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Is Vitamin D Level Associated with COVID-19 Infection?

D Vitamini Düzeyi COVID-19 Enfeksiyonu ile İlişkili midir?

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ABSTRACT

Aim: The effects of vitamin D, which has an antiviral and immune modulator in preventing the rapidly spreading COVID-19, which has been resulting in increasing number of deaths worldwide, is discussed. The aim of the present study was to determine whether 25-hydroxyvitamin D level is associated with COVID-19 risk.

Material and Methods: Ninety-six individuals (48 COVID-19 positive and 48 COVID-19 negative) were included in this cross-sectional study. Data were collected with a questionnaire form evaluating the individual and clinical characteristics of the study participants, their eating habits affecting vitamin D status and their sun exposures. 25-hydroxyvitamin D measurements and polymerase chain reaction test results were evaluated. Independent samples t test was used to compare the age, BFUI and vitamin D levels of the patient and control groups while Chi-square and Fisher's exact test were used for the ratio comparisons of categorical variables.

Results: It was found that 86.5% of the study participants had vitamin D deficiency. There was no significant difference between 25-hydroxyvitamin D levels of individuals who tested positive for COVID-19 and those who did not (11.50 ± 6.66 ng/ml and 12.95 ± 6.11 ng/ml, respectively, p = 0.271). Vitamin D status (severely deficient, deficient, insufficient) was similar in those with and without COVID-19 infection (p = 0.586).

Conclusion: Our findings do not support the potential link between COVID-19 infection risk and 25-hydroxyvitamin D level or vitamin D status.

Keywords: 25(OH)D, COVID-19, Infection, Sunlight, Vitamin D status

ÖZ

Amaç: Antiviral ve immün modülatör etkisi olan D vitamininin, dünya çapındaki artan ölüm sayısıyla birlikte hızla yayılan COVID-19'u önlemedeki etkisi tartışılmaktadır. Çalışmanın amacı 25-hidroksivitamin D düzeyinin COVID-19 riski ile ilişkili olup olmadığının belirlenmesidir.

Gereç ve Yöntemler: Kesitsel tipteki çalışmaya 96 birey (48 COVID-19 pozitif ve 48 COVID-19 negatif) dahil edildi. Çalışmaya katılanların bireysel ve klinik özelliklerini, D vitamini durumlarını etkileyen beslenme alışkanlıklarını ve güneş maruziyetlerini değerlendiren anket formu ile veriler toplandı. 25-hidroksivitamin D düzeyi ölçümleri ve Polimeraz Zincir Reaksiyonu test sonuçları değerlendirildi.

Bulgular: Çalışmaya katılanların %86,5'inde D vitamini eksikliği olduğu bulundu. Çalışmada COVID-19 testi pozitif olan ve olmayan bireylerin 25-hidroksivitamin D düzeyi ortalamaları arasında istatistiksel olarak anlamlı fark bulunmadı (sırasıyla 11,50 ± 6,66 ng/ml, 12,95 ± 6,11 ng/ ml, p = 0,271). D vitamini durumu (ciddi eksiklik, eksiklik, yetersizlik) COVID -19 enfeksiyonu olan ve olmayanlar arasında benzer bulundu (p = 0,586). Hasta ve kontrol gruplarının yaşı, BFUI ve D vitamini düzeylerinin karşılanmasında iki ortalama arasındaki farkın önemlilik testi; kategorik değişkenlerin oran karşılaştırmaları için Ki-kare ve Fisher'in kesin testi kullanıldı.

Sonuç: Bulgularımız 25- hidroksivitamin D düzeyi ve D vitamini durumu ile COVID-19 enfeksiyonu riski arasında potansiyel bağlantıyı desteklememektedir.

Anahtar Sözcükler: 25(OH) D, COVID-19, D vitamini durumu, Enfeksiyon, Güneş ışığı

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome (SARS-CoV2) and threatens the health of the world's population along with strong social and economic effects. It has become a pandemic despite the ongoing efforts by governments to slow down the infection and death rates (1). As of November 2021, more than 249 million cases and more than 5 million deaths were reported worldwide (2). With COVID-19 spreading worldwide, researchers indicated that region, climate, exposure to the sunlight and vitamin D could be linked with viral pathogenicity and death (3). Vitamin D is produced by previtamin D3 synthesis in the skin which is activated by sunlight, especially by ultraviolet B rays (UVB), and its production depends on various factors such as latitude, season, gender, age, etc. (4).

