
The risk of adenoid hypertrophy in children with allergic rhinitis

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Background: Adenoid hypertrophy (AH) may cause significant morbidity in children but its relationship to allergic rhinitis (AR) has not been studied.

Objective: To determine the risk factor of AH in patients with AR.

Methods: We studied 315 children (ages 1 to 18 years) who had AH and AR. We compared them with 315 age-matched controls who had AR alone. To identify risk factors, they were divided into four groups according to age and clinical parameters, including the prevalence of otitis media, sinusitis, lower respiratory infection, exposure to smoking, sleep disorders, use of antihistamine/decongestants, and results of allergy skin testing.

Results: The prevalence of upper or lower respiratory infections was higher in the group with AR and AH, but not in all age groups. A high prevalence of exposure to smoking and skin test reactivity against house dust mites were found in both groups. However, the prevalence of positive reactivity to molds was significantly higher in the group with AH and AR (P ranged from 0.013 to <0.0001 and the relative risk ranged from 1.609 to 2.375). Further, the risk of AH was positively correlated with number of skin test reactivity to mold spores (P ranged from 0.0035 to 0.0001). Positive skin test reactivity to animal danders or seasonal allergens failed to predict the risk of AH.

Conclusions: Sensitivity to mold allergens is an important risk factor for AH in children with AR; therefore, early prevention of exposure to molds may help reduce occurrence of AH.

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INTRODUCTION

The term adenoid normally refers to the nasopharyngeal tonsil. The tonsils are part of the lymphoid tissues that circle the pharynx and are known collectively as the Waldeyer ring. The ring consists of the lymphoid tissue on the base of the tongue (lingual tonsil), the two palatine tonsils, the adenoids, and the lymphoid tissues on the posterior pharyngeal wall. This tissue normally serves as a defense against upper respiratory infections, but it may become a site of acute or chronic infection. Disturbances of the adenoids tend to parallel those of the palatine tonsils,

but hypertrophy and infection may occur separately. The soft adenoid structure, which is normally widespread in the nasopharynx, especially on the posterior wall and the roof, undergoes hypertrophy, and masses of varying size are formed. These masses may almost fill the vault of the nasopharynx, interfering with the passage of air through the nose, obstructing the Eustachian tube, and blocking the clearance of nasal mucus. Persistent rhinitis is often cited as a risk factor for developing adenoid hypertrophy (AH), but this relationship has not been studied extensively. We reviewed a total of 315 children (from 1989 to 1999) diagnosed with AH. All of them had clinical history and signs of perennial allergic rhinitis (AR). We examined their clinical parameters and determined the risk of AH by comparing them with children who had only symptoms and signs of AR.

METHOD

Study Population

From 1989 to 1999, we registered consecutively a total of 315 pediatric patients (from age 1 to 18 years) with a diagnosis of AH confirmed radiologically. All the patients were seen in the allergy clinic initially for evaluation of AR. AR was diagnosed by history, physical findings, and skin test results, which are described below. To identify the risk factors of AH among patients with AR, we also randomly selected and reviewed records of a total of 315 patients who served as controls. The controls were referred for evaluation of AR and for possible sinusitis. All had sinus x-ray films and AH were ruled out by study of lateral view of the neck. They were matched in age and sex with the patients who had AH.

Study Design

AH was defined radiologically according to Cohen et al,¹ with a slight modification. In this study, we defined AH as a narrowing of the airway attributable to adenoid mass by as much as two-thirds of the airway caliber, which is the distance between the posterior to anterior pharyngeal wall. AR was defined clinically as the presence of a combination of symptoms including rhinorrhea, nasal congestion, postnasal drip, loud snoring, mouth breathing, and the presence of physical signs including the presence of allergic shiners, noticeable swelling of turbinates, and congested eyes for at least 3 months a year.

Patients were divided into four groups by age: group I, 1 to 3 years ($n = 35$); group II, 4 to 6 years ($n = 148$); group III, 7 to 12 years ($n = 88$); and group IV, 12 to 18 years ($n = 44$).

