



Research

Serum Vitamin D Levels and Food Sensitization in Atopic Dermatitis: A Single-center Study

Atopik Dermatitli Olgularda Serum D Vitamini Düzeyi ve Besin Duyarlanması: Tek Merkezli Çalışma

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ABSTRACT

Objective: Atopic dermatitis (AD) is a chronic, itchy, recurrent, and recurrent inflammatory skin disease that affects 2-20% of the population, especially in childhood. Its pathophysiology is complex and occurs as a result of genetic, immunological, and environmental factors, especially epithelial-barrier dysfunction. We determined the frequency of food sensitization and vitamin D deficiency in patients with AD.

Methods: This cross-sectional retrospective study was conducted by examining the files of patients who were admitted to the pediatrics allergy and immunology outpatient clinic with AD. A total of 72 patients with eczema were included in the study.

Results: 37.5% (n=27) of the patients were girls. The mean age was 3.8±3.6 years. Food sensitization was proven in 40.2% (n=29) of all cases included in the study. Vitamin D deficiency was found in 30.6% (n=22) of the cases. Serum 25-hydroxyvitamin D3 levels were found to be lower in the patient group than in the control group. The limitation of our study is that it was retrospective and blood tests could not be re-evaluated after treatment in all patients.

Conclusion: In patients with AD, serum vitamin D levels were significantly lower. We examined vitamin D deficiency in AD patients who applied to us as a clinical team. According to our study, we can say that both food sensitization and vitamin D deficiency should be investigated in AD patients.

Keywords: D vitamini deficiency, food allergy, eczema, atopik dermatitis

ÖZ

Amaç: Atopik dermatit (AD), özellikle çocukluk çağında, nüfusun %2-20'sini etkileyen, kronik, kaşıntılı ve tekrarlayan enflamatuvar bir deri hastalığıdır. Patofizyolojisi net olmamakla beraber, başta epitel bariyer disfonksiyonu olmak üzere genetik, immünolojik ve çevresel faktörlerin bir sonucu olarak gelişmektedir. Çalışmamızda AD olgularında besin duyarlılığı ve D vitamini eksikliği sıklığını saptamayı amaçladık.

Gereç ve Yöntem: Bu kesitsel retrospektif çalışma, hastanemizin çocuk alerji ve immünoloji polikliniğinde atopik dermatit tanısı ile izlenen hastaların dosyaları incelenerek yapıldı. Çalışmaya toplam 72 AD hastası dahil edildi.

Bulgular: Hastaların %37,5'i (n=27) kızdı. Ortalama yaş 3,8±3,6 idi. Çalışmaya dahil edilen tüm olguların %40,2'sinde (n=29) besin duyarlılığı tespit edildi. Olguların %30,6'sında (n=22) D vitamini eksikliği saptandı. Serum 25-hidroksivitamin D3 düzeyleri hasta grubunda kontrol grubuna göre daha düşük bulundu. Çalışmamızın kısıtlılığı retrospektif olması ve tüm hastalarda tedavi sonrası tekrar tetkik edilememesidir.

Sonuç: AD tanılı hastalarda serum D vitamini düzeyleri anlamlı olarak düşük bulundu. Klinik olarak AD tanısı ile izlenen hastalarda D vitamini eksikliği değerlendirilmektedir. Çalışmamızdaki istatistiksel sonuçlara göre AD tanılı olgularda hem besin duyarlanması hem de D vitamini eksikliği yönünden değerlendirilmesi gerektiğini söyleyebiliriz.

Anahtar Kelimeler: D vitamini eksikliği, besin alerjisi, egzama, atopik dermatit

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INTRODUCTION

Atopic dermatitis (AD) is a chronic, itchy, recurrent, and relapsing inflammatory skin disease that affects 2-20% of the population and is especially encountered in childhood. The pathophysiology is complex and occurs as a result of genetic, immunological, and environmental factors, especially epithelial-barrier dysfunction. Concomitant food allergy is observed in approximately 30% of AD cases (1-4).

