Importance of Vitamin D in COVID-19 Patients

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ABSTRACT

Objectives: The severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) virus, was identified as the cause of a severe respiratory illness in Wuhan, China three years ago. The COVID-19 infection, which was declared a pandemic in March 2020, caused more than 600 million people to get sick and close to 7 million people to die. Which people have the disease more severely and who have higher mortality are still the subject of research. We investigated whether vitamin D, whose role in immunity has been known for a long time, also affects the prognosis of COVID-19 infection. COVID-19 is currently the leading cause of death worldwide. Vitamin D is an important micronutrient and has been reported to protect against respiratory diseases by improving immunity. In this study, we aimed to reveal whether the 25-hydroxyvitamin D (25 (OH) D) concentration is associated with the risk and severity of COVID-19 by evaluating vitamin D levels in outpatients or hospitalized patients with the diagnosis of COVID-19.

Methods: In the study, vitamin D levels in 124 COVID-19 cases and clinical course and laboratory findings were analyzed retrospectively between March 11-May 31 2020. Statistical analysis was done using IBM SPSS 23. Kolmogorov Smirnov, Man Whitney U, Kruskal Wallis Test, Chi-square, and fisher extract and risk analysis tests were used. Categorical variables were expressed as %. P value < 0.05 was considered significant.

Results: Vitamin 25 (OH) D level in 32 patients (median 10.2) who were given antiviral treatment and needed oxygen. It was found to be significantly lower than the other 92 patients (median 16.25). When patients who needed oxygen treatment during COVID-19 treatment were examined in terms of vitamin D levels; It was observed that patients with 25 (OH) vitamin D level < 10 needed more O2 (OR: 2,833 CI 95% 1,230-6,528, p = 0.013). In patients with 25 (OH) vitamin D < 10, more patients had pulmonary involvement with thorax CT (OR: 2.225 CI 95% 0.999-4.952 p = 0.048) and these patients had more back pain symptoms (OR: 4,765 CI 95% 1,126-20,163 p = 0.022). Patients with 25 (OH) vitamin D <10 had a greater number of decreased senses of smell and taste (OR: 11,857 CI 95% 1,336-105,214 p = 0.006). In addition, 25 (OH) vitamin D levels were positively correlated with aPTT, while it was negatively correlated with neutrophil/monocyte ratio, glucose, ALT, AST, GGT, and LDH.

Conclusions: Our findings suggest a potential relationship between vitamin D concentrations and the prognosis of COVID-19 infection. Our results support the importance of vitamin D levels in the treatment of COVID-19 and the need for vitamin D supplements in treatment.

Keywords: COVID-19, vitamin D, pneumonia

The pandemic coronavirus disease (COVID-19) is currently the leading cause of death worldwide. To date, no curative medication has been found for the definitive treatment of this disease. Future measures, especially vaccines, masks, and social distancing are the most important ways to prevent the social transmission of this disease.

Vitamin D is an important micronutrient and has been reported to protect against respiratory diseases by improving immunity. [1,2]

In this study, we aimed to reveal whether the 25-hydroxyvitamin D (25 (OH) D) concentration is associated with the risk and severity of COVID-19 infection by evaluating vitamin D levels in outpatients or hospitalized patients with the diagnosis of COVID-19.

METHODS

In the study, the test results of 124 cases whose vitamin D levels were measured between March 11, 2020 and May 31, 2020 were analyzed retrospectively. COVID-19 RT-PCR results in nose and throat swab samples, clinical course, and laboratory findings of the patients were retrospectively analyzed. Statistical analysis was done using IBM SPSS 23. Kolmogorov Smirnov, Man Whitney U, Kruskal Wallis Test, Chi-square, and fisher extract and risk analysis tests were used. Categorical variables were expressed as %. P value < 0.05 was considered significant.

RESULTS

RT-PCR test was found positive in 33.9% of 124 patients whose 25(OH) vitamin D levels were checked out of 2800 patients included in the study and whose nose and throat swabs were tested for COVID-19. The 25(OH) vitamin D levels of these patients are shown in Table 1 according to their clinical characteristics. In 32 patients (median 10.2) who were given antiviral drug therapy after lung involvement, 25(OH) vitamin

Table 1. Vitamin D levels according to the clinical characteristics of the patients

		N	%		Median		
RT-PCR	RT-PCR positive	42	33,9	0,452	13,55	4,2	93
	RT-PCR negative	82	66,1		16,05	2,22	97,2
Follow up	In ICU	24	19,4	0,221	12,1	6,3	44,9
	Inpatient	100	80,6		16	2,22	97,2
	Outpatient						
Prognosis	Death	7	5,6	0,673	15,9	6,3	19,8
	Live	117	94,4		14,4	2,22	97,2
Gender	Male	58	46,8	0,896	14	4,2	93
	Female	66	53,2		15,45	2,22	97,2
Vitamin D	< 10	40	32,3				
	> 10	84	67,7				
Vitamin D	< 20	87	70,2				
	> 20	37	29,8				
Vitamin D	< 30	108	87,1				
	> 30	16	12,9				
Antiviral or O2	Take	32	25,8	0,013	10,2	4,2	47,3
	Not taking	92	74,2		16,25	2,22	97,2
Infitration on CT	Positive	66	53,2	0,212	12,9	4,2	97,2
	Negative	17	13,7		16,15	2,22	36,7
	No CT	41	33,1				
	Outpatient	32	25,8				
	Inpatient	92	74,2				

Table 2. Correlation analysis between vitamin D and laboratory values

25 (0H) Vitamin D	R value	*P* value
Neutrophil / monocyte	-0,182	0,058
APTT	0,240	0,029
Glucose	-0,321	0,016
ALT	-0,191	0,045
AST	-0,252	0,008
GGT	-0,261	0,017
LDH	-0,252	0,021

D levels were found to be significantly lower than the other 92 patients (median 16.25).