All patients had skin test using the percutaneous method for airborne al-

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lergens including house dust mites, molds (a total of 14), animal danders, cockroaches, and seasonal pollens (trees, grasses, and weeds). A positive reaction was defined as a wheal >3 mm larger than that of the negative control (saline) and was scored as 1+. A wheal 2 mm larger than that of the 1+ reaction was scored as 2+ or above. The frequency of the following symptoms as clinical parameter was compared between groups with and without AH:

The frequency of otitis media (more than six occurrences per year). Otitis media was defined as the presence of hyperemic, opaque, bulging tympanic membrane of poor mobility or purulent otorrhea;

The frequency of sinusitis (more than five occurrences per year in the last 3 years). Sinusitis was defined by the presence of at least one of the radiologic findings: presence of air-fluid level, mucosal thickening of at least 4 mm, or complete opacity of at least one of the sinus cavities;

The frequency of lower respiratory infection (more than three occurrences

of bronchitis, croup, or pneumonia per year in the last 3 years);

Exposure to smoking in the home (average of more than 2 weeks a month in the last 3 years);

The prevalence of sleep disorders (a positive history confirmed by physicians);

The frequency of the use of topical or systemic antihistamine/decongestant (more than 2 weeks in a month in the last 3 years); and

The results of allergy skin test.

Statistical Analysis

Fisher's exact test was used to compare the clinical parameters and skin test results between the groups with and without AH. GraphPad Prism (GraphPad Software, Inc, San Diego, CA) was used to calculate the significance of difference (*P* values) and relative risk for AH.

RESULTS

The statistical differences between the two groups with and without AH for each clinical parameter are summa-

rized as follows and illustrated in Figures 1 to 3.

Otitis Media (> Six Episodes a Year)

The group with AH had a significant increase of otitis media in children under the age of 6 ($P < 0.009$), but not in the group above the age of 6 (Fig 1A). The relative risk in the high-risk group ranged from 1.318 (95% confidence interval [CI] 1.185 to 1.465) to 1.455 (95% CI 1.106 to 1.913).

Lower Respiratory Infections (> Three Episodes a Year)

The patients with AH had a higher frequency of lower respiratory infections (Fig 1B). A statistically significant difference was seen in groups II, III, and IV with *P* values ranging from 0.0005 to 0.0042. Only in patients under the age of 3 was there no statistical difference. Patients with AH had a relative risk (95% CI) in the different groups as follows: group II, 2.5 (1.332 to 4.692); group III, 2.545 (1.353 to 4.789); and group IV, 4.750 (1.758 to 12.84).

Sinusitis (> Five Episodes a Year)

A statistically significant higher frequency of sinusitis was found in groups II ($P = 0.04$) and III ($P < 0.0001$) in children with AH, but not in the other groups (Fig 1C). The relative risk and 95% CI were as follows: group II, 1.209 (1.018 to 1.437) and group III, 1.349 (1.176 to 1.548).

Exposure to Smoking (>2 Weeks a Month)

The exposure to smoking was frequent in both groups (Fig 1D). However, it seems that only in group II was exposure to smoking higher in children with AH ($P = 0.0144$). Its relative risk and 95% CI was 1.373 (1.073 to 1.756).

Sleep Disorders

The children with AH showed a higher prevalence of sleep disorders than those without (Fig 2A). The difference in the prevalence of sleep disorders was statistically significant in all age groups (P from 0.0085 to <0.0001). The relative risk and 95% CI in the children with AH were as follows: group I, 2.500 (1.550 to 4.033); group