Low levels of 25-hydroxyvitamin D (25(OH)D) were reported to be linked with cancer, cardiovascular, autoimmune and infectious diseases (4, 5). Some recent studies have suggested that vitamin D deficiency may weaken respiratory immune function and increase the severity and risk of death in COVID-19 (6, 7). A study dealing with the association of vitamin D levels with COVID-19-related morbidity and mortality in European countries reported a negative association between COVID-19 frequency and vitamin D levels (8). However, a large sample study using data from 348,598 individuals in UK Biobank could not found an association between 25(OH)D levels and COVID-19 infection risk when ethnic factors were evaluated (9).

The present study aimed to determine whether blood 25(OH)D levels are associated with COVID-19 risk.

MATERIAL and METHODS

This cross-sectional study was carried out between July 1 and October 1, 2020 at Tokat State Hospital, which is a pandemic hospital. The sample of the study consisted of all PCR-positive COVID-19 patients followed up by the researchers during the planned study period. Of the 53 individuals who were 18 years of age and older, who tested positive for COVID-19 based on PCR test and treated at the hospital, two patients who had used vitamin D, one patient who had hyperparathyroidism history and two patients who did not want to take part in the study were excluded, and a total of 48 patients were included. Of the 81 individuals who tested negative for COVID-19 PCR test results, five individuals who used vitamin D and two individuals with malignancy were excluded. Among them, forty-eight individuals were included in the study using simple randomized sampling considering the 48 PCR-positive patients. The patients with malignancy, severe liver and kidney failure, hyperparathyroidism and malabsorption disorders, psychiatric illnesses, skin diseases that could prevent sun exposure, history of gastric bowel surgery, the patients who had used medicines that could have interfered with vitamin D, phosphorus, calcium, parathyroid hormone and albumin levels, and the patients who refused to participate in the study were not included.

Data Collection Tools

Survey form: It was composed of 20 questions evaluating age, gender, educational status, diagnosed disease information, medications, vitamin and calcium supplementation, alcohol consumption, smoking status, hospital admissions and complaints, eating habits affecting vitamin D levels (last three months) and sun exposure.

Benefiting from Ultraviolet Index (BFUI): Benefiting from ultraviolet index used in geriatrics science clinics of Ankara University Faculty of Medicine was used (10) to determine the efficiency of sunlight exposure. Calculation was made using the following formula:

BFUI = Point of exposure to sun / The level of sunlight prevention capacity of the outfit

25 (OH)D

Serum 25(OH)D Level was measured using an autoanalyzer (Roche Cobas e601, Roche Diagnostics, Mannheim, Germany) based on electrochemiluminescence method. 25(OH)D level classification was as follows: < 10 ng/ml severely deficient, < 20 ng/ml deficient, 20 - 30 ng/ml insufficient and > 30 ng/ml sufficient (4, 11).

Data Collection Method

Blood samples taken at the time of hospitalization of individuals who tested positive for COVID-19 PCR and were treated in hospital were used, and these patients were asked to fill the pre-discharge questionnaire themselves.

The study included the individuals who tested positive and individuals who presented to Physical Medicine and Rehabilitation clinic of Pandemic hospital about the time period and tested negative based on COVID-19 PCR test. Individuals who applied to the outpatient clinic were asked to fill and return the questionnaire form themselves at the end of the examination.

Study Ethics

The present study was approved by the Local Ethics Committee (20-KAEK-185). After obtaining permission from the Pandemic hospital, oral and written consent was obtained from the participants before starting the research.

Evaluation of the Data

Statistical analyses of the data obtained in the research were carried out using IBM SPSS software (SPSS Inc., Chicago, IL, USA, ver. 22.0). Descriptive statistics were reported as mean ± standard deviation for continuous data, and as frequency distributions and percentages (%) for categorical data. The normality of the distribution was examined by the Shapiro-Wilk test. For continuous variables, independent samples t test was employed to compare the means of two independent samples. Chi-square and Fisher's exact test were used for ratio comparisons of categorical variables between research groups. A statistical significance level of $p < 0.05$ was used.

RESULTS

Of all participants, 55.2% were women, 44.8% were primary school graduates, and 45.8% did not have any chronic diseases diagnosed. It was found that 74% of individuals consumed milk, 29.2% consumed meat and 62.5% consumed eggs every day. Vitamin D deficiency was observed in 86.5% of the study participants. The mean age was 57.11 ± 13.41 years, and mean BFUI score was 0.70 ± 0.47.

