



Original Article

Vitamin D in Mild to Moderate COVID-19: A Retrospective Cross-Sectional Study

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ABSTRACT

Background: Vitamin D linkage with COVID-19 is investigated in many studies, but there is still no single summation. Thus, this study aimed to evaluate the relationship between Vitamin D levels and clinical characteristics of COVID-19.

Methods: This was a retrospective cross-sectional study on floor admitted COVID-19 patients in the Jahrom province of Iran in 2020. The patients in this study were divided into different groups based on vitamin D status after the definitive diagnosis of COVID-19. Demographic and clinical characteristics of COVID-19 patients were analyzed based on the COVID-19 status.

Results: Vitamin D levels were normal for almost half of the patients (51.7%) and the rest were insufficient (25.9%) or deficient (22.4%). Serum vitamin D levels did not correlate with vital sign data and venous blood gas results ($P > 0.05$). Vitamin D status was not different among patients with different symptoms of COVID-19 ($P > 0.05$).

Conclusion: Our results revealed that vitamin D levels is not correlated to clinical characteristics in COVID-19 patients. In addition, well-designed studies with a good sample size are required to draw conclusions.

GRAPHICAL ABSTRACT



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Introduction

COVID-19 was first observed in late 2019, in China [1-3]. Clinical manifestations range from mild flue like symptoms to severe organ dysfunction [4-6]. According to the World Health Organizations (WHO), the disease is classified into 4 degrees based on severity: Grade 1: Feeling sick, Grade 2: Cold-like symptoms, runny nose, low-grade fever, low-grade cough, Grade 3: Flu-like symptoms, i.e., fever and chills, loss of appetite and muscle aches, and grade 4: Symptoms of acute respiratory distress syndrome [ARDS], severe Dyspnea, dry cough, and sometimes fever [7]. It has been found that the severity of symptoms is affected by different baseline biological and sociodemographic factors and current health status [8-9]. COVID-19 has caused many deaths worldwide, which has also been associated with economic risks. Therefore, immediate preventive and therapeutic measures are needed to further manage the disease and identify the risk factors associated with it [10]. So far, several risk factors have been identified concerning COVID-19. Major comorbidity, including diabetes, obesity, hypertension, and cardiovascular disease, and increased levels of cytokines and other inflammatory factors are predictors of COVID-19 [11-13]. Recently vitamin D supplementation is proposed for COVID-19 [14]. Pooled analysis of current evidence is also showing promising benefits of the vitamin D in COVID-19 disease course [15]. Vitamin D can regulate the immune system against viral infections in several different ways for example Increased levels of CD8 + T cells, calling immune cells to the site of infection, modification of interferon in respiratory epithelium, reducing the virus replication, and ultimately reduces the inflammatory storm induced by the innate and acquired immune system [16-17]. Many studies have shown that vitamin D deficiency increases the deterioration of COVID-19 symptoms, but there are still further studies to identify this mechanism. Therefore, we hypothesized a relationship between serum vitamin D levels and clinical characteristics of Covid-19.

Material and Methods

This was a retrospective cross-sectional study on COVID-19 patients referred to Peymanieh Hospital in Jahrom in 2020 and admitted to the COVID-19 ward. The study protocol was register under code of IR.JUMS.REC.1399.111 in the affiliated university.

The inclusion criteria in our research were included:

1. Positive RT-PCR test of COVID-19;
2. No cancer, chronic inflammatory and autoimmune diseases (rheumatology, COPD, liver, kidney, etc.);
3. No pregnancy and breastfeeding;
4. No ongoing or previous radiotherapy and chemotherapy;
5. Not taking immunosuppressive drugs;
6. Not taking psychotropic drugs and addiction; and,
7. Satisfaction to participate in the study

Exclusion criteria in this study included:

1. Dissatisfaction and lack of cooperation to participate in the study

Demographic information as well as the age, sex, occupation, place of residence, and history of the comorbidities, the patient's main complaints were recorded along with vital signs, arterial blood oxygenation (O₂ Sat), and blood gas analyses at admission. In this study, serum 25(OH)D was considered to be "Deficient" in case of serum levels of under 20 ng/ml, "insufficient" at 20-30 ng/ml, "Normal" above 30 ng/ml, respectively [18]. SPSS software version 21 was utilised to analysis data. Continuous data were expressed by mean and standard deviation being analysed by Pearson correlation and binominal data by number and percent being analysed by Chi-square and Fisher's exact test. P value of under 0.05 was considered statistically significant.

Results

Among 57 participants of study, 58.6% were female and 41.4% were male. The majority were married (93.1%) and literate (63.8%). Among comorbidities, diabetes (24.1%) and hypertension (37.9%) had the highest frequency (Table 1). Vitamin D levels were Normal for almost half of

the patients (51.7%) and the rest were insufficient (25.9%) or deficient (22.4%) (Chart 1).

Table 1: Baseline characteristics of study subjects

		Number	percentage
Sex	Male	24	41.4%
	Female	34	58.6%
Marital status	Single	4	6.9%
	Married	54	93.1%
Education level	Literate	37	63.8%
	Illiterate	21	36.2%
Co-morbidities	Diabetes	14	24.1%
	Kidney	6	10.3%
	Cancer	3	5.2%
	Hypertension	22	37.9%
	pulmonary	4	6.9%

