



Clinical characteristics of asymptomatic allergen sensitization with nasal septal deviation, often misdiagnosed as allergic rhinitis

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Abstract

Purpose Allergic rhinitis (AR) is often defined based on symptoms accompanied by a positive allergen sensitivity test result. However, a positive skin prick test (SPT) does not always imply the occurrence of clinical symptoms. If an asymptomatic allergen-sensitized patient has nasal septal deviation (DSN) that could cause nasal obstruction, the condition could easily be confused with typical symptomatic AR. This study investigated the clinical and laboratory characteristics of asymptomatic allergen-sensitization with septal deviation (ASSD).

Methods Patients from a nationwide AR cohort study, conducted in 8 university hospitals, were investigated. AR was diagnosed when there were at least 1 rhinitis symptom with a positive SPT result. The ASSD group included patients who had severe nasal obstruction with few other symptoms and a positive SPT, along with septal deviation. Clinical and laboratory characteristics were compared between the ASSD group and the true AR group.

Results In total, 728 patients were included. The average age was 32.2 ± 12.7 and 66% of the patients had DSN. SPT indicated that ASSD patients were less sensitized to house dust mite ($p=0.019$ for *Dp* and $p=0.021$ for *Df*). There was a significant sex difference: the male-to-female ratio was higher in the ASSD than in the AR group (3.59 vs. 1.77, $p=0.012$). However, no statistically significant differences in age, family history, and body mass index were found.

Conclusion ASSD can mimic AR. When dealing with allergen-sensitized patients with a predominant symptom of nasal obstruction, DSN might also be considered before confirming a diagnosis of AR.

Keywords Allergens · Allergic rhinitis · Cohort studies · Nasal obstruction · Nasal septum

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Introduction

Allergic rhinitis (AR) is clinically characterized by symptoms such as nasal obstruction, rhinorrhea, nasal itching, and sneezing, along with a positive allergen-sensitivity test result [1]. Many laboratory tests are used for the diagnosis of AR; among those methods, the skin prick test (SPT) is considered to be a valid, safe, low-cost, and easy-to-perform test for demonstrating the skin hyper-reactivity caused by IgE sensitization toward an aeroallergen [2]. However, a positive SPT result does not always imply the occurrence of AR symptoms. Previous studies have shown that only 30–40% of patients with a positive SPT experience clinical symptoms [3, 4]. In many reports, subjects without any allergic symptoms but with a positive SPT were called “asymptomatic sensitizers;” however, the mechanism underlying this phenomenon remains unclear [5].

Among the symptoms of AR, nasal obstruction can occur for many other reasons, of which nasal septal deviation (DSN) is the most common structural etiology [6]. Therefore, it can be assumed that, if an asymptomatic sensitizer has a DSN that causes nasal obstruction, the condition could easily be misdiagnosed as typical symptomatic AR, as the person has both an AR symptom and a positive SPT result, although asymptomatic sensitizers without DSN would not be misdiagnosed as AR patients, as they would not have any symptoms. For these misdiagnosed patients, it would be better to correct the septal deviation, rather than prescribing common AR medication. We have named this specific group as asymptomatic sensitizers with septal deviation (ASSDs).

In this study, we attempted to distinguish ASSD patients from patients diagnosed with AR in a nationwide cohort study. We investigated the clinical and laboratory characteristics of ASSD as distinct from those with true AR.

Materials and methods

Study design

We conducted a prospective, multicenter, nationwide allergic rhinitis cohort (ARCO) study, supported by National Strategic Coordinating Center of Clinical Research, to identify clinical information about Korean AR patients. Eight university hospitals participated in this cohort study. The information gathered included general clinical characteristics, physical examinations, and laboratory tests. Written informed consent was obtained from participants. The detailed protocol of this study was approved by the institutional review board of each participating hospital.

