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Original Article

Age related risk factors associated with severity of atopic dermatitis in children

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Abstract

Aim: Atopic dermatitis is a chronic, relapsing, and pruritic dermatitis, which generally develops in early childhood, and has a characteristic age-dependent distribution. To review age related risk factors associated with severity of atopic dermatitis in children.
Material and Methods: The medical records of 206 pediatric patients with the diagnosis of atopic dermatitis between August 2015 and August 2017 were reviewed retrospectively.
Results: The study included two hundred six patients who were diagnosed with atopic dermatitis (118 males, 88 females, median age: 20 months). The disease was found to have a more severe course in patients who were breastfed for less than six months, who were exposed to cigarette smoke, who had a food allergen and a history of atopy in the family ($p<0.047$, 0.046, 0.032, 0.012, respectively) in the 0-2 age group. The disease was found to have a more severe course in patients who had aeroallergen sensitivity, high serum total IgE level, who had eosinophilia, and low socioeconomic level ($p<0.016$, 0.023, 0.038, 0.032, respectively) in the patient older than 2 years old.
Conclusion: While parental atopy and diet determine the severity of the disease in the early period of life, environmental factors have a more obvious role in later periods.

Keywords: Atopic Dermatitis; Eczema; Vitamin D; SCORAD; Risk Factors; Severity; Children.

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by pruritic skin lesions, disrupted skin barrier function, dysregulation of the immune system, and allergic reactions to food and environmental allergens (1). It commonly presents during early infancy, but may persist or begin later in childhood or even in adulthood (2). In Europe, 10% to 20% of children and teenagers are affected by AD (3). Major clinical features are a pruritic and relapsing eczematous dermatitis in a typical distribution that changes with age. In infancy, the cheeks, scalp, trunk, and extremities are most commonly affected. In early childhood, the flexural areas are characteristic, whereas in adolescents and adults, hands and feet are typically involved (4). The objective of this study is to examine age related risk factors influencing the severity of atopic dermatitis in childhood by using SCORAD index.

MATERIAL and METHODS

This retrospective study was conducted in Gaziosmanpasa Taksim Education and Research Hospital Pediatric Allergy and also Immunology Department and İnönü University Medical Faculty Department of Pediatric Allergy and Immunology between August 2015 and August 2017.

Study Group: Two hundred six patients with atopic dermatitis (aged 2-180 months) children were included in the study. The diagnosis of atopic dermatitis was established according to the Hanifin and Rajka criteria (5). The patients were grouped in two as those younger than two years old and those older than two years old. Demographic data such as age of onset of atopic dermatitis, diagnosis age, and regular breast milk intake, exposure to tobacco smoke, accompanying atopic disease, family history of atopy, crowded life, socioeconomic status, and pet exposure were obtained from of electronic files of patients. Serum vitamin D concentrations, allergen-specific IgE, total serum IgE and peripheral eosinophilia values of all patients weremeasured on admission. The data about laboratory results were obtained from patient files. The severity of atopic dermatitis was determined

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using the SCORAD index. Patients with SCORAD score below 25 were classified as mild, 25-50 as moderate and over 50 as severe atopic dermatitis. Maximum SCORAD score was 103 (6,7). Patients receiving systemic or topical corticosteroids in last three months were excluded from the study. Also, the patients who had used not only naive topical steroid but also combine formulation (e.g. steroid and antifungal cream) were excluded.

Laboratory Studies: Total serum vitamin D levels were measured by nephelometry using commercially available kits. For Serum 25(OH) vitamin D, <30 ng/mL values were accepted as insufficiency, ≥30 ng/mL values were accepted as sufficiency (8). Total IgE and allergen-specific IgE were measured using capture ELISA and Radio Allergo Sorbent Test (RAST), respectively. Sensitization to food allergens and aeroallergens were defined as at least 1 specific IgE > 0.35 kU/L. The count and percentage of peripheral blood eosinophils were determined. Patients older than three months underwent skin prick test. Skin prick tests were performed on the volar aspect of the forearm for foods (cow's milk, egg white, egg yolk, wheat,) and common aeroallergens (house dust mites, cockroaches, animal dander, mold, and mixed grass pollen). The reaction was read 15 minutes later. The test was considered positive if the diameter of the wheal was at least 3 mm greater than that of the negative control. Patients positive for at least one skin prick test or specific IgE positivity were defined as sensitized, and those who did not have any positive result were defined as not sensitized. Atopy patch tests were applied on uninvolved skin of the child's back, according to the method described by Turjanmaa et al (9). We used 12 mm diameter integrated filter paper cups (IQ Chamber, Chemotechnique diagnostics, Sweden). The patch test formulation was prepared in all subjects using lyophilized foods allergen extract. The formulation was consisted of one part of petrolatum and two parts lyophilized foods allergen extracts which are cow milk, egg white, egg yolk, wheat, soy bean, fish, peanut, lentil, and beef. Isotonic saline solution was used as negative control to exclude false positive reactions. The occlusion time of patch test was 48 hours. The results were read for the first time 15 min after removal of the cups. If irritative redness was found in the test area, the results were read after 30 min. The second evaluation was done 72 hours after attaching the patch tests. Reactions were classified according to standards and considered as: 0 - negative – no reaction, either visible or palpable; + - redness – negative or doubtful reaction; ++ - redness and palpable infiltration with papules – positive reaction; +++ - redness, palpable infiltration with many papules and eczema – strong positive reaction. If the reaction was very intensive as: redness, edema, palpable infiltration and vesicles, the result was marked as ++++. Reactions 0 and + (redness without infiltration) were regarded as negative. Occurrence of alone redness can be the results of local irritation.

