

Investigation of asthma comorbidity in children with different severities of allergic rhinitis

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ABSTRACT

Background: Allergic rhinitis (AR) and asthma comorbidity is widely seen. However, the effects of AR on asthma are more likely to be studied in the literature.

Objective: To investigate the prevalence of asthma in children with AR who are followed-up and to evaluate the effect of asthma on the severity of AR.

Methods: A total of 509 children with AR who were followed-up in the pediatric allergy-immunology department between January 2012 and December 2013 were enrolled in the study. Asthma and AR are diagnosed by using the Global Initiative for Asthma and the Allergic Rhinitis and its Impact on Asthma, respectively. The patients were categorized into two groups according to the presence of asthma. The two groups were compared according to sociodemographic characteristics, clinical features, and laboratory findings. Skin-prick test results, serum immunoglobulin E levels, and the percentage of eosinophils of the patients were evaluated.

Results: A total of 299 of the patients were boys (58.7%) the mean age was 7.2 ± 3.5 years (range, 1.5–18 years). Patients with moderate-severe persistent rhinitis (40.5% of all patients) were the most common rhinitis subgroup. Mild intermittent rhinitis was diagnosed in 17.7%, mild persistent rhinitis in 11.2%, and moderate-severe intermittent rhinitis in 30.6% of the patients. Two hundred seventy-one children with AR (53.2%) also had concomitant asthma. The patients were categorized into two groups: AR-asthma comorbidity group (group I) and AR-only group (group II). There was no significant difference between these two groups when compared with the sex, age, familial atopy, exposure to smoke, and severity of AR ($p > 0.05$). The duration of illness, immunoglobulin E levels, number of positive sensitivity, sensitivity to house-dust mites, sensitivity to cockroaches, and polysensitization were significantly higher in the AR-asthma comorbidity group ($p < 0.05$).

Conclusion: This study showed that asthma comorbidity had no effect on the severity of AR. However, it was also shown that the majority of children with AR had asthma comorbidity. For these purposes, the presence of asthma should be investigated in children with AR, independent of severity.

(Am J Rhinol Allergy 30, 186–189, 2016; doi: 10.2500/ajra.2016.30.4315)

Allergic rhinitis (AR) and asthma are global health problems that cause major disability worldwide. Both AR and asthma are systemic inflammatory conditions seen often in comorbidity. Interactions between the lower and the upper airways are well known and have been extensively studied since 1990. More than 80% of patients with asthma have rhinitis, and 10–40% of patients with rhinitis have asthma. Most patients with asthma have rhinitis, which suggests the concept of “one airway one disease,” although there are differences between rhinitis and asthma.^{1–3} It is an expected issue that these disorders affect each other due to the high comorbidity.

Rhinitis is a risk factor for asthma, independent of allergy.^{4–6} The study by Guerra *et al.*⁵ showed that rhinitis increased the risk of development of asthma by ~3 times both among patients with atopy and patients without atopy. It also was shown that the presence of AR commonly exacerbates asthma and increases the frequency of asthma attacks, emergency department visits, and hospitalizations for asthma.^{1–3,7} An adequate number of studies that observed AR and its impact on asthma have been conducted, and a guideline (Allergic Rhinitis and its Impact on Asthma [ARIA]) was formed.¹ However, the relationship between the severity of AR and asthma in patients with AR was evaluated in fewer studies.^{8–15} These studies have contradictory results, and most of these studies were done in adults.^{8–11}

From the studies that were conducted in children, Ibáñez *et al.*¹² showed that odds ratios (OR) with asthma is not significant between moderate and mild and between severe and moderate AR; however, ORs were significantly associated with persistent versus intermittent and with severe versus mild AR. Dondi *et al.*¹³ evaluated children with pollen allergy and found the relationship between blocker-type

AR and asthma. Studies performed in both children and adult patients showed a correlation between asthma comorbidity and the duration or severity of AR.^{14,15} In this study, I aimed to identify the prevalence of asthma in children with AR and to evaluate the effect on severity of AR.

