

## Effects of wheezing in early childhood in the development of allergic rhinitis in later years

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**Background:** Studies on the long-term effects of wheezing in infancy have particularly focused on asthma. There isn't adequate information about the effects of wheezing in the development of allergic rhinitis in later years.

**Objective:** In this study, children with wheezing in the first year of life were investigated in terms of allergic rhinitis after five years of age.

**Methods:** The study consisted of children with early-transient wheezing or persistent wheezing. The study groups were evaluated in terms of allergic rhinitis with physical examination and a questionnaire translated from International Study of Asthma and Allergies in Children (ISAAC) questionnaire after five years of age.

**Results:** The study included 50 children; 23 (46%) had early-transient wheezing and 27 (54%) had persistent wheezing. The symptoms of allergic rhinitis were reported in 13 (48%) of children with persistent wheezing but in none of children with early-transient wheezing ( $p < 0.05$ ). Skin prick tests showed positive results in 4.3% of children with early-transient wheezing and in 48.1% of children with persistent wheezing ( $p < 0.05$ ).

**Conclusion:** Persistent wheezing, but not early transient wheezing seems to be a risk factor in the development of allergic rhinitis in children after five years of age.

**Key words:** Wheezing; Asthma; Allergic rhinitis; Childhood

### INTRODUCTION

The progression of atopic disorders, generally from eczema in early childhood to allergic rhinitis and asthma in later childhood has been described as "atopic march" [1]. But, the development of a particular allergic disease does not necessarily follow

this classical paradigm of the atopic march and any atopic disorder may precedes the others. Wheezing, as an important health problem among young children affect nearly half of the children in their first year of life [2]. The relationship between early childhood wheezing and asthma has been studied in detail [3, 4] and for identification the characteristics and risk

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factors associated with children that experience wheezing in early ages, some wheezing phenotypes have been defined [2]. To our knowledge, the effects of wheezing-without other atopic diseases such as atopic dermatitis-in the development of allergic rhinitis have never been investigated before.

The aim of this study was to investigate the effects of two types of wheezing in early life in the development of allergic rhinitis in later childhood.

## MATERIALS AND METHODS

The study consisted of children who had been diagnosed with early-transient wheeze or persistent wheeze in their first year of life and followed-up until they were older than five years of age in various institutions in Istanbul. Early-transient wheeze was described as “wheezing during the first three years, but no wheezing in the previous 12 months at age five.” Persistent wheeze was described as “wheezing during the first three years, and wheezing in the previous 12 months at age five” [2]. Children with atopic dermatitis or children with wheezing due to any organic cause (e.g., cystic fibrosis, gastroesophageal reflux disease, immune deficiencies, etc.) were excluded. Children were seen and examined thoroughly every 2–4 months and their sensitivity to environmental allergens and frequently consumed foods were investigated by skin prick tests in addition to total IgE level measurement in the end of five years of age.

Skin prick tests were performed with mixed extracts of certain grasses, trees, and weeds in addition to milk, egg, *Candida albicans*, and a mixture of *Dermatophagoides pteronyssinus* plus *Dermatophagoides farinae* (Laboratoire des Stallergenes, Fresnes Cedex, France). Skin prick tests were performed on the volar aspect of the forearm using Stallerpoint needles (Laboratoire des Stallergenes). Histamine phosphate and buffered saline were used as the positive control and negative control respectively. The cutaneous reactions were read after 15 minutes and were evaluated according to the size of wheal and erythema. Skin prick tests were defined as positive if the mean wheal diameter was at least 3 mm larger than the negative control [5].

The children were examined in detail especially in terms of signs and symptoms of allergic rhinitis and asthma after five years of age. In addition, a questionnaire translated from International Study of Asthma and Allergies in Children (ISAAC) questionnaire were filled by the parents [6]. The diagnosis of allergic rhinitis was

based on history, physical examination and results of skin prick tests [7]. The study was approved by the Ethics Committee of Maltepe University School of Medicine.

## Statistical analyses

Descriptive statistics were provided for the numeric and categorical variables using means, standard deviations and percent distributions where required. Chi-square and Fisher tests were used for the comparisons of data. Student *t*-test was used for the analysis of normally distributed data and Mann-Whitney U test was used for others. Analyses were performed with SPSS ver. 17.0 (SPSS Inc., Chicago, IL, USA).  $p < 0.05$  was considered statistically significant for tests.

## RESULTS

A total of 50 children (14 females) were included in the study; 23 (46.0%) of which had early transient wheezing and 27 (54.0%) had persistent wheezing (Table 1). The mean follow-up period was 4.8 years. Thirteen percent of children with early transient wheezing and 44.4% of persistent wheezing had at least one parent with allergic diseases.

The symptoms of allergic rhinitis were reported in 13 (48.0%) of children with persistent wheezing but in none of children with early transient wheezing ( $p < 0.05$ ). Skin prick tests have given positive results in only one case (4.3%) of children with early transient wheezing and in 13 (48.1%) of children with persistent wheezing ( $p < 0.05$ ). Allergic rhinitis was diagnosed in 8 of children with persistent wheezing and positive skin prick tests (61.5%). Cases were most commonly allergic to house dust mites and foods (Table 1).

