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Association Between Vitamin D Levels and COVID-19 Infection in Children: A Case-Control Study

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What is already known on this topic?

- *It is known that coronavirus disease 2019 (COVID-19) infection is more frequent and more mortal in patients with low vitamin D levels. However, studies examining the relationship between COVID-19 and vitamin D in the pediatric age group are extremely rare.*

What this study adds on this topic?

- *We compared the etiology, clinical, radiology, vitamin D, and other biochemical markers between those who had coronavirus disease 2019 (COVID-19) infection and healthy control group between November 2020 and January 2021. Our study examines the relationship between COVID-19 and vitamin D in the largest pediatric age group to date.*

ABSTRACT

Objective: Coronavirus disease 2019 (COVID-19) infection is seen in all age groups, and its symptoms are very variable. The course of the disease can be asymptomatic or mortal. In pediatric patients, vitamin D is thought to be protective against (COVID-19) with its immunomodulator, antiviral, anti-inflammatory, and epithelial integrity properties. Our aim is to investigate the relationship between (COVID-19) infection and vitamin D level.

Materials and Methods: We included (COVID-19) patients between 1 month and 18 years of age and healthy control groups. We compared epidemiological, clinical, laboratory, and imaging findings in patients.

Results: One hundred forty-nine patients were evaluated in our study. Seventy-three (49%) of them were (COVID-19)-positive patients and 76 (51%) of them were healthy control group. The mean 25(OH)-D vitamin level was 15.80 ng/mL (5-41.56) in (COVID-19) patients and 21.51 ng/mL (5-69.80) in the control group. Vitamin D level was shown to be statistically significantly lower in coronavirus disease 2019 patients ($P < .001$). It was observed that myalgia was more common in patients with low 25(OH)-D levels ($P < .048$).

Conclusion: Our study is one of the rare studies examining the relationship between (COVID-19) and 25(OH)-D vitamins in the pediatric age group. Children with (COVID-19) have a lower 25(OH)-D vitamin level than the control group.

Keywords: COVID-19, 25(OH)-D vitamin, pediatric, myalgia, epidemiology

INTRODUCTION

On October 31, 2019, it was reported by the World Health Organization (WHO) that 27 patients had pneumonia with an infection of unknown cause in Wuhan, Hubei, China. Coronavirus disease 2019 (COVID-19), which started in China, spread to the world in a short time. On March 11, 2020, COVID-19 was recognized as a pandemic by WHO, and the agent was named as severe acute respiratory syndrome coronavirus 2.[1] COVID-19 infection was detected in 634 million people by October 2022, causing 6.5 million deaths.[2]

COVID-19 infection occurs in all age groups, and its symptoms vary widely. It can be asymptomatic or it can be mortal. Acute upper respiratory tract and gastrointestinal system symptoms such as fever, cough, runny nose, refusal to feed, vomiting, and diarrhea are common in the pediatric age group.[3,4]

Angiotensin-converting enzyme II (ACE2) is the receptor for COVID-19. ACE2 is less common in children than adults. In patients in the pediatric age group, COVID-19 infection usually progresses with asymptomatic or mild-to-moderate symptoms. This is related to the low ACE2 level, as well as the stronger respiratory epithelial integrity in children compared

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to adult age, higher vitamin D levels, and different immune response mechanisms according to age.[5] In COVID-19 infection, mortality increases as a result of hyperinflammation.[6] Vitamin D is known to have a protective effect against acute respiratory infections, but its protective effect against COVID-19 is not clear.[7]

Vitamin D has immunomodulatory, antiviral, anti-inflammatory, and epithelial integrity protective properties. It shows its protective effect against viruses that infect the respiratory system by creating both an innate and adaptive immune response.[8] Vitamin D increases the synthesis of cathelicidin, an antimicrobial peptide, reduces the synthesis of dipeptidyl peptidase-4 receptor (DPP-4/CD26), and plays a protective role with its antibacterial, antiviral, and antioxidant effects.[9] Cathelicidin is protective against bacteria, viruses, fungi, and many pathogens. Its synthesis increases with vitamin D.[10] The spike protein of COVID-19 attaches to the respiratory epithelium by binding to the DPP-4/CD26 receptor.[11]