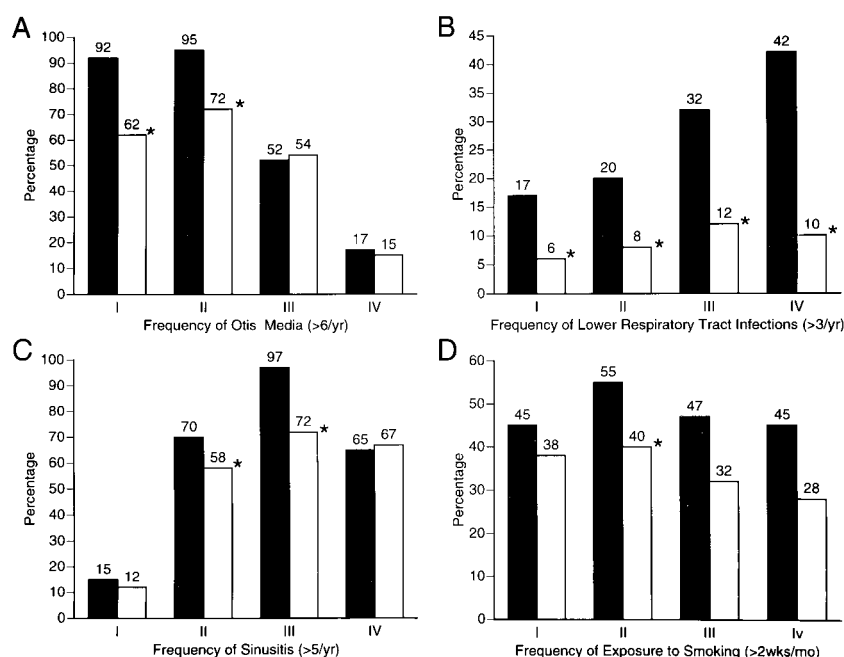


Figure 1. Comparison of the frequency of otitis media (A), lower respiratory infections (B), sinusitis (C), and exposure to smoking (D) between patients with (shaded bar) and without (white bar) AH. I, II, III, and IV within the graph represent the different age groups.

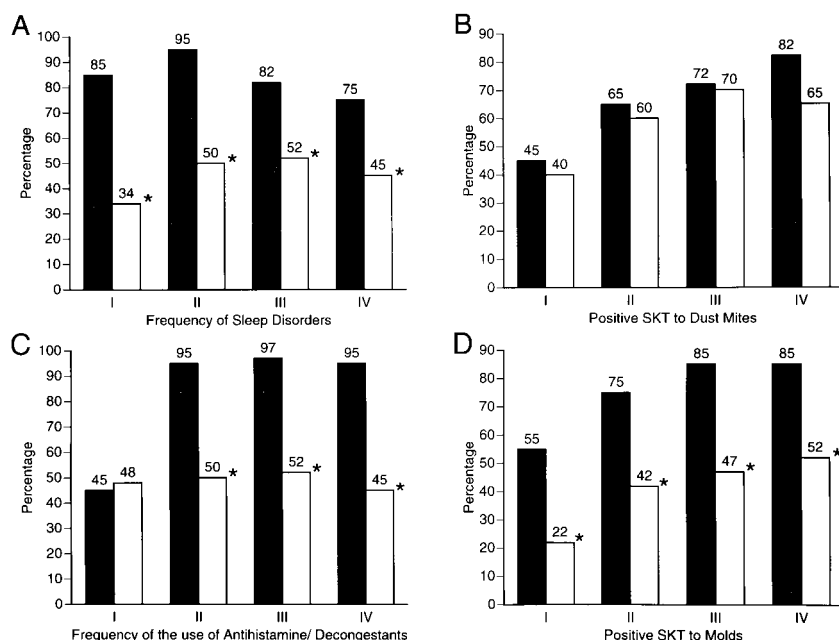


Figure 2. Comparison of the frequency of sleep disorders (A), positive skin test (SKT) on dust mites (B), use of antihistamine/decongestant (C), and positive SKT to molds (D) between patients with (shaded bars) and without (white bars) AH. I, II, III, and IV within the graph represent the different age groups.

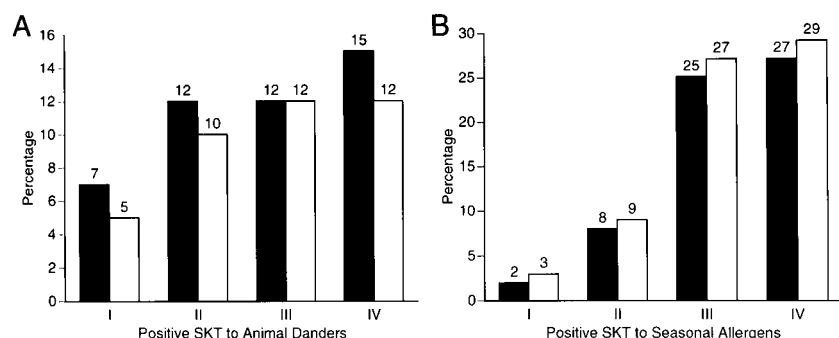


Figure 3. Comparison of SKT results to animal danders (A) and seasonal allergens (B) between patients with (shaded bars) and without (white bars) AH. I, II, III, and IV within the graph represent the different age groups.

II, 1.905 (1.615 to 2.247); group III, 1.565 (1.253 to 1.956); and group IV, 1.650 (1.144 to 2.379).

