Eskisehir Medical Journal
Eskişehir Tıp Dergisi

Eskisehir Med J. 2023; 4(supp): 195-200
doi: 10.48176/esmj. 2023.132

Araştırma Makalesi / Original Article

ASSOCIATION BETWEEN VITAMIN D STATUS AND ASTHMA CONTROL IN ADULTS

ERİŞKİNLERDE D VİTAMİNİ DÜZEYİ İLE ASTIM KONTROLÜ ARASINDAKİ İLİŞKİ

BİLGE SALIK[1] MERVE AYIK TÜRK[2] ÖZGÜR BATUM[1] BERNA KÖMÜRCÜOĞLU[1]

[1]Department of Pulmonology, Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital, Izmir, Turkey
[2]Department of Pulmonology, İzmir Bozyaka Training and Research Hospital, Izmir, Turkey

ÖZET

Giriş: Astım, hava yolu inflamasyonu ile ilişkili kronik solunum yolu hastalığıdır. Vasküler hastalıklar ve diabetes mellitus gibi bazı hastalıklarda, diyetin hastalığın kontrolündeki rolü vurgulanırken, astımda benzer bir nedensel faktör olarak tanımlanmamaktadır. Bu çalışmada, D vitamini düzeyi ile astım ilişkili solunum parametreleri arasındaki ilişkiyi değerlendirmek amaçlanmıştır.

Yöntemler: Bu çalışmada, astım tanısı konan toplam 87 hasta, tek merkezli retrospektif kohort olarak incelendi. Son 1 ay içinde herhangi bir nedenle D vitamini düzeyleri kontrol edilen hastalar çalışmaya dahil edildi. Hastaların astım kontrol durumu, Astım Kontrol Testi (AKT) ile belirlendi. Hastaların astım kontrolü ile D vitamini düzeyleri arasındaki istatistiksel ilişki incelendi.

Bulgular: AKT sonuçlarına göre, hastaların 43'ü kontrollü astım, 44'ü ise kontrolsüz astımdı. Tüm olguların medyan D vitamini düzeyi 12.80 (8.83-10.66) olduğu bulundu. D vitamini düzeyleri, kontrollü ve kontrolsüz astım gruplarında karşılaştırıldığında, aradaki fark istatistiksel olarak anlamlı bulundu ($p<0.001$).

Sonuç: Çalışmada diyetin astım ilişkili solunum parametreleri ve astım kontrolü üzerindeki etkisine odaklanılmıştır ve düşük D vitamini düzeyleri ile kontrolsüz astım arasında bir ilişki olduğunu gösterilmiştir. Maliyet-etkinlik göz önünde bulundurulduğunda astım kontrolünde, D vitamini düzeylerinin takibinin ve gerektiğinde D vitamini replasmanının yapılması, astım kontrolünün sağlanmasında, klinisyenlere katkı sağlayacağı düşünülmektedir.

Anahtar Kelimeler: Astım, D vitamini, Astım kontrol testi

ABSTRACT

Introduction: Asthma is a chronic respiratory disease associated with airway inflammation. In some diseases such as vascular diseases and diabetes mellitus, the role of diet in the control of the disease is emphasized, but it is not defined as a similar causal factor in asthma. This study was planned to evaluate the relationship between vitamin D status and asthma-related respiratory results.

Methods: This single-center retrospective cohort study examined a total of 87 patients diagnosed with asthma. Vitamin D levels that were checked for any reason in the past 1 month were included in the present study. The asthma control status of the patients was determined by the Asthma Control Test (ACT). The statistical relationship between asthma control and vitamin D levels of the patients was examined.

Results: According to ACT results, 43 of the patients had controlled asthma and 44 had uncontrolled asthma. The median vitamin D level of all cases was found to be 12.80 (8.83-10.66). When vitamin D levels were compared between the controlled and uncontrolled asthma groups, they were statistically significant ($p<0.001$).

Conclusion: The present study showed that there is an association between low vitamin D levels and uncontrolled asthma and the researchers focused on the effect of diet on asthma-related respiratory outcomes and asthma control. Considering the cost-effectiveness, it is thought that monitoring vitamin D levels in asthma control and vitamin D replacement when necessary will contribute to the clinicians.

