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Original Article

Effects of Vitamin D on Risks and Severity of COVID-19 Infection

Abdul Ridha Al-Awade, H[1], Shakir Abed Almjalawi, B[2] *

1. Department of Biology, College of Education for Pure Sciences, University of Kerbala, Kerbala, Iraq
2. General Directorate of Education in Kerbala, Kerbala, Iraq

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Corresponding Author: batoolshakir5@gmail.com

Abstract

In the last two decades, numerous studies have been carried out to find correlations between vitamin D and the efficiency of the lungs and respiratory system. This study aimed to find the relationship of taking vitamin D with the risks of the severity of infection with coronavirus disease 2019 (COVID-19) and the risk of infection of patients with chronic diseases. A total of 100 COVID-19 patients (61 males and 39 females) were included in the study and divided into groups, namely never taken vitamin D and taken a dose of 50 and 1,000 IU. The effects of gender, chronic diseases (i.e., hypertension and diabetes), and requiring intensive care unit (ICU) were evaluated. The results showed that females were at lower risks of infection with COVID-19 than males and taking 50 IU of vitamin D could lower the severe cases by 33%. It was also revealed that patients with chronic disease were more sensitive to COVID-19 and administering 50 units of vitamin D in these patients decreased the need for ICU from 49% to 9%. Given that vitamin D enhances the immune system and respiratory function, the findings of this research indicated that vitamin D reduced the risk of COVID-19; however, it was not able to prevent it.

Keywords: Chronic diseases, COVID-19, ICU, Iraq, Vitamin D

1. Introduction

Vitamin D is a cyclic hydrocarbon compound called prohormones. It is the fat-soluble substance that has an important role in bone health due to its main part in absorbing phosphorous, calcium, and magnesium and controlling the functions of the cellular cells. It also has highly considerable properties that enhance the immune system, such as neuroprotective, antioxidant, and anti-inflammatory. Vitamin D can control the expression of the genes and support the activities of the brain cells and the functions of the muscles. This vitamin is obtained from sun exposure, foods (e.g., eggs), fatty fish (e.g., salmon), fortified cereal, fortified milk, and other resources (1, 2). The human body is capable of synthesizing vitamin D through the reaction between skin and sunlight; nevertheless, the result of this process is affected by numerous factors, such as exposure time to sunlight, pigment on skin, latitude, and season (3, 4). The findings of numerous researches have exhibited a possible link between vitamin D deficiency and different diseases, including systemic infections (5)**.**Vitamin D is involved in activating immune systems and deficiency of this affected immune function (6). The proper concentration of vitamin D increased innate immunity by separating anti-viral peptides (7), improved the mucosal defenses. In the clinical studies, reduced vitamin D levels in the blood had been related to acute respiratory infections, which include pandemic influenza (8). Some recent studies had hypothesized

that deficiency in vitamin D might lead to respiratory and immunity failure and an increased risk and severity of coronavirus disease 2019 (COVID-19) infection and mortality in patients (9). In 2011, it was shown that vitamin D directly affected lung function by increasing the secretion of cathelicidin (an antimicrobial peptide), reducing chemokine production, leading to the activity of T cells, and inhibiting the activity of dendritic cells (10). Vitamin D deficiency affects respiratory diseases and increases the infection with mycobacteria. However, it has been noticed that increasing vitamin D levels in the blood can lead to recovery from asthma (11, 12). Recent data have suggested the antiviral effects of vitamin D may directly inhibit virus replication and has anti-inflammatory responses (13). During the COVID-19 pandemic, a lot of pieces of research and studies were carried out to find the correlation between the coronavirus infection and vitamins (14, 15). The results of the research have shown that although vitamin D cannot prevent COVID-19 infection, it can reduce the disease severity and mortality (15, 16). The findings of a number of recent reviews have found some of the pathways through which vitamin D reduces the risk of microbial infection (17). Vitamin D follows a variety of mechanisms to decrease viral infections and mortality. For the purpose of reducing the risks of respiratory infection, vitamin D utilizes three pathways, namely physical barrier, natural cellular immunity, and adaptive immunity (18). The outbreak and rapid spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus is a global health threat with unstable outcomes all over the world. The current study was carried to find the relationship between the severity of infection with COVID-19 and the level of vitamin D in the blood and compare it with the control group.

