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A Lower 25(OH)D Level in COVID-19 Patients is Associated with Increased Mortality: An Observational Study

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Abstract

Background: Recent studies have shown that insufficient vitamin D supply is correlated with increase in COVID-19 cases and its mortality. Potentially, it may play an important role in controlling virus proliferation.
Objectives: This study aimed to evaluate the association between serum vitamin D levels and clinical findings, and mortality rate in patients with COVID-19.
Methods: This cross-sectional study was conducted on 200 COVID-19 patients referred or admitted to Loghman-e-Hakim Hospital of Tehran, Iran, from February to June 2020. After patient selection, demographic information of all patients was recorded. Eventually, the relationship between basic demographic and clinical findings with vitamin D levels in all patients was evaluated.
Results: The mean Vit-D levels in intubated and non-intubated patients were 22.95 $\pm$ 22.23 ng/mL and 21.64 $\pm$ 29.20 ng/mL, respectively (P = 0.018). In most of the outpatients (46.7%), Vit-D levels were between 21 - 30 ng/mL, and 47.6% of admitted patients had Vit-D $\leq$ 20 ng/mL. The mean Vit-D level in survived patients was significantly higher than patients who died (28.2 $\pm$ 21.18 ng/mL vs. 19.91 $\pm$ 14.18 ng/mL, respectively; P = 0.021). While 34.2% (55 cases) of survived patients had Vit-D level $\geq$ 31 ng/mL, about 70% of death cases had Vit-D $\leq$ 20 ng/mL (P < 0.001).
Conclusions: According to our results, vitamin D supplementation could be beneficial in COVID-19 patients. However, further comprehensive clinical trials are needed to confirm these findings.

Keywords: COVID-19, Vitamin D, Mortality

1. Background

In December 2019, a novel coronavirus (COVID-19) was introduced to the world. Since then, more than 200 countries have been affected in less than six months (1). This pandemic has resulted in high mortality and morbidity worldwide. Fatality rate is reported to be about 6.6%, which is higher among patients with underlying diseases, such as diabetes, obesity, hypertension, as well as cardiovascular and cerebrovascular diseases (2). This highly contagious virus enters the body through upper respiratory tracts and causes severe respiratory tract infection. Prodromal symptoms include malaise, fever, dry cough, fatigue, and myalgia (3). Small number of patients may experience atypical symptoms such as nausea, vomiting, or diarrhea. Interestingly, 81% of patients have mild symptoms that recover with supportive care, 14% have more severe symptoms like dyspnea and low oxygen saturation, and 5% have life-threatening conditions such as acute respiratory distress syndrome (ARDS), septic shock, and multi-organ failure (4). Patients with severe COVID-19 infection are more prone to need emergent intubation and mechanical ventilation. Approximately 10% of all confirmed cases need intensive care unit (ICU) admission due to profound hypoxia (5).

Diagnosis of COVID-19 is based on epidemiological history, clinical manifestations, radiologic and laboratory findings. The most common laboratory items include lymphopenia, increase in transaminases, CRP, and ferritin (6). Chest computed tomography (CT) scan reveals bilateral parenchymal ground glass opacities or consolidative pulmonary opacities. Diagnosis is confirmed by real-time quantitative polymerase chain reaction (RT-PCR) from nasopharyngeal swabs, trans-tracheal aspiration, or bronchoalveolar lavage (BAL) fluid. However, its false-negative rate should be considered (7). Treatment is supportive care, and up to now, there is no clinically approved antiviral

agent for this novel virus.

Vitamin D (Vit-D) is a fat-soluble chemical which may regulate immune system response. Vit-D deficiency may correlate with increased risk of viral infections. Recent studies have shown that insufficient Vit-D supply is correlated with increase in COVID-19 cases and its mortality. Potentially, it may play an important role in controlling virus proliferation. Moreover, production of pro-inflammatory cytokines can be inhibited by Vit-D. Active metabolite of Vit-D is 1,25 OH Vit-D, which inhibits T cells proliferation and activation (8).

2. Objectives

This study aimed to evaluate the correlation between Vit-D levels and the incidence of infection with COVID-19 to clarify whether Vit-D deficiency is a risk factor for more severe COVID-19 events.

