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Exposure to mould allergens and rhinoconjunctivitis in Korean Children

Myung-Il Hahm, PhD^a, Jihyun Kim, MD, PhD^b, Ho-Jang Kwon, MD, PhD^b, Yoomi Chae, MD, PhD^d, Kangmo Ahn, MD, PhD^b, Hoo-Yeon Lee, MD, PhD^e

^aDepartment of Health Administration and Management, College of Medical Science, Soonchunhyang University, Asan, Korea

^bDepartment of Pediatrics, Samsung Medical Center, Environmental Health Center for Atopic Diseases, Sungkyunkwan University School of Medicine, Seoul, Korea

^cDepartment of Preventive Medicine, Dankook University College of Medicine, Cheonan, Korea

^dDepartment of Occupational and Environmental Medicine, College of Medicine, Dankook University, Cheonan, Korea

^eDepartment of Social Medicine, Dankook University College of Medicine, Cheonan, Korea

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Corresponding author: Ho-Jang Kwon, MD, PhD

Department of Preventive Medicine, Dankook University College of Medicine

201, Manghyang-ro, Dongnam-gu, Cheonan-si, Chungnam, 330-714, Korea

Telephone: 82-41-550-3879

Fax: 82-41-556-6461

E-mail: hojang@dankook.ac.kr, heroo75@hanmail.net

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Abstract

Background: Although rhinitis is the most common allergic disease in children, few studies have explored the causal relationships between mould allergens and rhinitis. Thus, this study aimed to identify factors, especially prior exposure to mould allergens, related to rhinitis and rhinoconjunctivitis in Korean children.

Methods: Subjects in this study were 12-13-year-old children from 40 national middle schools who were participants of the International Study of Asthma and Allergies in Childhood (ISAAC) study in Korea. A total of 3,852 children who completed the ISAAC questionnaire in 2010 and underwent a skin prick test (SPT) and blood test were enrolled in this study.

Results: The prevalence of symptoms suggestive of rhinitis or rhinoconjunctivitis in last 12 months was 42.7% and 19.4%, respectively. A parental history of allergies (OR = 2.08, 95% CI = 1.80-2.40; OR = 2.63, 95% CI = 2.20-3.15), visible mould or dampness (OR = 1.28, 95% CI = 1.09-1.51; OR = 1.23, 95% CI = 1.00-1.51), previous exposure to mould allergens (OR = 4.54, 95% CI = 2.32-8.84; OR = 4.98, 95% CI = 2.43-10.02), total IgE levels ≥ 78 kU/L (OR = 1.44, 95% CI = 1.22-1.69; OR = 1.99, 95% CI = 1.60-2.48) were risk factors for rhinitis and rhinoconjunctivitis.

Conclusions: This study suggested that previous exposure to mould allergens more influenced rhinitis and rhinoconjunctivitis than visible mould or dampness, and that total IgE levels of ≥ 78 kU/L, which was the criterion suggested in a study of Asian children, were risk factors for rhinitis diseases.

Key words: mould allergen, IgE, rhinitis, ISAAC

Introduction

Allergic diseases are the most common chronic diseases and have been increasing in children over the last several decades (1-3). The International Study of Asthma and Allergies in Childhood (ISAAC) study showed that symptoms of asthma, rhinoconjunctivitis, and eczema have increased in the Asia-Pacific region since the study's initiation (1). Allergic diseases decrease quality of life and increase medical costs for patients (4). For children living in developed countries, allergic diseases are the most common chronic childhood diseases and the most common cause of school absence (3).

Although fungi cause allergic reactions, the extent to which they cause allergic diseases, including allergic rhinitis and asthma, has been underestimated (5). Exposure to mould allergens could lead to IgE mediated rhinitis as well as asthma and dermatitis (6). *Alternaria* and *Aspergillus* are airborne fungal allergens (7, 8). These mould allergens are

very useful to assess exposure to moulds because these allergens are markers of mould exposure (8).

Asian dust storms (ADS), known as 'yellow sand', originate in China and are blown throughout East Asian countries, including Korea, Taiwan, and Japan (18-20). ADS contain industrial pollutants from China and are thought to increase the death rate from cardiovascular and respiratory diseases (19). A study by Chan *et al.* identified a correlation between ADS and clinical visits for allergic rhinitis in Taipei, Taiwan (20, 21). ADS are rich in fungal allergens (18) and other airborne substances, including sulphate and microbial agents (22). It has been hypothesised that rhinoconjunctivitis is a particular consequence of ADS, because fungi in the dust come into direct contact with the conjunctiva and eyelid margins (18).