Demographic and clinical characteristics of the individuals participating in the study are presented in Table 1. The individuals who tested positive and those who tested negative for COVID-19 were not different in terms of age, gender distribution, educational status, diagnosed diseases, milk, meat and egg consumption habits which affect 25(OH)D level, vitamin D status and BFUI score ($p > 0.05$). None of the participants consumed fish oil, salmon, mackerel and cod which affect 25(OH)D level and none of them were smokers or alcohol users.

The mean 25(OH)D level was 11.50 ± 6.66 ng/ml in the group of patients who tested positive for COVID-19 and 12.95 ± 6.11 ng/ ml in the group of individuals who tested negative, and the difference was not significant ($p = 0.271$) (Figure 1).

DISCUSSION

Vitamin D deficiency is a common but preventable public health problem across the world (12). Vitamin D was reported to reduce viral replication rates, to reduce pro-inflammatory cytokine concentrations that damage the lung membrane, and to be a potential protective factor against COVID-19 infection (6). In the present study conducted

Table 1. Demographic and clinical characteristics of the participants.

Feature		COVID-19 positive n (%)	COVID-19 negative n (%)	p
Gender	Female	25 (52.1)	28 (58.3)	0.538
	Male	23 (47.9)	20 (41.7)	
Education status	Illiterate	16 (33.3)	14 (29.2)	0.126
	Primary school and equivalent	17 (35.4)	26 (54.2)	
	High school and equivalent	15 (31.3)	8 (16.7)	
Diagnosed disease	No	19 (39,6)	25 (52.1)	0.412[a]
	Diabetes mellitus	11 (22.9)	7 (14.6)	
	Hypertension	14 (29.2)	9 (18.8)	
	Rheumatoid arthritis	1 (2.1)	3 (6.3)	
	Coronary artery disease	3 (6.3)	4 (8.3)	
How often milk is consumed?	Every day	40 (83.3)	31 (64.6)	0.062
	Two-three times a week	8 (16.7)	17 (35.4)	
How often meat is consumed?	Every day	14 (29.2)	14 (29.2)	0.371
	Once a week	11 (22.9)	11 (22.9)	
	Two-three times a week	9 (18.8)	15 (31.3)	
	Four-five times a week	14 (29.2)	8 (16.7)	
How often eggs are consumed?	Every day	31 (64.6)	29 (60.4)	0.883
	Two-three times a week	10 (20.8)	12 (25.0)	
	Four-five times a week	7 (14.6)	7 (14.6)	
Vitamin D status	Severely deficient	23 (47.9)	18 (37.5)	0.586
	Deficient	19 (39.6)	23 (47.9)	
	Insufficient	6 (12.5)	7 (14.6)	
Age	Mean ± SD	59.46 ± 13.18	54.77 ± 13.46	0.630[b]
Benefiting from Ultraviolet Index score	Mean ± SD	0.69 ± 0.39	0.72 ± 0.54	0.791[b]

Chi-square test was used. [a] Fisher's exact test was used.[b] Student t test was used.

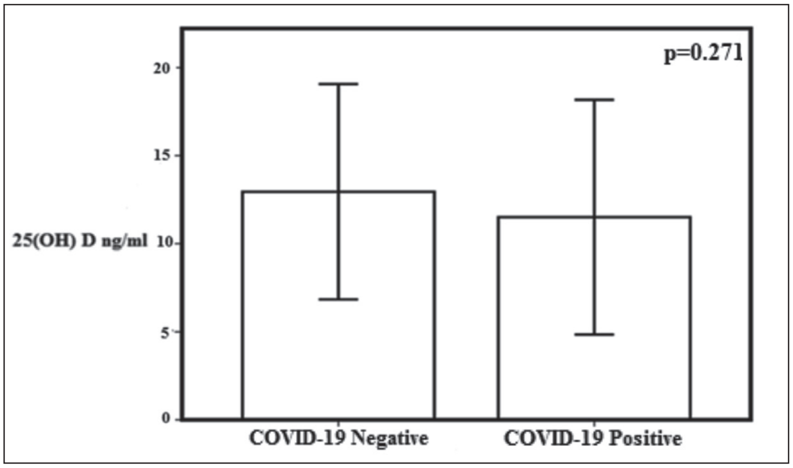

Figure 1: The relationship between 25(OH)D levels and COVID-19 infection.