3. Methods

3.1. Patients and Methods

This cross-sectional study was conducted on 200 COVID-19 patients referred or admitted to Loghman-e-Hakim Hospital of Tehran, Iran, from February to June 2020. The current study was approved by the institutional review board and ethical committee of Shahid Beheshti University of Medical Sciences (Tehran, Iran). Written informed consents were signed by all patients. COVID-19 was confirmed in all patients using PCR and chest CT methods. Inclusion criteria were as follows: (1) confirmed COVID-19, (2) aged > 18 years old, and (3) both genders. The exclusion criteria were as follows: (1) congenital anomalies, (2) use of Vit-D supplementation at the time of study, and (3) unwillingness to participate in the study. After patient selection, basic demographic information (including age, sex, weight, history of smoking, and underlying diseases) of all patients was recorded. Then, 5 ml of blood sample was collected from the antecubital veins of patients, and serum Vit-D levels were measured. Serum Vit-D levels were divided into three groups based on concentration: $\leq$ 20 ng/mL (Vit-D deficiency), 21 - 30 ng/mL (insufficient concentration of Vit-D), and $\geq$ 31 ng/mL (normal concentration of Vit-D). Additionally, basic clinical data of all patients along with routine laboratory test results (eg, CBC analysis), blood pressure, pulse rate, respiration rate, ventilation status, and mortality rate were evaluated. Eventually, the relationship between these basic demographic and clinical findings with Vit-D levels was evaluated in all patients.

3.2. Statistical Analysis

The results were analyzed by SPSS software (IBM, version 19). Quantitative data was analyzed using the descriptive program and presented as mean $\pm$ standard deviation (SD). Crosstabs and chi-square tests were used to compare the percentages or frequencies between the two groups. The comparison of the mean of parametric data was analyzed using independent student's *t*-test. One-way analysis of variance (ANOVA) and Tukey's post-hoc test was used to compare the data between three groups of Vit-D levels. In this study, $P < 0.05$ was considered statistically significant.

4. Results

In this study, a total of 200 COVID-19 patients (mean age: 58.72 $\pm$ 20.37 years; mean weight: 67.34 $\pm$ 8.69 kg) were included. Also, 101 patients (50.5%) were males, and 99 cases (49.5%) were females. The comparison of the demographic and basic clinical characteristics between outpatients and admitted cases is summarized in Table 1. The frequency of outpatients and admitted cases was 7.5% (15) and 92.5% (185), respectively. The mean age of outpatients was significantly higher than admitted cases (45.8 $\pm$ 19.29 years vs. 59.77 $\pm$ 20.14 years, respectively; P = 0.011). Moreover, 71 (35.5%) patients were smokers, of whom 84.5% (60 cases) were males, and 15.5% (11 cases) were females (P < 0.001). In addition, 25 (12.5%) patients were opiate users, 82% (18 cases) of whom were males and 28% (7 cases) were females (P = 0.022). There was no significant difference in the prevalence of smoking and opiate using between outpatients and admitted cases (Table 1). There was no significant difference in the frequency of ischemic heart disease (IHD), hypertension (HTN), and diabetes mellitus (DM) between the two groups. While none outpatients received intubation, 40.5% (75) of admitted cases underwent intubation (P = 0.002).

There was no significant difference in the mean Vit-D levels between admitted cases (26.52 $\pm$ 20.83 ng/mL) and outpatients (27.37 $\pm$ 11.21 ng/mL) (P = 0.87). Overall, 45.5% (91 cases) had serum Vit-D levels $\leq$ 20 ng/mL, 25.5% (51 cases) had Vit-D levels 21 - 30 ng/mL, and 29% (58 cases) had Vit-D levels $\geq$ 31 ng/mL. A tendency for lower mean Vit-D level was found in admitted cases (P = 0.07). While Vit-D levels in most of outpatients (46.7%) were between 21 - 30 ng/mL, 47.6% of admitted patients had Vit-D $\leq$ 20 ng/mL. The percentage of outpatients and admitted cases with mean Vit-D levels of $\geq$ 31 ng/mL was 33.3% and 28.6%, respectively (Table 2). A significant difference was observed in the prevalence of Vit-D concentration between males and females (P = 0.008). While 38.4% of females had Vit-D $\geq$ 31 ng/mL, more than 50% of males had Vit-D level $\leq$ 20 ng/mL.