Statistics analyses

We performed statistical analysis using Statistical Package for Social Sciences (SPSS) 21.0 software (SPSS Inc., Chicago, IL, United States). Descriptive statistics were expressed as frequency and percentage for categorical variables, whereas quantitative data were expressed as median for non-normally distributed data and as mean for normally distributed data. We used the Mann-Whitney U test compare two groups (Severe atopic eczema group and mild-moderate atopic eczema group in both ages group), and used the Chi-square test to compare the categorical variable.

The study was approved by the ethics committee of Inonu University and written informed consent was obtained from all the participant.

RESULTS

The study included two hundred six patients who were diagnosed with atopic dermatitis (118 males, 88 females, median age: 20 months). Demographic characteristics of the patients who were diagnosed with atopic dermatitis were summarized in Table 1.

Table 1. Demographics of children with atopic dermatitis

	n (%)
Male	118 (57.3)
Age, median,(min-max), month	20 (2-180)
The first eczema episode, month	5 (0-156)
Breast –feeding regular	135 (65.5)
Tobacco exposure	116 (56.3)
History of atopic disease, in parents	86 (41.7)
Co-existing atopic disease, in patient	122 (59.2)
Skin prick test	
Aeroallergen sensitivity	63 (30.6)
Food allergen sensitivity	111 (53.9)
Peripheral eosinophilia	79 (38.3)
Serum vitamin D level (<30)	85/123 (69.1)
Crowded life	100 (48.5)
Low socioeconomic level	111 (53.9)
Pet exposure	14 (6.7)
Serum IgE level elevation	85 (41.3)

Patients with atopic dermatitis were divided into two groups as 0-24 months and >24 months old. The groups were classified as mild-moderate and severe atopic dermatitis according to SCORAD index. There were 112 patients (62 males, 50 females, mean age 9 months) in the 0-2 age group. No statistically significant differences were found between mild-moderate atopic dermatitis and severe atopic dermatitis patients in terms of gender, diagnosis age, atopic dermatitis onset age, comorbid atopic disease, aeroallergen sensitivity, eosinophilia, serum vitamin D level, crowded life, socioeconomic level, exposure to pet and serum IgE level ($p>0.05$). The disease was found to have a more severe course in patients who were breastfed for less than six months, who were exposed to cigarette smoke, who had a food allergen and a history of atopy in the family ($p<0.047$, 0.046, 0.032,

0.012, respectively). There were 94 patients (56 males, 38 females, mean age 48 months) in the patient group older than 2 years old. No statistically significant differences were found between mild-moderate atopic dermatitis and severe atopic dermatitis patients in terms of gender, diagnosis age, atopic dermatitis onset age, comorbid atopic disease, atopy in the family, breast milk intake, exposure to cigarette smoke, food allergen sensitivity, serum vitamin D level, crowded life, socioeconomic level and exposure to pet (p>0.05). The disease was found to have a more severe course in patients who had aeroallergen sensitivity, high serum total IgE level, who had eosinophilia, and low socioeconomic level (p<0.016, 0.023, 0.038, 0.032, respectively). Age related risk factors associated with severity of atopic dermatitis were summarized in Table 2.

