Research Article

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Evaluation of serum 25-hidroxy vitamin D and zinc levels in asthmatic patients

Astımlı hastalarda serum 25 hidroksi vitamin D ve çinko düzeylerinin değerlendirilmesi

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Abstract

Introduction: We aimed to investigate the impact of serum zinc, and vitamin D levels on the development of asthma, and its clinical characteristics.
Methods: In our cross-sectional study; 50 patients who were diagnosed as atopic asthma and 70 healthy children consisted the control group. In both groups levels of vitamin D, and zinc were analyzed.
Results: A statistically significant intergroup difference was not detected as for age, gender, body height (percentile), and weight (percentile) of the patients ($p > 0.05$). Mean vitamin D levels in the asthmatic patient, and control groups were 32.61 ± 9.48 nmol/L, and 42.55 ± 15.42 nmol/L, respectively. Between two groups a statistically significant difference was found ($p = 0.001$). Zinc levels were higher in the control group without any statistically significant difference between groups ($p = 0.25$). A statistically significant negative correlation (−0.635) was found between vitamin D levels, and severity of asthma in the patient group. As the level of vitamin D increased, a decrease in severity of asthma was seen ($p = 0.04$).
Conclusion: Though larger series are needed to arrive at definitive conclusions, we think that vitamin D deficiency rather than zinc deficiency, might convey importance in the emergence, and exacerbation of asthma.

Keywords: Asthma; Child; Level; Vitamin D; Zinc

Özet

Giriş: Biz, serum çinko ve vitamin D düzeylerinin astım gelişimi ve klinik özellikleri üzerine olan etkisinin araştırılmasını amaçladık.
Yöntemler: Kesitsel çalışmamız, atopik astım tanısı konulan 50 hasta ve kontrol grubunu oluşturan 70 hastadan oluşmaktaydı. Her iki grubun D vitamini ve çinko düzeyleri analiz edildi.
Bulgular: Gruplar arasında yaş, cinsiyet, boy (percentil) ve kilo (percentil) açısından yapılan karşılaştırmada istatistiksel anlamlı farklılık tespit edilmedi ($p > 0,05$). Gruplar arasında D vitamini ortalamaları astımlı hastalarda ve kontrol grubunda sırasıyla 32,61 ± 9,48 nmol/L ve 42,55 ± 15,42 nmol/L bulundu. İki grup arasında, istatistiksel anlamlı farklılık bulundu ($p = 0,001$). Çinko düzeyleri, iki grup arasında istatistiksel anlamlı fark olmadan, kontrol grubunda daha yüksekti ($p = 0,25$). Hasta grubunda D-Vitamini ile astım şiddeti arasında, istatistiksel olarak anlamlı negatif bir korelasyon (−0,635) bulundu.
Sonuç: Daha geniş serilere ihtiyaç olmakla birlikte, astımın ortaya çıkması ve şiddetlenmesinde D vitamini düşüklüğünün önemli olabileceğini, çinkonun ise etkisi olmadığını düşünmekteyiz.

Anahtar Kelimeler: Astım; Çocuk; Düzey; Vitamin D; Çinko

Introduction

In the pediatric age group asthma is one of the most frequently encountered chronic diseases. In recent years, the

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roles of vitamin D, and zinc have been investigated throughly regarding their roles in the pathogenesis of asthma.

Presence of vitamin D receptor in many types of T lymphocytes, dendritic cells, and macrophages has suggested the possible role of vitamin D in the improvement of immune functions [1]. Among its immune modulator effects, vitamin D exerts protective effects against respiratory tract infections, suppresses remodeling, and decreases cell turnover. It inhibits formation of proinflammatory cytokines found in the cells of immune system namely interleukin-6, tumor necrosis factor α, and proinflammatory mediator COX2 [2, 3], and stimulates synthesis of antimicrobial peptides [4]. Binding of active vitamin D to vitamin D receptors in human monocytes, macrophages, and epithelial cells activates cathelicidin, and genes of cationic peptides including defensin 2, and 4 with resultant increase in its synthesis which consequently provides protection against respiratory system infections [5, 6]. As reported in many articles, lower vitamin D levels have been more frequently encountered in patients with asthma, and respiratory tract infections [7, 8]. With its above mentioned characteristics, it plays a protective role in the development of asthma. Besides, in some studies, it has been observed that it reinforces effects of glucocorticoids, and reduces steroid resistance with resultant decrease in steroid requirements of the patients. This phenomenon emphasizes the potential importance of vitamin D in the pathogenesis, severity and control of asthma [4].