Vitamin D deficiency is an important public health problem seen in many parts of the world, just like the COVID-19 pandemic. It is common in children. Vitamin D level is thought to be <20 ng/mL in approximately one-third of children around the world, and deficiency is more common in adolescence[12,13] Vitamin D deficiency has been reported to be a risk factor for COVID-19 infection. It has been suggested that vitamin D supplementation will reduce infections that will cause hospitalization, and therefore vitamin D supplements should be taken to protect against COVID-19.[14] Prophylactic vitamin D supplementation is thought to be an important adjuvant treatment option for both the COVID-19 pandemic and vitamin D deficiency.[15] In our study, the relationship between COVID-19 infection and vitamin D was investigated.

MATERIALS AND METHODS

The data of COVID-19 patients who applied to Gülhane Faculty of Medicine between November 2020 and January 2021 and healthy control group patients of the same age and sex were retrospectively analyzed.

Study Population

Seventy-three COVID-19 patients aged between 1 month and 18 years who applied to our hospital were included in the study. In the same period, 76 patients who applied to the pediatric outpatient clinic and had no symptoms suggestive of COVID-19 infection in her and her family were included in the study as a control group. The children included in the control group did not have a history of any chronic diseases, comorbidities, or regular medication use.

Coronavirus Disease 2019 and Vitamin D Test Results

In patients diagnosed with COVID-19, the severity of the disease, according to clinical and laboratory findings, was classified as asymptomatic, mild, moderate, severe, and critical.[16] Seventy-three patients with positive COVID-19 reverse-transcriptase polymerase chain reaction (RT-PCR) results were classified as asymptomatic and mild/moderate according to these criteria. Complete blood count (CBC), plasma parathyroid hormone levels, and calcium, phosphorus, alkaline phosphatase, and 25(OH)-D levels were measured in the patients and children in the control group. Levels of serum 25(OH)-D vitamin and other biochemical parameters were detected with an DXI800 instrument (Beckman Coulter, Brea, Calif, USA) via an immunoinhibition assay. COVID-2019 in nasopharyngeal samples (Bioksen ArGe Teknik Co., Ltd., İstanbul, Turkey; Biospeedy®), quantitative RT-PCR detection kit was used. Age, sex, biochemical characteristics and imaging findings of COVID-19 patients and children in the control group were compared.

The 25(OH)-D level was grouped according to the American Academy of Pediatrics.[17] Those with a 25(OH)-D level <5 ng/mL were classified as severe deficiency, those between 5 and 15 ng/mL as deficiency, those between 15 and 20 ng/mL as insufficiency, and those between 20 and 100 ng/mL as sufficiency. Patients diagnosed with COVID-19 were divided into 2 groups: 25(OH)-D level below <20 ng/mL and normal ≥20 ng/mL. Clinical and laboratory findings were compared between the 2 groups with low and normal 25(OH)-D. Coronavirus disease 2019 patients were divided into 2 groups according to their 25(OH)-D vitamin levels. Age, sex, clinical, and laboratory findings were compared between the 2 groups.

The study was conducted based on the rules of Declaration of Helsinki and approved by the Institutional Ethics Committee of the University of Health Sciences.

Statistical Analysis

Data analyses were examined by using Statistical Package for Social Sciences (SPSS) version 20.0 for Windows (IBM Corp.; Armonk, NY, USA). Scale datas were described as mean ± SD for normal distributions and median (minimum–maximum value) for skewed distribution and categorical variables expressed as either frequency (percentage). Statistical analysis differences in normally distributed variables between 2 independent groups were compared by the Student's *t*-test, Mann–Whitney *U* test was applied for comparisons of the non-normally distributed data, and categorical variables were compared using the Pearson's chi-square test. Spearman's correlation analysis was used to evaluate the degrees of relation between variables. Correlation analysis was shown to vary from –1 to +1. Regarding the strength of the correlation coefficient, the following definitions were made: 0.01-0.25, very weak relationship; 0.26-0.49, weak relationship; 0.50-0.69, intermediate relationship; 0.70-0.89, high relationship; 0.90-1.0, very high correlation.[18] *P*-values <.05 were considered statistically significant. Statistically significant *P*-values are indicated in bold.

