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The Effect of Nutrition and Micronutrients on Children with Atopic Dermatitis

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ABSTRACT

Objective: One of the most frequently investigated epigenetic factors in the pathogenesis of atopic dermatitis (AD) is food. There are different views on the effects of micronutrients on AD development and disease severity. In our study, we aimed to determine the feeding style and micronutrient levels and to investigate their relationship with AD clinical scores in infants with AD.

Materials and Methods: We determined the serum vitamin A, vitamin B12, vitamin D, vitamin E, zinc, and iron levels of infants with AD at the time of presentation to our pediatric allergy clinic. We recorded the feeding types and AD clinical scores of the infants. The relationship between micronutrient levels, nutrition type, and clinical scores of the patients was evaluated.

Results: A total of 63 patients, 34 (54%) male, with a median age of 6 (min-max: 2-21) months were included in the study. Breastfeeding (82.5%) was the most preferred feeding method. We did not detect any difference in terms of micronutrient levels between the feeding types. Micronutrients other than vitamin D and zinc were not correlated with disease severity. Moreover, low vitamin D levels were common despite the group receiving prophylaxis.

Conclusion: Prevention of vitamin D and zinc deficiencies in patients diagnosed with AD may be beneficial in reducing the severity of the disease. It may be useful to investigate whether low vitamin D in patients with AD is a cause or a result.

Keywords: Atopic dermatitis, child, micronutrients, vitamin D, zinc

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disease with itching and exacerbations, involving complex interactions between immunological, hereditary, and environmental effects (1). It affects approximately 1/5 of the children in the world (2).

In addition to genetic factors, the role of epigenetic factors, including nutrients, in the pathogenesis of AD has been investigated. In addition to allergen sensitivity to foods, it has been thought that vitamin and mineral deficiencies may be responsible for the development of AD through their effects on the immune system (3,4). The effects of micronutrients have been shown in the regulation of immunity, the elimination of skin barrier disorders, and the prevention of itching (5). The effects of micronutrients such as vitamin D and zinc on AD pathogenesis and disease scores are still debated (6-8).

In our study, we aimed to determine the feeding type and serum vitamin A, vitamin B12, vitamin D, vitamin E, zinc, and iron levels in infants diagnosed with AD. We investigated the relationship between micronutrient levels, type of feeding, and AD clinical scores.

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MATERIALS and METHODS

Between October 2021 and March 2022, pediatric patients aged 0-2 years who were followed up with the diagnosis of AD according to the Hanifin and Rajka diagnostic criteria (9) were determined in the Pediatric Allergy and Immunology clinic. Those whose vitamin (A, B12, D, E) and trace element (Fe, Zn) levels were studied in serum samples were included in the study.

Malnutrition was graded according to Gomez (weight for age) and Waterlow (weight for height) evaluations (10). Patients with additional chronic disease, food allergy, and/or malnutrition were excluded from the study. In our country, 400 IU/day vitamin D is given routinely in the first 1 year of life, and prophylactic iron support is given from the 4th month to 1 year of age, at the recommendation of the Ministry of Health. Other than these, patients who took supplements were not included in our study.

AD disease severity was evaluated using the SCORAD (SCORing Atopic Dermatitis) index. Those with a SCORAD score <25 were classified as mild, those with ≥25 to <50 as moderate, and those with ≥50 as severe (11).

The feeding types of the patients were categorized as breastfeeding, standard formula, and complementary food. The duration of breast milk intake and the initiation of additional food were recorded.

Analyzes of vitamin and trace element levels were obtained from patient records retrospectively. Current analyses were carried out at the Central Laboratory of the Dokuz Eylul University Hospital, which has ISO15189 laboratory quality management system accreditation and is certified by the Ministry of Health.