between July and October months (36 °-42 °N Latitudes), the mean 25(OH)D levels of individuals who tested positive and negative for COVID-19 were 11.50 ± 6.66 and 12.95 ± 6.11 ng/ml, respectively. Contrary to our findings, in the retrospective study conducted by Chodick et al. in Israel (31°N- 46° N Latitudes) between February and April, the mean 25(OH)D levels were 23.6 ± 8.6 and 24.1 ± 9.1 ng/ml in individuals who were positive for COVID-19 and in those who were not (13). In a population-based study in Israel by Merzon et al., the mean the mean plasma vitamin D level was 19.00 ng/mL (95% confidence interval [CI] 18.41 -19.59) in individuals who tested for positive for COVID-19 and 20.55 (95% CI 20.32 -20.78) in those who were not positive. (14). In a cross-sectional study conducted by Mardani et al. in Iran (35-41° N Latitudes) in March, the mean 25(OH)D levels of individuals who tested positive for COVID-19 and who did not were 18.5 and 30.2 ng/ml, respectively (15). Turkey has a sunny climate. However, lower 25(OH)D levels in the present study compared to the ones conducted in countries with similar latitudes (13-15) could be explained with lower BFUI scores of individuals who were COVID-19 positive and who were not (0.69 ± 0.39 and 0.72 ± 0.54, respectively, p = 0.791) in the present study. Vitamin D is produced through the activation of previtamin D3 synthesis on the skin, especially with ultraviolet B rays (UVB) (4). Studies in the literature indicating that higher exposure to sunlight increases 25(OH)D levels (10, 16, 17) support this finding.

There was no significant difference between the 25(OH)D levels of individuals who tested positive for COVID-19 and who did not (p = 0.271). In support of our findings, a study evaluating the ethnic factors in the UK for the relationship between 25(OH)D concentrations and COVID-19 infection found no significant relationship between vitamin D concentrations and COVID-19 infection (9). In a retrospective study conducted by Avelio et al. in Switzerland evaluating individuals aged 70 and under who tested positive for COVID-19 and who did not, no significant association was found between the medians of vitamin D and COVID-19 infection (18). In another study which evaluated the association between angiotensin-converting enzyme inhibitors and increased COVID-19 cases in Israel, on the other hand, no correlation was found between vitamin D levels and COVID-19 infection risk (13). Contrary to our findings, there were also studies reporting that low 25(OH)D levels were associated with an increased risk of COVID-19 infection (19-23). Regarding the extra-skeletal effects of 25(OH)D, including the immune system, it was suggested that a blood 25(OH) D level greater than 30 ng/ml is required, and a 4 ng/ml increase in 25(OH)D level was reported to be associated with a 7% lower risk of infection (24). It was reported that individuals with blood 25(OH)D levels of < 20 ng/ml had a 54% higher COVID-19 positivity rate than those with a blood level of 30-34 ng/ml (25). The fact that the majority of the individuals included in the study had 25(OH)D levels less than 20 ng/ml may be the reason why there was no significant difference between the 25(OH)D levels of individuals who tested positive for COVID-19 and those who did not in the present study.

The present study is the first to assess the relationship between COVID-19 and vitamin D level of adults in Turkey. The fact that there were no individuals with sufficient vitamin D level in the study was a limitation of the study.

In conclusion, our findings did not support the potential link between the risk of COVID-19 infection and 25 (OH) D levels or vitamin D status (severely deficient, deficient, insufficient). Studies with larger samples are needed to evaluate the relationship between vitamin D and COVID-19.

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Author Contributions

Concept, Design, Supervision: **Fatih Okan,** Materials, Data Collection: **Fatih Okan, Sevil Okan, Yasemin Hanoğlu,** Analysis or Interpretation, Literature Search, Writing Manuscript: **Fatih Okan, Sevil Okan, Yasemin Hanoğlu,** Critical Review: **Fatih Okan, Sevil Okan.**

Conflicts of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Ethical Approval

The approval was obtained from the Non-Interventional Research Ethics Committee of Tokat Gaziosmanpasa University (20-KAEK-185).

Review Process

Extremely peer reviewed and accepted.