RESULTS

Demographic and Laboratory Data

Of the 149 patients in the study, 73 (49%) were patients with COVID-19, and 76 (51%) comprised the healthy control group. The mean age of COVID-19 patients was 87.26 months ± 53.28 (minimum: 6 months, maximum: 18 years). The mean age of the control group was 97.62 ± 64.99 (minimum: 6 months, maximum: 18 years). Thirty-seven (50.7%) of the COVID-19 patients and 38 (50%) of the control group were male. There was no significant difference in age and sex distribution between the groups ($P = .933$). The mean 25(OH)-D vitamin level was 15.80 ng/mL (5-41.56) in COVID-19 patients and 21.51 ng/mL (5-69.80)

in the control group. A statistically significant difference was found in the 25(OH)-D vitamin level between COVID-19 patients and the control group ($P = .002$). Calcium, phosphorus, alkaline phosphatase, and parathyroid hormone levels were similar in both groups (Table 1).

25(OH)-D Levels and Coronavirus Disease 2019

Severe deficiency in 25(OH)-D vitamin was detected in 6 (8.2%) of the patients, deficiency in 26 (35.6%) patients, insufficiency in 17 (23.3%) patients, and sufficiency in 24 (32.9%) patients. In the control group, 5 (6.6%) patients had severe deficiency, 21 (27.6%) patients had deficiency, 9 (11.8%) patients had insufficiency, and 41 (53.9%) patients had sufficiency. COVID-19 patients and control group were compared according to 25(OH)-D vitamin levels. The results of the control group were higher than the patient group and were statistically significant($P = .015$) (Table 2).

Myalgia finding was more common in the group with 25(OH)-D insufficiency, and it was statistically significant ($P = .048$). There was no significant difference in other laboratory and clinical findings between the 2 groups. The distribution of demographic, clinical, and laboratory data is shown in Table 3.

Coronavirus disease 2019 patients were grouped according to the severity of clinical findings, and 25(OH)-D vitamin levels were compared (Table 4). There was no significant difference between the 2 groups ($P = .418$). The 25(OH)-D vitamin level was found to be correlated with calcium, phosphorus, alkaline phosphatase, and parathyroid hormone, but no significant correlation was found between myalgia and 25(OH)-D vitamin (Table 5).

DISCUSSION

As far as we know, there was very little research on the relationship between 25(OH)-D vitamin and COVID-19 infection in the pediatric age group in the English literature. In this study, we aimed to investigate the relationship between 25(OH)-D vitamins in the pediatric age group with COVID-19 infection in a larger patient population.

In some previous clinical studies, 25(OH)-D vitamin has been shown to protect children against respiratory tract infections. In Esposito and Lelii's[19] study, it was reported that low 25(OH)-D vitamin in the pediatric age group increased the frequency of acute respiratory tract infections. Martineau et al[20] reported that 25(OH)-D vitamin is generally protective against acute respiratory tract infection. In the study of Li et al[21] with 1582 children, the group with community-acquired pneumonia was compared with the control group, and the low 25(OH)-D vitamin level was found to be lower in the group with community-acquired pneumonia. In addition, in a case–control study conducted by Velarde López et al.[22] 25(OH)-D vitamin deficiency was found to be significantly low in children with lower respiratory tract infections.