Table 1. Comparison of the Demographic and Basic Clinical Characteristics Between Outpatients and Admitted Cases [a]

Variable	Outpatients	Inpatients	P-Value
Age (y)	45.8 ± 19.29	59.77 ± 20.14	0.011
Gender			0.81
Male (%)	50.3	53.3	
Female (%)	49.7	46.7	
Smoking			0.34
Yes	7 (46.7)	64 (34.6)	
No	8 (53.3)	121 (65.4)	
Opiate using			0.47
Yes	1 (6.7)	24 (13)	
No	14 (93.3)	161 (87)	
IHD			0.57
Yes	4 (26.7)	38 (20.5)	
No	11 (73.3)	147 (79.5)	
HTN			0.79
Yes	7 (46.7)	80 (43.2)	
No	8 (53.3)	105 (56.8)	
DM			0.41
Yes	4 (26.7)	69 (37.3)	
No	11 (73.3)	116 (62.7)	
Intubation			0.002
Yes	0	75 (40.5)	
No	15 (100)	110 (59.5)	

[a] Values are expressed as No. (%) unless otherwise indicated.

Smoker patients had a tendency for lower mean serum Vit-D levels compared to non-smoker patients (23.38 ± 18.5 ng/mL vs. 28.35 ± 21.01 ng/mL; P = 0.07). While 33.3% of non-smokers had Vit-D levels ≥ 31 ng/mL, more than 50% of smokers had Vit-D ≤ 20 ng/mL (Table 2).

Patients who underwent intubation had significantly lower mean Vit-D levels compared to non-intubated patients (22.12 ± 16.95 ng/mL vs. 29.20 ± 21.64 ng/mL; P = 0.018). While 39.2% of non-intubated patients had Vit-D levels ≥ 31 ng/mL, more than 50% of intubated cases had Vit-D levels ≤ 20 ng/mL (Table 2; P < 0.001). There was no significant relationship between the history of HTN, DM, and IHD with mean Vit-D levels (Table 2).

The comparison of laboratory results between patients with different concentrations of Vit-D showed no significant correlation between Vit-D levels and the other laboratory test results (Table 3).

Overall, the mortality rate among all COVID-19 patients was 19.5% (39 cases), 17.8% of whom were males and 21.2% (21 cases) were females (P = 0.54). A significant difference was found in the mean Vit-D levels between survived patients and death cases (P = 0.021). The mean Vit-D levels in survived patients were significantly higher than death cases (28.2 ± 21.18 ng/mL vs. 19.91 ± 14.18 ng/mL, respectively) P-value is 0.001.

While 34.2% (55 cases) of survived patients had Vit-D levels ≥ 31 ng/mL, about 70% of death cases had Vit-D levels ≤ 20 ng/mL (P < 0.001). Approximately 40% of survived patients had Vit-D levels ≤ 20 ng/mL (Table 2).

The comparison of the demographic and basic clinical characteristics between survived patients and death cases is summarized in Table 4. The mortality rate among outpatients and admitted cases was 6.7% and 20.5%, respectively (P = 0.16). The mean age in death cases was significantly higher compared to survived cases (68.05 ± 18.37 vs. 56.46 ± 20.24 years, respectively; P = 0.001). Also, death cases had a lower mean weight compared to survived patients (64.07 ± 6.21 vs. 68.13 ± 9.03 kg, respectively; P = 0.009). The mortality rate among patients with a history of HTN was significantly higher than those without this problem (59% vs. 39.8%, respectively; P = 0.03). a trend was also found for increased mortality rate among cases with a history of IHD (died patients: 30.8% vs survived patients: 18.6%, P-value: 0.077) and DM (died patients: 48.7% vs survived patients: 33.5%, P-value: 0.07). Mortality rate in patients who underwent intubation process was considerably higher compared to non-intubated cases (92.3% vs. 24.2%, respectively; P < 0.001).

The comparison of laboratory results between death cases and survived patients is depicted in Table 5. The mean of CRP and systolic blood pressure (SBP) in death cases (34.82 ± 19.8 mg/L and 144.1 ± 13.66 mmHg, respectively) were significantly higher than those in survived cases (26.75 ± 18.37 mg/L and 138.78 ± 15.09 mmHg, respectively).