For the 25 (OH) D level, ≥30 ng/ml was considered sufficient, 21-29 ng/ml insufficient, and ≤20 ng/ml deficiency (12). For other parameters, normal reference ranges were determined according to our laboratory's reference data: Serum iron level 40-100 ug/dL, Zinc 70-114 ug/dL, Vitamin A 316-820 µg/L, Vitamin B12 126.5-505 pg/mL, and Vitamin E 6.6-14.3 µg/L. Levels below the reference ranges were considered low. These parameters were evaluated in all patients.

Ethical Statement

Ethics committee approval was received for this study from the Local Ethics Committee of Dokuz Eylül University, School of Medicine (Approval number: 2022/16-06)

Statistical Analysis

To select the statistical methods to be employed, the Kolmogorov–Smirnov normality test was conducted; however, if any of the groups did not meet the assumption of normality, then nonparametric testing methods were selected. The univariate logistic regression model and Pearson's correlation were used to examine the relationship between serum Vitamin D and zinc level and the severity of atopic dermatitis. Statistical analysis of the study was performed using IBM SPSS Statistics for Windows, Version 25 and the statistical significance limit was determined as $p \leq 0.05$.

RESULTS

A total of 63 patients, 34 (54%) male, with a median age of 6 (min-max: 2-21) months were included in the study.

Breastfeeding (82.5%) was the most preferred feeding method. Twenty (31.7%) of our patients were fed only with breast milk, 32 (50.8%) with breast milk and standard formula and/or complementary food, and 11 (17.5%) with standard formula and/or complementary food. The median duration of breastfeeding was 6 (min-max: 0-15) months in our 52 breastfed patients; the median time to the onset of solid food was 5.5 (3-7) months in the 38 patients who received complementary food.

There were 37 (58.7%) patients who received vitamin D and iron supplementation. Vitamin D was insufficient in 17 (27%) patients and deficient in 21 (33.3%) patients. The serum levels of vitamin A were low in 35 (55.6%), vitamin B12 in 11 (17.5%), vitamin E in 2 (3.2%), iron in 17 (27%), and zinc in 10 (15.9%) patients. Demographic data and laboratory findings of the patients are summarized in Table I.

There was no difference between the feeding type of the patients and their serum micronutrient levels ($p>0.05$) (Table II).

According to the SCORAD scores of the patients, 38 (60.3%) had mild, 20 (31.7%) had moderate, and 5 (7.9%) had severe atopic dermatitis. There was no difference between SCORAD scores and gender, feeding type, duration of breastfeeding, and time to start complementary food ($p=0.793$, $p=0.518$, $p= 0.176$, $p= 0.945$, respectively).

Vitamin D and zinc levels were found to be significantly lower in patients with moderate-severe AD compared to patients with mild AD (respectively; p=0.017, p= 0.041) (Table III).

Low vitamin D and serum zinc levels were associated with the risk of developing moderate-to-severe AD (Table IV).

DISCUSSION

A total of 63 patients with a median age of 6 (min-max: 2-21) months were included in our study. The majority of our patients were breastfed, and we did not find any difference between feeding types and serum micronutrient levels of the patients. Mild AD was present in 60% of our patients. Serum vitamin D and zinc levels were significantly lower in the moderate-severe AD group than in the mild ones. However, more than half of our patients were using prophylactic doses of vitamin D.

A balanced diet containing vitamins and minerals is important in the development of a strong immune system. Despite the popular opinions and information in the literature, scientific data proving its importance in the patho-

Table I: Demographic data and laboratory findings of the patients.