Clinical and laboratory data were investigated to assess the relationship between low 25(OH)-D vitamin levels and respiratory tract infection. A negative association was shown between hospitalizations with pneumonia, increased risk of sepsis, acute respiratory distress syndrome, and increased proinflammatory cytokines such as CRP and IL-6 in patients with low 25(OH)-D vitamin levels.[23-27] Likewise, the 25(OH)-D vitamin association with COVID-19 infection was evaluated in those. Studies have shown that low 25(OH)-D vitamin levels both increase the frequency of COVID-19 infections and increase the mortality. In the study conducted by Kaufman et al.[28] it was shown that those with low 25(OH)-D vitamin levels were more frequently infected with COVID-19. In a study conducted by Ilie et al.[29] each country's COVID-19 cases and the average 25(OH)-D vitamin values were compared, and a negative correlation between the number of deaths due to COVID-19 infection and 25(OH)-D vitamin was shown. In the study conducted by Carpagnano et al.[30] mortality was shown to be 50% higher in patients hospitalized with COVID-19 infection with acute respiratory failure in patients with 25(OH)-D levels <10 ng/mL. On the other hand, in the study by Tiosano et al.[31] patients with low 25(OH)-D vitamin levels do not exhibit increased rates of infections or inflammatory diseases, and vitamin D deficiency is just associated with asthmatic exacerbations. There are many articles in the literature that report that vitamin D deficiency increases infections or does not cause infections. However, in these studies, it is difficult to evaluate the relationship between mortality and 25(OH)-D vitamin levels due to comorbidity factors in most of the patients with low 25(OH)-D vitamin levels.

Table 1. Demographic and Laboratory Data of the COVID-19 Patient and Control Groups

Parameters	COVID-19 Patients ($n = 73$)	Healthy Controls ($n = 76$)	P
Age (months)	87.26 ± 53.28	97.62 ± 64.99	.288*
Sex			
Male	37 (50.7%)	38 (50.0%)	.933β
Female	36 (49.3%)	38 (50.0%)	
Serum calcium (mg/dL), reference: 7.6-10.4	9.77 ± 0.42	9.82 ± 0.45	.459*
Serum phosphorus (mg/dL), reference: 4-7	4.71 ± 0.65	4.62 ± 0.76	.438*
Alkaline phosphatase (U/L), reference: 25–150	223.21 ± 81.63	224.59 ± 102.63	.929*
Vitamin D levels (ng/mL)	15.80 (5-41.6)	21.51 (5-69.8)	**.002**α
Parathyroid hormone levels (pg/mL), reference: 12–88	43.87 ± 24.94	39.02 ± 17.59	.171*

COVID-19, coronavirus disease 2019.
*Student's *t*-test.
αMann–Whitney *U* test.
βPearson's chi-square test.

Table 2. 25(OH)-D Levels in COVID-19 Patient and Control Groups

25(OH)-D Vitamin Levels	COVID-19 Patients (*n* = 73) (%)	Healthy Controls (*n* = 76) (%)	*P*
Severe deficiency	6 (8.2)	5 (6.6)	.374[β]
Deficiency	26 (35.6)	21 (27.6)	.297[β]
Insufficiency	17 (23.3)	9 (11.8)	.685[β]
Sufficiency	24 (32.9)	41 (53.9)	**.015**[β]

COVID-19, coronavirus disease 2019.
[β]Pearson's chi-square test.

In this study, clinical and biochemical markers associated with 25(OH)-D vitamin deficiency were evaluated in COVID-19-positive patients admitted to our hospital. There was a low 25(OH)-D vitamin level in 84 (56.4%) of the cases. In our study of the cases, 11 (7.4%) patients had severe deficiency, 47 (31.5%) patients had deficiency, and 26 (17.4%) patients had insufficiency. No hospitalization or mortality was reported in our cases.