REFERENCES

1. Ferrari D, Locatelli M, Briguglio M, Lombardi G. Is there a link between vitamin D status, SARS-CoV-2 infection risk and COVID-19 severity? Cell Biochem Funct 2021;39(1):35-47.
2. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU) https://coronavirus.jhu.edu/ map.html. Accessed November 1, 2021.
3. Laird E, Rhodes J, Kenny RA. Vitamin D and Inflammation: Potential implications for severity of Covid-19. Ir Med J 2020;113(5):81.
4. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM; Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011;96(7):1911-1930.
5. Grant WB, Boucher BJ. Randomized controlled trials of vitamin D and cancer incidence: A modeling study. PLoS One 2017; 12(5): e0176448.
6. Grant WB, Lahore H, McDonnell SL, Baggerly CA, French CB, Aliano JL, Bhattoa HP. Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. Nutrients 2020;12(4):988.
7. Watkins J. Preventing a covid-19 pandemic. BMJ 2020;368:m810.
8. 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.
9. Hastie CE, Mackay DF, Ho F, Celis-Morales CA, Katikireddi SV, Niedzwiedz CL, Jani BD, Welsh P, Mair FS, Gray SR, O'Donnell CA, Gill JM, Sattar N, Pell JP. Vitamin D concentrations and COVID-19 infection in UK Biobank. Diabetes Metab Syndr 2020;14(4):561-565.
10. Atli T, Gullu S, Uysal AR, Erdogan G. The prevalence of Vitamin D deficiency and effects of ultraviolet light on Vitamin D levels in elderly Turkish population. Arch Gerontol Geriatr 2005;40(1):53-60.
11. http://temd.org.tr. Osteoporoz ve Metabolik Kemik Hastalıkları Tanı ve Tedavi Kılavuzu. METABOLIK_KH_BOOK_web_.pdf. [cited May 1, 2021] Available from: http://temd.org.tr.
12. Palacios C, Gonzalez L. Is vitamin D deficiency a major global public health problem? J Steroid Biochem Mol Biol 2014;144:138-145.
13. Chodick G, Nutman A, Yiekutiel N, Shalev V. Angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers are not associated with increased risk of SARS-CoV-2 infection. J Travel Med 2020;27(5):taaa069.
14. Merzon E, Tworowski D, Gorohovski A, Vinker S, Golan Cohen A, Green I, Frenkel-Morgenstern M. Low plasma 25(OH) vitamin D level is associated with increased risk of COVID-19 infection: An Israeli population-based study. FEBS J 2020;287(17):3693-3702.
15. Mardani R, Alamdary A, Mousavi Nasab SD, Gholami R, Ahmadi N, Gholami A. Association of vitamin D with the modulation of the disease severity in COVID-19. Virus Res 2020;289:198148.
16. Okan F, Okan S, Zincir H. Effect of sunlight exposure on vitamin D status of individuals living in a nursing home and their own homes. J Clin Densitom 2020;23(1):21-28.
17. Livingstone KM, Celis-Morales C, Hoeller U, Lambrinou CP, Moschonis G, Macready AL, Fallaize R, Baur M, Roos FF, Bendik I, Grimaldi K, Navas-Carretero S, San-Cristobal R, Weber P, Drevon CA, Manios Y, Traczyk I, Gibney ER, Lovegrove JA, Saris WH, Daniel H, Gibney M, Martinez JA, Brennan L, Hill TR, Mathers JC; Food4Me Study. Weekday sunlight exposure, but not vitamin D intake, influences the association between vitamin D receptor genotype and circulating concentration 25-hydroxyvitamin D in a pan-European population: The Food4Me study. Mol Nutr Food Res 2017;61(2).
18. D'Avolio A, Avataneo V, Manca A, Cusato J, De Nicolò A, Lucchini R, Keller F, Cantù M. 25-Hydroxyvitamin D concentrations are lower in patients with positive PCR for SARS-CoV-2. Nutrients 2020;12(5):1359.
19. Abdollahi A, Kamali Sarvestani H, Rafat Z, Ghaderkhani S, Mahmoudi-Aliabadi M, Jafarzadeh B, Mehrtash V. The association between the level of serum 25(OH) vitamin D, obesity, and underlying diseases with the risk of developing COVID-19 infection: A case-control study of hospitalized patients in Tehran, Iran. J Med Virol 2021;93(4):2359-2364.
20. Luo X, Liao Q, Shen Y, Li H, Cheng L. Vitamin D Deficiency Is Associated with COVID-19 Incidence and Disease Severity in Chinese People. J Nutr 2021;151(3):742-743.
21. Bassatne A, Basbous M, Chakhtoura M, El Zein O, Rahme M, El-Hajj Fuleihan G. The link between COVID-19 and VItamin D (VIVID): A systematic review and meta-analysis. Metabolism 2021;119:154753.
22. Demir M, Demir F, Aygun H. Vitamin D deficiency is associated with COVID-19 positivity and severity of the disease. J Med Virol 2021;93(5):2992-2999.
23. Bayraktar N, Turan H, Bayraktar M, Ozturk A, Erdoğdu H. Analysis of serum cytokine and protective vitamin D levels in severe cases of COVID-19. J Med Virol 2022;94(1):154-160.
24. Berry DJ, Hesketh K, Power C, Hyppönen E. Vitamin D status has a linear association with seasonal infections and lung function in British adults. Br J Nutr 2011;106(9):1433-1440.
25. 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.