5. Discussion

In this study, we investigated the relationship between serum vitamin D levels and the severity of clinical findings and mortality rate among 200 patients with COVID-19. Since the COVID-19 virus has been recently spread throughout the world, no comprehensive study, especially in Iran, has been conducted on this disease so far. Our data revealed that the mortality rate among all patients was 19.5%. Interestingly, we found that the mean serum vitamin D levels in survived patients were significantly higher than those of death cases. While approximately 35% of survived patients had serum Vit-D levels ≥ 31 ng/mL, only 7.7% of death cases had Vit-D levels ≥ 31 ng/mL. Although there

Table 2. Comparison of the Demographic and Basic Clinical Characteristics Between Patients with Different Concentrations of Vit-D [a]

Variable	≤ 20 ng/mL	21 - 30 ng/mL	≥ 31 ng/mL	P-Value
Patients				0.07
Outpatients	3 (20)	7 (46.7)	5 (33.3)	
Admitted patients	88 (47.6)	44 (23.8)	53 (28.6)	
Survival				0.001
Survived	64 (39.8)	42 (26.1)	55 (34.2)	
Died	27 (69.2)	9 (23.1)	3 (7.7)	
Age (y)	60.78 ± 19.53	58.96 ± 20.34	55.13 ± 21.52	0.24
Weight (kg)	67.31 ± 8.89	66.76 ± 9.09	67.87 ± 8.1	0.8
Gender				0.008
Male	55 (54.5)	26 (25.7)	20 (19.8)	
Female	36 (36.4)	25 (25.3)	38 (38.4)	
Smoking				0.14
Yes	38 (53.5)	18 (25.4)	15 (21.1)	
No	53 (41.1)	33 (25.6)	43 (33.3)	
IHD				0.69
Yes	20 (47.6)	12 (28.6)	10 (23.8)	
No	71 (44.9)	39 (24.7)	48 (30.4)	
HTN				0.59
Yes	42 (48.3)	23 (26.4)	22 (25.3)	
No	49 (43.4)	28 (24.8)	36 (31.9)	
DM				0.62
Yes	36 (49.3)	16 (21.9)	21 (28.8)	
No	55 (43.3)	35 (27.6)	37 (29.1)	
Intubation				< 0.001
Yes	39 (52.0)	27 (36.0)	9 (12)	
No	52 (41.6)	24 (19.2)	49 (39.2)	

[a] Values are expressed as No. (%) or mean ± SD.

Table 3. Comparison of the Laboratory Results Between Patients with Different Concentrations of Vit-D [a]

Variables	≤ 20 ng/mL	21 - 30 ng/mL	≥ 30 ng/mL	P-Value
ESR (mm/h)	44.38 ± 22.01	40.15 ± 15.6	42.82 ± 17.08	0.45
CRP (mg/L)	29.52 ± 22.47	28.3 ± 15.0	26.47 ± 15.62	0.63
HB (g/dL)	13.24 ± 9.79	11.91 ± 2.02	13.4 ± 12.09	0.65
WBC (×1000/mL)	9.22 ± 10.72	7.41 ± 3.45	7.13 ± 2.75	0.19
SBP (mmHg)	139.61 ± 14.04	144.11 ± 14.16	136.37 ± 16.21	0.025
DBP (mmHg)	83.02 ± 5.52	83.92 ± 5.68	80.77 ± 6.86	0.017
PR (n/min)	81.07 ± 4.64	82.43 ± 8.08	81.53 ± 6.09	0.44
RR (n/min)	23.2 ± 2.67	23.07 ± 4.63	23.12 ± 4.63	0.97

[a] Values are expressed as mean ± SD.

Table 4. Comparison of the Demographic and Basic Clinical Characteristics Between Survived Patients and Death Cases [a]

Variable	Survived Patients	Death Cases	P-Value
Patients			0.16
Outpatients	14 (93.3)	1 (6.7)	
Admitted patients	147 (79.5)	38 (20.5)	
Age (y)	56.46 ± 20.24	68.05 ± 18.37	0.001
Weight (kg)	68.13 ± 9.03	64.07 ± 6.21	0.009
Gender			0.54
Male	83 (51.6)	18 (46.2)	
Female	78 (48.4)	21 (53.8)	
Smoking			0.66
Yes	56 (34.8)	15 (38.5)	
No	105 (65.2)	24 (61.5)	
IHD			0.077
Yes	30 (18.6)	12 (30.8)	
No	131 (81.4)	27 (69.2)	
HTN			0.03
Yes	64 (39.8)	23 (59)	
No	97 (60.2)	16 (41)	
DM			0.07
Yes	54 (33.5)	19 (48.7)	
No	107 (66.5)	20 (51.3)	
Intubation			< 0.001
Yes	39 (24.2)	36 (92.3)	
No	122 (75.8)	3 (7.7)	

[a] Values are expressed as No. (%).