Keywords: Asthma, Vitamin D, Asthma control test

Corresponding Author: Merve Ayık Türk
E-mail: merve.ayik@hotmail.com
ORCID: 0000-0003-3106-7403
Received Date: 26.03.2023 **Accepted Date:** 07.08.2023

Cite as: Salık B, Ayık Türk B, Batum Ö, Kömürcüoğlu B. Association Between Vitamin D Status And Asthma Control In Adults. Eskisehir Med J. 2023; 4(supp): 195-200. doi: 10.48176/esmj.2023.132.

INTRODUCTION

Asthma is a chronic lung disease characterized by reversible obstruction of the airways, increased bronchial reactivity, and chronic inflammation of the airways. Although asthma has a variable distribution all over the world according to genetic and environmental factors, it is a common respiratory disease that affects 1-18% of the population (1).

Studies conducted on asthma over the past 20 years has largely revealed the complex immunological mechanisms behind the inflammation in the airways. In the pathogenesis of asthma, airway inflammation is divided into eosinophilic inflammation and non-eosinophilic inflammation. It has been shown in recent years that in addition to classical treatment methods with phenotypic approaches, different methods can be effective in the treatment of different phenotypes. One of the mechanisms that has been investigated is the relationship between asthma and vitamin D (2).

Vitamin D is from the group of fat-soluble vitamins whose most important biological and chemical components are cholecalciferol (vitamin D3) and ergocalciferol (vitamin D2) (3). Endogenous production of vitamin D is the main source of vitamin D. This endogenous production is made from 7-dehydrocholesterol in the skin by the action of ultraviolet rays (4). Some studies have been done to determine normal vitamin D levels. Many studies were designed to identify the normal vitamin D level, and with these studies, vitamin D deficiency was defined as a 25(OH)D level below 20 ng/ml (5-7). Although vitamin D was traditionally associated with calcium homeostasis regulation, it is also expressed in lymphocytes and monocytes and is considered to have an additional role in inflammation and the immune system (8-10).

The purpose of the present study was to examine Vitamin D levels and deficiency in asthma patients and to investigate their relationship with asthma control and severity.

METHODS

Study Design

The study had a single-center retrospective cohort design. The patients who were followed up with a diagnosis of asthma in the chest diseases clinic for at least 6 months were evaluated retrospectively. The diagnosis of asthma was made by clinical, physical examination and reversible respiratory function test with FEV1 <80%, FEV1/FVC <80% and an increase of >12% and 200 ml in FEV1 when compared to the baseline values 10-15 minutes following 200-400 mcg salbutamol or equivalent. The patients followed up with the diagnosis of asthma and whose vitamin D levels were checked for any reason in the last 1 month were enrolled in the present study. Patients were also excluded that:

1. who had diagnosed with osteoporosis,
2. who got pregnant through the follow-up period,
3. when the patients' recent medical records were examined, who had diagnosed with metabolic syndrome, and malabsorption syndrome (pancreatitis, inflammatory intestinal disease, amyloidosis, celiac disease and malabsorptive bariatric surgical interventions etc.),
4. who had insufficient clinical data.

Plasma 25-hydroxy vitamin D (25-OH Vit D) measurement was used to determine the vitamin D level. The reference range for vitamin D in adults was taken as 40-100 ng/ml. If the 25(OH)D level was less than 20 ng/mL, it was considered vitamin D deficiency, and if it was between 21 and 29 ng/mL, it was defined as insufficient vitamin D (6). In the present study, vitamin D levels below 30 ng/ml were recorded as Vitamin D deficiency.

In the present study, the asthma control of the patients was determined by the Asthma Control Test (ACT). ACT is a survey in which asthma control is evaluated numerically as a test consisting of 5 questions that can be applied to patients over the age of 12.

The questions in the contents of the test are as follows.

1. In the last 4 weeks, how much has your asthma affected what you want to do at work, school, or home?
2. How often did you feel short of breath during the last 4 weeks?
3. How many times during the night or morning did asthma symptoms (wheezing, cough, shortness of breath, chest tightness, or pain) wake you up before your normal getting up time during the last 4 weeks?
4. How many times have you used your reliever inhaler or Salbutamol-type nebulizer in the last 4 weeks?
5. How would you rate your asthma control for the last 4 weeks?

The total score at the end of the test is 25 (5-15 uncontrolled asthma, 16-19 poorly controlled asthma, and 20-25 good control).

According to ACT results, the patients who had a score of 20 and above were grouped as the controlled asthma group (Group 1) and patients who had an ACT score of 19 and below were grouped as the uncontrolled asthma group (Group 2).