When patients who need oxygen therapy during COVID-19 treatment are examined in terms of vitamin D level; It was observed that patients with 25 (OH) vitamin D levels < 10 ng/ml had higher oxygen demand and antiviral therapy was started in these patients (OR: 2,833 CI 95% 1.230-6.528, *p* = 0.013). It was observed that patients with 25 (OH) vitamin D < 10 ng/ml had more frequent lung involvement with thorax CT compared to those without (OR: 2.225 CI 95% 0.999-4.952 *p* = 0.048). It was also observed that myalgic symptoms such as low back pain were more common in patients with 25 (OH) vitamin D < 10 ng/ml (OR: 4.765 CI 95% 1.126-20.163 *p* = 0.022). We determined that the symptom of decreased sense of smell and taste also occurred more frequently in patients with 25 (OH) vitamin D < 10 ng/ml (OR: 11,857 CI 95% 1.336-105.214 *p* = 0.006).

In addition, 25 (OH) vitamin D levels were positively correlated with aPTT, while negatively correlated with neutrophil/monocyte ratio, glucose, ALT, AST, GGT, and LDH (Table 2).

When the 25(OH) vitamin D levels of the patients who were followed up in the outpatient, hospitalized or intensive care unit after the diagnosis of COVID-19 were compared, there was no significant difference. Similarly, when the 25(OH) vitamin D levels of the patients whose COVID-19 infection resulted in cure or death were compared, no significant difference was found.

DISCUSSION

When we look at the literature, it is seen that the number of studies examining the relationship between the clinical course of COVID-19 infection and vitamin D levels is increasing day by day.

In a retrospective study, the levels of vitamin D at the time of diagnosis in 212 patients with SARS-CoV-2 infection were examined and it was found that there is a relationship between the prognosis of the disease and vitamin D levels. [3] In our study, we found that patients with low vitamin levels had more severe COVID-19 and needed additional supportive treatments.

In a cohort study of 43 patients, the group was given vitamin D (1000 IU), Mg (150 mg), and vitamin B12 (500 μg) worsened less frequently (*p* = 0.041) than the control group. [4] In a retrospective observational study conducted in Belgium, 186 SARS-CoV-2 PCR positive and 2717 negative patients were examined and it was found that the vitamin D levels of positive cases were lower than the control group (p: 0.0016). [5] We also found in our study that COVID-19 PCR-positive cases had lower 25(OH) vitamin D levels than negative cases. (*p*: 0.452)

In a retrospective cohort study conducted in Indonesia, 780 patients were examined and a correlation was established between low 25(OH) vitamin D levels and mortality due to COVID-19. [6] A similar study was conducted retrospectively on health records in the United States of America and very large patient populations were examined. Exposure to sunlight, vitamin D levels, and COVID-19 infection and mortality were compared over the latitude lived. It has been shown that high vitamin D levels reduce the risk of both COVID-19 infection and related mortality. [7] On the other hand, in a study conducted in the United Kingdom between May and October 2021, Jolliffe and colleagues looked at 25-hydroxyvitamin D concentrations in the blood of 3100 participants, and those < 75 nmol/L were treated with vitamin D3 at a dose of 200IU/day or 800IU/day for 6 months. The control group of 3100 people was not examined or treated. The authors found that none of the vitamin D doses had any effect on the incidence of COVID-19. [8] This trial had several strong aspects: a high prevalence of participants (64.6%) within adequate 25-hydroxyvitamin D levels (< 50 nmol/L), good protocol compliance, and a definitive endpoint with COVID-19 confirmed by polymerase chain reaction.

Although most of the studies in the literature have shown a relationship between vitamin D levels and COVID-19 infection, a small number of studies have not found any relationship between them. In our study, there was no finding that patients with low vitamin D levels had a more fatal course. It was considered that

this was probably due to the low number of deceased patients in our study.

CONCLUSION

Our findings suggest a potential link between vitamin D concentrations and the risk and prognosis of COVID-19 infection. The fact that 25(OH) vitamin D levels are low, especially in patients with involvement in thorax CT and progressing with more severe symptoms, reveals the necessity of vitamin D supplementation. On the other hand; It was evaluated that the lack of significant difference in 25(OH) vitamin D levels in intensive care, hospitalized or outpatient patients due to COVID-19 infection may be due to the rapid replacement of the vitamin when the vitamin level is found to be low or the relatively small number of patients.

It must be admitted that during the pandemic era, which threatens almost the entire society, it is obvious that it is impossible to measure 25(OH) vitamin D levels in all patients who apply to the doctor. At this point; In selected patient groups, it is considered that it would be appropriate to plan treatment according to the result by looking at 25(OH) vitamin D levels or to start 25(OH) vitamin D treatment empirically in patients with certain clinical features. Larger, prospective randomized controlled studies are needed to strengthen this recommendation and confirm the relationship between 25(OH) vitamin D levels and the course and prognosis of COVID-19 infection.

Authors' Contribution

Study Conception: MK, YO,; Supervision: YO, İK,; Desing: MK, YO, İK, ÖÇ,; Data Collection and/or Processing: MK, YO, İK,; Statistical Analysis and/or Data Interpretation: MK, YO, İK, ÖÇ,; Literature Review: MK, YO, İK,; Manuscript Preparation: MK and Critical Review: MK, YO, İK, ÖÇ.

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