Table 2. Age related risk factors associated with severity of atopic dermatitis in children

	0-24 months n (%)	p-value	>24 months	p value
Male	62 (55.3)	0.593	56 (59.5)	0.785
Age, median, (min-max), month	9 (2-22)	0.186	48 (24-180)	0.514
The first eczema episode, month	3 (0-16)	0.429	12 (0-156)	0.772
Breast –feeding regular	58 (51.7)	0.047	77 (81.9)	0.307
Tobacco exposure	61 (54.4)	0.046	55 (58.5)	0.920
History of atopic disease, in parents	41 (36.6)	0.032	45 (47.8)	0.078
Co-existing atopic disease, in patient	55 (49.1)	0.098	67 (71.2)	0.152
Skin prick test				
Aeroallergen s ensitivity	7 (6.2)	0.229	56 (59.5)	0.016
Food allergen sensitivity	76 (67.8)	0.012	35 (37.2)	0.421
Peripheral eosinophilia, (%)	45 (40.1)	0.624	34 (36.1)	0.038
Serum vitamin D level (<30)	31/60 (51.6)	0.965	54/63 (85.7)	0.601
Crowded life	51 (45.5)	0.230	49 (52.1)	0.734
Low socioeconomic level	60 (53.5)	0.770	51 (54.2)	0.032
Pet exposure	3 (2.6)	0.263	11 (11.7)	0.310
Serum IgE level elevation	27 (24.1)	0.863	58 (61.7)	0.023

DISCUSSION

The development of atopic dermatitis in infancy and subsequent allergic rhinitis and asthma in later childhood is known as the atopic march (10). Atopic dermatitis is associated with both disruption of the epithelial barrier of the skin and allergic inflammation in the skin of hosts whose genetic background results in a predisposition to atopy. Atopic dermatitis, along with food allergy present in the first years of life and are the initial steps in the 'atopic march' (11). The prevalence of food allergy in all children in the first 5 years of life is approximately 5%. In children with AD the prevalence of food allergy is approximately 30% to 40% (4). Sensitization to food allergens (cow's milk and hen's eggs) is associated with infantile AD and severity of disease. Food allergen sensitization is also predictive for persistence of symptoms throughout childhood (12). In our study, a significant association was found between food allergen sensitivity and atopic dermatitis severity in patients younger than two years old. Our study supported literature with this aspect.

Parental atopy was associated with early age and severe atopic dermatitis. The association between exposure to second hand tobacco smoke and atopic dermatitis has not been clearly determined yet (13). In our study, parental atopy, breast milk intake of less than six months and exposure to cigarette smoke were found to be associated with atopic dermatitis severity in patients younger than two years old. Similar results were not found in patients older than two years old. These results bring to mind that environmental factors come to the forefront in atopic dermatitis severity as age gets older. The reason for this may be exposure to environmental allergen with increasing age. It was demonstrated in a recent meta-analysis that the incidence of atopic dermatitis was lower in breastfed infants (at least four months) (14). In our study, atopic dermatitis was found to have a milder course in patients who were breastfed for longer than six months. This result shows that breast milk decreases not only the incidence of atopic dermatitis but also its severity. In addition, although its mechanism is unknown, exposure to cigarette smoke in early age causes atopic dermatitis to course more severely.

The data about the association between serum D vitamin and atopic dermatitis severity are contradictory in literature. While there are studies in literature which report that atopic dermatitis is more severe in patients with low serum D vitamin, there are also studies which report the reverse or which report that there is no association (15-17)). In our study, no association was found between serum vitamin D level and atopic dermatitis severity in both age groups. Recent studies have shown that both high serum IgE levels and eosinophils are associated with atopic dermatitis severity (18,19). In our study, both high serum IgE levels and eosinophils were found to be associated with atopic dermatitis severity especially in patients older than two years old. No association was found in patients younger than two years old. The reason for this difference can be atopic march. Most probably, asthma or allergic rhinitis comorbid to atopic dermatitis in patients older than two years old may have caused an increase in serum IgE levels and eosinophil count.

Although great majority of children with atopic dermatitis

are sensitive to one or more aeroallergens, the association between exposure to aeroallergens and atopic dermatitis is unknown. Up to date, no clear evidence for the relationship between early exposure to aeroallergens and increased risk for atopic dermatitis has been found (20). A recent meta-analysis of randomized clinical trials on subcutaneous immunotherapy with house dust mite preparation in patients with AD provided a moderate-level evidence of the efficacy for AD (21). The most significant aspect of our study was the result that inhalant allergen sensitivity was found to be associated with atopic dermatitis severity in patients older than two years old. This result brings to mind that inhalant allergens are in the etiology of atopic dermatitis in patients older than two years old. Another risk factor associated with atopic dermatitis in patients older than two years old was low socioeconomic level. This shows that environmental factors are more on the forefront in the etiology of atopic dermatitis as age gets older.

CONCLUSION

As a conclusion, this is the first study in literature classifying risk factors associated with atopic dermatitis severity according to age groups. While parental atopy and diet determine the severity of the disease in the early period of life, environmental factors have a more obvious role in later periods.

Competing interests: The authors declare that they have no competing interest.
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