ASTHMA ALLERGY IMMUNOLOGY

Asthma Allergy Immunol 2014;12:97-103

**ARAŞTIRMA** RESEARCH ARTICLE

# An evaluation of characteristics and concomitant allergic diseases in children with atopic dermatitis

## Atopik dermatitli çocukların özellikleri ve eşlik eden allerjik hastalıkların değerlendirilmesi

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**ABSTRACT**

**Objective:** The aims of the study were to evaluate the characteristics of children with atopic dermatitis and presence of concurrent atopic diseases among these patients.

**Materials and Methods:** One hundred and eighty-one patients followed-up with a diagnosis of atopic dermatitis were evaluated. The age of the patients ranged from 2 months to 13 years and 70.2% were male. Of these patients, 146 had been diagnosed with atopic dermatitis, 29 with atopic dermatitis and asthma, and 6 with atopic dermatitis and allergic rhinitis.

**Results:** Of the patients 37.6% were found to have allergic sensitization by skin prick test. The IgE level and eosinophil count of the sensitized group were higher (p: < 0.001, 0.002; respectively). The rate of concurrent asthma or rhinitis in the sensitized group was 38.2%, while it was 8% in the group without sensitization (p: < 0.001).

**Conclusion:** The most important factors affecting sensitization were high IgE levels and eosinophilia. In the presence of sensitization, asthma or rhinitis development is more common. More cohort studies are

**ÖZ**

**Giriş:** Çalışmanın amacı atopik dermatit tanılı hastaların özelliklerini ve astım ve/veya allerjik rinit birlikteliği için risk faktörlerini değerlendirmektir.

**Gereç ve Yöntem:** Yaşları 2 ay ile 13 yıl arasında değişen %70.2'si erkek olan atopik dermatit tanılı 181 hasta değerlendirildi. Hastaların 146'sı atopik dermatit, 29'u astım + atopik dermatit ve 6'sı atopik dermatit + allerjik rinit tanısı ile izleniyordu.

**Bulgular:** Hastaların %37.6'sında deri prik testinde allerjik duyarlanma vardı. Allerjik duyarlanması olan grupta IgE düzeyi ve eozinofil sayısı daha yüksekti (sırasıyla p: < 0.001, 0.002). Allerjik duyarlanması olan grupta astım/allerjik rinit birlikteliği %38.2 iken; olmayan grupta %8 olarak bulundu (p: < 0.001).

**Sonuç:** Atopik dermatitte allerjik duyarlanmayı en çok etkileyen faktörler yüksek IgE düzeyi ve eozinofili olarak bulundu. Atopi varlığında atopik dermatite astım ve alerjik rinit daha sık eşlik etmekteydi. Atopik dermatitli çocuklarda astım gelişimi ile ilişkili risk faktörlerinin belirlenmesi için daha fazla kohort çalışmalara ihtiyaç vardır.

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needed to unravel the factors associated with development of asthma in children with atopic dermatitis.

*(Asthma Allergy Immunol 2014;12:97-103)*

**Key words:** Atopy, asthma, atopic dermatitis, childhood, eosinophilia

Received: 18/09/2013 • Accepted: 14/01/2014

*(Asthma Allergy Immunol 2014;12:97-103)*

**Anahtar kelimeler:** Atopi, astım, atopik dermatit, çocukluk çağı, eozinofili

Geliş Tarihi: 18/09/2013 • Kabul Ediliş Tarihi: 14/01/2014

## INTRODUCTION

Atopic dermatitis is a common, chronic inflammatory disease. It is characterized by pruritis, erythema, vesiculation, papulation, exudation, excoriation, crusting, scaling, and sometimes lichenification. It occurs most frequently in children. The prevalence of atopic dermatitis is on the rise. In industrialized countries, it affects 15% to 30% of children[1,2].

The pathogenesis of atopic dermatitis involves complex interactions between susceptible genes, immunologic factors, skin infection, environmental factors and defects in the skin barrier. Atopic dermatitis frequently starts in early infancy (early onset atopic dermatitis) and in adults (late-onset atopic dermatitis). Eighty-five per cent of all cases of atopic dermatitis begin before five years of age[1]. Approximately 60% to 80% of patients have associated IgE-mediated sensitization (extrinsic form, IgE associated form); 20% or 40% of patients are without IgE mediated sensitization (intrinsic form, non-atopic eczema)[1,2]. Th2 cytokines interleukin (IL)-4/-5/-6/-10/-13 contribute to hypereosinophilia and high IgE levels. Compared with extrinsic atopic dermatitis, the intrinsic form is associated with less IL-4 and IL-13 production[2].

