

## Atopy and House Dust Mite Sensitization as Risk Factors for Asthma in Children

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Asthma is commonly described as an atopic disease in childhood, but some cases of this disorder do not fit this description. The aim of this study was to evaluate the frequency of atopy, asthma, and sensitization to house dust mites in children with allergic symptoms. This study was performed at the Severance Hospital of Yonsei University with patients who visited the allergy clinic for evaluation of nonspecific upper respiratory symptoms, typical symptoms of asthma, or a general health workup. The patients were divided into three age groups: 0-3 years (group 1), 4-7 years (group 2), and 8-12 years (group 3). Of the 1,244 children examined, 844 (67.8%) were atopic and 400 (32.2%) were non-atopic. The frequency of atopy and asthma increased with age. Asthma was diagnosed in the same proportion (64%) of atopic and non-atopic children. As risk factors for asthma symptoms, the positive values of house dust mite (HDM) sensitivity were significantly increased in groups 1, 2, and 3 to 53.5%, 68.9%, and 80.2%, respectively. A significant difference between the percentage of asthmatics sensitized to HDM and that of asthmatics not sensitized to HDM was found only in group 3. In conclusion, asthma is related to atopy with increasing age, and house dust mite sensitization seems to be an important determinant of asthma in older children in Korea.

**Key Words:** Asthma, atopy, house dust mite

### INTRODUCTION

Asthma is one of the most common disorders

in children. The prevalence of childhood asthma has been on the rise over the last decade.<sup>1</sup> Although some studies noted that the prevalence of asthma has stabilized,<sup>2</sup> the incidence is increasing in several Westernized Asian countries. Among Korean adolescents, the overall lifetime prevalence of wheeze was 12.8% in 2000 and the prevalence of asthma symptoms has increased each year from 1995 to 2000.<sup>3</sup>

Asthma is commonly recognized as an atopic disease.<sup>4</sup> There is considerable evidence for the strong relationship between allergic sensitization and atopic disorders such as asthma, eczema, and rhinitis.<sup>5</sup> However, the role of atopy can be overestimated, because environmental factors such as respiratory infections and exposure to allergens can cause asthma symptoms, particularly during the first year of life.<sup>6</sup>

Identification of factors that could predict the development of asthma in children is useful for early intervention, because atopic disorders usually manifest for the first time in childhood and often lead to chronic disease that may continue into adulthood.<sup>7</sup> Studies have been carried out in different communities, and they have confirmed that sensitization to indoor allergens, especially to house dust mites (HDM), is a major risk factor for asthma.<sup>8,9</sup> We previously reported on the correlation between specific IgE of inhalant allergens such as HDM and pulmonary function in children with asthma.<sup>10</sup>

The aim of this study was to evaluate the frequency of atopy, asthma, and sensitization to house dust mite in children who visited an allergy clinic.

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## MATERIALS AND METHODS

### Study populations

In a cross-sectional retrospective survey lasting 26 months (November 2001-December 2003), we studied 1244 children who came to our allergy clinic in Seoul for a general health workup or with physician-referred or self-reported symptoms of atopic disease. We included in the study children for whom a diagnosis of asthma, allergic rhinoconjunctivitis, or atopic dermatitis was confirmed by a pediatric allergologist. We divided the patients into three age groups: 0-3 years (group 1), 4-7 years (group 2), and 8-12 years (group 3).

### Diagnostic criteria for bronchial asthma and allergic disease

The diagnosis of asthma was made on the basis of American Thoracic Society (ATS) criteria.<sup>11</sup>

The children with asthma reported having typical wheezing or episodic shortness of breath and had a positive response to any question concerned with the following asthma-related symptoms: chest tightness, difficulty in breathing, occasional or persistent wheeze, breathlessness or cough after exposure to cold air or exercise, chest noise while breathing, chronic cough persisting for more than<sup>3</sup> weeks, or nocturnal symptoms that disturb sleep.<sup>12</sup> Children who could not answer any of the questions confidently were excluded from the asthma group.

Atopy was defined by one or more positive specific IgE test of eight common allergens in Korea or total serum IgE level >100 IU/mL. Allergic rhinoconjunctivitis was diagnosed if sneezing, nasal obstruction, watery rhinorrhea, nasal itching,

conjunctival hyperemia or photophobia appeared after exposure to a particular allergen and was unrelated to infection. Atopic dermatitis was defined as a pruritic, chronic or chronically relapsing dermatitis with typical features and distribution according to Hanifin and assessed with the Scrad index.<sup>13</sup>

### Specific IgE test

Specific IgE test was performed on house dust mites (HDM) (*Dermatophagoides pteronyssinus* (Der p.), *D. farinae* (Der f.)), ragweed, *Alternaria*, egg, cow's milk, cockroach, and timothy using the CAP system FEIA (Pharmacia Diagnostics, Uppsala, Sweden). A specific IgE value greater than 0.35 kUA/L was considered positive.