In our study, we analyzed the ARCO data from 2013 to 2015. Patients aged 18 years and older, who were diagnosed with AR, were included in this study. Patients with chronic rhinosinusitis or with a history of sinus surgery were excluded. AR was diagnosed when a patient had at least 1 rhinitis symptom, along with a positive SPT result. The AR symptoms included nasal obstruction, nose itching, sneezing, and watery rhinorrhea. A visual analogue scale (VAS) was used for evaluating AR symptoms. AR was classified as persistent (symptoms lasting at least 4 days/week and ≥ 4 weeks/year) or intermittent (symptoms of < 4 days/week or < 4 weeks/year), according to the recent guidelines [7].

Grouping

We presumed that, among patients who were diagnosed with AR in this cohort study, some would be misdiagnosed ASSD patients. To select the ASSD patients, we attempted to identify patients who had (1) severe nasal obstruction, with (2) no or minimal other AR symptoms and (3) septal deviation on endoscopic examination. According to these criteria, patients with a VAS score of nasal obstruction > 5 and a VAS score of other AR symptoms ≤ 5 were defined as the ASSD group. The remaining typical allergic-sensitization patients were considered as the true AR group. Clinical and laboratory characteristics were compared between the ASSD and true AR groups.

Survey questionnaires

General clinical information was collected by self-reported survey questionnaires covering medical and social history. Medical history included previous physician-diagnosed diseases and nasal and ocular symptoms related to AR; both their duration and severity were recorded. The diagnosed diseases included atopic dermatitis, allergic conjunctivitis, food allergy, drug allergy, asthma, otitis media, and pneumonia. The social history included residential area, occupation, smoking status, education, family size, and lifetime drinking history.

Endoscopic examination and laboratory tests

Anterior rhinoscopy and endoscopic examination were performed in all subjects by a trained ear, nose, and throat (ENT) specialist. DSN was defined when the nasal septum deviated greater than half of the total distance from the midline septum to the lateral wall after vasoconstriction of the nasal mucosa. Blood samples were collected from all subjects for measurement of white blood cell counts, total eosinophil counts, and total IgE levels.

Allergy tests

The SPT was performed by using standardized extracts (Allergopharma, Reinbek, Germany) for 13 common aeroallergens, including house dust mites (*Dermatophagoides pteronyssinus* [Dp] and *Dermatophagoides farinae* [Df]), molds (*Aspergillus fumigatus* and *Alternaria alternata*), animal dander (cat and dog epithelia), pollens (tree pollen mixture I, tree pollen mixture II, grass pollen mixture, mugwort, ragweed, and oak) and cockroach (*Blattella germanica*). Histamine and isotonic saline were used as positive and negative controls, respectively. A positive SPT was diagnosed when the mean wheal diameter of the allergen was 3 mm larger than that of the negative control.

Statistical analysis

The values of the true AR group and ASSD group were compared by chi-square or Fisher's exact tests for categorical variables and by Student's *t* test for continuous variables. SPSS statistical software version 18.0 (SPSS Inc, Chicago, IL, USA) was used for statistical analyses. A *p* value less than 0.05 was considered statistically significant.

Results

A total of 752 consecutive subjects were initially enrolled in our study. After excluding 2 participants with incomplete questionnaires, 6 who refused the SPT, and 16 with saline positivity in the SPT, 728 patients (477 male, 251 female) were finally included in this study.

The average age of the patients overall was 32.2 ± 12.7 (range 18–78 years). The mean VAS symptom score was 6.72 ± 2.56 for nasal obstruction, 5.25 ± 2.78 for sneezing, 5.69 ± 2.93 for rhinorrhea, and 4.07 ± 3.20 for nose itching. After dividing the study group, 78 patients (10.7%)

met the criteria of ASSD, and 650 (89.3%) were classified as having true AR. The general demographics of the patients in each group are presented in Table 1.

Clinical characteristics

Among the general characteristics, there was no statistically significant difference in age ($p=0.255$), body mass index ($p=0.112$), and family history of allergic disease ($p=0.806$) between the ASSD and true AR groups. However, the male-to-female ratio was significantly higher in the ASSD group than in the true AR group (3.59 vs. 1.77, $p=0.012$). After classifying each subject using the Allergic Rhinitis and its Impact on Asthma classification, the distribution pattern did not differ between the groups (Table 2).