Statistical Methods

The data of the study were entered into the database that was created in the SPSS 18.0 program and the MecCalc and SPSS programs were used in statistical analyzes. The conformity of the continuous variables to the normal distribution was tested. In the comparisons of independent groups, the variables with normal distribution were evaluated with the Student’s t-test, and those not with the “Mann-Whitney U-Test”. The most appropriate cut-off value was selected according to the Youden Index by ROC Analysis for the significant variables, and the ODDS Ratio was calculated according to this value. The qualitative variables were given in cross-tables as frequencies and percentages, and their distribution was compared with the Chi-Square Test.

The margin of error for the first type was found to be α:0.05 in all statistical comparison tests and it was tested with two tails. When the “p” value was < 0.05, the difference was considered statistically significant.

RESULTS

A total of 87 patients were examined, 73 (83%) patients were female and the mean age was 50.62 ± 13 years. According to ACT results, 43 of the patients had controlled asthma and 44 had uncontrolled asthma. A total of 79% of the controlled asthma group and 88% of the uncontrolled asthma group consisted of female patients, and no gender difference was found in this respect (p> 0.05). No significant difference was detected between the age distributions of both groups (p=0.33). When the ACT scores were compared between the controlled and uncontrolled asthma groups, statistically significant differences were found (p<0.001).

The median vitamin D level of all cases was found to be 12.80 (8.83-10.66). When vitamin D levels were compared between the controlled and uncontrolled asthma groups, they were statistically significant (p<0.001) (Figure 1).

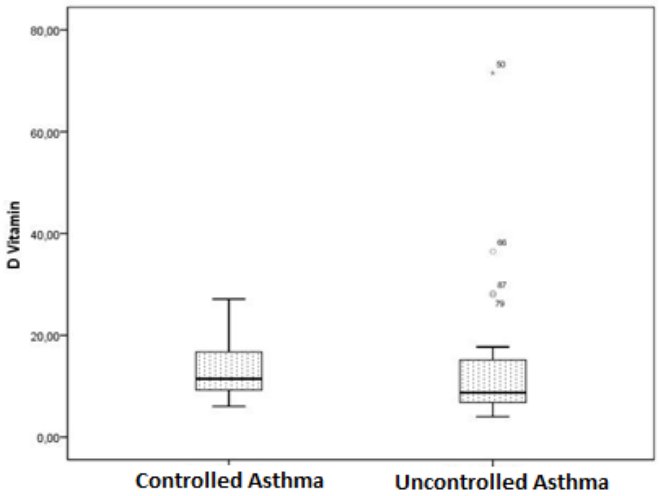

Figure 1. Distribution of Vitamin D Levels in Controlled and Uncontrolled Asthma Groups

The cut-off efficacy of vitamin D in determining asthma control was examined with the ROC Analysis. The cut-off value for vitamin D was calculated as 8.72 with the Youden Index. Sensitivity and specificity were calculated as 52% and 79% for the determined cut-off value (Figures 2, 3). It was found that a vitamin D value of less than 8.72 elevated the risk of uncontrolled asthma 5.26 times (OR: 5.26 95% CI 1.73-15.95, p<0.003).

The distribution of respiratory parameters in the controlled and uncontrolled asthma groups is given in Table 1. A positive correlation was found in the correlation analysis between vitamin D and ACT and PEF values (r=0.498, r=0.337, respectively; p=0.01).