The role played by zinc in the cellular, and humoral response mechanism, and its presence in respiratory tract epithelium suggests its possible involvement in the pathogenesis, and control of asthma. The effects of zinc at a molecular level have been demonstrated in asthma, however, in various studies performed, a significant difference in the incidence of asthma in cases with zinc deficiency could not be found. Since incidence of allergic diseases, mainly asthma has gradually increased within the last decades, relevant studies have still retained their up-to-dateness. Outcomes of meta-analyses have demonstrated that lack or deficiency of vitamin D may increase the risk of asthma during childhood [9, 10]. However in the pathogenesis of asthma many changes in environmental factors in addition to genetic factors have been held responsible. Though asthma is a multifactorial disease, since very limited number of studies have investigated dietary molecules as vitamin D and zinc in its pathogenesis, we planned to perform this study. Besides, we tried to analyze the effects of these two molecules on both the development, and many clinical features of asthma from many perspectives.

Materials and methods

Our article presents a cross-sectional study. Fifty patients who were referred to Topçular district outpatient clinic, and outpatient clinic of Haseki Training and Research Hospital affiliated with Istanbul Fatih Association of Public Hospitals between May 1st 2013, and July 1st 2013 were included in the study. These patients were diagnosed with atopic asthma by a pediatric allergist based on proper anamnesis, physical examination findings, respiratory function, and skin test results, and measurements of total/specific serum IgE, and eosinophil levels. In our study, serum 25-hydroxy vitamin D, and zinc levels of 50 patients diagnosed with atopic asthma were compared to those of age- and gender-matched 70 healthy controls. Approval was obtained from the Ethics Committee of Haseki Training and Research Hospital and parents signed this consent form. A detailed questionnaire containing information about demographic characteristics of the patient, personal and family history, duration, and characteristics of asthma symptoms, concomitant symptoms of atopic disease, drugs taken for the treatment of asthma, level of asthma control, and severity of asthma during the previous 3 months, number of asthmatic attacks experienced during the previous 1 year, and concomitant diseases diagnosed by a physician was applied, and physical examination was performed. Each patient underwent asthma control test applied by a physician, and asthma score of the patient was recorded. From patients' medical files the most recent respiratory function, and skin test results, total/specific IgE level, peripheral blood eosinophil counts were reviewed. Zinc, and 25 (OH) vitamin D levels were measured in two cc-venous blood samples. The patients were questioned about the use of vitamin D or zinc containing supplements.

Pretreatment severity of asthma was determined based on the Table of Determination of the Severity of Asthma Based on Clinical Symptoms in Turkish Thoracic Society 2010 Guideline on Diagnosis, and Treatment of Asthma. The clinical status of patients followed up with the diagnosis of asthma was determined according to the Table of Asthma Control Levels in Turkish Thoracic Society 2010 Guideline on The Diagnosis, and Treatment of Asthma.

Patients aged 5–18 years with the diagnosis of atopic asthma were included in the patient group:

1. Patients with established diagnosis of deranged vitamin D metabolism.
2. Patients with established diagnosis of deranged zinc metabolism.
3. Patients who had received or had been receiving vitamin D replacement therapy within the previous 6 months.

4. Patients who had received or had been receiving zinc replacement therapy within the previous 6 months were excluded from the study.

Seventy healthy patients over the age of 5 years, who were referred to the outpatient clinics of the Department of Children's Health, and Diseases of Haseki Training and Research Hospital affiliated with Istanbul Fatih Association of Public Hospitals within working hours constituted the control group.

After application of the questionnaire form, body height, and weight measurements, and physical examination of the children were performed by the resident of the department of children's health and diseases in the outpatient clinics of pediatric allergy, and general pediatrics.

(a) Measurements of body height, and weight: were performed with the children in their indoor dresses, empty stomach, and standing upright.
(b) Body mass index (BMI): BMI was calculated as the ratio of weight (kg) to the square of body height (m^2).

According to the World Health Organization, the following BMI criteria were used:

– <18.5 kg/m^2: thin
– 18.5–25 kg/m^2: normal
– 25–30 kg/m^2: overweight
– ≥30 kg/m^2: obese.