METHODS

Five hundred nine children with AR who were followed-up in pediatric allergy-immunology department tertiary outpatient clinics between January 2012 and December 2013 were enrolled into the study. A detailed allergy history, including age, familial atopy history, and exposure to cigarette smoke, were recorded. Familial atopy was accepted as a positive sign when allergic disease was seen in first-degree relatives (parents and siblings). AR and asthma were diagnosed by using the international guidelines.^{1,16} AR severity was assessed according to the four ARIA items (sleep; daily activities, sport, leisure; academic performance; and troublesome symptoms) and were classified according to different severity levels, such as mild (no affected items) or moderate-severe (one or more affected items) based on the ARIA classification. The duration of AR was classified according to the ARIA guidelines as follows: persistent (symptoms that last >4 days a week and for >4 weeks) or intermittent (symptoms that last up to 4 days a week or up to 4 weeks). The patients were categorized into two groups by the presence of asthma: AR-asthma comorbidity group (group I) and AR-only group (group II). The study was approved by the ethics committee of Zeynep Kamil Woman and Children's Diseases Training and Research Hospital, and adhered to the principles of Declaration of Helsinki. An oral consent was obtained from all the subjects and/or their parents.

Application and Evaluation of Skin-Prick Test

Skin-prick tests for common aeroallergens (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinea*, mixture of grass pollens, mixture of grain pollens (oats, wheat, barley, corn), mixture of tree pollens, weed-mix pollens, *Alternaria alternaria*, cockroaches (*Blattella germanica*), cat dander, and dog dander (Stallergenes SA, Antony,

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The author has no conflicts of interest to declare pertaining to this article

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Table 1 Demographic characteristics and classification of allergic rhinitis of the patients

Sample size	509
No. boys/girls	299/210
Age, y	
Mean (standard deviation)	7.2 ± 3.5
Minimum-maximum (median)	1.5–18 (6.4)
Familial atopy, no. (%)	228 (44.8)
Exposure to smoke, no. (%)	232 (45.6)
Rhinitis classification, no. (%)	
Mild intermittent	90 (17.7)
Moderate-severe intermittent	156 (30.6)
Mild persistent	57 (11.2)
Moderate-severe persistent	206 (40.5)

France) were performed by using stallerpoint (Stallergenes). Patients with a positive history of food reactions underwent skin-prick tests with the suspected food. Skin-prick tests were applied on the anterior forearm. The patients were considered eligible for the skin test if they had not received antihistamines for at least 1 week. Histamine (10 mg/mL) and physiologic saline solution were used as positive and negative references, respectively. Skin reactions were evaluated at the 20th minute of the application. A positive reaction was characterized as ≥ 3 mm than that of the negative control. If sensitization to a single allergen group was detected, then patients were classified as “mono-sensitized.” If sensitization to different allergen groups was detected, then the patients were classified as “polysensitized.”

Statistical Analyses

Data were analyzed by using the Statistical Package for Social Sciences program (SPSS for Windows 15.0; SPSS Inc., Chicago, IL). Results are given as either mean (standard deviation [SD]) or as mean (SD) (median) according to the distribution. The Student's *t*-test was used for the comparison of normally distributed variables. The χ^2 and Mann-Whitney U-tests were used for non-normally distributed variables. A *p* < 0.05 was considered significant.

RESULTS

Demographic Characteristics and Classification of Rhinitis of the Patients

Two hundred ninety-nine patients (58.7%) were boys, and the mean (SD) age of the patients was 7.2 ± 3.5 years (range, 1.5–18 years). Two hundred twenty-eight patients (44.8%) had familial atopy, and 232 patients (45.6%) had exposure to smoke. The patients with moderate-severe persistent rhinitis (40.5% of all the patients) were the most common rhinitis subgroup. Mild intermittent rhinitis was diagnosed in 17.7%, mild persistent rhinitis in 11.2%, and moderate-severe intermittent rhinitis in 30.6% of the patients. (Table 1).

Comorbidity with Asthma

Asthma comorbidity was observed in 271 children with AR (53.2%). The patients were categorized into two groups: AR–asthma comorbidity group (group I) and AR-only group (group II). One hundred sixty-two patients (59.8%) in group I were boys, and the mean (SD) age of the patients was 7.1 ± 3.2 years (range, 1.5–18 years). One hundred thirty-seven patients (57.6%) in group II were boys, and the mean (SD) age of the patients was 8.3 ± 3.7 years (range, 1.5–17.1 years). There was no significant difference between these two groups when compared with sex, age, history of familial atopy, exposure to smoke (*p* > 0.05). (Table 2).