In terms of comorbidities, ASSD patients less frequently had allergic conjunctivitis ($p=0.004$) than the true AR group. Food allergy ($p=0.163$), atopic dermatitis ($p=1.000$), asthma ($p=1.000$), otitis media ($p=0.704$), pneumonia ($p=0.743$), hypertension ($p=0.788$), diabetes mellitus ($p=0.136$), and depression ($p=0.348$) were not associated with either group.

Laboratory results

The mean serum total IgE level was 315.0 kU/L of true AR group and 322.9 in the ASSD group ($p=0.899$). The white blood cell count showed no statistically significant difference between the true AR and ASSD groups (6.734×10^3 vs. 6.477×10^3 , $p=0.697$). The true AR group showed a tendency to have a higher percentage of eosinophils than did the ASSD group (4.2% vs. 3.5%), but this was not statistically significant ($p=0.106$) (Fig. 1).

Table 1 Baseline selected characteristics of true allergic rhinitis (AR) and asymptomatic sensitization with septal deviation (ASSD) in 728 subjects from the Allergic Rhinitis Cohort Study (ARCO), 2013–2015

Variable	Total subjects (N=728)	True AR (N=650)	ASSD (N=78)	P value*
Demographics				
Male, n (%)	477 (65.6)	416 (64.0)	61 (78.2)	0.012
Age, year, mean (SD)	32.2 (12.7)	32.4 (12.7)	30.7 (13.0)	0.255
Body mass index	23.3 (3.4)	23.2 (3.5)	23.9 (3.1)	0.112
Allergies in family				
Father	151 (20.7)	131 (20.2)	20 (25.6)	0.163
Mother	172 (23.6)	154 (23.7)	18 (23.1)	0.516
Endoscopic findings				
Septal deviation, n (%)	480 (65.9)	402 (61.8)	78 (100.0)	<0.001

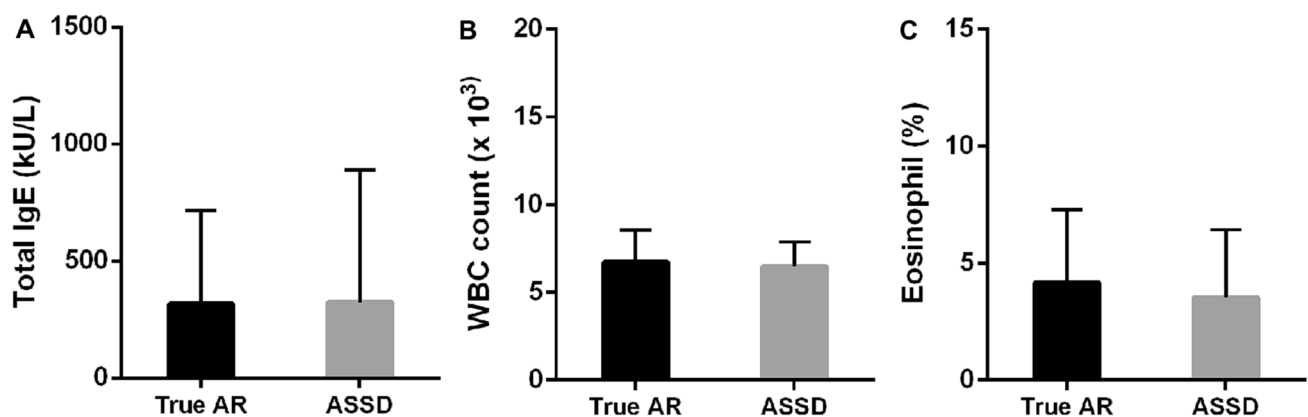
*For between-group differences, using *t* test for continuous variables, and Pearson χ^2 test for categorical variables

Table 2 Allergic symptoms and classification of true allergic rhinitis (AR) and asymptomatic sensitization with septal deviation (ASSD) in 728 subjects from the Allergic Rhinitis Cohort Study (ARCO), 2013–2015