The etiology, symptoms, and laboratory findings were compared between the groups with low and normal 25(OH)-D vitamin levels. Myalgia was found to be significant in the group with low 25(OH)-D vitamin ($P = .048$). However, there was no significant correlation between low 25(OH)-D vitamin and myalgia ($P = .198$). The frequency of myalgia in COVID-19 infection was 35.8% in Li et al's[32] study and 23.75% in Wang et al's[33] study. In our study, it was 16.4%. In a study conducted by Lechien et al[34] with 1420 COVID-19 patients, myalgia was seen at a rate of 62.5%, and it was shown that the possibility of myalgia was higher in elderly patients. Myalgia is less common in the pediatric age group than in adults. Pennisi et al[35] reported that statin-related muscle symptoms, including myalgia, myopathy, and rhabdomyolysis, were more common in people with low 25(OH)-D vitamin levels. However, there are also articles reporting that myalgia is not associated with low 25(OH)-D vitamin levels.[36,37] We think that more research should be done to understand the relationship between 25(OH)-D vitamins and myalgia. In studies conducted in the adult age group, there is a relationship between COVID-19 infection and low 25(OH)-D vitamin levels. In the study conducted by Meltzer et al.[38] COVID-19 infection was found to be high in the group with low vitamin D levels. Similarly, in the study conducted by Merzon et al.[39] it was stated that low 25(OH)-D vitamin levels increased COVID-19 infection. Until now, the study including COVID-19 infection and its relationship with vitamin D level in pediatric population was only conducted by Yılmaz and Şen[40] with 85 patients. In this study, those who had COVID-19 infection were compared with the healthy group, and those who had COVID-19 infection were found to be low in 25(OH)-D vitamins. In our study, similar results were obtained with other studies. We think that low levels of 25(OH)-D vitamin increase the frequency of COVID-19 infection. We think that randomized controlled studies with

Table 3. Demographic, Clinical, and Laboratory Data by 25(OH)-D Levels

Parameters	25(OH)-D ≤20 ng/mL (*n* = 49)	25(OH)-D >20 ng/mL (*n* = 24)	*P*
Age (months)	100 (6-205)	58.5 (6-195)	.194[α]
Sex			
Male	25 (51.0%)	12 (50.0%)	.935[β]
Female	24 (49.0%)	12 (50.0%)	
Fever >38°C	36 (73.5%)	15 (62.5%)	.337[β]
Dry cough	12 (24.5%)	8 (33.3%)	.426[β]
Loss of taste	2 (4.1%)	0 (0%)	.316[β]
Myalgia	11 (22.4%)	1 (4.2%)	**.048**[β]
Diarrhea	1 (2%)	0 (0%)	.481[β]
Pharyngeal pain	10 (20.4%)	2 (8.3%)	.191[β]
Rhinorrhea	0 (0%)	3 (12.5%)	.083[β]
Abdominal pain	0 (0%)	1 (4.2%)	.150[β]
Nausea/vomiting	1 (2%)	0 (0%)	.481[β]
Vitamin D (ng/mL)	12.03 (4.51-19.70)	28.34 (21.70-41.56)	**<.001**[α]
PTH (pg/mL)	45.64 (14.10-171.30)	40.26 (17.00-92.40)	.390[α]
Serum calcium (mg/dL)	9.70 (8.80-10.68)	9.90 (9.00-10.70)	**.040**[α]
Serum phosphorus (mg/dL)	4.66 ± 0.67	4.82 ± 0.62	.337[*]
Alkaline phosphatase (U/L)	222 (56-425)	220.5 (136-406)	.239[α]
CRP (mg/L), reference: 0-5	4.32 (0.17-37.60)	5.50 (0.10-33.97)	.692[α]
WBC (10^3/μL)	7.57 ± 1.55	7.14 ± 1.88	.311[*]
Oxygen saturation %	98 (92-99)	98 (92-100)	.339[α]
Respiratory rate	24.56 ± 9.06	22.43 ± 6.45	.870[*]
PA chest x-ray findings	24 (49%)	11 (45.8%)	.638[β]

CRP, C-reactive protein; PA, posteroanterior; PTH, parathyroid hormone; WBC, white blood cell.
*Student's *t*-test.
[α]Mann–Whitney *U* test.
[β]Pearson's chi-square test.