Table 5. Comparison of the Laboratory Results Between Survived Patients and Death Cases [a]

Variable	Survived Patients	Death Cases	P-Value
ESR (mm/h)	42.78 ± 20.25	43.15 ± 13.94	0.91
CRP (mg/L)	26.75 ± 18.37	34.82 ± 19.8	0.016
HB (g/dL)	13.26 ± 10.33	11.63 ± 1.51	0.32
WBC ($\times 10^3/\mu L$)	8.15 ± 8.16	8.18 ± 4.93	0.93
SBP (mmHg)	138.78 ± 15.09	144.1 ± 13.66	0.046
DBP (mmHg)	82.60 ± 5.81	82.56 ± 7.15	0.96
PR (n/min)	81.42 ± 6.16	82.07 ± 5.85	0.55
RR (n/min)	22.95 ± 3.41	23.94 ± 4.14	0.12

[a] Values are expressed as mean ± SD.

was no significant difference in the mean Vit-D levels between admitted patients and outpatients, most of the hospitalized patients had Vit-D levels ≤ 20 ng/mL, indicating a possible role of Vit-D in the severity of the disease. However, because of the limited number of outpatients in this study (n = 15 cases), further research with greater sample size of outpatients is needed to achieve a more accurate result. Therefore, these results indicate that not only COVID-19 patients have a tendency for lower mean Vit-D levels, but also decreased mean serum Vit-D levels (especially ≤ 20 ng/mL) are significantly associated with increased mortality rates among these patients. Therefore, further clinical studies are recommended to investigate the effect of Vit-D administration on clinical findings, mortality, and morbidity in these patients. Biesalski et al. (9) reported that serum Vit-D levels in COVID-19 patients were significantly lower than healthy individuals; thus, it could be considered as a risk factor for mortality rate among these patients. Similarly, in another study, Lau et al. (10) showed that serum Vit-D levels were significantly reduced in COVID-19 patients admitted to the ICU, which is in line with our findings. In another study, Alipio et al. (11) reviewed the findings of 212 COVID-19 patients and concluded that Vit-D administration significantly improved Vit-D deficiency, and consequently, clinical symptoms of these patients. Panfili et al. (12) reported that Vit-D administration was effective in preventing SARS-COV-2 by regulating the immune system in both children and adults. A recent survey demonstrated that Vit-D plays an important role in preventing the disease and decreasing the mortality rate among COVID-19 patients (13). Marik et al. (14) reported that a decrease in mean serum Vit-D levels was significantly associated with increased mortality rate in patients with SARS-CoV-2, which is consistent with our findings.

We also found that older patients had a tendency for lower mean Vit-D levels. The mean age of patients with Vit-D ≤ 20 ng/mL (60.78 years) was higher compared to those with Vit-D levels ≥ 31 ng/mL (55.13 years). This indicates that a decrease of mean Vit-D levels in older people is a probable reason for higher mortality rate in these patients. Daneshkhah et al. (15) showed that a decrease in serum Vit-D concentration (less than 25 ng/mL) in older patients was significantly associated with increased mortality rate, which is consistent with the findings of our study. Interestingly, we found that serum Vit-D levels in patients undergoing intubation were significantly lower than non-intubated patients. Approximately, half of the intubated patients had Vit-D levels ≤ 20 ng/mL, and only 12% of them had Vit-D levels ≥ 31 ng/mL. However, about 40% of non-intubated patients had Vit-D levels ≥ 31 ng/mL. Approximately 92% of intubated patients died, and about half of them had serum Vit-D levels ≤ 20 ng/mL; this might indi-

cate a strong association between serum Vit-D levels with a need for intubation, and subsequently, mortality rate in these patients. We also found that patients with history of smoking and opiate using and hypertension had a tendency for lower mean Vit-D levels; however, further studies with larger sample size are required to confirm this issue.

According to the results of this study, the decreased Vit-D levels were significantly associated with increased mortality rate among COVID-19 patients. Thus, further clinical trials are recommended to determine the effect of Vit-D administration on clinical outcomes and mortality in these patients. Given that COVID-19 has recently become widespread around the world, many studies are undergoing, and studies on the association between Vit-D and clinical outcomes in patients with COVID-19 are currently limited. However, studies have reported a positive effect and a strong association between Vit-D levels and disease severity (16).

5.1. Conclusions

The results of our study showed that patients with COVID-19 had significantly lower mean serum Vit-D levels. Also, a decreased level of vitamin D, especially $\leq$ 20 ng/mL, was significantly associated with an increased mortality rate in these patients. On the other hand, a decrease in mean Vit-D level was significantly associated with an increased risk of ventilation and higher blood pressure. Older patients had a greater tendency for lower mean Vit-D levels and higher mortality rate, which requires further investigation. Therefore, Vit-D supplementation is recommended for COVID-19 patients, especially those with serum Vit-D levels $\leq$ 20 ng/mL.