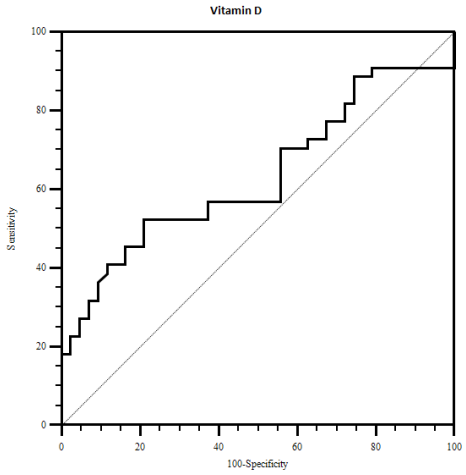

Figure 2. Vitamin D level ROC-Curve

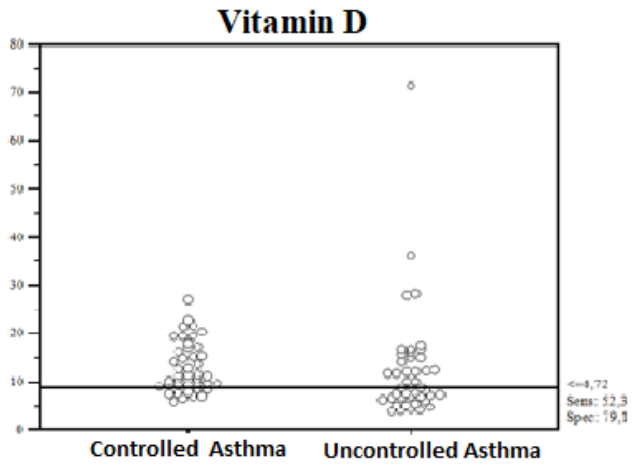

Figure 3. Population distribution according to vitamin D cut-off value

Table 1. Comparison of asthma control and pulmonary function test parameters with t-test

		n	Mean ± SD	P-value
FEV1	Controlled Asthma	43	81.91 ± 17.95	0.001
	Uncontrolled Asthma	44	69.02 ± 18.37	
FVC	Controlled Asthma	43	84.07 ± 18.02	0.006
	Uncontrolled Asthma	44	73.36 ± 17.31	
FEV1/FVC	Controlled Asthma	43	82.42 ± 9.73	0.048
	Uncontrolled Asthma	44	78.32 ± 9.35	
PEF	Controlled Asthma	43	73.86 ± 20.97	0.007
	Uncontrolled Asthma	44	62.27 ± 18.36	

DISCUSSION

The roles of vitamin D in the pathogenesis of asthma were investigated in many studies over the past two decades. The results obtained from these studies show that lung functions and asthma symptoms are worse in asthmatic patients who had vitamin D deficiency (11, 12). In the present study, a relationship was found between low vitamin D levels and increased asthma severity, and poor asthma control.

Vitamin D plays roles in the regulation of T and B cells causing decreased IL-17 production while inhibiting CD4+ T cell proliferation (13, 14). It was shown in a mouse model study that airway inflammatory response and IL-4 levels in Bronchoalveolar Lavage (BAL) fluid were significantly reduced when 1.25(OH)2D3 was given at the beginning of asthma induction or after completion of Th2 cell differentiation (15). Vitamin D levels were associated with airway hyperreactivity, inflammatory response, and response to steroids. For this reason, low vitamin D levels were attributed to poor asthma control and an elevated risk of asthma attacks.

In a pediatric meta-analysis, evidence was reported that polymorphisms in the gene encoding the vitamin D receptor (VDR) were associated with increased susceptibility to asthma (16). Also, decreased vitamin D levels were associated with increased TNF-alpha expression. The increase in TNF-alpha levels results in increased expression of pro-inflammatory cytokines, suggesting a potential pathway by which reduced vitamin D levels may exert pro-inflammatory effects in asthma (17, 18). In the study conducted by Korn et al., it was reported that vitamin D levels below 30 ng/ml were common in adults with asthma and low vitamin D was found to be more pronounced in patients who had uncontrolled asthma (19). Also, in another study conducted in Canada, vitamin D levels below 20ng/ml were associated with an increased risk of asthma attacks (20). It was reported in a study that children with asthma (5711 participants) had a significantly lower 25-OHD level than children without asthma (21.561 participants) (21.7 ng/ml vs. 26.5 ng/ml, p=0.01) (21). In the study conducted by Tamašauskienė L. et al., it was reported that low vitamin D levels elevated the risk of asthma 1.2-fold (OR, 1.194; 95% CI, 1.109-1.286, P<0.01) (22). In the study conducted by Kavitha et al., no relationship was detected between vitamin D levels and asthma control (23). In the present study, it was found that the risk of uncontrolled asthma increased 5.26-fold with vitamin D levels below 8.72 ng/dL (OR: 5.26 95%CI 1.73-15.95, p<0.003). Also, an 8.72 cut-off value could detect uncontrolled asthma with high specificity.

PEF is the peak expiratory airflow rate and is a spirometry measure used to evaluate airway restriction. The daily variability of the PEF value is >10% in adults and >13% in children in PEF meter monitoring. This supports the diagnosis of asthma. For this reason, PEF measurement is important in the diagnosis and follow-up of asthma. In the present study, a positive relationship was detected between vitamin D level and the PEF variable. Sarioglu et al. reported a positive relationship between FVC, FEV1, and PEF, which were similar, and vitamin D levels (r, 0.221-0.236; p ≤ 0.001) (24). In a cross-sectional study, a positive relationship was reported between vitamin D levels and FEV1 and FEV1/FVC (25). In a study that was conducted by Tamašauskienė L. et al., a relationship was found between vitamin D levels and FEV1/FVC in asthmatic smokers (22).