Apart from all these, vitamin D deficiency among etiological factors and even vitamin replacement among treatment approaches has been the subject of discussion for a long time. Vitamin D is a special vitamin for the immune system that has hormone-like properties, bioactive metabolites, and acts by binding to nuclear hormone receptors in different tissues and cells. Vitamin cholecalciferol (Pre-D3) is synthesized in the skin from 7-dehydrocholesterol due to sunlight, especially ultraviolet B radiation (270-300 nm wavelengths) (5). Pre-D3 is then converted to 25-hydroxyvitamin D3 [25(OH)-D3] by 25-alpha-hydroxylase in the liver, which is the main metabolite in the circulation and can alternatively be consumed by nutrition. Finally, D3 and its most physiologically active metabolite, 1,25-dihydroxy D3 (calcitriol), are mainly produced in the kidneys by 1-alpha-hydroxylase (6,7). Calcitriol plays an immunoregulatory role by binding to the vitamin D receptor and acting on immune cells in an autocrine or paracrine manner (6). Epithelial cells, antigen-presenting cells, lymphocytes, mast cells, eosinophils, and innate lymphoid cells play a role in AD immunopathogenesis. T helper 2 (TH2) differentiation is stimulated by alarmins produced by epithelial cells. While there is TH2 dominance in the early period, other lymphocyte subgroups and the cytokines they produce come to the fore in the chronic phase along with TH2. In the acute phase, IL-4, IL-5, and IL-13 are produced from TH2 lymphocytes. Calcitriol, on the other hand, stimulates T-regulatory (Treg) cell differentiation and thus helps suppress the increased and uncontrolled inflammation observed in AD (5-7). Therefore, we hypothesized that vitamin D deficiency may be more common in patients with AD than in the normal population. There are not many studies in the literature examining both vitamin D deficiency and food sensitization in AD cases. In our study, we aimed to comparatively evaluate vitamin D levels in AD patients with and without food sensitization.

METHODS

The study was approved by the Biruni University Non-invasive Research Ethics Committee (decision no: 2021/64-6, approval date: 17.12.2021). Informed consent was obtained from all participants. This cross-sectional retrospective

study was conducted by examining the files of patients who were referred to our pediatrics allergy and immunology outpatient clinic because of persistent or recurrent eczema.

Patients

The study started by examining the files of patients who were diagnosed with eczema among the patients who applied to our hospital between August 2021 and February 2022. During this period, 250 eczema cases were detected, and it was noted that 113 cases were referred to the pediatric allergy and immunology outpatient clinic. Upon examining the files, 137 patients were excluded from the study because they did not come for follow-up, and 41 patients were excluded because their file data was not complete (Figure 1). As a result, it was found appropriate to include 72 patients in the study. A control group comprised healthy children who applied to the pediatric outpatient clinic for routine control or check-up. Children with serum 25(OH)D3 levels and blood test results were selected. Eighty healthy children of equivalent age and gender were randomized as the control group. Later the same parameters were compared between the patient and control groups.

Study Design

Demographic data, gender, age, blood tests, absolute eosinophil count (AEC), serum 25(OH)D3 levels, presence of additional atopic disease, specific and total IgE levels, skin prick test results, examination findings, treatments applied, and responses given to treatment were noted from patient files. Values with serum 25(OH)D3 levels below 20 ng/mL were accepted as "vitamin D deficiency". Cases with proven food sensitivity by serum-specific IgE and skin prick test. Total IgE levels below 100 kU/L were considered normal. Food-specific IgE levels below 0.35 kUA/L were considered negative. Histamine (10 mg/mL) was used as the positive control and saline as the negative control in the skin prick test panel. An induration greater than 3 mm was considered positive. Patients with a SCORAD index below 25 were considered "mild", between 25 and 50 "moderate", and above 25 "severe".