Zinc was analyzed in the biochemistry laboratory of Haseki Training and Research Hospital using AU2700 Beckman Coulter device. The principle of the method is based on the formation of a red-colored chelate between zinc and 2-(5-Brom-2-pyridylazo)-5-(N-propyl-N-sulfopropylamino)-phenol. Total amount of zinc is consistent with an increase in its absorbance at 570 nw wavelength. Normal levels of zinc are considered as 60–135 µg/dL between ages 1 month and 15 years, and 70–150 µg/dL above 15 years of age.

Vitamin D levels were measured using LiaiSon ELISA analyzer. The Liaison 25 OH Vitamin D assay is a direct competitive chemiluminescence immunoassay (CLIA) for quantitative determination of total 25 OH vitamin D in serum. The DiaSorin LIAISON 25 OH Vitamin D TOTAL Assay measures between 4.0 and 150 ng/mL. The lowest reportable value is 4.0 ng/mL which is based on an inter-assay precision that approximates 20% CV (functional sensitivity). Values below 4.0 ng/mL should be reported as <4.0 ng/mL. The highest reportable value without dilution is 150 ng/mL.

Precisìon of intraassay measurement is about 4.0 and 6.3 for interassay mesurement as CV%.

The results were expressed in nmol/L. Accepted normal reference values range between 12 and 132 nmol/L. Vitamin D deficiency (<20 ng/mL; <50 nmol/L), insufficiency (20–32 ng/mL; 50–80 nmol/L), and adequacy (>32 ng/mL; >80 nm/L) were considered when values indicated in parentheses were detected [11, 12].

Statistical analysis

For statistical analysis, SPSS 15.0 Windows program was used. Descriptive statistical data was expressed as means, standard deviation, minimum, maximum, median, and categorical variables as frequencies and percentages. Comparisons of numerical variables in independent two groups were performed with Student t-test, and Mann-Whitney U-test for data with normal, and non-normal distribution, respectively. In cases where conditions of normal distribution among more than two groups were met, comparisons were made using One-way ANOVA test. Since relationship between numerical variables could not meet the parametric test conditions, correlation between ordinal, and numerical variables was analyzed using Spearman Correlation Analysis. Chi-square test was used for intergroup comparisons of rates. Level of statistical significance (α) was accepted as $p < 0.05$.

Results

Fifty patients with the diagnosis of asthma, and 70 healthy (control group) individuals were included in the study. The groups were compared for age gender, height (cm, and percentile), body weight (kg, and percentile), and BMIs (kg/m^2), and a statistically significant intergroup difference was detected regarding body height (cm), body weight (kg), and BMIs (kg/m^2) ($p < 0.05$). However a statistically significant intergroup difference was not detected as for age, gender, body height (percentile), and weight (percentile) ($p > 0.05$) (Table 1).

In our study, severity of the asthma was evaluated as mild intermittent (60%), mild persistent (20%), and moderate persistent (20%) asthma. The patients were under complete (50%) or partial control (34%), while asthmatic control could not be achieved in 16% of the patients.

Mean vitamin D levels of the groups were compared, and statistically significant lower vitamin D levels were detected in the asthmatic groups ($p < 0.05$). In the asthmatic group vitamin D insufficiency (50–80 nmol/L) was detected in one, and vitamin D deficiency (<50 nmol/L) in 49 patients.

Table 1: Intergroup comparisons of demographic data.

	Asthmatic patient group (n = 50)	Control group (n = 70)	p-Value
Age	8.66 ± 2.88	9.57 ± 3.09	0.084
Mean ± SD (min–max/median)	(5–18/8)	4.5–18/9.3)	
Gender			
Female	25	35	1.000
Male	25	35	
Height (Cm)	128.03 ± 14.50	137.70 ± 19.14	**0.009**
Mean ± SD (min–max/median)	(107.4–161/124)	(102.8–174.3/136.15)	
Body weight (Kg)	27.73 ± 9.28	35.53 ± 15.09	**0.009**
Mean ± SD (min–max/median)	(15.9–52/25.25)	(15.2–67/29.85	
BMI[a]	16.39 ± 1.89	17.76 ± 2.92	**0.040**
Mean ± SD (min–max/median)	(12.4–20.8/16.1)	(14–27.2/17.1)	

[a]BMI, Body mass index. Bold values indicate statistical significance.