Atopic dermatitis is often associated with other atopic disorders, such as allergic rhinitis and asthma. The dermatitis and asthma association has been explained by invoking the atopic march whereby children with dermatitis have a high risk of progression to asthma and/or allergic rhinitis later in childhood[3-7]. Nevertheless, progression to asthma/allergic rhinitis is not seen in all children with atopic dermatitis; and history of atopic dermatitis does not necessarily have to be positive in the history of asthmatic children.

In this study, we aimed to evaluate the characteristics of children with atopic dermatitis and presence of concurrent atopic diseases among these patients.

## MATERIALS and METHODS

We reviewed the medical records of all children with a diagnosis code of AD who were seen in the Department of Allergy and Asthma Ankara Dr. Sami Ulus Woman's Health and Children Education and Research Hospital between 01 September 2008 and 31 August 2009.

The patients who visited our clinic for control in this period with atopic dermatitis or newly diagnosed for atopic dermatitis were enrolled into the study. Skin prick test was performed in all the patients. If the last control was 3 months ago, the patients were called and reevaluated for asthma and rhinitis symptoms. Exclusion criteria were dermatitis other than atopic dermatitis and immunodeficiency. Atopic dermatitis was diagnosed by using diagnostic criteria described by Hanifin and Rajka[7]. Patients were also considered to have asthma if there was a history of physician-diagnosed asthma according to GINA[8].

The following demographic and historical information were recorded:

- Age, month of birth, feeding history, past diseases,
- Symptoms, characteristics of symptoms,
- Predisposing factors or factors increasing the severity,

- Family history of allergic disease,
- Characteristics of the residence, passive smoking, pets at home, usage of wool.

In the laboratory studies, serum total IgE levels, eosinophil counts and results of skin prick tests of the patients were recorded. The total IgE was studied with ELISA (Enzyme linked immunoassay) method. The eosinophil count was determined from the peripheral blood smear or counter and values higher than 4% were considered eosinophilia.

#### Skin Prick Test

The patient's antihistaminic medication, if any, was stopped three days before the test. A drop of the allergen solution at standard activity and concentration was placed on the skin and allowed to seep into the epidermis with the help of a stallerpoint. The allergens used included pollens, fungal spores, mites, animal fur and various food substances (Stallergenes S.A.-France). The skin reaction was evaluated 20 minutes later. The wheal and flare reactions were compared with the size of negative (antigen diluting solution) and positive (histamine hydrochloride 10 mg/mL) controls and enduration > 3 mm was considered positive[9].

In the patients younger than 5 years, SPT was performed to egg (yolk, white), milk (and fresh milk prick to prick), soy, wheat, potato, Dp (*Dermatophagoides pteronysssinus*), and cockroach (*Blatella germanica*). In patients older than 5 years, SPT was performed to egg, milk, pollens, fungal spores, mites, and animal fur. Additional foods or aeroallergens were tested based on parental concern.

The study was approved by local ethics committee.

#### Statistical Analysis

SPSS 15.0 package program was used in statistical analysis. The definitions were provided as number and percentage for discrete variables and mean and standard deviation for continuous variables. Chi-square test was used for discrete variables of two unrelated groups. Mann-Whitney-U test was used for constant variables that were not suitable for normal distribution of the two groups. p value < 0.05 was considered statistically significant.

### RESULTS

Two hundred thirty patients were identified as atopic dermatitis during ICD code scanning. Data of 49 patients were insufficient and these patients were not included and 181 patients were enrolled. The files of 181 patients were evaluated retrospectively.

#### Sociodemographic Characteristics

The age of the patients ranged from 2 months to 13 years and 70.2% were male. The characteristics of these patients are detailed in Table 1.

#### Skin Prick Test Results

The skin prick test was performed in all patients and 68 (37.6%) were found to have allergic sensitization. Thirty five (51.5%) patients had sensitization to food, 19 (27.9%) to aeroallaergen, 14 (20.6%) to both food and aeroallergen. The distribution of food sensitization were 4 milk, 2 egg yolk, 6 egg white, 17 egg white and egg yolk, 7 milk and egg, 3 hazelnut, 1 wheat flour and 1 egg yolk with potato. In addition 9 house dust mite, 1 animal, 5 mold, and 12 pollen sensitizations were determined. The median age of the patients sensitive only to food was 17 months (6-120 months), only to aero-allergens, 108 months (12-156 months), and to both food and aero-allergens, was 60 months (6-120 months) (p< 0.0001).

Comparisons of characteristics of patients with and without allergic sensitization are shown in Table 2. IgE level and eosinophil count were higher in the group with allergic sensitization (p< 0.0001, p: 0.002; respectively).