Statistical Analysis

Data were analyzed using SPSS statistical software, version 22 (SPSS Inc, Chicago, IL). Continuous variables are expressed as mean \pm standard deviation and categorical variables as number (%). For comparisons, we used independent t-test and One-Way ANOVA for continuous variables and chi-square test for categorical variables. Pearson's test was used for correlation analysis. $P < 0.05$ was considered statistically significant.

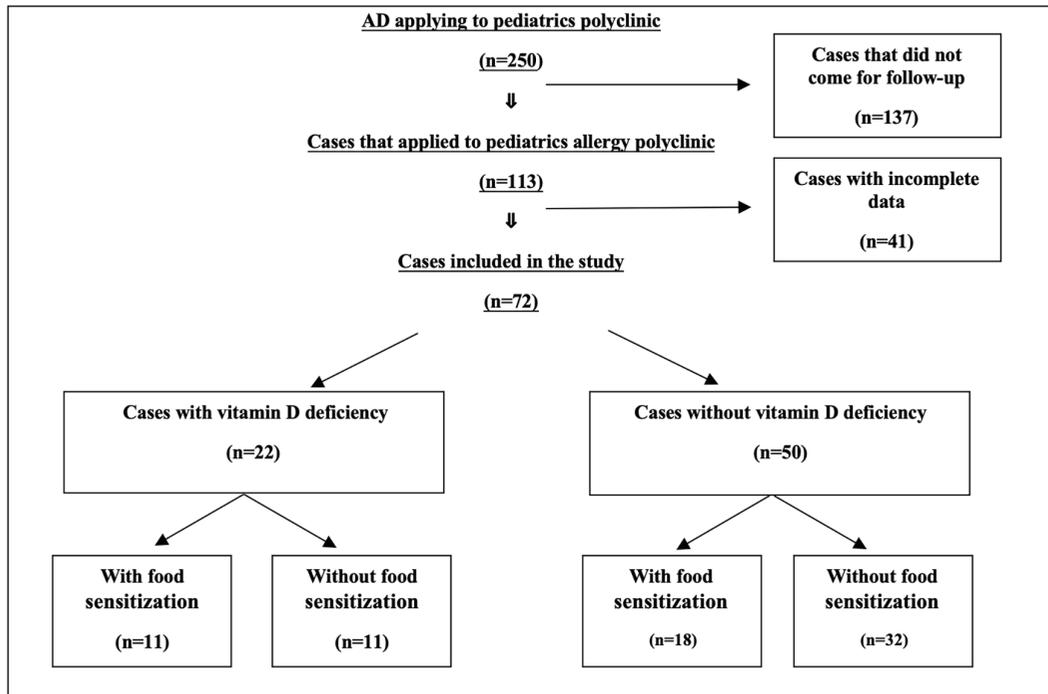


Figure 1. Study design

RESULTS

37.5% (n=27) of 72 patients included in the study were girls. The mean age was 3.8±3.6 years. When the file records of the patients were examined, the mean AEC was 632±711,4/mm³, and the mean total IgE level was 134 kU/L. The highest AEC was 4080/mm³, whereas the highest IgE value was 2000 kU/L. The mean AEC of the patient group was higher than that of the control group and was statistically significant (p<0.0001). The mean serum 25(OH)D3 level was 20.3±9.2 ng/mL. Vitamin D deficiency was detected in 30.6% (n=22) of the patients. In the control group, vitamin D deficiency was detected in 12.5% (n=10). It was statistically significant (p<0.0001). A comparison of the patient and control groups is given in Table 1.