## DISCUSSION

There has been a significant increase in the frequency of all allergic diseases, especially of food allergy and asthma in recent years [8, 9]. Allergic rhinitis is another common allergic disease with a frequency between 10% and 40% in the general population with a considerable variability among countries and regions [10]. The symptoms of allergic rhinitis usually develop before age six in 40% of cases and before age 20 in 80% of cases [11]. Although many factors have been implicated in the increase of allergic diseases,

**Table 1.** Some demographic, clinical, and laboratory findings of children with wheezing

Feature	Early transient wheezing	Persistent wheezing	p value
Number	23	27	
Gender (male/female)	6/17	8/19	
Age at first wheezing (mo)	10.0 ± 4.8	13.0 ± 6.2	> 0.05
Age at present (yr)	6.3 ± 0.83	6.11 ± 0.93	> 0.05
Duration of wheezing (yr)	1.7 ± 0.6	4.2 ± 0.87	< 0.05 <sup>*</sup>
Allergic disease in parents (%)	3 (13.0)	12 (44.4)	< 0.05 <sup>†</sup>
Allergic disease in sibling (%)	3 (13.0)	4 (14.8)	
Total serum IgE (kU/L)	11.3 ± 25.8	62.8 ± 66.4	< 0.05 <sup>†</sup>
Positive skin prick tests (%)	1 (4.3)	13 (48.1)	< 0.05 <sup>†</sup>

\*Mann Whitney U test. †Chi-square test.

the exact cause has not been well elucidated yet. Genetics and familial history, sensitization to food allergens in early life, exposure to inhaled allergens, outdoor and indoor air pollution, doctor-diagnosed eczema and recurrent wheeze are the most important risk factors in the development of allergic rhinitis [12].

Another factor responsible for the increase in allergic diseases is the sequential development of allergic disease manifestations during early childhood is the process referred to as “atopic march” [13]. The classical way of the atopic march is usually from atopic dermatitis towards asthma and allergic rhinitis [14].

The emergence of signs and symptoms related to allergic rhinitis in 50% of our cases with persistent wheezing makes it necessary to monitor the remaining of the children in terms of similar symptoms and signs in the subsequent years [11]. On the other hand, it seems that transient early wheeze is not associated with impaired lung function [15] and therefore is not a risk factor for the sensitization to environmental allergens and development of allergic rhinitis.

Mixture of house dust mites was the leading cause of sensitivity among our cases with persistent wheezing and it was followed by the foods. Aeroallergens are very often implicated in the development allergic rhinitis and asthma [16]. Since most of our children (61.5%) with persistent wheezing were allergic to any antigen this may contribute to the development of allergic rhinitis in these children.

Any allergic disease among the parents of children with persistent wheezing (44.4%) also seems to be an important risk factor in the development of allergic rhinitis in this group [17]. Allergic rhinitis is closely related to other atopic diseases especially atopic dermatitis and asthma [18, 19]. Since atopic dermatitis has

been shown as a risk factor in the development of allergic rhinitis in previous studies [20], the children with atopic dermatitis were excluded from our study group to see the effects of wheezing alone in the development of allergic rhinitis.

Although asthma and allergic rhinitis are very common in the community alone they also contribute to the development of each other and generally rhinitis precedes the development of asthma [21]. In most of the studies on the relationship between allergic rhinitis and asthma, the effect of allergic rhinitis in the development of asthma has been emphasized [22]. Rhinitis has generally been accepted as a significant risk factor for the development of asthma both in atopic and nonatopic individuals [23]. On the other hand, there are very few studies on the effects of asthma in the development of allergic rhinitis. Greisner et al. [24] evaluated college students who have been diagnosed with asthma or allergic rhinitis after 23 years and reported allergic rhinitis in 85.7% among asthmatics and asthma in 21.3% of those with allergic rhinitis. Eriksson et al. [25] also reported similar proportions: a 64% prevalence of allergic rhinitis in asthmatic patients and a 20% prevalence of asthma in rhinitis patients. According to the results of The Tucson Children’s Respiratory Study, children whose rhinitis began in the first year of life had more respiratory symptoms at age 6 and were more likely to have a diagnosis of asthma [26].

Some researchers working on the relationship between asthma-rhinitis have suggested a two-way relationship between bronchial and nasal mucosa by which these two conditions may influence each other [27, 28]. Some others proposed that there is an epithelial-mesenchymal tropic unit which functions from nose towards lungs [29]. We think the development of allergic

rhinitis in our study group with persistent wheezing is a result of a mechanism similar to asthma-allergic rhinitis relationship. In addition, development of sensitivity to environmental allergens may also have contributed to development of allergic rhinitis in these children.

The main limitation of our study is the less number of the subjects. Another limitation is the shortness of the follow-up period. So, we need more long-term studies with more subjects.

In conclusion, transient early wheeze doesn't seem to be a risk factor in the development of allergic rhinitis in later childhood among our patients. On the contrary, persistent wheeze might contribute to the occurrence of the allergic rhinitis in children older than five years of age.

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