Studies have found that patients with severe asthma responded to mould allergens (9-12); however, most of these studies focused on adults. Multiple studies confirmed the effects of mould on allergic diseases using dampness, visible mould, and mould odour models from participants in the ISAAC study; however, these studies were also limited due to using visible mould or dampness as a risk factor which was measured at cross sectional survey (13-17). Previous studies had identified an association between exposure to visible mould and symptoms of rhinitis in present time.

Serum immunoglobulin E (IgE) is a good predictor of allergic disease since allergies cause inflammation (23). However, Total IgE has a relatively poor specificity because high level of total IgE was associated with allergic disease as well as other diseases (24). Although studies have suggested that a critical level of IgE could diagnose allergic disease (25-27), the levels of total IgE vary among individuals and increase with age (23). Tu *et al.* (2013) suggested that total IgE level was ≥ 78 kU/L for the assessment of allergic diseases based on their study in 1,321 Asian children aged 5-18 years (25).

Since ADS occur frequently in Korea, the possibility of previous exposure to mould allergens might be higher among Korean children. Thus, studies detailing the relationships between exposure to mould allergens and allergic diseases in children are necessary, as most studies have focused on adults. This study aimed to identify the relationship between the exposure to fungal allergens and rhinitis in last 12 months (especially rhinoconjunctivitis) among 12-13-year old Korean children. This study also aimed to identify whether the higher level of total IgE would be correlated with symptoms of rhinitis or rhinoconjunctivitis in last 12 months.

Methods

Study population

This study used data collected from the ISAAC study that was conducted in Korea between October and November 2010. To guarantee representativeness, this survey was conducted among 12- and 13-year-old students from 40 middle schools nationwide.

The sampling method followed a stratified two-stage cluster based on a comprehensive list of national schools. First, schools were stratified by geographic region and school location (i.e., metropolitan, urban, and rural). For each stratum, sample schools

were selected using the systematic 'probability proportional to size' (PPS) sampling procedure, and the size was based on the number of classes in each school. In the second stage of sampling, three classes were selected randomly from the first grade of each sample school, and all children were asked to participate. The response rates among children aged 12-13 years was 93.8%. In total, 4,112 students aged 12-13 years participated.

A total of 3,852 children who completed the ISAAC questionnaire in 2010 and underwent a SPT and a blood test were included in the study. This study was approved by the Dankook University Institutional Review Board (IRB approval number: DKUH IRB 2010-09-0260). Informed written consent was obtained from the parents or guardians of all subjects.

Measures

Children aged 12-13 years were asked to complete a validated questionnaire regarding asthma and allergies, based on the ISAAC Phase III questionnaire. Parents or guardians of the participating children were asked to complete a validated questionnaire on their environmental exposures and socioeconomic status. Students who completed the survey underwent a SPT to identify exposure to the following 18 standard inhalant allergens: : *Der p*, *Der f*, *Tyrophagus putrescentiae* (*Tyr p*), cockroach, cat, dog, alder, birch, oak, Japanese cedar (Lofarma, Milan, Italy), orchard grass, Bermuda grass, timothy, mugwort, ragweed, Japanese hop, *Alternaria*, and *Aspergillus fumigatus*. Histamine was used as a positive control and normal saline as a negative control. Positive skin prick test was defined if the calculated value, which was calculated from the largest diameter plus perpendicular diameter, was ≥ 3 mm and controls showed adequate reactions. We categorized the sensitization to 18 aeroallergens into four groups; (1) no sensitization to any aeroallergens, (2) sensitization to only mould allergens, *Aspergillus fumigates* or *Alternaria*, (3) sensitization to mould allergens and to one or more allergens among other 16 aeroallergens, (4) sensitization to one or more aeroallergens except for mould allergens (Figure 1).

<Figure 1. Venn diagrams illustrating 4 sensitization categories to aeroallergens>

We obtained blood samples from subjects and measured their total IgE levels. A positive total IgE level was defined as ≥ 78 kU/L, which is based on the results of a previous study in Asian children (25). Tu *et al.* (2013) suggested this reference value for the assessment of allergic diseases based on their study in 1,321 Asian children aged 5-18 years (25).

We defined the symptoms suggestive of rhinitis and rhinoconjunctivitis using the questionnaire and in accordance with the ISAAC Phase III protocol (28). To assess rhinitis and rhinoconjunctivitis, the following two questions were asked: (1) "In the past 12 months, have you had a problem with sneezing or a runny, or blocked nose when you did not have a cold or the flu?" (Yes/No); and (2) "In the past 12 months, has this nasal problem been

accompanied by an itchy, watery nose?" (Yes/No). Rhinitis was considered when a subject answered 'yes' to the first question, and rhinoconjunctivitis was considered rhinitis when accompanied by itchy, watery eyes (28).