### Statistical analysis

All data analysis was performed using the statistical analysis program SPSS. A chi-square test was used to analyze the difference between proportions. A *p*-value < 0.05 was considered significant. The odds ratio (OR) was calculated to evaluate the independent effect of atopy on the development of asthma. The odds ratio was considered significant when a 95% confidence interval excluded unity.

## RESULTS

In the 1244 children examined, 844 (67.8%) were atopic and 400 (32.2%) were non-atopic. Asthma was diagnosed in 542 (64%) atopic children and in 250 (64%) non-atopic children. In the overall population studied, there was no significant dif-

**Table 1.** Demographics and Classification of the Groups of Children Who Enrolled in This Study (n = 1,224)

Age group (years)	Total patients	Males (%)	Asthma (%)	Atopy (%)
Group 1	424	61%	54.7%	54.7%
Group 2	446	60%	69.5%	71.7%
Group 3	374	55%	78.1%	78.1%
<i>p</i> -value	-	-	0.00	0.02

*p*-values were calculated by the Pearson chi-square test.

Group 1, children between 0 and 3 years of age; Group 2, children between 4 and 7 years of age; Group 3, children between 8 and 12 years of age.

**Table 2.** Percentage of Asthma Cases Attributable to Atopy

Age group (years)	Non asthmatic children		Asthmatic children		Odds ratio (95% CI)
	Patients (n)	Atopy (%)	Patients (n)	Atopy (%)	
Group 1	106/192	55.2	126/232	54.3*	0.97 (0.706-1.523)
Group 2	106/136	77.9	214/310	69.0* <sup>†</sup>	0.63 (0.989-2.540)
Group 3	60/82	73.2	232/292	79.5 <sup>†</sup>	1.42 (0.401-1.541)

*p*-values were calculated by the Pearson chi-square test.

CI, confidence interval.

Group 1, children between 0 and 3 years of age; Group 2, children between 4 and 7 years of age; Group 3, children between 8 and 12 years of age.

\* $\chi^2 = 12.6$ ; <sup>†</sup> $\chi^2 = 8.9$ .

**Table 3.** Association of HDM Sensitization and Asthma

Age group (years)	HDM positive atopic asthmatics		HDM negative atopic asthmatics		Odds ratio (95% CI)
	Patients (n)	HDM positive (%)	Patients (n)	HDM negative (%)	
Group 1	46/86	53.5%*	80/146	54.8% <sup>†</sup>	0.94(0.585-1.511)
Group 2	168/244	68.9%* <sup>†</sup>	46/76	60.5% <sup>†</sup> §	1.44(0.623-1.401)
Group 3	202/252	80.2% <sup>†</sup>	30/40	75.0% <sup>§</sup>	1.34(0.664-2.389)

*p*-values were calculated by Pearson chi-square test.

CI, confidence interval.

Group 1, children between 0 and 3 years of age; Group 2, children between 4 and 7 years of age; Group 3, children between 8 and 12 years of age.

\* $\chi^2 = 6.9$ ; <sup>†</sup> $\chi^2 = 8.4$ ; <sup>‡</sup> $\chi^2 = 0.5$ ; <sup>§</sup> $\chi^2 = 2.52$ .

**Table 4.** Association of HDM-Sensitized Asthma and Atopy

Age Group (years)	HDM positive atopic asthmatics		HDM negative atopic asthmatics	
	Patients (n)	% of total atopy (%)	Patients (n)	% of total atopy (%)
Group 1	46/126	36.5%	80/126	63.5%
Group 2	168/214	78.5%	46/214	21.5%
Group 3	202/232	87.0%*	30/232	13.0%*

Group 1, children between 0 and 3 years of age; Group 2, children between 4 and 7 years of age; Group 3, children between 8 and 12 years of age.

\* $\chi^2 = 56.3$ .

ference between atopic and non-atopic asthmatics.

The frequencies of atopy in age groups 1, 2, and 3 were 54.7%, 72%, and 78%, respectively, and the frequencies of asthma were 54.7%, 69.5%, and 78.1%, respectively. The frequency of atopy and asthma increased with age (Table 1,  $p < 0.05$ ).