Variable	Total subjects (N=728)	True AR (N=650)	ASSD (N=78)	P value*
Allergic symptoms, VAS score, mean (SD)				
Nasal obstruction	6.7 (2.5)	6.6 (2.6)	7.7 (1.3)	<0.001
Sneezing	5.3 (2.7)	5.6 (2.7)	2.7 (1.6)	<0.001
Rhinorrhea	5.7 (2.9)	6.1 (2.8)	2.5 (1.9)	<0.001
Nose itching	4.1 (3.2)	4.4 (3.1)	1.2 (1.5)	<0.001
Eye itching	4.1 (3.2)	4.4 (3.2)	1.4 (1.7)	<0.001
ARIA classification (%)				
Intermittent mild	56 (7.7)	52 (8.0)	4 (5.1)	
Intermittent moderate–severe	228 (31.3)	203 (31.2)	25 (32.0)	
Persistent mild	36 (4.9)	33 (5.0)	3 (3.8)	
Persistent moderate–severe	408 (56.0)	362 (55.7)	46 (58.9)	

VAS visual analogue scale, ARIA allergic rhinitis and its impact on asthma

*For between-group differences, using *t* test for continuous variables and Pearson χ^2 test for categorical variables

**Fig. 1** Laboratory test results. **a** Serum total IgE level, **b** white blood cell (WBC) count, and **c** percentage of eosinophils

Allergy tests

SPT analysis showed that, among the allergens, the proportion of patients showing sensitization to house dust mite was lower in the ASSD group (*Dp* 67.9%; *Df* 70.5%) than in the true AR group (*Dp* 79.8%; *Df* 82.2%), and the difference was statistically significant ($p=0.019$ for *Dp* and $p=0.021$ for *Df*) (Fig. 2). However, the average wheal size in response to histamine ($p=0.221$), *Dp* ($p=0.416$), and *Df* ($p=0.356$) were not significantly different between the groups. There was no statistically significant difference in the sensitization rates for other allergens.

Discussion

As AR is one of the most common chronic diseases encountered in ENT clinics [8], and as the diagnosis of AR is made based on a history of AR symptoms, with laboratory test confirmation, it is easy to misdiagnose and treat a patient with a positive SPT as well as only nasal obstruction due to DSN as having AR. However, our study suggests that symptoms and laboratory allergy tests are not sufficient to conclude a diagnosis of AR. Moreover, we firstly define and report the characteristics of this prone to misdiagnose group, ASSD.

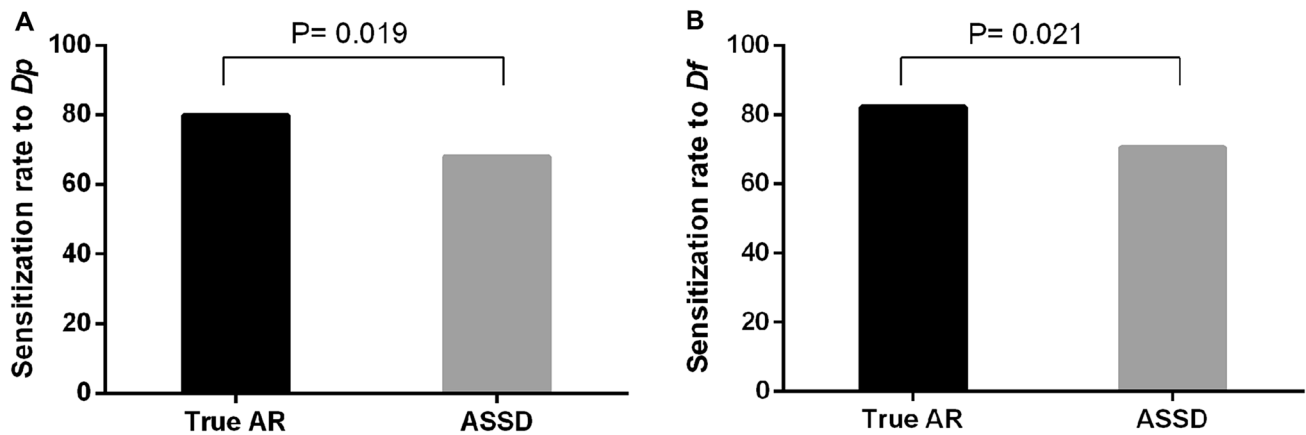


Fig. 2 The sensitization rate to house dust mites. **a** *Dermatophagoides pteronyssinus*, **b** *Dermatophagoides farinae*