Footnotes

Authors' Contribution: Study concept and design: Z.A. and S.J.E.; Analysis and interpretation of data: F.D.; Drafting of the manuscript: A.SH.; Critical revision of the manuscript for important intellectual content: Z.A., F.D., and A.SH.; Statistical analysis: F.D.

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References

1. Peng M. Outbreak of COVID-19: An emerging global pandemic threat. *Biomed Pharmacother*. 2020;**129**:110499. doi: 10.1016/j.biopha.2020.110499. [PubMed: 32768974]. [PubMed Central: PMC7334916].
2. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. *JAMA*. 2020;**323**(18):1775–6. doi: 10.1001/jama.2020.4683. [PubMed: 32203977].
3. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;**395**(10223):497–506. doi: 10.1016/s0140-6736(20)30183-5.
4. Brewster DJ, Chrimes N, Do TB, Fraser K, Groombridge CJ, Higgs A, et al. Consensus statement: Safe Airway Society principles of airway management and tracheal intubation specific to the COVID-19 adult patient group. *Med J Aust*. 2020;**212**(10):472–81. doi: 10.5694/mja2.50598. [PubMed: 32356900]. [PubMed Central: PMC7267410].
5. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;**395**(10223):507–13. doi: 10.1016/s0140-6736(20)30211-7.
6. Velavan TP, Meyer CG. Mild versus severe COVID-19: Laboratory markers. *Int J Infect Dis*. 2020;**95**:304–7. doi: 10.1016/j.ijid.2020.04.061. [PubMed: 32344011]. [PubMed Central: PMC7194601].
7. Li X, Geng M, Peng Y, Meng L, Lu S. Molecular immune pathogenesis and diagnosis of COVID-19. *J Pharm Anal*. 2020;**10**(2):102–8. doi: 10.1016/j.jpha.2020.03.001. [PubMed: 32282863]. [PubMed Central: PMC7104082].
8. Chun RF, Liu PT, Modlin RL, Adams JS, Hewison M. Impact of vitamin D on immune function: lessons learned from genome-wide analysis. *Front Physiol*. 2014;**5**:151. doi: 10.3389/fphys.2014.00151. [PubMed: 24795646]. [PubMed Central: PMC4000998].
9. Biesalski HK. Vitamin D deficiency and co-morbidities in COVID-19 patients – A fatal relationship? *NFS J*. 2020;**20**:10–21. doi: 10.1016/j.nfs.2020.06.001.
10. Lau FH, Majumder R, Torabi R, Saeg F, Hoffman R, Cirillo JD, et al. Vitamin D insufficiency is prevalent in severe COVID-19. *medRxiv*. 2020. doi: 10.1101/2020.04.24.20075838.
11. Alipio M. Vitamin D Supplementation Could Possibly Improve Clinical Outcomes of Patients Infected with Coronavirus-2019 (COVID-2019). *SSRN Electronic J*. 2020. doi: 10.2139/ssrn.3571484.
12. Panfili FM, Roversi M, D'Argenio P, Rossi P, Cappa M, Fintini D. Possible role of vitamin D in Covid-19 infection in pediatric population. *J Endocrinol Invest*. 2021;**44**:1–9. doi: 10.1007/s40618-020-01327-0. [PubMed: 32557271]. [PubMed Central: PMC7299247].
13. Ilie PC, Stefanescu S, Smith L. The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality. *Aging Clin Exp Res*. 2020;**6**:1–4.
14. Marik PE, Kory P, Varon J. Does vitamin D status impact mortality from SARS-CoV-2 infection? *Med Drug Discov*. 2020;**6**:100041. doi: 10.1016/j.medidd.2020.100041. [PubMed: 32352080]. [PubMed Central: PMC7189189].
15. Daneshkhah A, Agrawal V, Eshein A, Subramanian H, Roy HK, Backman V. The Role of Vitamin D in Suppressing Cytokine Storm in COVID-19 Patients and Associated Mortality. *Med Drug Discov*. 2020. doi: 10.1101/2020.04.08.20058578.
16. Razdan K, Singh K, Singh D. Vitamin D Levels and COVID-19 Susceptibility: Is there any Correlation? *Med Drug Discov*. 2020;**7**:100051. doi: 10.1016/j.medidd.2020.100051. [PubMed: 32835212]. [PubMed Central: PMC7266578].