Use of Antihistamine/Decongestants

Unlike group I, the patients with AH in groups II, III, and IV showed a significant increase in the use of these medications compared with those without AH ($P < 0.0001$; Fig 2C).

Skin Reactivity to House Dust Mites

There was virtually no statistical difference in the frequency of skin test positivity against house dust mites in

any of the age groups, whether they had AH or not. More than 50% of the patients in any group, but especially in groups II, III, and IV, were sensitive to house dust mites (Fig 2B).

Skin Reactivity to Molds

The higher frequency of positivity to molds was prevalent in all age groups of children with AH but not in those without AH (P ranged from 0.013 to < 0.0001 ; Fig 2D). The relative risk and 95% CI were: group I, 2.375 (1.203 to 4.690); group II, 1.790

(1.449 to 2.212); group III, 1.829 (1.439 to 2.326); and group IV, 1.609 (1.180 to 2.194).

Skin Reactivity to Animal Danders

There was no statistical difference between the two groups in frequency of positivity against animal danders (Fig 3A).

Skin Reactivity to Seasonal Allergens

There was no statistical difference between the two groups in skin test positivity against the seasonal allergens (primarily the pollens of weeds, trees, and grasses; Fig 3B).

Increase in Positive Skin Reactivity to Molds and Relationship to the Development of AH

Figure 4 shows a comparison of the mold reactivity between the two groups. We found that the patients with AH showed a stronger reactivity in skin test (score of reaction $> 2+$) to more than three mold allergens. There were 10 patients with AH who had a 2+ reaction to six or more antigens, but no AR patients without AH showed such a reactivity. The P values in all four age groups were statistically significant (ranging from 0.0035 to 0.0001), whereas their relative risks ranged from 1.833 to 2.111.

DISCUSSION

Anatomically, the adenoids are the lymphoid tissues located on the posterior pharyngeal wall. They are sometimes called pharyngeal tonsils in reference to two other known tonsillar tissues in man, palatine tonsils and sublingual tonsils, which are located in the oral cavity. Those tonsils form an important frontline defense against intruding microorganisms. Unlike palatine tonsils, which are more visible in routine physical examination, adenoids are not easily seen without the aid of an endoscope or a reflecting mirror. They are on the posterior pharyngeal wall and are situated above the limit of inspection. It has been stated in the literature that adenoid and tonsillar hypertrophy co-exist.²⁻⁴ A study was subsequently carried out to examine this issue. Stearns⁵ weighed removed ade-

noids and tonsils in 45 children, and found that there was no correlation in weight between these two tissues. He concluded that tonsil size cannot be used to predict the size of adenoids from the same person. Therefore, it is important to investigate the size of adenoids independent of the size of tonsillar tissue. Further, when we determine the clinical significance of the adenoids for a patient, we should take into consideration the growth of the surrounding anatomical structures in the oropharynx.⁶

The clinical importance of adenoid tissue does not become apparent until its enlarged mass begins to encroach on airflow. Clinically, however, the evaluation of the size of the adenoids remains somewhat conjectural. Traditionally, measurement is done by lateral x-rays of the neck. This approach has been challenged, especially once nasopharyngeal endoscopy became available.^{6,7} Endoscopy allows for a better view of the adenoid mass in three dimensions. However, a recent study suggested that careful evaluation of clinical signs of nasopharyngeal obstruction, with the aid of radiologic findings, may be a better gauge of the necessity for surgical intervention in these children⁸ (Fig 5A and B).

The cause of AH in children remains unknown. A review of previous studies suggests that the cause could be multifactorial. In a study of 18 children whose adenoids were dissected and cultured, Brook⁹ found mixed aerobic and anaerobic flora from all specimens, yielding an average of 7.8 isolates (4.6 anaerobes and 3.2 aerobes). Among the 97 anaerobes isolated, the predominant ones included: bacteroid species, *Fusobacterium* sp., Gram-positive anaerobic cocci, and *Veillonella* sp. Among the 138 isolates, the predominant aerobes included: α - and γ -hemolytic streptococci, β -hemolytic streptococci (groups A,B,C, and F), *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae* type B. The findings indicate the polymicrobial nature of deep adenoid flora and demonstrate the presence of many β -lactamase-producing organ-