In the asthmatic children of groups 1, 2, and 3, the frequencies of atopy were 54.3% (126 of 232 asthmatic children), 69.0%, and 79.5%, respectively, and atopy increased significantly with age (group 1 vs. group 2  $\chi^2 = 12.6$ ; group 2 vs. group 3  $\chi^2 = 8.9$ ). However, there was no significant

association between asthma and atopy in all three groups (Table 2). The percentage of asthmatic children who were HDM-positive increased significantly, especially in group 3 (group 1 vs. group 2  $\chi^2 = 6.9$ ; group 2 vs. group 3  $\chi^2 = 8.4$ ). As risk factors for asthma symptoms, the positive values of house dust mite (HDM) were significantly increased in age groups 1, 2, and 3 to 53.5% (46 of 86 HDM positive children), 68.9%, and 80.2%, respectively. However, a significant difference between the percentage of asthmatics sensitized to HDM and that of asthmatics not sensitized to

HDM was found only in group 3 (Table 4, 87% vs. 13%  $\chi^2 = 56.3$ ). The percentages of HDM-negative asthmatic patients was not significant between groups (Table 3; group 1 vs. group 2  $\chi^2 = .5$ ; group 2 vs. group 3  $\chi^2 = 2.52$ ).

## DISCUSSION

The prevalence of atopy and asthma are increasing in all populations around the world. Higher prevalence rates are reported in more Westernized countries, with wheezing occurring in over 30% of infants in the first year of life,<sup>14</sup> atopy in 40% of children,<sup>15</sup> and physician-diagnosed asthma in over 20% of children. Therefore, it is important to evaluate the risk factors for asthma and the sensitization period after exposure to allergens. It is reported that the sensitization occurs early in atopic children with asthma established before 7 years of age, without any significant changes after this age.<sup>16</sup> But atopy combines with other environmental factors to predispose children to asthma. Before the seventh year of age, the development of asthma depends mainly on factors other than atopy, such as viral respiratory illnesses.<sup>17</sup> The majority of infants with wheezing have transient conditions such as diminished airway function at birth. Non-atopic asthmatics produce IgE directed against unknown antigens of viral origin,<sup>18</sup> a molecular response in which IL-5 could play a key role.<sup>19</sup> Also, in younger children, other factors like food are important in stimulation of allergic symptoms. Han *et al.*<sup>20</sup> reported that, clinically, food sensitization is important in Korean infants and younger children with moderate to severe atopic dermatitis.

We evaluated infants and children who had symptoms of atopic disease to clarify the relationship between atopy and asthma. Although many reports describe a relationship between atopy and asthma, we evaluated this connection further in our country with a large data set. In Korea, the majority of adults and children with allergy are highly sensitized to Der p. and Der f. (house dust mites), and the sensitizing antigens can be causal allergens of asthma. In our study, atopy to some allergens such as HDM may be more important than atopy to other allergens in predisposing chil-

dren to asthma. Early sensitization to mite allergen might lead to asthma and persistent wheeze, especially in high-risk subgroups defined by maternal atopy.<sup>21,22</sup> Continuing exposure to mite allergens causes airway inflammation that leads to the development of asthma in childhood,<sup>23</sup> and several studies have shown that there is a strong relationship between exposure to house dust mite allergens and the prevalence and severity of asthma.<sup>22,24-26</sup> House dust mite allergens may be more potent than other allergens, because they are ubiquitous or because the airborne particles are small and are easily respired. Our data showed a significant correlation between atopic asthma and risk of developing HDM sensitization, especially for children over 8 years. Several cross-sectional studies in older children indicate that specific sensitization to house dust mites is related to dust mite allergen concentrations in mattress dust.<sup>27,28</sup> Cole *et al.*<sup>29</sup> investigated the relationship of dust mite allergen exposure during early life to allergic sensitivity and asthma at 6 to 7 years of age, using a relatively large birth cohort. Although HDM sensitization often occurs in early childhood and is dependent on the level of exposure,<sup>30-32</sup> the incidence of sensitization to inhalant allergen increases with age during the first decade of life. Sporik *et al.*<sup>22</sup> reported that after age 2, the children who later became allergic developed IgG, IgG4, and IgE antibodies to Der p. in parallel with the symptoms. Because the correlation between atopic asthma and HDM sensitization was not as strong in the younger age groups, we should consider other factors in younger children. Sarah *et al.*<sup>33</sup> reported that aeroallergens like house dust mites play little role in the development of wheeze in the first 4 years of life. They concluded that early childhood asthma relied on other genetic and environmental factors such as maternal atopic history and smoking.

As sensitization to HDM depends on exposure to such allergens, it is important to attempt to reduce exposure before the sensitization occurs in early childhood. Lee<sup>34</sup> reported that environmental control of house dust mites is effective in relieving symptoms and reducing peak expiratory flow rate in asthmatic children. We need longer-term follow-up studies to investigate whether the development of asthma can also be prevented by

environmental control of HDM. Furthermore, asthma itself is a heterogeneous disease with many different genetic and environmental determinants, and we should consider other factors such as family history and smoking in future studies.

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