The response to treatment must be reviewed in the evaluation of asthma and the long-term follow-up of asthmatic patients and the treatment must be rearranged according to the status of asthma. In the follow-up of the patients, the symptoms, attack status, respiratory functions, and future risks are determined. Although there are many methods for the evaluation of symptom control of patients, ACT is one of the tests in which asthma control is evaluated numerically and its validity has been determined by studies today. These scores can sensitively evaluate the changes in the asthma symptom control level of the patients. In the present study, a positive relationship was detected between vitamin D levels and ACT results. The anti-inflammatory response and decreased bronchial hyperreactivity provided by vitamin D will ensure that asthma is monitored under control. This relationship confirms the correlation between vitamin D and ACT, which was detected in the current study.

Supplementation with vitamin D (60.000 IU per month for six months) was found to reduce the rate of asthma exacerbations, steroid requirement, and emergency department visits in patients who had asthma. An improvement at a significant level was observed in FEV 1 in patients who had mild-to-moderate persistent asthma 24 weeks after vitamin D supplementation (26). Although low vitamin D levels are attributed to uncontrolled asthma, integrating the monitoring of vitamin D levels into daily practice in patients followed up with a diagnosis of asthma may contribute to maintaining asthma control and reducing the risk of exacerbation.

Vitamin D levels of patients were evaluated in a cohort study, and it was reported that while variables such as age, gender and seasonal factors affect vitamin D levels, using a physiologic cut-off value of 20 ng/ml as the cut-off value of vitamin D level better reflects the population (27). Different vitamin D levels have been identified even throughout populations, raising the question ‘specific vitamin D levels’. The identification of a specific vitamin D level for asthma is necessary due to these variations in vitamin D cut-off levels.

The limitations of the study were that it had a single-centered retrospective design. The second limitation was the small number of cases. Another limitation is changes in the seasons affect vitamin D levels. Vitamin D levels were not able to be measured in all patients at the same time interval due to the retrospective nature of the research. The factors affecting vitamin D levels are another limitation. The amount of physical activity, obesity, dietary habits, and sun exposure time are all related to vitamin D levels.

In the future the association between vitamin D levels and asthma control must be developed, and understanding the dose-response relationship will provide ideas for future research. As a result, while our findings indicate an association, it may be naïve to generalize this finding to the general population. In order to strengthen the idea that serum vitamin D levels and asthma control are related, further study must be done in a single season with bigger patient sample sizes and multicentric levels.

CONCLUSION

The present study showed that there is a relationship between low vitamin D levels and uncontrolled asthma. Measuring the vitamin D level in the group in which asthma control cannot be achieved with standard treatment and evaluating it in terms of vitamin D supplementation in the patient group with low asthma levels may contribute to the provision of asthma control. Considering the cost-effectiveness, it is thought that monitoring vitamin D levels in asthma control and vitamin D replacement when necessary will contribute to the clinicians.

Ethics Committee Approval: This is a retrospective study, local ethical approval was received with the ethical approval date and number 21.09.2018-7153. All procedures that involved human participants were performed following the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments/comparable ethical standards.

Informed Consent: Informed consent was waived because of the retrospective design of the study.

Authorship Contributions: Idea/Concept: BS, BK, Design: BK, BS, MAT, Supervision: BK, Data Collection or Processing: ÖB, BS, Analysis or Interpretation: BK, MAT, Literature Search: MAT, Writing: MAT, BK, Critical Review: MAT, BK, Fundings: -, Materials: ÖB, BS.

Conflict Of Interest: The author declares there are no potential conflicts of interest. This article is protected by copyright. All rights reserved.

Financial Disclosure: The authors declare there is no financial support for this study.

REFERENCES

1. The Global Asthma Network. The Global Asthma Report; 2022.

2. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention (Update 2020). Avaliable from: https://ginasthma.org/gina-reports/.

3. Öngen B, Kabaroğlu C, Parıldar Z. D vitamininin biokimyasal ve laboratuvar değerlendirmesi Türk Klinik Biyokimya Derg 2008;6:23-31.