#### Concomitant Allergic Diseases

One hundred fourty six patients had been diagnosed with atopic dermatitis, 29 with atopic dermatitis and asthma, and 6 with atopic dermatitis and allergic rhinitis. There were no statistically significant differences between the patients who had only atopic dermatitis and the patients who had asthma/allergic rhinitis concomitantly

**Table 1. The sociodemographic characteristics of the patients**

| | n= 181 | % |
|---|---|---|
| Gender | | |
| Male | 127 | 70.2 |
| Age (months) | | |
| Minimum-maximum | 2 months-13 year | |
| Median | 24 | |
| Age groups | | |
| < 3 years | 109 | 60.2 |
| 3-6 years | 39 | 21.5 |
| ≥ 6 years | 33 | 18.2 |
| No breast-feeding | 6 | 3.3 |
| Average breast-feeding duration (months) | | |
| Minimum-maximum | 1-48 | |
| Median | 14 | |
| Age at onset of symptoms | | |
| First 6 months | 109 | 60.2 |
| First year | 145 | 80.1 |
| First five years | 177 | 97.8 |
| Duration of follow-up in allergy clinic (months) | | |
| Minimum-maximum | 1-136 | |
| Median | 7 | |
| Positive family history of allergic disease | 41 | 22.7 |
| Consanguineous marriage | 22 | 12.2 |
| Number of sibling | | |
| One | 93 | 51.4 |
| More than one | 33 | 18.3 |
| Number of patients whose sibling was enrolled in daycare | 48 | 26.5 |
| Passive smoking | 59 | 32.6 |
| Pets in the house | 5 | 2.8 |
| Wool use | 90 | 49.7 |

for gender, breastfeeding time, the beginning of the symptoms, passive smoking, history of family atopy, and eosinophil counts. Allergic sensitization was determined in 26 (74.3%) of 35 patients who had asthma/allergic rhinitis with atopic dermatitis, while it was determined in 42 (28.8%) of 146 patients who had only atopic dermatitis (p< 0.0001) (Table 3).

## DISCUSSION

In the present study, the clinical and laboratory characteristics and concomitant other allergic disease of 181 children with atopic dermatitis were evaluated retrospectively. Of these patients, 146 had been diagnosed with atopic dermatitis, 29 with atopic dermatitis and asthma, and 6 with atopic dermatitis and allergic rhinitis. Aeroallergen and/or food allergen sensitization was found in 68 (37.6%) patients. The percent of peripheral blood eosinophils and IgE level were significantly higher in the sensitized group. The allergic sensititization rate was significantly higher among patients who had concurrent asthma/allergic rhinitis.

The onset of atopic dermatitis is within the first 6 months of life in 45% of all cases, during the first year in 60%; and before 5 years of age in 85%[1]. In our study, our patients' age at onset was younger than reported in the literature. In 60% of our patients, the onset was within the 6 months of life and before 5 years of age in 97.8%. Literature reveals no significant difference between boys and girls for prevalence rates[7]. However, in our study, the prevalence of atopic dermatitis was higher (72.2%) in boys.

Atopic dermatitis is a complex genetic disease that arises from gene-gene and gene-environment interactions. There is a strong genetic predisposition in 30% to 50% of children who have one affected parent[1,2]. Of the parents of our patients, 41 (22.7%) had a history of allergic disease in the family.

In children, a transient form of atopic dermatitis has been shown with low IgE serum levels without any detectable sensitization. Nevertheless, some patients (extrinsic form) have increasing IgE serum levels and develop sensitizations against allergens later in life[6]. Elevated total serum IgE has been determined in 70-80% of patients with atopic dermatitis. On the other hand, a normal total serum IgE does not preclude the diagnosis of atopic dermatitis[10]. Consistent

**Table 2. Comparison of patients with and without allergic sensitization**

| | Sensitized n= 68 n (%) | Not sensitized n= 113 n (%) | p |
|---|---|---|---|
| Gender | | | |
| Male | 47 (69) | 80 (70) | 0.469* |
| Age at onset of symptoms | | | |
| Minimum-maximum | 1-84 | 1-72 | 0.772** |
| Median (months) | 5.5 | 5 | 0.653** |
| Average breast-feeding duration (months) | 14 | 14 | 0.341* |
| Positive family history of allergic disease | 17 (25) | 24 (21.2) | **< 0.0001*** |
| Associated asthma or rhinitis | 26 (38.2) | 9 (8) | |
| IgE (IU/mL) | | | |
| Minimum-maximum | 2-2170 | 2-907 | **< 0.0001**** |
| Median | 111 | 18 | |
| Eosinophilia (≥ 4%) | 38 (63.3) | 39 (38.6) | **0.002*** |