Table 4. 25(OH)-D Vitamin Levels in Patients According to the Severity of COVID-19 Clinical Findings

	Asymptomatic	Mild	Moderate	Severe	*P*
Normal level of vitamin D, *n* (%)	10 (20.4)	36 (73.5)	3 (6.1)	0 (0)	.418[β]
Low level of vitamin D, *n* (%)	8 (33.3)	14 (58.3)	2 (8.3)	0 (0)	

COVID-19, coronavirus disease 2019.
[β]Pearson's chi-square test.

Table 5. Correlation Analysis of 25(OH)-D Vitamin Levels and Parameters

	r	*P*
Serum calcium (mg/dL)	0.307[β]	**<.001**
Phosphorus (mg/dL)	0.255[β]	**.001**
Alkaline phosphatase (U/L)	0.232[β]	**.004**
Parathyroid hormone (pg/mL)	−0.290[β]	**.003**
Myalgia	0.106[β]	.198

[β]Spearman's correlation analysis.

25(OH)-D vitamin supplements are needed for the prevention and treatment of COVID-19 infection. But this research is a correlation research of previously published vitamin D studies, and it is not possible to establish a cause–effect relationship with just these data. First of all, we know that vitamin D is a negative acute-phase reactant, so in cases with severe inflammation such as COVID-19, the total 25(OH)-D vitamin level is expected to drop.[41]

There are some limitations to our study. First, it is possible that the data are incomplete and incorrect due to our retrospective study design. Second, some clinical symptoms such as abdominal pain, pharyngeal pain, loss of taste, and myalgia cannot be evaluated in all age groups. Third, although the patients we included in the control group were said to have no COVID-19 infection in themselves and their immediate surroundings, we could not confirm this with RT-PCR in all of our patients in the control group. Fourth, we do not have data for serious and critically ill patients, since our patient group can reach COVID-19 patients with asymptomatic, mild, and moderate clinical course. The effect of COVID-19 and 25(OH)-D vitamin relationship on hospitalization and mortality has not been clearly evaluated. In addition, the number of patients in our study may be insufficient, but despite all these limitations, it may guide future studies to evaluate the association between Covid-19 and 25(OH)-D vitamin level.

Our study is one of the rare studies examining the relationship between COVID-19 and 25(OH)-D vitamins in the pediatric age group. Children with COVID-19 have a lower 25(OH)-D vitamin level compared to the control group. Whether 25(OH)-D vitamin has a protective effect against COVID-19 infection needs to be investigated further.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of University of Health Sciences University (Approval No: 2020-493).

Informed Consent: Informed consent was obtained from the patient's family, who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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REFERENCES