2. Materials and Methods

The statistical sample of this study included 100 (61 males and 39 females) COVID-19 patients that their infection was confirmed by a specialist physician using a computed tomography scan or positive reverse transcription polymerase chain reaction test for SARS-CoV-2. Informed consent was obtained from patients to enter the study. The patients were divided into two groups, including those who never took vitamin D and those that received vitamin D (50-1000 IU). The effect of the gender and chronic diseases, such as hypertension and diabetes, for which patients needed care at intensive care unit (ICU), were also evaluated. Patients' clinical symptoms and conditions during the infection, such as headache, diarrhea, shortness of breath, and loss of sense of smell and taste, were measured and recorded.

2.1. Statistical Analysis

All the collected data were statistically analyzed in SAS software 2012 (19). Statistical tests were analyzed by ANOVA, t-test, and Chi-square. A p-value of less than 0.05 was considered significant.

3. Results and Discussion

This study was conducted to evaluate the role of vitamin D in patients with COVID-19. Patients were classified according to gender, and a dosage of vitamin D was given to them according to table 1. It was revealed that the number of infected cases was much higher in pertains who never took a dose of vitamin D; however, it could not protect the patient from infection, which was consistent with the results of other studies (11, 14).

Based on the data in table 2, chronic diseases could increase the possibility of infection with COVID-19. The results of a study conducted by Liu (20) showed that chronic diseases affected the severity and mortality of COVID-19.

According to table 2, the number of non-infected people with coronavirus is much higher in those who never had any chronic diseases. This number is higher in those with both hypertension and diabetes than in those with only one of them.

Table 3 presents a comparison between males and females regarding the severity of the infection with coronavirus.

Table 1. Effects of vitamin D intake on infection with COVID-19 and its comparison with control for males and females

Gender	Number and percentage	Never take Vitamin D	Dose 50 IU	Dose 1,000 IU	Total	P-value
Males	Number	34	5	22	61	0.105
	Horizontal percentage	55.7%	8.2%	36.1%	100%	
	Vertical percentage	66.7%	35.7%	62.9%	61.0%	
Females	Number	17	9	13	39	
	Horizontal percentage	43.6%	23.1%	33.3%	100%	
	Vertical percentage	33.3%	64.3%	37.1%	39.0%	

Table 2. Effect of chronic diseases on infection with COVID-19 in males and females

Gender	Number and percentage	Nonchronic disease	Hypertension	Diabetes	Hypertension and diabetes	Total	P-value
Males	Number	55	1	1	4	61	0.940
	Horizontal percentage	90.2%	1.6%	1.6%	6.6%	100%	
	Vertical percentage	62.5%	50.0%	25.0%	66.7%	61.0%	
Females	Number	33	1	3	2	39	
	Horizontal percentage	84.6%	2.6%	7.7%	5.1%	100%	
	Vertical percentage	37.5%	50.0%	75.0%	33.3%	39.0%	

Table 3. Effect of gender on the severity of infection with COVID-19

Gender	Number and percentage	Severe infection	Moderate infection	Light infection	Total	P-value
Males	Number	14	28	19	61	0.310
	Horizontal percentage	23%	45.9%	31.1%	100%	
	Vertical percentage	73.7%	62.2%	52.8%	61.0%	
Females	Number	5	17	17	39	
	Horizontal percentage	12.7%	43.6%	43.6%	100%	
	Vertical percentage	26.3%	37.8%	47.2%	39.0%	

According to table 3, the percentage of severe infections is double in men, while it is almost equal in moderate infections, and for mild infections, the percentage is higher in women than in men, which is consistent with the results of a study conducted by Jin, Bai (21)**.**

Table 4 shows a comparison between male and female patients who needed ICU, indicating that male cases needed ICU more than their female counterparts (14.8% vs. 10.3%, respectively); this percentage may vary depending on the place and country.

The results of this study demonstrated that vitamin D administration could reduce the risk of coronavirus in patients suffering from chronic diseases, such as hypertension and diabetes.

According to table 5 and the findings of other studies, vitamin D could reduce the severity of the infection with COVID-19 (22, 23). The severe cases were decreased by 33% in those who took 50 IU of vitamin D (Table 6).

In table 7, a significant correlation was found between patients who needed ICU and vitamin D uptake (P=0.01). The percentage of patients in need of ICU dropped from 49% for patients who had never taken a dose of vitamin D to 9% for patients who received 50 IU for vitamin D, these findings were in agreement with those of other studies (24-26).