Currently, laboratory tests evaluating sensitization to allergens, including SPT and immunoCAP, are widely used, along with the physical examination and symptom history, to diagnose AR. The SPT, which examines the skin reaction to allergic stimulation, demonstrating IgE sensitization toward an allergen, is one of the most popular methods as it is easy to perform and less expensive cost [9]. The known sensitivity range of SPT is 79–100% and its specificity is 79–91%, which implies that a certain proportion of patients who have a positive SPT do not express allergic symptoms [10, 11]. A large study, conducted by 17 allergy centers in 14 European countries, reported that, among patients sensitized to allergens as determined by SPT, 59.9–88.4% showed a correlation of the SPT results with clinical symptoms [12]. In another study, it was demonstrated that, among patients who had a positive SPT, 7.5–19% had no symptoms of AR [13]. The mechanism of this asymptomatic sensitization remains unclear and no convincing explanation has been provided. It is assumed that the phenomenon could be due to, except for simple false-positive test result, the relatively low level of effector cells and specific IgE in target organs, or that it represents an intermediate clinical state between non-atopy and true allergy, with a potential risk of allergy development [14–16].

AR is suspected when patients complain of symptoms such as nasal obstruction, rhinorrhea, sneezing, and an itching nose. Nasal obstruction is the most common symptom in AR patients [17, 18]. However nasal obstruction also can be found in other diseases, such as DSN, sinusitis, and tumorous conditions. Among these, DSN is the most common condition. Min et al. reported the prevalence of DSN to be 22.4% in a nationwide examination [19, 20]. In this study, the prevalence of DSN among AR patients was 65.9%. We assumed that patients who have DSN are more likely to be given a diagnosis of AR. In addition, although DSN is known to aggravate AR symptoms [21], we found

that the average symptom score of sneezing, rhinorrhea, and itching sense was lower in the DSN group than in the non-deviated septum group in a subgroup analysis (data not shown). Therefore, we presume that among the DSN subgroup, there might be a certain portion of patients who do not have sneezing, rhinorrhea, or itching sense, but whose only symptom is nasal obstruction. Such patients would be mistakenly included in the AR cohort and may contribute to a lower symptom score in the DSN subgroup. We named this specific entity as “asymptomatic sensitizer with septal deviation.”

In our comparison of the ASSD group with the true AR group, we found several distinct differences. First, the male-to-female ratio was significantly higher in the ASSD group. This may be because DSN per se has a male preponderance [19]. Second, the ASSD group was less sensitized to house dust mites. Patients who were sensitized to house dust mites tended to have more allergic symptoms, such as sneezing, rhinorrhea, and itching sense; this finding was in agreement with those of previous studies. House dust mites, especially *Dp* and *Df*, are the most common sensitized allergen in the Korean population [22]. Moreover, it has been demonstrated that symptoms worsen when patients are sensitized to multiple allergens, including house dust mites [23]. Third, the ASSD group showed less allergic conjunctivitis. The main symptoms of allergic conjunctivitis are redness, tearing, itching, and edema of the eyes. Most of these symptoms are due to the release of histamine and other active substances by mast cells, sharing the same pathophysiology as AR. Therefore, an ASSD subject, who tends to have fewer allergic responses, may also be less likely to have allergic conjunctivitis.

The above findings suggest that physicians dealing with allergy should consider the diagnosis of AR carefully. First, physical examination, especially endoscopic findings, is crucial to establish whether there are other factors,

such as DSN, that could cause nasal symptoms. Second, matching the allergy test results with the clinical history of AR itself is important. Not all of the sensitized allergens cause symptoms and the spatial and temporal correlation between allergen exposure and clinical symptoms should be evaluated, especially in for allergens other than a house dust mite. Third, the diagnosis of AR with only 1 symptom, in particular nasal obstruction, although it is the most common AR symptom, can cause misdiagnosis. Physicians should rather focus on other symptoms, such as sneezing, itching sense, and rhinorrhea, which seems to be more truly allergic symptoms.