1. Kakodkar P, Kaka N, Baig MN. A comprehensive literature review on the clinical presentation, and management of the pandemic coronavirus disease 2019 (COVID-19). *Cureus*. 2020;12(4):e7560. [CrossRef]
2. Worldometer; 2022. Available at: https://www.worldometers.info/coronavirus. Accessed October 26, 2022.
3. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. *Pediatrics*. 2020;145(6):e20200702. [CrossRef]
4. Parri N, Lenge M, Cantoni B, et al. COVID-19 in 17 Italian pediatric emergency departments. *Pediatrics*. 2020;146(6):e20201235. [CrossRef]
5. Zimmermann P, Curtis N. Why is COVID-19 less severe in children? A review of the proposed mechanisms underlying the age-related difference in severity of SARS-CoV-2 infections. *Arch Dis Child*. 2020. [CrossRef]
6. Sinha P, Calfee CS, Cherian S, et al. Prevalence of phenotypes of acute respiratory distress syndrome in critically ill patients with COVID-19: a prospective observational study. *Lancet Respir Med*. 2020;8(12):1209-1218. [CrossRef]
7. Jolliffe DA, Camargo CA Jr, Sluyter JD, et al. Vitamin D supplementation to prevent acute respiratory infections: a systematic review and meta-analysis of aggregate data from randomised controlled trials. *Lancet Diabetes Endocrinol*. 2021;9(5):276-292. [CrossRef]
8. Greiller CL, Martineau AR. Modulation of the immune response to respiratory viruses by vitamin D. *Nutrients*. 2015;7(6):4240-4270. [CrossRef]
9. Jain SK, Parsanathan R. Can vitamin D and L-cysteine co-supplementation reduce 25(OH)-Vitamin D Deficiency and the Mortality Associated with COVID-19 in African Americans? *J Am Coll Nutr*. 2020;39(8):694-699. [CrossRef]
10. Gombart AF, Borregaard N, Koeffler HP. Human cathelicidin antimicrobial peptide (CAMP) gene is a direct target of the vitamin D receptor and is strongly up-regulated in myeloid cells by 1,25-dihydroxyvitamin D3. *FASEB J*. 2005;19(9):1067-1077. [CrossRef]
11. Vankadari N, Wilce JA. Emerging WuHan (COVID-19) coronavirus: glycan shield and structure prediction of spike glycoprotein and its interaction with human CD26. *Emerg Microbes Infect*. 2020;9(1):601-604. [CrossRef]
12. Holick MF. The vitamin D deficiency pandemic: approaches for diagnosis, treatment and prevention. *Rev Endocr Metab Disord*. 2017;18(2):153-165. [CrossRef]
13. Gül İ, Gür E, Erener Ercan T, Can G. The effect of vitamin D prophylaxis on 25-OH vitamin D levels in children. *Turk Arch Pediatr*. 2021;56(6):618-623. [CrossRef]