Table 4. Effect of the severity of the infection with COVID-19 on the need for ICU in male and female patients

Gender	Number and percentage	Does not need ICU	Need ICU	Total	P-value
Males	Number	52	9	61	0.510
	Horizontal percentage	85.2%	14.8%	100%	
	Vertical percentage	59.8%	69.2%	61.0%	
Females	Number	35	4	39	
	Horizontal percentage	89.7%	10.3%	100%	
	Vertical percentage	40.2%	30.8%	39.0%	

ICU: Intensive care unit

Table 5. Effects of vitamin D dose on individuals with chronic diseases and COVID-19

Dose	Number and percentage	Without chronic disease	Hypertension	Diabetes	Hypertension and diabetes	Total	P-value
Never take vitamin D	Number	46	1	20	2	51	0.900
	Horizontal percentage	90.2%	2.0%	3.9%	3.9%	100%	
	Vertical percentage	52.3%	50.0%	50.0%	33.3%	51.0%	
50 unit	Number	13	0	0	1	14	
	Horizontal percentage	92.9%	0.0%	0.0%	7.1%	100%	
	Vertical percentage	14.8%	0.0%	0.0%	16.7%	14.0%	
1,000 unit	Number	29	1	2	3	35	
	Horizontal percentage	82.9%	2.9%	5.7%	8.6%	100.0%	
	Vertical percentage	33.0%	50.0%	50.0%	50.0%	35.0%	

Table 6. Effects of vitamin D dose and severity of infection by COVID-19

Dose	Number and percentage	Severe infection	Moderate infection	Light infection	Total	P-value
Never take vitamin D	Number	6	22	23	51	0.170
	Horizontal percentage	11.8%	43.1%	45.1%	100%	
	Vertical percentage	31.6%	48.9%	63.9%	51.0%	
50 IU	Number	4	5	5	14	
	Horizontal percentage	28.6%	35.7%	35.7%	100%	
	Vertical percentage	21.1%	11.1%	13.9%	14.0%	
1,000 IU	Number	9	18	8	35	
	Horizontal percentage	25.7%	51.4%	22.9%	100.0%	
	Vertical percentage	47.4%	40.0%	22.2%	35.0%	

Table 7. Effect of vitamin D dose and the need to ICU for people with COVID-19

Dose	Number and percentage	Need ICU	Not need ICU	Total	P-value
Never take vitamin D	Number	49	2	51	0.01
	Horizontal percentage	96.1%	3.9%	100%	
	Vertical percentage	56.3%	15.4%	51.0%	
50 IU	Number	9	5	14	
	Horizontal percentage	64.3%	35.7%	100%	
	Vertical percentage	10.3%	38.5%	14.0%	
1000 IU	Number	29	6	35	
	Horizontal percentage	82.9%	17.1%	100.0%	
	Vertical percentage	33.3%	46.2%	35.0%	

ICU: Intensive care unit

It is important to note here that the effectiveness and value of vitamin D, as a supplement in the treatment of coronavirus, are unclear and there is no understandable explanation for its mechanism *in vivo* condition. However, the results of a study conducted by Murai, Fernandes (27) revealed that increasing vitamin D intake would not affect the length of staying in the hospital. The study eventually did not encourage raising vitamin D dose to supplement the treatment of coronavirus patients. The same finding was confirmed in a study carried out by Hernandez, Nan (28) reporting that there was no relation between the dosage of vitamin D and recovery from the COVID-19 virus.

The results of the present study indicated that females were at lower risks of infection with COVID-19 than males, and taking 50 IU of vitamin D could reduce the severe cases by 33% and the need for ICU from 49% to 9%. It was also found that vitamin D enhanced the immunity and respiratory systems, and although it lowered the risks of infection with COVID-19, it was not able to prevent it. Patients with chronic diseases were more susceptible to the coronavirus than others. On the other hand, the findings of a study demonstrated that maintaining a level of vitamin D could participate in coping with the COVID-19 virus pandemic (29). However, it is important to consider other factors, such as chronic diseases, environment, and genetic history of the patients.

Authors' Contribution

Study concept and design: H. A. R. A.
Acquisition of data: B. S. A. A.
Analysis and interpretation of data: H. A. R. A.
Drafting of the manuscript: B. S. A. A.
Critical revision of the manuscript for important intellectual content: H. A. R. A.
Statistical analysis: B. S. A. A.
Administrative, technical, and material support: H. A. R. A.

Ethics

The study protocol was approved by the Ethics Committee of the University of Kerbala, Iraq.

Conflict of Interest

The authors declare that they have no conflict of interest.

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