To identify risk factors influencing rhinitis, we selected factors from previous reports (16, 17, 29-33). The questionnaire included questions about age, gender, income, residential area, current environmental tobacco smoke (ETS) exposure, father's education level, the parents' history of allergic disease, the housing type, floor of the house, age of the building, dampness or mould presence, and remodelling of the home in which the child lived, and a history of moving to a newly built home during the first year after birth. We defined a parental history of allergic disease as positive when one or both parents previously experienced asthma, rhinitis, or dermatitis. Exposure to mould allergens was defined as sensitisation to at least one of the two mould allergens *Alternaria* and *Aspergillus fumigatus*.

Statistical analyses

Comparisons of the prevalence of rhinitis and rhinoconjunctivitis among children were made in terms of the socioeconomic status of the parents, environmental factors, the parents' history, and indoor environmental factors, using the chi-square test. Some variables were included in the final logistic model, because they were considered important, even if they did not differ significantly according to the prevalence of rhinitis.

Univariate logistic regression models were used to identify individual associations between independent variables and rhinitis. Multivariate logistic regression models were used to determine the effects of an experience of exposure to mould allergens, and total serum IgE level, on the prevalence of rhinitis diseases after controlling for independent variables. Statistical analyses were performed using SAS software (ver. 9.3; SAS Institute, Cary, NC, USA).

Results

Point prevalence of rhinitis and rhinoconjunctivitis in children aged 12-13 years

A total of 3,852 students who completed questionnaires, the SPTs, and a blood test were selected in this study (figure 2). Among them, prevalences of symptoms suggestive of rhinitis or rhinoconjunctivitis were 42.7% (1,644 students) and 19.4% (737 students), respectively (Figure 2; Table 1). Children who had positive reactions to the mould allergens *A. fumigatus* or *Alternaria* were more likely to have symptoms of rhinitis than other groups (63.3% for sensitization to mould allergens, 57.7% for overlapped sensitization, 52.3% for sensitization to the other allergens, and 29.7% for no sensitization for rhinitis; 32.7% for sensitization to mould allergens, 28.8% for overlapped sensitization, 27.0% for sensitization to the other allergens, and 19.1% for no sensitization for rhinoconjunctivitis, respectively).

The prevalences of rhinitis and rhinoconjunctivitis in children with ≥ 78 kU/L total IgE were 50.9% and 26.4%, respectively, compared with 32.7% and 10.8% for children with < 78 kU/L IgE.

<Figure 2. Flow chart of study subjects>

<Table 1. Prevalence of the rhinitis and rhinoconjunctivitis in the last 12 months among 12-13-year-old students based on socio-demographic and indoor environmental factors >

Factors associated with rhinitis and rhinoconjunctivitis

Based on previous studies of rhinitis or rhinoconjunctivitis and on the results of the chi-square test, we selected independent variables for the logistic regression models. Table 2 shows the results of the univariate logistic regression analyses. Children whose parents had a history of allergic disease were more likely to have symptoms of rhinitis or rhinoconjunctivitis than were children whose parents had no history of allergic disease (OR = 2.26, 95% CI = 1.98-2.59; OR = 2.63, 95% CI = 2.23-3.10). Children with a positive reaction to aeroallergens, especially mould allergens were more likely to have symptoms of rhinitis (OR=4.08, 95% CI=2.26-7.36 for sensitization to mould allergens, OR=3.23, 95% CI=2.49-4.19 for overlapped sensitization, and OR=2.60, 95% CI=2.27-2.99 for sensitization to the other allergens for rhinitis; OR=5.16, 95% CI=2.76-9.64 for sensitization to mould allergens, OR=4.13, 95% CI=3.03-5.63 for overlapped sensitization, and OR=3.78, 95% CI=3.11-4.59 for sensitization to the other allergens for rhinoconjunctivitis, respectively). Children who moved to a newly built home within their first year of life were 1.29-fold and 1.48-fold more likely to have symptoms of rhinitis or rhinoconjunctivitis ($p < 0.05$), respectively, than those who had not. Regarding the total IgE levels, children with ≥ 78 kU/L were more likely to have rhinitis and rhinoconjunctivitis than those with < 78 kU/L (OR = 2.14, 95% CI = 1.87-2.44; OR = 2.96, 95% CI = 2.47-3.54).