Age at diagnosis of AD (months) median (min-max)	3 (1-11)
Feeding type n (%)	
Only breastfeeding	20 (31.7)
Breastfeeding+ Standard formula	4 (6.3)
Breastfeeding+ Complementary food	21 (33.3)
Breastfeeding+ Standard formula + Complementary food	7 (11.1)
Standard formula + Complementary food	4 (6.3)
Standard formula	1 (1.6)
Only complementary food	6 (9.5)
Vitamin/Element levels median (min-max)	
Vitamin A (µg/L)	293.98 (108.47-608.58)
Vitamin B12 (pg/mL)	218 (71-997)
Vitamin D (ng/ml)	28.30 (12.29-71.55)
Vitamin E (µg/L)	9.47 (6.59-23.47)
Iron (ug/dL)	49 (16-129)
Zinc (ug/dL)	87 (48-133)
SCORAD score * median (min-max)	22.1 (8.9-63.7)

* SCORAD score, Scoring Atopic Dermatitis

Table II: Comparison of micronutrient levels according to feeding types.

	Only breastfeeding*	Breastfeeding+ Standard formula and/or Complementary food†	Standard formula and/or Complementary food‡	p
Vitamin A (µg/L)	281.15 (108.47-411)	323 (123.78-608.58)	303.95 (182-448)	0.103
Vitamin B12 (pg/mL)	208.5 (104-761)	219.5 (71-997)	223 (189-614)	0.132
Vitamin D (ng/ml)	27.02 (13.08-46.65)	30.11 (12.29-71.55)	26.03 (17.41-39.88)	0.138
Vitamin E (µg/L)	9.64 (6.8-18.2)	9.63 (6.59-23.47)	8.8 (6.8-17.5)	0.915
Iron (ug/dL)	49 (20-129)	49 (16-112)	55 (33-93)	0.357
Zinc (ug/dL)	87 (62-133)	87.5 (48-121)	80 (56-123)	0.652

*: for 20 patients, †: for 32 patients, ‡: for 11 patients.

Table III: Comparison of serum vitamin and mineral levels according to the severity of AD.

	Mild AD*	Moderate-Severe AD*	p
Vitamin/Element levels median (min-max)			
Vitamin A (µg/L)	302.49 (108.47-563.17)	290.40 (152.60-608.58)	0.316
Vitamin B12 (pg/mL)	245 (71-614)	203.5(102-481)	0.593
Vitamin D (ng/ml)	29.63 (15.35-71.55)	23.45 (12.29-45.40)	0.017
Vitamin E (µg/L)	9.35 (6.59-17.66)	8.85 (6.80-22.49)	0.710
Iron (ug/dL)	49.5 (16-93)	52 (19-112)	0.817
Zinc (ug/dL)	89 (48-123)	80 (58-133)	0.041

***AD:** Atopic dermatitis

Table IV: The relationship between the risk of developing moderate-severe AD and serum vitamin D and zinc levels.

	B*	EXP(B)†	95% confidence interval [CI] for EXP(B)		p
			Lower	Upper	
Vitamin D	-0.069	0.933	0.878	0.991	0.023
Zinc	-0.032	0.968	0.938	1.000	0.048

***B:** The coefficient for the constant. †**Exp(B):** The exponentiation of the B coefficient, which is an odds ratio.

genesis and treatment of AD are insufficient (4,13). In particular, although vitamin D supplementation has been popular in recent years, the results of studies are conflicting (14,15). However, it has been reported that the severity of AD decreases with a serum 25(OH) D level above 20ng/ml (16). A recent study evaluated 36 infants, 19 with mild and 17 with moderate AD. Vitamin D deficiency was found in 50% of the cases, and insufficiency in 25% of the cases. The 25(OH)D level was reported to be lower in the moderate AD group (17). In another study, it was found that vitamin D supplementation could decrease disease severity in children with AD; however, it has been emphasized that the information for the recommended dose and duration of administration is insufficient (18).

Low serum zinc levels have also been reported in patients with AD. In addition, an inverse correlation was found between zinc levels and SCORAD scores (5). Studies on the role of micronutrients other than vitamin D and zinc in AD are limited (19,20). Another study reported that current study results on vitamin/mineral supplements in patients with AD are inconsistent and supplementation should not be recommended unless patients have a documented deficiency (21).