There were a few limitations in this study. First, although we tried to develop a criteria for ASSD group, we could not clearly exclude patients who have minimal AR symptoms with SD. However, along with the ASSD group these patients also need management of the septal deviation after accurate physical examination instead of AR medication. Second, we assumed that the nasal obstruction of the ASSD group was caused by DSN. However, not all DSN induces nasal obstruction [24] and there may be a certain portion of patients in the ASSD group who have nasal obstruction due to true AR. Checking symptom changes in response to medication for AR may be another method for differentiating true AR patients from ASSD patients. Third, we evaluated the symptoms using a VAS score, which can be subjective and has high interpersonal variation. To overcome these limitations in future studies, an objective examination of symptoms, such as acoustic rhinometry, rhinomanometry, a thread test for evaluating secretion [25], and detailed endoscopic examination, could be used to provide more precise symptom evaluation.

Conclusion

We show that patients with ASSD are often misdiagnosed as having AR, but that there are some differences in clinical characteristics. Use of symptom history and a positive SPT is not sufficient to diagnose AR unequivocally. Understanding the clinical characteristics of ASSD by performing detailed endoscopic examination could help avoid this mismanagement.

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Declarations

Conflict of interest The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval This study was approved by the Institutional Review Board of each hospital.

References

1. Skoner DP (2001) Allergic rhinitis: definition, epidemiology, pathophysiology, detection, and diagnosis. *J Allergy Clin Immunol* 108:S2–S8. <https://doi.org/10.1067/mai.2001.115569>
2. Verstege A, Mehl A, Rolinck-Werninghaus C et al (2005) The predictive value of the skin prick test weal size for the outcome of oral food challenges. *Clin Exp Allergy* 35:1220–1226. <https://doi.org/10.1111/j.1365-2222.2005.2324.x>
3. Majamaa H, Moisio P, Holm K et al (1999) Cow's milk allergy: diagnostic accuracy of skin prick and patch tests and specific IgE. *Allergy* 54:346–351. <https://doi.org/10.1034/j.1398-9995.1999.00834.x>
4. Salo PM, Calatroni A, Gergen PJ et al (2011) Allergy-related outcomes in relation to serum IgE: results from the National Health and Nutrition Examination Survey 2005–2006. *J Allergy Clin Immunol* 127:1226–35.e7. <https://doi.org/10.1016/j.jaci.2010.12.1106>
5. Bodtger U (2004) Prognostic value of asymptomatic skin sensitization to aeroallergens. *Curr Opin Allergy Clin Immunol* 4:5–10. <https://doi.org/10.1097/00130832-200402000-00003>
6. Corey JP, Houser SM, Ng BA (2000) Nasal congestion: a review of its etiology, evaluation, and treatment. *Ear Nose Throat J* 79:690–702. <https://doi.org/10.1177/014556130007900908>
7. Bousquet J, Khaltaev N, Cruz AA et al (2008) Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy* 63(Suppl 86):8–160. <https://doi.org/10.1111/j.1398-9995.2007.01620.x>
8. Hellings PW, Fokkens WJ (2006) Allergic rhinitis and its impact on otorhinolaryngology. *Allergy* 61:656–664. <https://doi.org/10.1111/j.1398-9995.2006.01109.x>
9. Fornadley JA (2014) Skin testing for inhalant allergy. *Int Forum Allergy Rhinol* 4(Suppl 2):S41–S45. <https://doi.org/10.1002/alr.21393>
10. Sampson HA, Albergo R (1984) Comparison of results of skin tests, RAST, and double-blind, placebo-controlled food challenges in children with atopic dermatitis. *J Allergy Clin Immunol* 74:26–33. [https://doi.org/10.1016/0091-6749\(84\)90083-6](https://doi.org/10.1016/0091-6749(84)90083-6)
11. Nevis IF, Binkley K, Kabali C (2016) Diagnostic accuracy of skin-prick testing for allergic rhinitis: a systematic review and meta-analysis. *Allergy Asthma Clin Immunol* 12:20. <https://doi.org/10.1186/s13223-016-0126-0>
12. Burbach GJ, Heinzerling LM, Edenharter G et al (2009) GA(2) LEN skin test study II: clinical relevance of inhalant allergen sensitizations in Europe. *Allergy* 64:1507–1515. <https://doi.org/10.1111/j.1398-9995.2009.02089.x>
13. Bodtger U, Poulsen LK, Malling HJ (2003) Asymptomatic skin sensitization to birch predicts later development of birch pollen allergy in adults: a 3-year follow-up study. *J Allergy Clin Immunol* 111:149–154. <https://doi.org/10.1067/mai.2003.37>
14. Fuiano N, Fusilli S, Passalacqua G et al (2010) 10 Allergen-specific immunoglobulin E in the skin and nasal mucosa of