The comparison according to the presence of vitamin D deficiency and food sensitization in the patient group is shown in Table 2. When the cases with vitamin D deficiency were compared according to gender, no significant difference was found (p=0.265). While food sensitization was observed in half of these cases (n=11), no food sensitization was observed in the other half. Food sensitization was proven in 40.2% (n=29) of all patients included in the study. When vitamin D deficiency was compared between patients with and without food sensitization, no statistically significant difference was found (p=0.921). When the total IgE level was compared between those with and without vitamin D deficiency, no statistically significant difference was found (p=0.48). There was a statistically significant difference

Table 1. Comparison of study groups

	Patients (n=72)	Control (n=80)	p-value
Gender			
Female (n, %)	27 (37.5%)	23 (28.8%)	0.252
Male (n, %)	45 (62.5%)	57 (71.2%)	
Age (years, mean ± SD)	3.8±3.6	3.5±2.8	0.563
25(OH)D3 (ng/mL, mean ± SD)	20.3±9.2	29.3±6.7	<0.0001
Eosinophil (count/mm ³ , mean ± SD)	632±711.4	120±169.5	<0.0001

SD: Standard deviation, 25(OH)D3: 25-hydroxyvitamin D3

in male gender between patients with and without food sensitization (p=0.006). Patients were compared according to the SCORAD index. Serum 25(OH)D3 levels and eosinophil counts were evaluated. There was a statistically significant difference between the groups, and the results are shown in Table 3.

DISCUSSION

Serum 25(OH)D3 levels have been examined in different patient groups in various scientific studies (8-11). Calcitriol increases its affinity and migration to cutaneous tissue by increasing the expression of C-C chemokine receptor type 10 in T lymphocytes. The calcitriol produced suppresses

Table 2. Comparison of patient groups

	D vitamin deficiency		p-value
	Positive (n=22)	Negative (n=50)	
	n (30.6%)	n (69.4%)	
Gender			
Female	9 (40%)	18 (36%)	0.692
Male	13 (60%)	32 (64%)	
Age, years	4.5±3.6	3.5±3.6	0.29
Food sensitization			
Positive	11 (50%)	18 (36%)	0.265
Negative	11 (50%)	32 (64%)	
Eosinophil (count /mm ³), mean ± SD	551.3±588.2	667.4±762.1	0.52
Total IgE (IU/mL), mean ± SD	128.6±186	129.8±317	0.98
	Food sensitization		p-value
	Positive (n=29)	Negative (n=43)	
	n (%)	n (%)	
Gender			
Female	5 (17%)	22 (51%)	0.006
Male	24 (83%)	21 (49%)	
Age, years	2.7±2.6	4.5±4	0.03
25(OH)D (ng/mL), mean ± SD	19.1±10.7	21.2±8.1	0.34
Eosinophil (count /mm ³), mean ± SD	791.5±830.8	524.3±604.9	0.11
Total IgE (IU/mL), mean ± SD	150.2±347	98.7±138	0.38

SD: Standard deviation, 25(OH)D3: 25-hydroxyvitamin D3

TH1 differentiation in T lymphocytes, while inducing differentiation in the Treg cell direction. It also activates tolerogenic dendritic cells in skin tissue (6,7,11,12). In line with the basic information about this immune system, we can say that vitamin D plays an important immunoregulatory role in chronic cutaneous inflammation such as AD. Therefore, we evaluated the 25(OH)D3 levels in our patients with AD. There was statistically significant eosinophilia in our patients with severe eczema. Serum 25(OH)D3 levels were also significantly lower in these patients. We know that the number of eosinophils bound to IL-4 and IL-5 produced by TH2 cells increases. Vitamin D deficiency may have led to decreased T regulatory cell differentiation and increased TH2 differentiation. We hypothesized that vitamin D deficiency may also facilitate eosinophilia and food sensitization.

While the mean serum 25(OH)D3 level of our study subjects (n=72) was 20.3±9.2 ng/mL, Galli et al. (13) found (n=89) 48.3±40.6 ng/mL in their patients and Lara-Corrales et al. (14) found (n=77) 62.6±27.8 nmol/L in the study they conducted. Tromp et al. (15) found that low vitamin D levels were associated with increased eczema in their cohort study. In our study, we discussed the frequency of food sensitization and vitamin D deficiency in patients with eczema.

There is still no consensus on the optimal serum 25(OH)D3 vitamin level (15). As a clinical team, we analyzed vitamin D deficiency and food sensitivity in patients with eczema. In our study, eleven of the eczema cases had both vitamin D deficiency and food sensitization.