Table 2: Intergroup comparisons of serum vitamin D, and zinc levels.

	Asthmatic patient group (n = 50)	Control group (n = 70)	p-Value
Vitamin D level (nmol/L)	32.61 ± 9.48	42.55 ± 15.42	**<0.001**
Mean ± SD (min–max/median)	(10–52.5/32.6)	(12.5–76.8/41.6)	
Vitamin D deficiency	49 (98.0%)	46 (65.7%)	**<0.001**
Vitamin D insufficiency	1 (2.0%)	24 (34.3%)	**<0.001**
Zinc	81.17 ± 26.04	87.62 ± 32.76	0.251
Mean ± SD (min–max/median)	(43–168/81.6)	(29–197/84.7)	

Bold values indicate statistical significance.

Higher levels of vitamin D were detected in the control group. Vitamin D insufficiency was detected in 24, and vitamin D deficiency in 46 patients. Adequate serum levels of 32 ng/mL were not encountered in both groups. However higher levels of zinc were detected in the control group, without any statistically significant intergroup difference (Table 2).

Data concerning current or past history of atopic dermatitis, allergic rhinitis, montelukast and/or steroid therapy, mean RFT (Respiratory Function Test) (FEV1/FVC) values, average age at the onset of asthma, mean eosinophil percentage, and mean total IgE level, and family history of smoking patients are presented in Table 3.

Mean vitamin D level in the patient group receiving steroids (36.28 ± 8.38 ng/mL) was significantly lower when compared with the other groups (30.73 ± 9.57 ng/mL) ($p < 0.05$).

A statistically significant but a negative correlation was detected in the asthmatic patient group between vitamin D levels, and severity of asthma. In other words vitamin D levels increased as the severity of asthma decreased ($p < 0.05$) (Table 4).

In the patient group when vitamin D levels and asthma control criteria were compared, a negative correlation was not detected as anticipated ($p > 0.05$). We can attribute this phenomenon to the use of steroids in the group whose asthma was under control, and as we indicated in Table 5 contrary to the outcomes of other studies, steroid use decreased serum vitamin D levels.

A statistically significant correlation was detected in comparison between mean vitamin D levels, and the presence of atopic dermatitis, steroid therapy and allergic rhinitis in the patient group. In patients with atopic dermatitis, steroid therapy and allergic rhinitis statistically significant lower levels of vitamin D were detected. On the contrary, a statistically significant correlation was not noted between vitamin D levels, and family history of atopy/asthma, and smoking ($p > 0.05$) (Table 6).

In the asthmatic patient group, serum zinc levels were compared between subgroups with the current or past history of atopic dermatitis, allergic rhinitis, montelukast and/or steroid treatment, family history of asthma/atopy, and smoking. Serum zinc level was found to be significantly lower in patients with a family history of atopy/asthma ($p < 0.05$). Any statistically significant difference was not detected in all other parameters ($p > 0.05$).

Discussion

Detection of vitamin D receptor (VDR) and 1-α hydroxylase enzyme in many tissues, and cells of the body

Table 3: Data of the asthmatic patients.

	Asthmatic patient group n (%)
Atopic dermatitis	
Absent	36 (72%)
Present	14 (28%)
Allergic rhinitis	
Absent	24 (48%)
Present	26 (52%)
Family history of atopy/asthma	
Absent	19 (38%)
Present	31 (62%)
Montelukast therapy	
No	10 (20%)
Yes	40 (80%)
Steroid therapy	
No	17 (34%)
Yes	33 (66%)
Family history of smoking	
No	19 (38%)
Yes	31 (62%)
	Mean ± SD (min–max/median)
FEV1/FVC ratio	82.28 ± 7.12 (67–91/84)
Age at onset of asthma (years)	6.32 ± 3.20 (2–17/5.9)
Eosinophilia %	5.89 ± 4.01 (0.4–17/4.5)
Total IgE (IU/L)	323.57 ± 275.69 (2–1258/258.1)

Table 4: Comparison between vitamin D levels, and severity of asthma, FEV1/FVC ratio, age at onset of asthma, eosinophilia, total IgE.