- symptomatic and asymptomatic children sensitized to aeroallergens. *J Investig Allergol Clin Immunol* 20:425–430
15. Droste JH, Kerkhof M, de Monchy JG et al (1996) Association of skin test reactivity, specific IgE, total IgE, and eosinophils with nasal symptoms in a community-based population study. *J Allergy Clin Immunol* 97:922–932. [https://doi.org/10.1016/s0091-6749\(96\)80066-2](https://doi.org/10.1016/s0091-6749(96)80066-2)
 16. Kerkhof M, Schouten JP, De Monchy JG (2000) The association of sensitization to inhalant allergens with allergy symptoms: the influence of bronchial hyperresponsiveness and blood eosinophil count. *Clin Exp Allergy* 30:1387–1394. <https://doi.org/10.1046/j.1365-2222.2000.00907.x>
 17. Wang DY, Niti M, Smith JD et al (2002) Rhinitis: do diagnostic criteria affect the prevalence and treatment. *Allergy* 57:150–154. <https://doi.org/10.1034/j.1398-9995.2002.1s3402.x>
 18. Wang DY, Raza MT, Gordon BR (2004) Control of nasal obstruction in perennial allergic rhinitis. *Curr Opin Allergy Clin Immunol* 4:165–170. <https://doi.org/10.1097/00130832-200406000-00005>
 19. Min YG, Jung HW, Kim CS (1995) Prevalence study of nasal septal deformities in Korea: results of a nation-wide survey. *Rhinology* 33:61–65
 20. Min YG, Jung HW, Kim HS et al (1997) Prevalence and risk factors for perennial allergic rhinitis in Korea: results of a nationwide survey. *Clin Otolaryngol Allied Sci* 22:139–144. <https://doi.org/10.1046/j.1365-2273.1997.00879.x>
 21. Karatzanis AD, Fragiadakis G, Moshandrea J et al (2009) Septoplasty outcome in patients with and without allergic rhinitis. *Rhinology* 47:444–449. <https://doi.org/10.4193/Rhin08.126>
 22. Jeong KY, Park JW, Hong CS (2012) House dust mite allergy in Korea: the most important inhalant allergen in current and future. *Allergy Asthma Immunol Res* 4:313–325. <https://doi.org/10.4168/aair.2012.4.6.313>
 23. Gelardi M, Ciprandi G, Incorvaia C et al (2015) Allergic rhinitis phenotypes based on mono-allergy or poly-allergy. *Inflamm Res* 64:373–375. <https://doi.org/10.1007/s00011-015-0826-9>
 24. Salihoglu M, Cekin E, Altundag A et al (2014) Examination versus subjective nasal obstruction in the evaluation of the nasal septal deviation. *Rhinology* 52:122–126. <https://doi.org/10.4193/Rhin13.057>
 25. Yagi N, Ada EH, Ichikawa R (1987) The validity of the thread test for evaluating nasal secretion in nasal allergy. *Acta Otolaryngol* 103:312–317. <https://doi.org/10.3109/00016488709107800>

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