<Table 2. Results of univariate logistic regression analyses for identifying risk factors for rhinitis disease in the last 12 months >

Based on univariate logistic regression, we excluded certain variables from the multiple logistic regression. The results of the multivariate logistic regression analyses are listed in Table 3. The risk factors for rhinitis and rhinoconjunctivitis were the same as those from the univariate logistic regression analyses. Children whose parents had a history of allergic diseases were more likely to experience rhinitis or rhinoconjunctivitis (OR=2.03, 95% CI=1.75-2.35; OR=2.55, 95% CI = 2.13-3.06), and children with ≥ 78 kU/L total IgE were more likely to have allergic diseases (OR=1.44, 95% CI=1.22-1.69 for rhinitis;

OR=1.99, 95% CI=1.60-2.48 for rhinoconjunctivitis). Positive SPT to mould allergens was also a most important risk factor for rhinitis and rhinoconjunctivitis (OR=4.53, 95% CI=2.32-8.84 and OR=4.98, 95% CI=2.43-10.20, respectively). Other sensitization groups to aeroallergens were also risk factors for both rhinitis symptoms (OR=2.37, 95% CI=1.76-3.19 for overlapped sensitization, and OR=2.09, 95% CI=1.77-2.47 for sensitization to the other allergens for rhinitis; OR=2.65, 95% CI=1.85-3.78 for overlapped sensitization, and OR=2.68, 95% CI=2.12-3.37 for sensitization to the other allergens for rhinoconjunctivitis). Children living in a home with visible mould or dampness were more likely to have rhinitis and rhinoconjunctivitis than children living in a home with no mould or dampness (OR=1.28, 95% CI = 1.22-1.69; OR=1.23, 95% CI=1.00-1.51, respectively).

<Table 3. Results of multiple logistic regression analyses for identifying risk factors for rhinitis disease in the last 12 months >

Discussion

This study aimed to identify causal relationships between the exposure to mould allergens and rhinitis or rhinoconjunctivitis. Previous studies have been performed; however, they were limited by their sample size or measuring whether any visible mould or dampness exist in present and symptoms of rhinitis were measured at the same time (34). This study attempted to overcome these limitations and was the first nationwide study conducted among Korean middle school students aged 12-13 years. Sensitization to mould allergens could be useful to measure previous exposure to mould because mould allergens, such as *A. fumigatus* and *Alternaria*, are markers of mould exposure in various environments (8). Therefore, positive SPT to mould allergens means that there was previous exposure to mould.

Among 12-13 year olds in this study, the prevalences of symptoms associated with rhinitis and rhinoconjunctivitis were 42.7% and 19.4%, respectively. In a previous study of Korean children aged 6-7 years, the prevalences of symptoms associated with rhinitis were 43.4% and 22.1%, respectively (35). Thus, the overall prevalence of symptoms of rhinitis was similar between the different age groups. Also, the prevalence of rhinoconjunctivitis was higher in Korea than in most other countries that participated in the ISAAC study, with the exception of Thailand, Hong Kong, Paraguay, Tunisia, and South Africa. However, these differences may be due to the fact that the studies were carried out multiple years apart. For example, the worldwide prevalence of symptoms of rhinitis in the ISAAC study was estimated in 2002 to 2003, while the Korean ISAAC study was performed in 2010. Asher *et al.* suggested that the prevalence of allergic diseases has increased over time (1).

In the multivariate logistic regression model, a parental history of allergies, exposure to mould allergens, visible mould or dampness at home, moving to newly built house during infancy period, and a total IgE level of ≥ 78 kU/L were identified as risk factors for symptoms of rhinitis and rhinoconjunctivitis. Specifically, the study results suggested that the

occurrence of current symptoms of rhinitis and rhinoconjunctivitis in Korean children aged 12–13 years was strongly associated with past exposure to mould allergens.

Exposure to fungi may represent a risk factor for allergic disease as is true for patients with asthma (5, 9). This result suggests that rhinoconjunctivitis may be affected more by previous exposure to mould allergens, rather than by visible mould or dampness at home. On the other hand, visible mould and odour are associated with an increase in the concentrations of fungal allergens, including *Alternaria* and *A. Fumigatus* (36). This study identified the correlates with exposure to fungal allergens and symptoms of rhinitis and rhinoconjunctivitis, and confirmed the association between visual mould or dampness in the home and rhinitis diseases that was identified in previous cross-sectional studies (13-17). We also identified that exposure to other aeroallergens exception of mould allergens could be risk factors of rhinitis and rhinoconjunctivitis. Sensitization to more than one airborne allergen is common in atopic children (37).