14. Grant WB, Lahore H, McDonnell SL, et al. Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. *Nutrients*. 2020;12(4):988. [CrossRef]
15. Kara M, Ekiz T, Ricci V, Kara Ö, Chang KV, Özçakar L. 'Scientific Strabismus' or two related pandemics: coronavirus disease and vitamin D deficiency. *Br J Nutr*. 2020;124(7):736-741. [CrossRef]
16. Shen K, Yang Y, Wang T, et al. Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement. *World J Pediatr*. 2020;16(3):223-231. [CrossRef]
17. Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M, Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. *Pediatrics*. 2008;122(2):398-417. [CrossRef]
18. Köse K. Korelasyon ve Regresyon Analizi. Available at: http://file.toraks.org.tr/TORAKSFD23NJKL4NJ4H3BG3JH/mse-ppt-pdf/Kenan_KOSE3.pdf. Erişim Tarihi: 31.10.2022.
19. Esposito S, Lelii M. Vitamin D and respiratory tract infections in childhood. *BMC Infect Dis*. 2015;15:487. [CrossRef]
20. Martineau AR, Jolliffe DA, Greenberg L, et al. Vitamin D supplementation to prevent acute respiratory infections: individual participant data meta-analysis. *Health Technol Assess*. 2019;23(2):1-44. [CrossRef]
21. Li PL, Tian YJ, Wang YH, et al. The prevalence of vitamin D deficiency among schoolchildren: a cohort study from Xinxiang, China. *J Pediatr Endocrinol Metab*. 2015;28(5-6):629-633. [CrossRef]
22. Velarde López AA, Gerber JS, Leonard MB, Xie D, Schinnar R, Strom BL. Children with lower respiratory tract infections and serum 25-hydroxyvitamin D3 levels: a case-control study. *Pediatr Pulmonol*. 2016;51(10):1080-1087. [CrossRef]
23. Zhou YF, Luo BA, Qin LL. The association between vitamin D deficiency and community-acquired pneumonia: a meta-analysis of observational studies. *Med (Baltim)*. 2019;98(38):e17252. [CrossRef]
24. Lu D, Zhang J, Ma C, et al. Link between community-acquired pneumonia and vitamin D levels in older patients. [Zusammenhang zwischen ambulant erworbener Pneumonie und vitamin-D-Spiegel bei älteren Patienten]. *Z Gerontol Geriatr*. 2018;51(4):435-439. [CrossRef]
25. Dalvi SM, Ramraje NN, Patil VW, Hegde R, Yeram N. Study of IL-6 and vitamin D3 in patients of pulmonary tuberculosis. *Indian J Tuberc*. 2019;66(3):337-345. [CrossRef]
26. Manion M, Hullsiek KH, Wilson EMP, et al. Vitamin D deficiency is associated with IL-6 levels and monocyte activation in HIV-infected persons. *PLoS One*. 2017;12(5):e0175517. [CrossRef]
27. Poudel-Tandukar K, Poudel KC, Jimba M, Kobayashi J, Johnson CA, Palmer PH. Serum 25-hydroxyvitamin d levels and C-reactive protein in persons with human immunodeficiency virus infection. *AIDS Res Hum Retrovir*. 2013;29(3):528-534. [CrossRef]
28. Kaufman HW, Niles JK, Kroll MH, Bi C, Holick MF. SARS-CoV-2 positivity rates associated with circulating 25-hydroxyvitamin D levels. *PLoS One*. 2020;15(9):e0239252. [CrossRef]
29. 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;32(7):1195-1198. [CrossRef]
30. Carpagnano GE, Di Lecce V, Quaranta VN, et al. Vitamin D deficiency as a predictor of poor prognosis in patients with acute respiratory failure due to COVID-19. *J Endocrinol Invest*. 2021;44(4):765-771. [CrossRef]
31. Tiosano D, Abrams SA, Weisman Y. Lessons learned from hereditary 1,25-dihydroxyvitamin D-resistant rickets patients on vitamin D functions. *J Nutr*. 2021;151(3):473-481. [CrossRef]
32. Li LQ, Huang T, Wang YQ, et al. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. *J Med Virol*. 2020;92(6):577-583. [CrossRef]
33. Wang X, Liu W, Zhao J, et al. Clinical characteristics of 80 hospitalized frontline medical workers infected with COVID-19 in Wuhan, China. *J Hosp Infect*. 2020;105(3):399-403. [CrossRef]
34. Lechien JR, Chiesa-Estomba CM, Place S, et al. Clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. *J Intern Med*. 2020;288(3):335-344. [CrossRef]
35. Pennisi M, Di Bartolo G, Malaguarnera G, Bella R, Lanza G, Malaguarnera M. Vitamin D serum levels in patients with statin-induced musculoskeletal pain. *Dis Markers*. 2019;2019:3549402. [CrossRef]
36. Kurnik D, Hochman I, Vesterman-Landes J, et al. Muscle pain and serum creatine kinase are not associated with low serum 25(OH) vitamin D levels in patients receiving statins. *Clin Endocrinol (Oxf)*. 2012;77(1):36-41. [CrossRef]
37. Khayznikov M, Hemachrandra K, Pandit R, Kumar A, Wang P, Glueck CJ. Statin intolerance because of myalgia, myositis, myopathy, or myonecrosis can in most cases be safely resolved by vitamin D supplementation. *N Am J Med Sci*. 2015;7(3):86-93. [CrossRef]
38. Meltzer DO, Best TJ, Zhang H, Vokes T, Arora V, Solway J. Association of vitamin D status and other clinical characteristics with COVID-19 test results. *JAMA Netw Open*. 2020;3(9):e2019722. [CrossRef]
39. Merzon E, Tworowski D, Gorohovski A, et al. Low plasma 25(OH) vitamin D level is associated with increased risk of COVID-19 infection: an Israeli population-based study. *FEBS Journal*. 2020;287(17):3693-3702. [CrossRef]
40. Yılmaz K, Şen V. Is vitamin D deficiency a risk factor for COVID-19 in children? *Pediatr Pulmonol*. 2020;55(12):3595-3601. [CrossRef]
41. Scott MG, Gronowski AM, Reid IR, Holick MF, Thadhani R, Phinney K. Vitamin D: the more we know, the less we know. *Clin Chem*. 2015;61(3):462-465. [CrossRef]