The comparison of clinical and laboratory findings revealed no significant difference between the groups for severity of AR, percent-

Table 2 Comparison of the sociodemographic characteristics of the groups

	Group I (<i>n</i> = 271)	Group II (<i>n</i> = 238)	<i>p</i>
No. boys/girls	162/109	137/101	0.612*
Age, mean (standard deviation) (median), y	7.1 ± 3.2 (6.3)	8.3 ± 3.7 (6.4)	0.803#
Familial atopy, no. (%)	120 (42.3)	108 (45.4)	0.719*
Exposure to smoke, no. (%)	98 (36.1)	134 (56.3)	0.076*

* χ^2 test.

#Mann-Whitney U test.

age of eosinophils in complete blood count, sensitivity to pollens, sensitivity to dander, and sensitivity to *A. alternata*. However, the duration of illness, serum immunoglobulin E (IgE) levels, the number of positive sensitivity, sensitivity to house-dust mites (HDM), sensitivity to cockroaches, and polysensitization were significantly higher in group I (*p* < 0.05) (Table 3).

DISCUSSION

No relationship between asthma comorbidity and severity of AR was found in this study. There are a limited number of reports that are related to asthma's effect on AR control. Bousquet *et al.*⁸ evaluated the characteristics of persistent and intermittent AR in 591 adult patients and found that the prevalence of asthma was associated with the duration (intermittent versus persistent, *p* < 0.05) and severity of rhinitis (mild versus moderate-severe, *p* < 0.05). The diagnosis of AR was based on a score for AR of ≥ 7 .¹⁷ For this reason, most of the patients whose ARs were classified by using ARIA were persistent (63%) and moderate-severe (76%) rhinitis.

Also, the question “diagnosed asthma” was used to assess asthma. In this study, the results were inconsistent with the Bousquet *et al.*⁸ study, which may be due to the differences in age groups, inclusion criteria, and diagnosis criteria. The study performed by Antonicelli *et al.*,⁹ which also was performed on an adult population, evaluated 1321 patients with AR. The ISAAC questionnaire¹⁸ was used to diagnose asthma in this study. It was shown that both the duration and the severity of AR is not related with the presence of asthma. Another two adult studies also had similar results that implicated no significant difference between AR groups and the presence of asthma.^{10,11} In studies in children, Ibáñez *et al.*¹² evaluated the approach on AR treatment and comorbidities in a Spanish pediatric population. Inclusion criteria of the study were as follows: children with a diagnosis of AR, which was determined by an allergist, children who were 6–12 years old, and children who had symptoms of AR for at least 2 years. Moderate-severe AR was found in 90% of these children. Findings both of asthma and of severity of rhinitis showed that ORs with asthma were not significant between moderate versus mild and severe versus moderate AR, but ORs were significantly associated with persistent versus intermittent and severe versus mild AR.

In this study, the results were inconsistent with the study by Antonicelli *et al.*⁹ The methods to diagnose asthma were not defined, and the modified ARIA classification was used in their study.¹⁹ In addition, their study studied children who were only 6–12 years old. In contrast to their study, this study was of children ages 1.5–18 years old and better projected real life. Another study, performed by Dondi *et al.*¹³ in Italy, evaluated the children who had pollen-induced AR. Patients with AR were grouped by “sneezer” and “blocker.” A relationship was suggested between asthma and blocker-type AR. However, no relationship between asthma and mild and/or moderate-severe or intermittent and/or persistent rhinitis was observed. One study that involved both adult and children populations revealed that there was a relationship between long-term AR (>5 years) and