Total serum IgE is a key indicator of atopy (27). This study identified a positive correlation between total serum IgE levels ≥ 78 kU/L and both rhinitis and rhinoconjunctivitis. The standard IgE level used in this study was based on a previous study in Asian children (25). Serum IgE levels are correlated with allergic diseases; however, this relationship varies by ethnicity, age (23, 25), sex, and geographic area (26). Therefore, the true IgE levels indicative of allergic diseases may be variable. Tu *et al.* suggested a critical IgE level for diagnosing allergic diseases, which was based on a ROC curve analysis conducted in Asian children (25). Drkulec *et al.* also suggested that a cut-off level of total serum IgE of 116.6 kU/L for distinguishing allergic asthma from chronic coughs in Croatian hospital patients (27). Sharpe *et al.* suggested that asthma was associated with total IgE levels of ≥ 170 kU/L among adult U.S. participants of the National Health and Nutrition Examination Survey (NHANES) in 2005-2006 (36). The current study suggests that children with total IgE levels ≥ 78 kU/L are more likely to have rhinitis and allergic rhinitis than are children with total IgE levels < 78 kU/L.

This result showed that infants living in a newly built home are likely to be at increased risk of rhinitis and rhinoconjunctivitis symptoms. The 2010 ISAAC Phase III study, conducted in Korea previously as part of the same project, confirmed an effect of moving to a newly built house during infancy on rhinitis and allergic rhinitis in children aged 6–7 years (35). A newly built apartments has much higher volatile organic compounds (VOCs) than other older homes in Korea (38). Therefore, it could be assumed that exposure to VOCs during infancy might cause symptoms of rhinitis (35). When considering that rhinoconjunctivitis is the best predictor of allergic rhinitis (39), this result also supports a relationship between moving to a newly built house and allergic rhinitis. Some studies (32, 40, 41) defined allergic rhinoconjunctivitis using the definition of rhinoconjunctivitis used in our study.

When interpreting the findings of this study, a few limitations should be considered. Limitation to this study is the recall bias that is common among cross-sectional studies. Questionnaires were completed by students aged 12-13 years and their parents or guardians. Because information on allergic diseases and environmental exposures were obtained retrospectively (42), this may have facilitated recall bias. For validating the prevalence of allergic diseases, this study used a standardised and validated written questionnaire from the ISAAC protocol (43).

Second, caution should be taken when interpreting the causal relationship between risk factors and rhinitis diseases, since this study could not identify the precise past times that subjects were exposed to mould allergens. It was only possible to identify whether subjects of this study had prior exposure to mould allergens using the SPT to mould allergens. It is needed to consider that some subjects had no sensitization although they were exposure to mould allergens in the past because of individual immunity. However, this factor remains superior to the question of visual household mould and dampness for correlating the effect of fungi on rhinitis diseases.

In conclusion, this study showed that the factors associated with rhinitis diseases in 12-13-year-old Korean children were similar to those of 6-7-year-old Korean children or subjects in western countries. The key environmental risk factors associated with rhinitis or rhinoconjunctivitis in this study were previous exposure to mould allergens, visible mould or dampness at home, moving to newly built house during infancy period, and total serum IgE levels ≥ 78 kU/L. The result of this study suggested that living environment remediation measures to remove not only visible mould or dampness but also invisible mould allergens are important to prevent rhinitis development.

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Table 1. Prevalence of the rhinitis and rhinoconjunctivitis in the last 12 months among 12-13-year-old students based on socio-demographic and indoor environmental factors

	Rhinitis			Rhinoconjunctivitis	
	Total	n(%)	p-value	n(%)	p-value
Gender					
Female	1944	789(40.6)	0.0088	368(19.2)	0.7626
Male	1908	855(44.8)		369(19.6)	
Total	3852	1644(42.7)		737(19.4)	
Father's education (years)					
≤ 9 (middle school or less)	137	44(32.1)	0.0009	15(11.0)	0.0042
9 < ≤12 (high school)	1459	594(40.7)		262(18.2)	
12 < (post-high school)	2074	938(45.2)		429(21.0)	
Total	3670	1576(42.9)		706(19.5)	
Household Income (US\$/month)					
<2,000	581	232(39.9)	0.0333	103(17.9)	0.1586