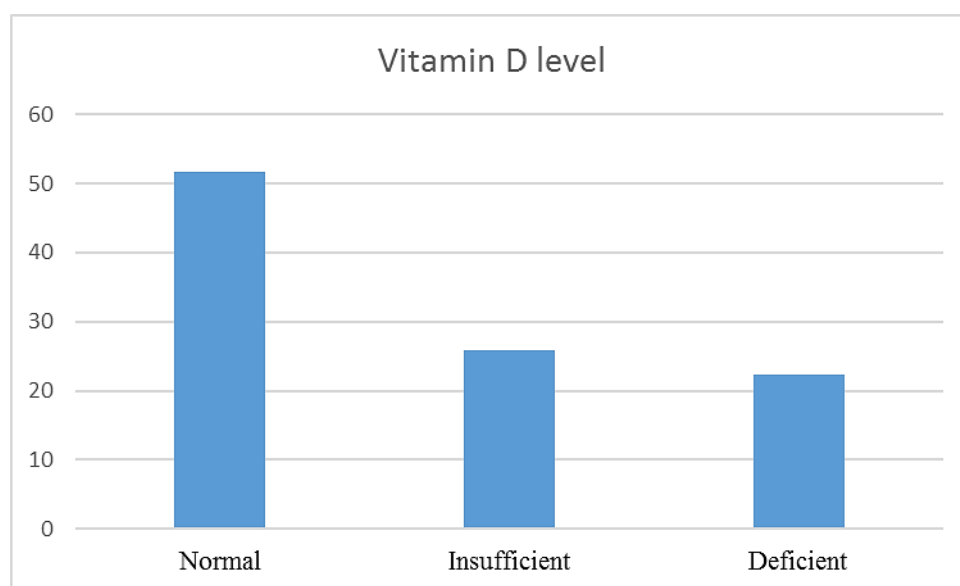


Chart 1: Vitamin D status of participants

The results of the Pearson correlation coefficient correlate with vital sign data and venous blood gas showed that serum vitamin D levels did not results ($P > 0.05$). (Table 2).

Table 2: Correlation of vital signs and venous blood gas analysis with vitamin D levels

Systolic Blood pressure	Diastolic Blood pressure	Pulse rate	Temperature	Number of breaths	PCO2	PO2	O2SAT	
-0.008	0.060	-0.12	0.009	-0.16	-0.10	0.04	-0.12	r
0.95	0.65	0.36	0.95	0.23	0.77	0.90	0.56	p-value

The results showed that patients with Covid-19 with vitamin D deficiency, symptoms of Dyspnea (61.5%) and fever (53.8%) were more common. In patients with COVID-19 with insufficient levels of vitamin D, rales in lung auscultation (46.7%), Dyspnea (66.7%) and myalgia (40%) were the

most frequent findings. The results of chi-square and Fisher's exact test showed that there was no significant relationship between serum vitamin D levels and clinical symptoms in patients with COVID-19 ($p > 0.05$) (Table 3).

Table 2: Vitamin D status and clinical symptoms

	Vitamin D level						P-value
	Normal		Insufficient		Deficient		
	Number	Percentage	Number	Percentage	Number	Percentage	
Rales in auscultation	16	53.3%	7	46.7%	6	46.2%	0.87
Wheezing	0	0.0%	1	6.7%	0	0.0%	0.2*
Lethargy	13	43.3%	3	20.0%	5	38.5%	0.30
Dyspnea	22	73.3%	10	66.7%	8	61.5%	0.75
Loss of appetite	4	13.3%	2	13.3%	4	30.8%	0.34*
Fatigue	4	13.3%	1	6.7%	1	7.7%	0.86*
Myalgia	12	40.0%	6	40.0%	5	38.5%	0.99
Sore throat	3	10.0%	0	0.0%	1	7.7%	0.65*
Fever	8	26.7%	2	13.3%	7	53.8%	0.07

*In some cases, the Fisher test is used and in other cases, the Chi-square test is used

Discussion

In this study, we found that 22.4% of our evaluated patients were vitamin D deficient. While we did not recruit any control group of healthy people to assess vitamin D status as a predisposing factor of COVID-19, our data suggested that none of the clinical factors was associated with vitamin D levels. Tekin et al.'s study found a similar finding of the no association of vitamin D levels with disease severity [19]. In controversy to our results, Vasheghani *et al.* [20], Campi *et al.* [21], and Meltzer *et al.* [22] found a significant relationship between vitamin D and the severity of COVID-19. The difference between our studies with these studies was that we did not include severe cases of COVID-19 that required advanced care in the ICU or mechanical ventilation.

Im et al., elucidated that zinc and Vitamin D levels of COVID-19 patients are even higher than healthy subjects [23]. These results are similar to our study and level of the vitamin D is normal in most COVID-19 patients. Like our study, AlKhafaji et al., did not find any relationship with COVID-19 severity [24]. Also, Tehrani *et al.* [25] did not find any link with mortality comparing the expired and survived patients. Furthermore, Murai *et al.* [26] elucidated that a strong dose of vitamin D cannot significantly improve clinical symptoms in COVID-19 patients in critical conditions. Vitamin D level and duration of hospitalization were not

correlated in another study [27], while ICU admitted patients had lower vitamin D levels than floor admitted ones. Some other studies are showing the conflict results. Meltzer *et al.* [22] that observed that vitamin D deficiency is associated with the risk of SARS-Cov2 infection. In another study, it was observed that vitamin D deficiency is associated with mortality and prognosis of COVID-19 patients. This may be due to the role of vitamin D in modulating the immune system (29). Studies showed that several confounding factors play a role in the relationship between Vitamin D status and the severity of COVID-19 infection that it is not possible to administer them even with advanced statistical methods, such as underlying diseases, socioeconomic status, and quality of health services correlated with lower Vitamin D status [30-31], as well as reverse causality bias due to rapid publication of results [28] and the small sample size [32].

Conclusion

Our results revealed that vitamin D levels is not correlated to clinical characteristics in COVID-19 patients. In addition, well-designed studies with a good sample size are required to draw conclusions.

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Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

There are no conflicts of interest in this study.

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