean±SD). To determine statistical significance, the Student's t-test was employed. When the p value was lower than 0.05, the difference was considered significant.

2.5. Ethics

The study protocol was approved by the local ethics committee at the Najaf Health Department's Public Health Laboratory. Written informed consent was obtained from patients (when possible) or from their authorized representatives.

3. Results and Discussion

The results of the primary screening in the current study showed no significant differences in the age and BMI between group A and group B. However, there was a significantly lower level of vit D3 levels in patients with corona virus (p < 0.05) as shown in table 1. In group B the level of Vit D3 was 15.92± 9.83 compared to the healthy groups (30.61± 11.15). Group A consisted of people with normal level of Vit D3 and infected with COVID-19 while group B showed sever deficiency in case of Vit D3 level. Results showed that the rate of hospitalization in group B (41.3%) is significantly increased compared with group A (12.5%).

Table 1. parameters in subjects in group A (control) and group B

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A (control) (60)</th>
<th>Group B (60)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>35.48 ± 14.34</td>
<td>39.24 ± 17.1</td>
<td>0.3</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.5± 1.49</td>
<td>24.3 ± 2.34</td>
<td>0.67</td>
</tr>
<tr>
<td>25OH Vit D3 Total (ng/mL)</td>
<td>30.61± 11.15</td>
<td>15.92.± 9.83</td>
<td>0.000</td>
</tr>
</tbody>
</table>

In addition to that there was a significantly higher level of Vit D3 levels in patients with corona virus (p < 0.05) after treated with Vit D3 supplement (5000 i.u) for four weeks compared with group B (without treated with Vit D3 supplement) as shown in table 2. In this regards Vit D3 therapy lead to significant increase in the level of Vit D3 and the patients who received Vit D3 were recovered from Hospital 5 days in average sooner than group B.

Table 2. Levels of 25OH Vit D3 Total (ng/mL) in subjects in group B (without Vit D3 supplement) and group C (treated with Vit D3 supplement)
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group B (60)</th>
<th>Group C (60)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>25OH Vit D3 Total (ng/mL)</td>
<td>15.92 ± 9.83</td>
<td>32.3± 3.5</td>
<td>0.000</td>
</tr>
</tbody>
</table>

In the several studies previously published by different research team, 25 (OH) D concentrations in the blood samples of COVID-19 patients were found to be low. This low level of 25(OH) D was associated with the severity of the COVID-19 disease (11, 12). The results of a study conducted by Meltzer et al. showed that 489 patients who had PCR tests with documented 25(OH) D levels measured in the last 1 year; the rate of patients who were positive for COVID-19 was found to be 12.2% in the group with sufficient Vit D3 levels and 21.6% in the group with Vit D3 deficiency (12). In another study conducted by Kaufman, Niles (11) involving 191,779 patients with COVID-19 tests, people with 30–34 ng/mL of vitamin D level had a 54% lower risk of COVID-19 compared to people with 25(OH) D <20 ng/mL. Similar to the mentioned results, the 25(OH) D levels of COVID-19 hospitalized patients was found to be low in our study.

A single oral dose of 200,000 IU vitamin D3 was given to 240 hospitalized patients with COVID-19 who were moderate to severely ill. Between the vitamin D3 group (n = 120) and the placebo group (n = 120), there was no difference in length of stay and inhospital mortality rate (11). In another study by Han et al. (13) mechanically ventilated adult ICU patients showed that administering high doses of oral vitamin D3 did not differ between ICU length of stay and hospital mortality. These findings are in contrast with findings of the current study.

Adequate intake of Vit D3 through diet or sun exposure can compensate the daily need of Vit D3. The COVID-19 patients in group C in the current study were patients with malnutrition without adequate exposure to sunlight. The proper function of the immune system is depend on good nutrition status, optimal nutrition is important in establishing an appropriate immune response. Therefore, nutritional deficiencies and insufficient sunlight exposure can weaken the immune system, susceptibility to all infections. Therefore, as a sign of malnutrition, it can be said that patients with malnutrition may have a more severe infection as Vit D3 levels reflect the nutritional level of the person rather than the direct effect of low Vit D3 on the severe course of COVID-19 infection and high mortality rate. Patients who received more Vit D3 when treating their corona infection healed faster than those who did not get additional Vit D3.

Vit D3 ingestion increases glutathione reductase synthesis, which is a strong antioxidant (14). It is well approved that any prescriptions which can increase antioxidant capacity in the living organisms subsequently lead to a significant increase in the capacity of the immune system.

References