2,000 ≤ < 4,000	1598	654(40.9)		287(18.2)	
2,000 ≤ < 6,000	1027	469(45.7)		218(21.5)	
6,000 ≤	506	228(45.1)		99(19.8)	
Total	3712	1583(42.7)		707(19.3)	
Residential Area					
Metropolitan	1702	731(43.0)	0.1494	318(18.9)	0.0367
Urban	1562	683(43.7)		324(21.1)	
Rural	588	230(39.1)		95(16.3)	
Total	3852	1644(42.7)		737(19.4)	
Total number of cigarettes*					
No	1734	730(42.1)	0.4191	327(19.2)	0.7891
1~20	1665	702(42.2)		325(19.7)	
≥21	241	112(46.5)		43(17.9)	
Total	3640	1544(42.4)		695(19.3)	
Parent history of atopic disease					
No	2394	841(35.1)	<.0001	319(13.5)	<.0001
Yes	1458	803(55.1)		418(29.1)	
Total	3852	1644(42.7)		737(19.4)	
Breast feeding					
No	1285	542(42.2)	0.6772	238(18.8)	0.5274
Yes	2495	1070(42.9)		486(19.7)	
Total	3780	1612(42.7)		724(19.4)	
Visible mould or dampness at home					
No	2845	1185(41.7)	0.0184	532(18.9)	0.2169
Yes	957	441(46.1)		197(20.9)	
Total	3802	1626(42.8)		729(19.4)	
Positive SPT to aeroallergens					
No	1729	513(29.7)	<.0001	156(9.0)	<.0001
Sensitization to fungal allergens	49	31(63.3)		16(32.7)	

Overlapped sensitization**	274	158(57.7)		79(28.8)	
Sensitization to other 16 allergens	1800	942(52.3)		486(27.0)	
Total	3852	1644(42.7)		737(19.1)	
Carpet use at home					
No	3137	1373(43.8)	0.0048	616(19.9)	0.1383
Yes	638	240(37.6)		109(17.3)	
Total	3775	1613(42.7)		725(19.5)	
House Type					
Detached house	658	247(37.5)	0.0020	97(14.8)	0.0019
Town house	605	244(40.3)		108(18.1)	
Apartment	2453	1101(44.9)		511(21.1)	
Others	103	38(36.9)		16(15.8)	
Total	3819	1630(42.7)		732(19.4)	
Floor of house					
Over 1st floor	3707	1588(42.8)	0.4675	712(19.5)	0.7932
Basement or semi-basement	91	35(38.5)		16(17.8)	
Total	3798	1623(42.7)		728(19.4)	
Building' age					
> 2 years	3653	1557(42.6)	0.9290	702(19.5)	0.9677
≤ 2 years	164	71(43.3)		31(19.0)	
Total	3817	1628(42.7)		733(19.5)	
Pets at home when pregnant or with infants					
Yes	199	72(36.2)	0.0670	38(19.3)	1.0000
No	3573	1538(43.1)		682(19.3)	
Total	3772	1610(42.7)		720(19.3)	
Pets at home					
Yes	610	260(42.6)	1.0000	122(20.3)	0.5965
No	3148	1342(42.6)		598(19.2)	
Total	3758	1602(42.6)		720(19.4)	
Remodeling within last 12					

months

No	3130	1321(42.2)	0.1329	578(18.72)	0.0252
Yes	646	294(45.5)		145(22.66)	
Total	3776	1615(42.8)		723(19.4)	

New furniture within last 12 months

No	3039	1272(41.9)	0.0511	570(19.0)	0.3382
Yes	768	352(45.8)		156(20.6)	
Total	3807	1624(42.7)		726(19.3)	

Moving to newly built house when infant

No	3201	1336(41.7)	0.0058	582(18.4)	0.0003
Yes	588	282(48.0)		145(25.0)	
Total	3789	1618(42.7)		727(19.4)	

Positive IgE (i.e., ≥ 78 kU/L)

No	1741	569(32.7)	<.0001	186(10.8)	<.0001
Yes	2111	1075(50.9)		551(26.4)	
Total	3852	1644(42.7)		737(19.4)	

*Total number of cigarettes: sum of number of cigarettes smoked daily by each smoker living in a child's home.