Galli et al. (13) included 89 eczema cases in their study, and the median age was reported to be 68 months. In this study, patients were categorized into two groups: susceptible with serum IgE levels above 40 IU/mL and non-sensitive with serum IgE levels below 40 IU/mL. 57% of the cases were accepted as sensitive. The food sensitization rate was found to be 20.2% (n=18). When compared with this study, the rate of food sensitization in our study was higher,

Table 3. Comparison of patient groups according to SCORAD index

	Mild (n=35)	Moderate (n=29)	Severe (n=8)	p-value
Gender				
Female (n, %)	13 (37.1%)	10 (34.4%)	4 (50%)	0.72
Male (n, %)	22 (62.9%)	19 (65.6%)	4 (50%)	
Eosinophil (count/mm ³ , mean ± SD)	451.8±373.8	551.3±587.2	1712.5±1045.8	<0.0001*
25(OH)D3 (ng/mL, mean ± SD)	24.9±8.6	17.3±6.8	11.3±9.2	<0.0001*

*Post-hoc analyzed with tukey test: For eosinophil mild versus moderate p=0.79; mild versus severe p<0.0001; moderate versus severe p<0.0001. For 25(OH)D3 mild versus moderate p=0.001; mild versus severe p<0.0001; moderate versus severe p=0.154

SD: Standard deviation, 25(OH)D3: 25-hydroxyvitamin D3

quantitatively 40.2% (n=29). However, we grouped the cases that we considered sensitive not only by looking at the IgE level but also according to the results of the food-specific IgE skin prick test. While the mean total IgE value of the case group with food sensitivity in the study of Galli et al. (13) was 577.0 ± 994 kU/L and the mean vitamin D level was 48 ± 41.6 ng/mL, the mean total IgE value of our cases with food sensitization accompanied was 150.2 ± 347 kU/L and their mean vitamin D level was 19.1 ± 10.7 ng/mL.

Patients with food sensitization had a higher mean AEC than those without food sensitization. In case of vitamin D deficiency, it can be predicted that a predisposition may develop to hypersensitivity response or autoimmunity. Various scientific studies have shown that calcitriol replacement may be clinically beneficial for the treatment of inflammatory and autoimmune diseases (5,6,12,16). There is no definite consensus regarding the use of 25(OH)D3 replacement as a treatment (17-19). Kim et al. (17) suggested in their meta-analysis that serum 25(OH)D3 levels are important for the treatment of AD. In this meta-analysis, a significant difference was observed between serum 25(OH)D3 levels when the patient and control groups were compared. Detection of vitamin D deficiency and vitamin D replacement in patients with eczema may benefit treatment. However, prospective studies are required to evaluate the efficacy of vitamin D replacement in treatment.

The limitation of our study is that it was retrospective and blood tests could not be re-evaluated after treatment in all patients. Therefore, serum 25(OH)D3 levels should be checked again after treatment.

CONCLUSION

In patients with severe eczema, serum vitamin D levels were significantly lower. We examined vitamin D deficiency in eczema patients who applied to us as a clinical team. According to our study, both food sensitization and vitamin D deficiency should be investigated in patients with eczema.

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ETHICS

Ethics Committee Approval: The study was approved by the Biruni University Non-invasive Research Ethics Committee (decision no: 2021/64-6, approval date: 17.12.2021).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: Ö.A., A.S., Y.M.R., E.C., B.T.B., Concept: Ö.A., İ.T., A.S., Y.M.R., Design: Ö.A., A.S., B.T.B., Data Collection or Processing: Ö.A., A.S., Y.M.R.,

E.C., B.T.B., Analysis or Interpretation: İ.T., Y.M.R., Literature Search: İ.T., E.C., Writing: Ö.A., İ.T., A.S., Y.M.R.

Conflict of Interest: No conflict of interest was declared by the authors.

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