isms in children with recurrent adenoiditis.⁷ The persistence of these infections can lead to a chronic inflammatory state, which can result in hyperplasia of lymphoid tissues such as adenoids. It has also been suggested that part of the reason for the persistence or recurrence of infections of the adenoids is poor mucociliary clearance. For instance, Maurizi et al¹⁰ used scanning electron microscopy to determine the characteristics of adenoid tissues and found that a small or poorly developed adenoid is covered with a compact layer of ciliated cells. In contrast, a severely hypertrophied adenoid is characterized by a metaplastic epithelium with an almost complete loss of cilia. The authors postulated that the poor mucociliary effect allowed for a prolonged inflammatory process in adenoid tissue.¹⁰ One other confronting issue that faces us when studying the cause of AH is that it is often difficult to differentiate infected adenoids from other upper respiratory infections. Counting 10 bacteria per gram of tissue as a criteria of infection, Kveton et al¹¹ reported that 90% of children with nasal obstruction and severe, recurrent otitis media had infected adenoids. This contrasted with finding of only 8% in groups with either nasal obstruction or otitis media alone.¹¹

Obviously, environmental factors also play a role in the development of AH. When Finkelstein et al¹² examined smoking-induced nasopharyngeal lymphoid hyperplasia in 17 heavy smokers, transmission electron microscopy revealed emperipolesis characterized by mucosal invasion and epithelial cell damage by an unusual population of migrating lymphocytes. These cytotoxic lymphocytes were attached to epithelial, ciliated, and goblet cells, resulting in cell damage. These findings confirm a direct effect of smoking on the nasopharyngeal lymphoid tissue.

Significant morbidity of patients with AH has been reported in the past, but the emphasis was limited to a few selected areas. First, otitis media was reported to occur often in children with AH.^{7,13,14} We found that it occurred more commonly in children with AH <6 years old (Fig 2A). Second, the influence of enlarged adenoids on recurrent infection of the lower airways in children was reported previously.¹⁵ We observed similar findings (Fig 2B) but were surprised to learn that the difference in the frequency of infections between those with AH and those without was noted across all age groups. Third, sleep apnea was reported to be the most common respiratory disturbance found among chil-

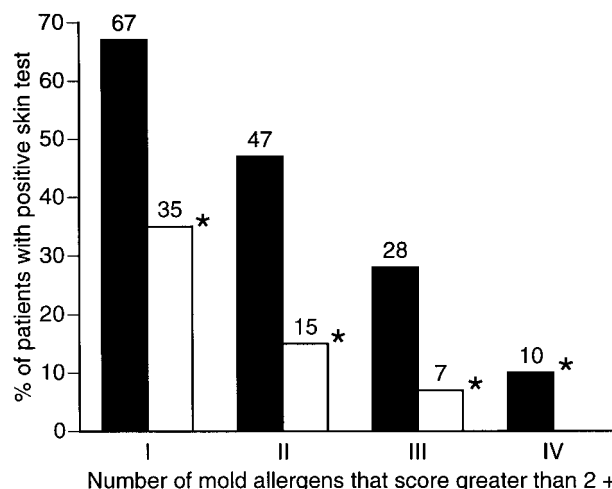


Figure 4. Comparison of the number of mold allergens to which the patients showed a skin test reaction equal to or greater than 2+ between patients with (shaded bars) and without (white bars) AH. *, the difference between the patients with (shaded bars) and without (white bars) AH is statistically significant ($P < 0.05$).