**Overlapped sensitization: positive SPT to fungal allergens (*A. fumigatus* or *Alternaria*) and to one or more allergens except for fungal allergens

Table 2. Results of univariate logistic regression analyses for identifying risk factors for rhinitis disease in the last 12 months

	Rhinitis			Rrhinoconjunctivitis		
	Odds Ratio	95% CI		Odds Ratio	95% CI	
Gender						
Female	1.00			1.00		
Male	1.19	1.05	1.35	1.03	0.88	1.21
Father's education level (years)						
≤ 9 (middle school or less)	1.00			1.00		
9 < ≤12 (high school)	1.45	1.00	2.11	1.80	1.04	3.14

12 < (post-high school)	1.75	1.21	2.52	2.16	1.25	3.74
Household Income (US\$/month)						
<2,000	1.00			1.00		
200≤ < 400	1.04	0.86	1.27	1.02	0.80	1.31
400≤ < 600	1.26	1.03	1.55	1.26	0.97	1.63
600≤	1.23	0.97	1.57	1.14	0.84	1.54
Parent history of atopic diseases						
No	1.00			1.00		
Yes	2.26	1.98	2.59	2.63	2.23	3.10
Residential area						
Metropolitan	1.00			1.00		
Urban	1.03	0.90	1.19	1.14	0.96	1.36
Rural	0.85	0.71	1.03	0.83	0.65	1.07
Total number of cigarettes*						
No smoking	1.00			1.00		
1≤ < 20	1.00	0.88	1.15	1.03	0.87	1.23
20≤	1.19	0.91	1.57	0.92	0.65	1.31
Visible mould or dampness at home						
No	1.00			1.00		
Yes	1.20	1.03	1.39	1.13	0.94	1.35
Positive SPT to aeroallergens						
No	1.00			1.00		
Sensitization to fungal allergens	4.08	2.26	7.36	5.16	2.76	9.64
Overlapped sensitization**	3.23	2.49	4.19	4.13	3.03	5.63
Sensitization to other 16 allergens	2.60	2.27	2.99	3.78	3.11	4.59
Carpet use at home						
No	1.00			1.00		
Yes	0.78	0.65	0.92	0.84	0.67	1.05
Remodeling within the last 12 months						
No	1.00			1.00		

Yes	1.14	0.97	1.36	1.27	1.04	1.56
New furniture within the last 12 months						
No	1.00			1.00		
Yes	1.18	1.00	1.38	1.11	0.91	1.35
Moving to newly built home when an infant						
No	1.00			1.00		
Yes	1.29	1.08	1.54	1.48	1.20	1.82
Positive IgE (i.e., ≥ 78 kU/L)						
No	1.00			1.00		
Yes	2.14	1.87	2.44	2.96	2.47	3.54

*Total number of cigarettes: sum of number of cigarettes smoked daily by each smoker living in a child's home.

**Overlapped sensitization: positive SPT to fungal allergens (*A. fumigatus* or *Alternaria*) and to one or more allergens except for fungal allergens

Table 3. Results of multiple logistic regression analyses for identifying risk factors for rhinitis disease in the last 12 months

	Rhinitis			Rhinoconjunctivitis		
	Odds Ratio	95% CI		Odds Ratio	95% CI	
Gender						
Female	1.00			1.00		
Male	1.10	0.96	1.27	0.90	0.75	1.08
Father's education level (years)						
≤ 9 (middle school or less)	1.00			1.00		
9 < ≤12 (high school)	1.49	0.98	2.26	1.96	1.03	3.72
12 < (post-high school)	1.55	1.02	2.37	2.08	1.09	3.97
Household Income (US\$/month)						
<2,000	1.00			1.00		
200≤ < 400	1.00	0.80	1.26	0.89	0.67	1.19
400≤ < 600	1.07	0.84	1.37	0.94	0.69	1.29
600≤	1.07	0.80	1.43	0.86	0.60	1.25

Parents' history of atopic diseases

No	1.00			1.00		
Yes	2.03	1.75	2.35	2.55	2.13	3.06

Visible mould or dampness at home

No	1.00			1.00		
Yes	1.28	1.09	1.51	1.23	1.00	1.51

Positive SPT to aeroallergens

No	1.00			1.00		
Sensitization to fungal allergens	4.53	2.32	8.84	4.98	2.43	10.20
Overlapped sensitization**	2.37	1.76	3.19	2.65	1.85	3.78
Sensitization to other 16 allergens	2.09	1.77	2.47	2.68	2.12	3.37

Carpet use at home

No	1.00			1.00		
Yes	0.84	0.69	1.02	0.86	0.66	1.11

Remodeling within the last 12 months

No	1.00			1.00		
Yes	1.13	0.93	1.38	1.30	1.03	1.65

New furniture within the last 12 months

No	1.00			1.00		
Yes	1.14	0.95	1.37	1.05	0.84	1.32

Moving to newly built home when an infant

No	1.00			1.00		
Yes	1.21	1.00	1.47	1.46	1.16	1.84

Positive IgE (i.e., ≥ 78 kU/L)

No	1.00			1.00		
Yes	1.44	1.22	1.69	1.99	1.60	2.48

*Total number of cigarettes: sum of number of cigarettes smoked daily by each smoker living in a child's home.