	Vitamin D level	
	ρ	p-Value
Severity of asthma	**– 0.635**	**0.049**
FEV1/FVC ratio	0.189	0.188
Age at onset of asthma (years)	0.123	0.396
Eosinophilia %	0.090	0.535
Total IgE (IU/L)	– 0.091	0.529

Bold values indicate statistical significance.

demonstrates that vitamin D involves not only in the bone mechanism, but also in the functioning of many organs, and tissues. Its inhibitory, and occasionally regulatory (stimulatory) effects have been demonstrated in cells containing vitamin D [13, 14]. Vitamin D deficiency or treatment with higher doses of vitamin D has been thought to increase sensitivity to aeroallergens leading to development of asthma [15].

Each receptor contains a binding site for active vitamin D, two finger-like protuberances which allow binding of the receptor to DNA, and a zinc atom which holds them in a steady state. Although the effects of zinc at a molecular level have been demonstrated in asthma, in most of the patients a significant correlation between the level of zinc, and asthma could not be displayed.

In our study, levels of 25-hydroxy vitamin D, and zinc were compared between 50 patients diagnosed as atopic asthma in the outpatient clinic of pediatric allergy, and in age- and gender-matched 70 healthy children. Ten patients were newly diagnosed cases, and 40 patients were previously diagnosed, and already under treatment. Mean age of the cases was 8.66 ± 2.88 years, and the patient population consisted of equal percentages (50%) of male, and female cases. Mean age of the control group volunteers was 9.57 ± 3.09 years. Gender and mean ages of both groups did not differ between groups ($p > 0.05$). Healthy children over age 5 years were selected as the control group. In the patient population asthma was either under complete (50%) or partial (34%) control or was intractable (16%). In our study we could not find a significant difference between our asthmatic, and control groups matched as for age, gender, height, and weight percentiles. Even though height, weight, and BMI values were higher in the control groups, it won't effect our study adversely. Indeed, risk of asthma increases in direct correlation with increases in height, weight, and these parameters effect asthma negatively. Therefore, it may be suggested that comparison between a group with relatively higher BMIs, and asthmatic patients won't effect the study adversely. As a matter of fact, in studies cited in the literature also in non-asthmatic healthy individuals serum vitamin D levels decreased in contrast to higher body weights, and BMI values [16].

During the assessment process, scarce number of patients in our study, its cross-sectional rather than longitudinal design, incomplete evaluation of nutrition, exposure to solar rays, and way of dressing, inability both to investigate genetic variants of VDR (vitamin D receptors), and also to reevaluate vitamin D deficient patients after vitamin D

Table 5: Comparison of vitamin D, and asthma control levels.

	Evaluation of asthma control	n	Mean ± SD (min–max/median)	p-Value
Vitamin D level (nmol/L)	Under complete control	25	32.51 ± 9.78 (10–52.5/33.5)	0.681
	Under partial control	17	34.25 ± 9.51 (20.5–49.5/37.5)	
	Uncontrolled	8	30.12 ± 7.32 (22–37/32.75)	

Table 6: Comparison of atopic dermatitis, steroid therapy, allergic rhinitis, and levels of vitamin D.

	Vitamin D level	p-Value
	Mean ± SD (min–max/median)	
Atopic dermatitis		
Present	27.67 ± 10.26 (10–42.8/26.75)	**0.020**
Absent	34.54 ± 8.55 (16.7–52.5/34.75)	
Allergic rhinitis		
Present	29.98 ± 9.37 (10–52.5/30)	**0.040**
Absent	35.46 ± 8.93 (20–49.5/36)	
Family history of atopy/asthma		
Present	30.88 ± 9.88 (10–49.5/29)	0.098
Absent	35.45 ± 8.24 (20.5–52.5/35)	
Montelukast therapy		
No	33.50 ± 8.53 (20–44/33.75)	0.746
Yes	32.40 ± 9.79 (10–52.5/32.5)	
Steroid therapy		
No	36.29 ± 8.39 (21.9–49.5/35.25)	**0.049**
Yes	30.73 ± 9.58 (10–52.5/31.25)	
Family history of smoking		
Present	32.77 ± 10.19 (10–52.5/32.75)	0.888
Absent	32.37 ± 8.45 (14.6–49.5/32.5)	

Bold values indicate statistical significance.

supplementation, partial difference between mean ages of the patients, and the control subjects, conduction of the study during summer months, lack of evaluation of seasonal differences should be taken into consideration.