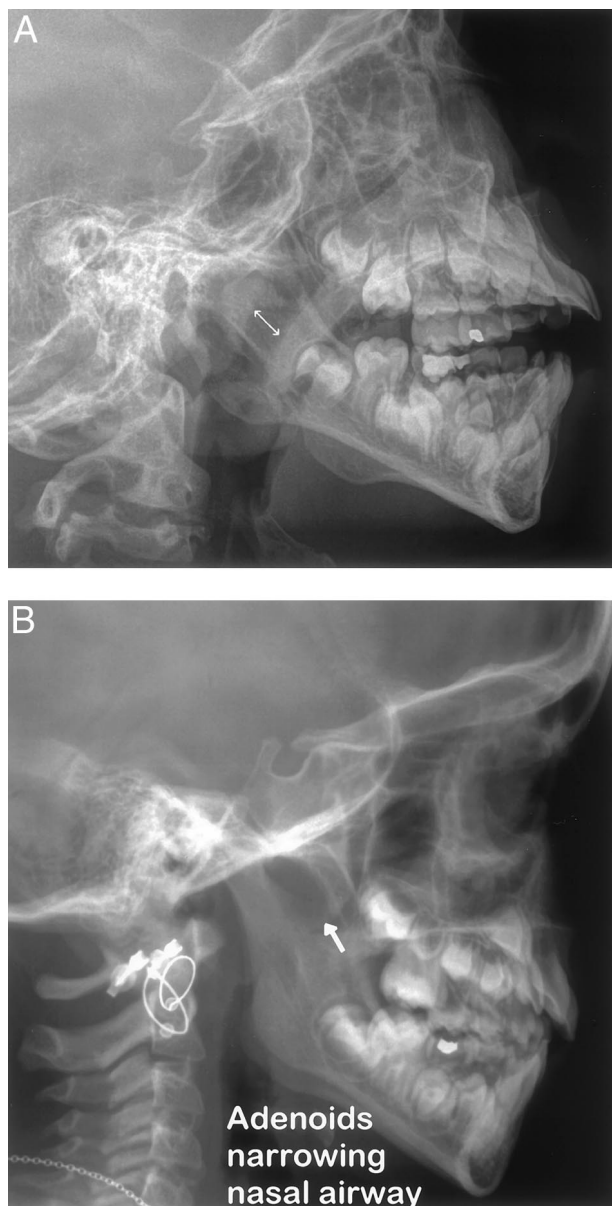


Figure 5. Radiographs showing a normal nasal airway (A) and adenoids narrowing nasal airway (B).

dren with AH.¹⁶ We found that sleep disorders were far more common in children of all age groups with AH, and the difference in children without AH was also statistically significant (Fig 3A).

Other problems that have not been well recognized in the past include the frequent occurrence of sinusitis, especially in AH patients in their early teens (Fig 1C), and frequent use of

antihistamine/decongestants in children with AH across all age groups, which suggest that these children suffered from clinical symptoms more often than those who had AR alone. In this study, we did not determine the pulmonary function of children with AH. A previous study, nonetheless, reported pulmonary function abnormalities evidenced by increased residual volume and ventilatory defects in

nearly two-thirds of patients with AH.¹⁷ Also, in a separate clinical review,¹⁸ it was cited that a subset of patients with AH may develop pulmonary hypertension because of chronic upper airway obstruction.

Although the association with AH in patients with AR is casually cited in the literature, to our knowledge, no study has been done so far to establish this relationship unequivocally. The main thrust of our study was to explore the possible link between these two clinical conditions by comparing the skin test results between patients with AH and those without. It was easier to compare between these two groups because all our patients had proven AR clinically and we had previously obtained skin test results for all of them. We found no statistical difference in terms of frequency of skin test positivity against house dust mites, animal danders, or seasonal allergens (Fig 2B, Fig 3A and B). The only striking difference we found was that of positive skin test to mold antigens (Fig 2D). The difference was statistically significant across all age groups. This difference in mold sensitivity became more apparent when we compared the intensity of skin test reactivity to mold allergen: patients with AH showed a greater reactivity (Fig 4). These results may imply that the allergic reaction to molds allergens compared with other allergens might have caused a more vigorous inflammation in the lymphoid tissue. This is possibly because of the uniqueness of mold allergens which may carry its mycotoxins, lipopolysaccharides, or its propensity to interact with other pollutants such as SO₂, ozone, or NO₂.¹⁹

We suggested this possibility in a recent study in which we found a strong association between mold allergy and sinusitis in children with allergic rhinitis.²⁰ This theory needs further investigation to establish a cause-and-effect relationship. We also need to emphasize that although no significant difference was found between children with and without AH in regard to exposure to tobacco smoking, it was disturbing to find such a

high frequency of exposure to smoking in both groups of children across all ages (Fig 1D). Again, those with AH tended to receive more exposure to tobacco smoking.

CONCLUSION

The findings of our study have two important implications: first, AH is strongly associated with exposure and reactivity to mold allergens in patients from a very young age. Second, the treatment of patients with mold allergy should include aggressive control of medical symptoms, as well as proper home environmental control such as reducing humidity in the house, using an air cleaner with a high-efficiency particulate air filter in the bedroom, and rigorous cleaning in mold-contaminated areas of the house (especially in regions where high humidity prevails throughout the year). Total smoking cessation is also highly recommended. These measures may help to reduce the risk of development of AH and its complications, which are associated with a high clinical morbidity.

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