**Overlapped sensitization: positive SPT to fungal allergens (*A. fumigatus* or *Alternaria*) and to one or more allergens except for fungal allergens

Figure 1. Venn diagrams illustrating 4 sensitization categories to aeroallergens

Figure 2. Flow chart of study subjects

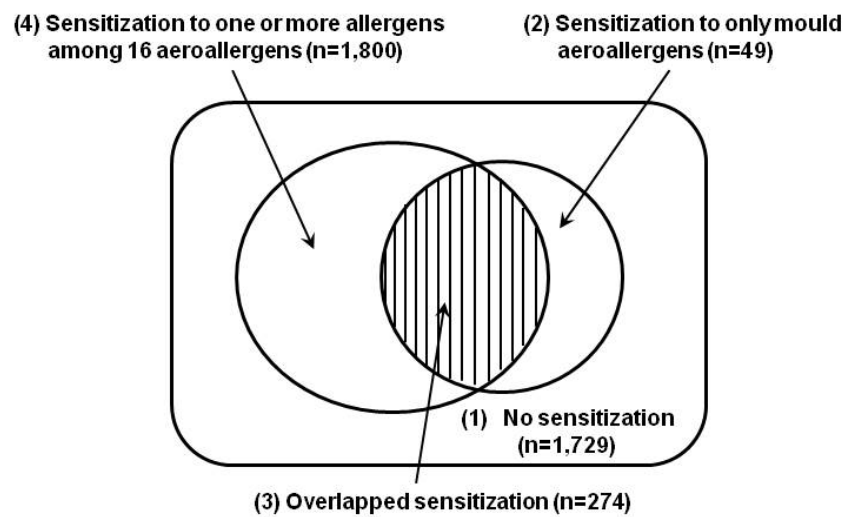


Figure 1 . Venn diagrams illustrating 4 sensitization categories to aeroallergens

- (1) No Sensitization to any aeroallergens
- (2) Sensitization to only mould allergens (*A. fumigatus* or *Alternaria*)
- (3) Sensitization to mould allergens and one or more allergens among other 16 aeroallergens
- (4) Sensitization to 16 aeroallergens except for 2 fungal allergens

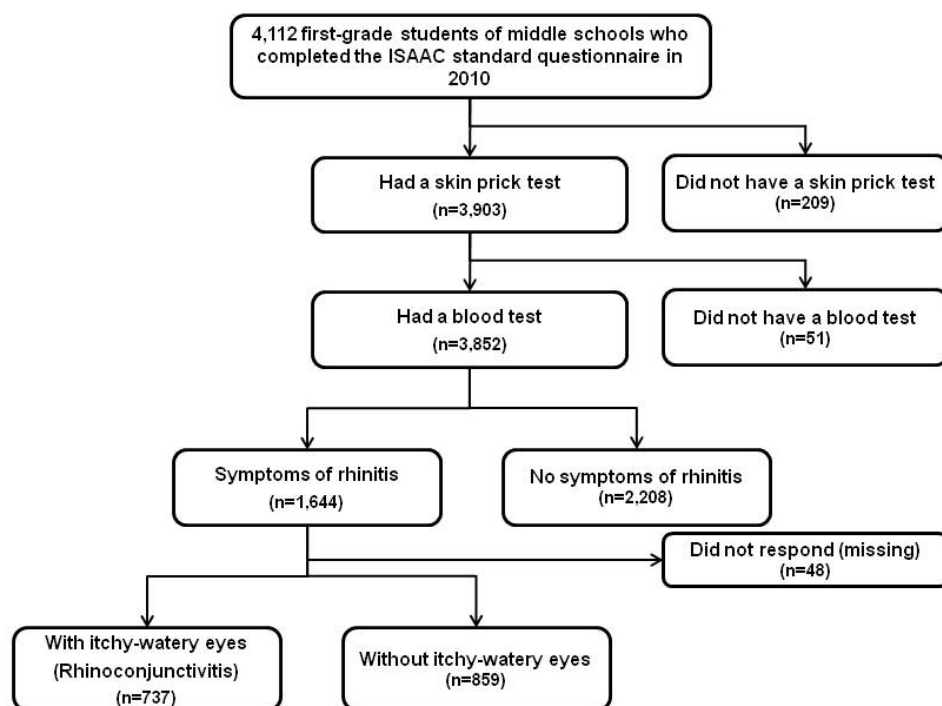


Figure 2. Flow chart of study subjects