Table 3 Comparison of clinical and laboratory findings of the groups

	Group I (n = 271)	Group II (n = 238)	p
Duration of disease, mo			0.007*
Mean (SD)	26.3 ± 15.5	22.9 ± 19.7	
Minimum-maximum	3–72	3–120	
Median	24	18	
Severity of allergic rhinitis, no. (%)			0.335#
Mild intermittent	48 (17.7)	42 (17.6)	
Mild persistent	35 (12.9)	22 (9.2)	
Moderate-severe intermittent	87 (32.1)	69 (29)	
Moderate-severe persistent	101 (37.3)	105 (44.1)	
Eosinophils, mean (SD) (median), %	5.3 ± 3.9 (4.6)	4.6 ± 3.4 (3.7)	0.087*
Immunoglobulin E level, mean (SD) (median), IU/mL	558 ± 583 (339)	331 ± 415 (168)	0.001*
Positive sensitivity, mean (SD) (median), no.	2.61 ± 1.3 (2)	2.19 ± 1.1 (2)	0.001*
Sensitivity, no. (%)			
To house-dust mite	247 (91.1)	196 (82.6)	0.003#
To pollens	80 (29.5)	69 (29)	0.896#
To dander	57 (21)	40 (16.8)	0.226#
To <i>A. alternata</i>	17 (6.3)	7 (2.9)	0.077#
To cockroaches	34 (12.5)	11 (4.6)	0.002#
Polysensitization, no. (%)	230 (84.9)	171 (71.8)	0.001#

SD = standard deviation.

*Mann-Whitney U test.

χ^2 test.

asthma.¹⁴ Despite the contradictorily findings, these results should be taken into consideration because this study was performed within a single center with patients of various ages who were followed-up by a single allergist.

In this study, 53.2% of children with AR also had concomitant asthma. The incidence of asthma in cases with AR varied from 5.33 to 49.5%.^{8–14} Changes of incidences were due to criteria such as age, asthma and/or AR diagnostic criteria, single- and multicentric, the kind of sensitivity, and the study region. To my knowledge, this is the first study in my country to investigate the presence of asthma in persons with AR and the relationship between asthma and AR severity. According to the ARIA guidelines, asthma prevalence in patients with AR is 10–40%.¹ However, these percentages were acquired from studies that were conducted in adults, and prevalence studies in children are rare. This study revealed some information about this area.

In this study, a comparison of the cases showed that children with asthma were likely to have a higher duration of AR, IgE levels, HDM sensitivity, sensitivity to cockroaches, and polysensitization of children who were not diagnosed with asthma. The relationship between asthma and AR duration was also demonstrated in other studies.^{8,13,14} Higher levels of IgE were not evaluated in other studies.^{8–15} Although the IgE level is not recommended to screen and diagnose allergic diseases,¹ I detected higher levels of IgE in children who had both asthma and rhinitis.

Further studies are required to enlighten the role of IgE in the presence of asthma in patients with AR. HDM and cockroach sensitivities were found to be the only two sensitivities that are higher in patients with both asthma and rhinitis. Antonicelli *et al.*⁹ found similar findings. They found that indoor allergens (HDM and cat dander) were most likely to be a risk factor for asthma. Hong *et al.*¹⁴ found no difference in terms of HDM sensitivities. According to the study by Hong *et al.*,¹⁴ patients with AR had a higher sensitivity to *Artemisia vulgaris* and ragweed pollen compared with the patients with both AR and asthma. Cockroach sensitivity was not evaluated. Although this study showed that the cockroach sensitivity was higher in rhinitis with asthma, it may be due to the cross-reaction that occurs in HDM and cockroach allergens.²⁰ It is hard to distinguish this because I could not evaluate specific IgE for cockroach. The study by Antonicelli *et al.*⁹

revealed the relationship between the presence of asthma and allergic sensitization. This study showed that the prevalence of asthma was significantly higher in patients who were polysensitized (49.3%) than in the patients who were monosensitized (39.3%) ($p = 0.002$). In this study, polysensitization was more likely to be seen in patients who had both asthma and AR, which correlated with the study by Antonicelli *et al.*⁹

This study had some limitations. The main limitation was that the study groups did not reflect the whole community because I recruited the patients from our allergy clinic. Another limitation was the lack of assessment by objective measures for the severity of AR, such as symptom scores and/or visual analog scales. Despite these deficiencies, this study had some positive aspects: broad coverage for all the childhood period and a high number of cases.

CONCLUSION

This study showed that asthma comorbidity had no effect on the severity of AR. However, it also showed that the majority of children with AR had asthma comorbidity. The presence of asthma should be investigated in children with AR, independent of severity.

ACKNOWLEDGMENTS

The author thanks fellows of pediatrics in Zeynep Kamil Woman and Children's Diseases Training and Research Hospital for their help in data collection of the patients.

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