In a study performed by Brehm et al. between the years 2001 and 2006 in Costa Rica the authors detected vitamin D insufficiency (28%), and deficiency (3.4%) in respective number of patients among 616 asthmatic patients aged between 6 and 14 years of age. Geographical lattitude (10°) of Costa Rica was held responsible for lower vitamin D concentration [17].

In a study by Sutherland et al. mean serum vitamin D level of 54 adult patients with the diagnosis of asthma was found as 28.1 ± 7.3. Increase in vitamin D levels has been shown to be strongly correlated with improved pulmonary functions [18].

In Qatar Bener et al. performed a study on 671 patients with the diagnosis of asthma, and 603 healthy children, and detected vitamin D deficiency in 68% of the asthmatic children with a mean serum vitamin D level of 17.2 ± 11.0 ng/mL. Vitamin D deficiency was detected more frequently in the asthmatic group with a significantly lower mean serum vitamin D levels when compared with the control group [19].

In two studies performed in children, decrease in the frequency of respiratory tract infection and asthmatic attacks has been shown in children receiving vitamin D supplementation [20].

Still vitamin D is considered as a potential new marker in asthmatic patients for the prevention of the impairment of airway tract, and its treatment [21–23]. Vitamin D exerts its effects by means of suppression of proliferation of pulmonary smooth muscle, secretion of mucus and tissue metalloproteinases [11, 24].

In asthmatic patients, vitamin D deficiency downregulates glycocorticoid receptors which involve in the pathogenesis of steroid-resistant asthma which can be seen in 15% of asthmatic patients. This condition can lead to increase in the dosages of corticosteroids, and leukotriene antagonists [22, 23]. Vitamin D decreases resistance to steroids, and demonstrates synergistic effects when used in combination with steroids [25]. In a randomized controlled study, vitamin D deficiency is found to be associated with severe asthmatic crisis, and the lowest risk of asthmatic crisis was seen in patients with serum vitamin D levels over 75 nmol/L [26].

In our study mean vitamin D and zinc levels were compared between groups, and significantly lower vitamin D levels were detected in the asthmatic patient group ($p < 0.05$). Intergroup differences regarding mean zinc levels were not detected ($p > 0.05$). Mean vitamin D levels in the asthmatic patient and control groups were 32.61 ± 9.48 nmol/L and 42.55 ± 15.42 nmol/L, respectively. In our study, mean zinc levels were 81.17 ± 26 μg/dL in the patient, and 87.62 ± 32.76 μg/dL in the control group without any significant intergroup difference ($p > 0.005$). Vitamin D levels were <50 nmol/L (deficiency) in 98%, 50–80 nmol/L (insufficiency) in 2%, and adequate in 0% of the asthmatic patients. In the control group vitamin D deficiency (<50 nmol/L) was detected in 52%, insufficiency (50–80 nmol/L) in 48%, and adequate in 0% of the members. Vitamin D deficiency was more frequently seen in the asthmatic group when compared with the control group. Lack of adequate vitamin D levels in both groups suggests some considerations. Some conditions which we thought will cause vitamin D deficiency include living indoors in line with worldwide industrialization, children's growing in kindergartens because of the parents' work hours, way of dressing in accordance with the beliefs of the community, use of sun cream with protective factors, air pollution for those living in urban areas, and western type life style. In our country we need large scale studies which will investigate mean vitamin D levels in children. and adults.

Only a few number of studies have investigated the correlation between vitamin D levels, and gender of the patients. In the United States of America, Black et al. reviewed the data of the NHANES II study performed on 14.091 individuals, and found significantly lower mean serum vitamin D levels in women (28.72 ng/mL) when compared with men (31.37 ng/mL) [13].

In our study mean vitamin D levels in the asthmatic girls, and boys were 30.87 ± 8.43 nmol/L, and 34.36 ± 10.29 nmol/L, respectively without any significant difference between genders ($p = 0.19$). In the control group mean vitamin D levels in the girls, and boys were 43.48 ± 9.54 nmol/L, and 55.71 ± 10.56 nmol/L, respectively without any significant difference between genders ($p = 0.001$).

In conclusion, even though studies with larger series are needed, we think that determination of vitamin D status in children, and vitamin D supplementation in case of need will potentially decrease the severity, and incidence rate of asthma.

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