4. Glerup H, Mikkelsen K, Poulsen L, et al. Commonly recommended daily intake of vitamin D is not sufficient if sunlight exposure is limited. Journal of Internal Medicine 2000;247:260-68.

5. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2011;96:1911–30.

6. Wacker M, Holick MF. Vitamin D-Effects on Skeletal and Extraskeletal Health and the Need for Supplementation. Nutrients 2013;5:111-48.

7. Spiro A, Buttriss JL. Vitamin D: An overview of vitamin D status and intake in Europe. Nutr Bull 2014;39:322-50.

8. DeLuca HF. Vitamin D: Historical Overview. Vitam Horm 2016;100:1-20.

9. Provvedini DM, Tsoukas CD, Deftos L J, et al. 1,25-dihydroxyvitamin D3 receptors in human leukocytes. Science 1983;221:1181–3.

10. Veldman CM, Cantorna MT, DeLuca HF. Expression of 1,25-dihydroxyvitamin D(3) receptor in the immune system. Arch Biochem Biophys 2000;374:334-8.

11. Yawn J, Lawrence LA, Carroll WW, et al. Vitamin D for the treatment of respiratory diseases: Is it the end or just the beginning? J Steroid Biochem Mol Biol 2015;148:326–37.

12. Bozzetto S, Carraro S, Giordano G, et al. Asthma, allergy and respiratory infections: The vitamin D hypothesis. Allergy 2012;67:10–7.

13. Mahon BD, Wittke A, Weaver V, et al. The targets of vitamin D depend on the differentiation and activation status of CD4 positive T cells. J Cell Biochem 2003;89:922–32.

14. Tang J, Zhou R, Luger D, et al.Calcitriol suppresses antiretinal autoimmunity through inhibitory effects on the Th17 effector response. J Immunol 2009;182:4624–32.

15. Topilski I, Flaishon L, Naveh Y, et al. The anti-inflammatory effects of 1,25-dihydroxyvitamin D3 on Th2 cells in vivo are due in part to the control of integrin-mediated T lymphocyte homing. Eur J Immunol 2004;34:1068–76.

16. Han JC, Du J, Zhang YJ, et al. Vitamin D receptor polymorphisms may contribute to asthma risk. J Asthma 2016;53:790–800.

17. Berry MA, Hargadon B, Shelley M, et al. Evidence of a role of tumor necrosis factor alpha in refractory asthma. N Engl J Med 2006;354:697–708.

18. Mora JR, Iwata M, von Andrian UH. Vitamin effects on the immune system: vitamins A and D take centre stage. Nat Rev Immunol 2008;8:685–98.

19. Korn S, Hubner M, Jung M, et al. Severe and uncontrolled adult asthma is associated with vitamin D insufficiency and deficiency. Respir Res 2013;14(1):25.

20. Niruban SJ, Alagiakrishnan K, Beach J, et al. Association between vitamin D and respiratory outcomes in

canadian adolescents and adults. J Asthma 2015;52(7):653–61.

21. Wang Q, Ying Q, Zhu W, et al. Vitamin D and asthma occurrence in children: A systematic review and meta-analysis. J Pediatr Nurs 2022;62:e60-8.

22. Tamašauskienė L, Gasiūnienė E, Lavinskienė S, et al. Evaluation of vitamin D levels in allergic and non-allergic asthma. Medicina (Kaunas) 2015;51:321-7.

23. Kavitha TK, Gupta N, Kabra SK, et al. Association of Serum Vitamin D Levels with Level of Control of Childhood Asthma. Indian Pediatr 2017;54:29-32.

24. Sarıoglu N, Yalcın AD, Sahin F, et al. Does vitamin D deficiency in asthma affect clinical and functional parameters? A Turkish multicenter study. Allergy Asthma Proc 2021;42:e152-8.

25. Searing DA, Zhang Y, Murphy JR, et al. Decreased serum vitamin D levels in children with asthma are associated with increased corticosteroid use. J Allergy Clin Immunol 2010;125:995-1000.

26. Jat KR, Goel N, Gupta N, et al. Efficacy of vitamin D supplementation in asthmatic children with vitamin D deficiency: a randomized controlled trial (ESDAC trial) Pediatric Allergy and Immunology 2021;32:479–488.

27. Katrinaki M, Kampa M, Margioris A, et al. Vitamin D levels in a large Mediterranean cohort: reconsidering normal cut-off values. Hormones (Athens) 2016;15:205-223.