Vitamins A and E are fat-soluble micronutrients that are important in maintaining the development and health of children. Vitamin A (retinol) is an important immunomodulator and has the ability to strengthen epidermal barrier function, while Vitamin E (α-tocopherol) acts as an antioxidant and plays important roles in regulating cell proliferation and gene expression. In individuals with AD, the use of vitamin A derivatives is not more effective than steroids; it has even been reported that it may cause irritation in patients with an impaired skin barrier (22,23). It has been reported that minerals such as magnesium, zinc, iron, and iodine may be beneficial for reducing inflammation in AD (23). Vitamin A was low in more than half of the patients with a median level of 293.98 μg/L, but it was not associated with disease severity. A low level of vitamin E was detected in very few of our patients and there was no relationship between vitamin E level and disease severity. Breastfeeding has been thought to be protective against vitamin E deficiency. The fact that vitamin A deficiency is common despite breast milk rich in vitamin A, suggested that this situation may be related to the pathogenesis of the disease and it may be beneficial to replace it, especially in patients who are found to be deficient.

Serum zinc level deficiency was present in approximately one of 6 patients, and zinc levels were significantly lower in infants with moderate-to-severe AD. More than half of our patients were taking iron supplements at prophylactic doses. Still, 27% of patients had iron deficiency. We did not find a significant difference between the iron level and AD severity. It may be beneficial to prevent low levels of iron and zinc in infants with AD who are predominantly breastfed. In particular, prevention of zinc deficiencies may benefit the AD clinical picture. Therefore, we started replacement therapy in patients with Fe and Zn deficiency.

In our study, although 58.7% of our patients received vitamin D prophylaxis, low vitamin D was present in 60.3% of the patients. In addition, 25 (OH) D levels of our patients with moderate-severe AD were significantly lower. This situation suggested that there could be a problem in vitamin D synthesis and metabolism in children with AD. Loss of skin barrier functions in AD may affect vitamin D synthesis. Concomitantly, vitamin D deficiency may contribute to the pathogenesis of AD and disease severity. We think that there is a complex relationship between vitamin D and AD. High-dose vitamin D replacement may be beneficial in children with AD. There is a need for comprehensive studies to be planned on this subject.

The role of breastfeeding in the prevention and treatment of AD has been evaluated in previous studies. Available data suggest that exclusive breastfeeding for at least 3 to 4 months has a beneficial effect for the prevention of AD (13,24). While there are results showing that breastfeeding has a protective effect compared to standard for-

mula, opposing views have also been reported (25-28). It is recommended that the transition to solid foods should not be delayed to after 4 to 6 months, including in high-risk infants (29,30).

About one third of our patients were exclusively breast-fed; in total, 82.5% were fed with breast milk. We could not detect a significant difference between the feeding style of the patients and micronutrient levels and the clinical scores. In line with the literature recommendations, the median duration of breast milk intake in our patients was 6 months, while the median time to start complementary food was 5.5 months. Severe AD was detected in only 7.9% of our patients. We believe that the recommended breastfeeding periods and complementary food transition periods are protective for AD. Most of our patients were fed with breast milk and additional food transition periods were in accordance with the literature recommendations.

The biggest shortcoming of our study is its retrospective design and the lack of a control group.

While the search for safe and effective treatment methods for AD continues, we believe that nutrition will continue to be an area of interest. Supporting breast feeding and starting complementary foods in the first 4-6 months of life may be protective for AD severity. Analyzing micronutrient deficiencies in patients diagnosed with AD may contribute to the treatment and prognosis of the disease. It can also enable the use of unnecessary vitamin and mineral supplements and the prevention of possible toxicities. In particular, the prevention of vitamin D and zinc deficiencies and intermittent level controls may be beneficial both in preventing the development of AD and in reducing the severity of the disease. In addition, there is a need for comprehensive studies investigating the relationship between vitamin D levels and skin barrier disorders.

Conflict of Interest

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Authorship Contributions

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