* Chi-square test
** Mann-Whitney U test

**Table 3. Comparison of the characteristics of the patients having asthma/allergic rhinitis with atopic dermatitis and the patients who had only atopic dermatitis**

| | Atopic dermatitis n= 146 n (%) | Atopic dermatitis + Asthma/Allergic rhinitis n= 35 n (%) | p |
|---|---|---|---|
| Age (months) | | | |
| Minimum-maximum | 2-120 | 6-156 | **0.017**** |
| Median | 24 | 48 | |
| Gender | | | |
| Male | 101 (69.2) | 26 (74.3) | 0.682* |
| Positive family history of allergic disease | 30 (20.5) | 11 (31.4) | 0.181* |
| Allergic sensitization | 42 (28.8) | 26 (74.3) | **< 0.0001*** |
| IgE (IU/mL) | | | |
| Minimum-maximum | 2-907 | 2-2170 | **0.004**** |
| Median | 32.2 | 68.5 | |

* Chi-square test
** Mann-Whitney U test

with literature, in our patients, serum IgE levels were significantly higher in patients with allergen sensitization. Eosinophilia in patients who have atopic dermatitis is a nonspecific finding and that can be seen in patients who have asthma, allergic rhinitis, and other diseases[1]. In a recent study, however, it has been shown that eosinophilia plays a role in persistence of symptoms[11]. Seventy seven of our patients had eosinophilia. Elevated serum eosinophil count was higher among children with allergic sensitization.

In atopic dermatitis, 60-80% of patients are reported to have IgE mediated sensitization to foods, aeroallergens or both[1]. The atopy rate was lower in our patients as 37.6%. Food allergy plays an important immunopathogenic role in 30% to 50% of young children with atopic dermatitis. Most children who have food allergy react to only one or two of the most common allergens such as egg, cow's milk, nut, peanut, soy, and wheat. Food allergen sensitization is also predictive for persistence of symptoms throughout childhood[6]. Food allergy (51.5%) was the most common type of sensitization in our patients. The majority of our patients were sensitive to egg and milk. Aeroallergens such as house dust mites, animal dander, and pollens might cause exacerbations of atopic dermatitis[2]. Pollens and house dust mite were the most frequently determined aeroallergens among our patients.

The protective effect of breastfeeding is controversial[2]. The American Academy of Dermatology Guidelines Task Force reviewed the subject in 2004 and found no conclusive evidence that exclusive breastfeeding influences the development of atopic dermatitis[5]. In high-risk infants, exclusive breastfeeding for the first 6 months of life is recommended[2]. In one study, it was shown that breastfeeding might not always be beneficial in allergy prevention in some high-risk infants[12]. In our study, except 6 patients, all the patients had been breastfed. The mean time for breastfeeding was 14 months.

Atopic dermatitis is more prevalent in children who belong to families with a smaller size and higher socioeconomic class. Likewise 81.7% of our patients were the only child of the family or had only one sibling, and 26.5% had a sibling enrolled in daycare. The role of passive tobacco smoke exposure in atopic dermatitis is inconclusive[6]. Fifty nine (32.6%) of our patients were reported passive-smoking. Furthermore, wool is an irritant, and half of our patients were using wool.

Atopic dermatitis may be accompanied by asthma in childhood, or atopic dermatitis patients may develop asthma in later stages of life. The term atopic march has been used to explain the sequential development of dermatitis, allergic rhinitis and asthma. One third of children with atopic dermatitis before age 4 will develop asthma by 6 years of age or older[13]. Children with atopic dermatitis have been reported to have asthma or rhinitis frequently (respectively 34.1% and 57.6%)[14]. In the study by Yüksel et al. the prevalence of concomitant rhinitis was 1.9% and asthma, 28.1% in children with atopic dermatitis[15]. In our study, 19.3% (16% asthma and 3.3% allergic rhinitis) of the patients had asthma and/or allergic rhinitis concurrently.

The prevalence rates of atopic disease in the children of our country have been reported to be as follows: asthma, 5.6%; allergic rhinitis, 23.2%, and atopic dermatitis, 5.0%[16]. In another study by Yüksel et al. the prevalence rate of current atopic dermatitis was 3.2%; current allergic rhinitis, 14.5%, and the rate of physician diagnosed asthma in those older than 3 years were 7.9% [15]. In our study, the prevalence rate of asthma (16%) was higher in the sensitized atopic dermatitis group than in the normal population. In the sensitized group the rate of concurrent asthma or rhinitis was 38.2%, while in not sensitized patients, it was 8%. The rate of concurrent asthma in not sensitized patients was similar to the rate in the normal population.

Limitation of our study was its retrospective nature. More cohort studies are needed to unravel the factors associated with development of asthma/allergic rhinitis in children with atopic dermatitis.

In conclusion, the progression of atopic dermatitis into asthma/allergic rhinitis is complex. Both genetic and clinical factors contribute to the progression and there is not one way. Our results have shown that the presence of allergic sensitization in atopic dermatitis is an important marker for coexisting asthma or rhinitis.

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