Clinical features of allergic rhinitis in children of Shanghai, China

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ABSTRACT. The aims of the current study were to assess the clinical features of allergic rhinitis (AR) in children in Shanghai. Serum-specific IgE (sIgE) tests were performed on samples from patients with AR symptoms from January 2011 to December 2014. A disease-related questionnaire was completed after AR diagnosis. The allergen profile and clinical features of AR were analyzed. In total, 2713 AR patients were enrolled in this study. *Dermatophagoides pteronyssinus* was found to be the most common offending allergen in the study population. With increasing age, the prevalence of sIgE against inhalant allergens was significantly increased; however, the opposite trend was observed for food allergens. Additionally, the proportion of children with high levels of sIgE against *D. pteronyssinus* increased with age. Of the AR cases, 8.6% were classified as intermittent mild, 4.2% as persistent mild, 40.5% as intermittent moderate-severe, and 46.7% as persistent moderate-severe. A family history of allergies and a patient history of allergies within 6 months of birth were significantly associated with the duration and severity of AR symptoms. The occurrence of co-morbidities, such as allergic conjunctivitis, cough, and asthma, gradually increased from intermittent mild, persistent mild, and intermittent moderate-severe to persistent moderate-severe. The most frequently used drugs were topical corticosteroids and oral antihistamines, which were used by 86.7 and 79.0% of patients, respectively. These results confirm the adequacy of the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines for classifying AR patients, and advance the understanding of clinical features of AR in children in Shanghai, China.

Key words: Allergic rhinitis; Children; ARIA classification; Phenotypes; Risk factors; Serum-specific IgE

INTRODUCTION

Allergic rhinitis (AR) has received attention because of a globally increasing prevalence (Asher et al., 2006), including in China. AR is a symptomatic disorder of the nose that is induced after allergen exposure, and is caused by immunoglobulin E (IgE)-mediated inflammation of the nasal membrane. The burdens of AR include substantial social and economic costs related to its high prevalence and to the impairment of children's cognitive performance, daily activities, and quality of sleep (Nathan, 2007). AR is also the most common form of noninfectious rhinitis in children, affecting approximately 0.5-28% of children under 18 years old (Baena-Cagnani, 2004), and as many as 11% of children aged 3-6 years in China (Kong et al., 2009).

Finding the causative allergen of AR is crucial for diagnosing and managing this disorder. The serum-specific IgE (sIgE) test is a popular diagnostic allergy test that is commonly used in the clinical setting. Multiple allergens can be detected *in vitro* simultaneously with this test, which also avoids the occurrence of allergic reactions. AR may have different clinical presentations according to the types of symptoms and their duration. Additionally, AR has been classified as seasonal or perennial according to its seasonal profile, but these classifications do not define the clinical importance or the duration of the allergens. The Allergic Rhinitis and its Impact on Asthma (ARIA) document, which is endorsed by the World Health Organization and was published in 2001, introduced a new classification of AR based on the duration profile (intermittent/persistent) rather than on the seasonal profile, and a severity grading (mild/moderate-severe) based on symptom intensity and impairment of a patient's quality of life (Bousquet et al., 2001). This classification system is currently used worldwide. Recent studies have shown that the ARIA severity classification clearly discriminates among the impact of AR in all domains of quality of life and categorizes the symptom scores (Zicari et al., 2013). The duration and severity of AR are affected by numerous complex factors such as genetics, age, exposure time, exposure amount, and environmental factors (Li et al., 2014; Rhee et al., 2014; Portelli et al., 2015). Furthermore, large worldwide variations in the prevalence of AR symptoms have been explained based on these factors. However, factors contributing to AR development remain unknown. Although several epidemiologic studies have evaluated the prevalence of AR in China (Li et al., 2011; Chen et al., 2014), few studies have examined the different clinical presentations and factors that may influence them. In order to facilitate the diagnosis, management, and prevention of AR, we assessed the clinical presentation of AR in children in Shanghai. Particularly, we studied the profile of offending allergens in children of different age groups, and examined various potential contributing risk factors that could affect the duration and severity of clinical symptoms based on different AR classifications. Current drug treatment strategies are also discussed.

MATERIAL AND METHODS

Patients

This was a prospective study. All patients with hyperactive nasal symptoms (at least two symptoms from nasal obstruction, nasal itching, sneezing, and rhinorrhea) that persisted or accumulated for more than 1 h per day were included. Patients with nasal infections or tumors as determined during the examination were excluded. AR diagnosis was based on a detailed clinical history, positive results in the sIgE test for one or more allergens, and on the concordance between the clinical history and sIgE results. Patients with negative sIgE results were excluded from the study. With the help of their physicians, the parents of each AR patient completed a standardized questionnaire. This study was conducted in accordance with the declaration of Helsinki, and was conducted with approval from the Ethics Committee of Shanghai Jiaotong University. Written informed consent was obtained from the guardians of all study participants.

Serum-sIgE test

Peripheral blood samples were collected from all patients. The serum concentrations of total IgE and allergen sIgE antibodies were measured using the AllergyScreen system from Mediwiss Analytic GmbH (Moers, Germany) according to manufacturer instructions. Serum concentrations of sIgE antibodies against 10 common inhalant allergens were determined, including those against *Dermatophagoides pteronyssinus*, house dust, mulberry, cat dander, dog dander, cockroach, *Amaranthus retroflexus*, mixed grass pollen (mugwort, ragweed, *Humulus japonicus*, and gray quinoa), mixed tree pollen (oak, *Firmiana simplex*, and willow), and mixed mold (*Penicillium notatum*, branch spore mold, *Alternaria alternate*, *Aspergillus fumigatus*, and *Aspergillus niger*). Additionally, the concentrations of antibodies against nine common food allergens were evaluated, including those against egg white, milk, shrimp, beef, mussel, crab, mango, cashew nut, and pineapple.

A serum concentration of total IgE less than 100 IU/mL was regarded as normal and results of sIgE ^{3}0.35 IU/mL were considered positive. The quantitative test results of sIgE were divided into the following 6 allergic grades according to their concentrations: level 0: <0.35 IU/mL; level 1: 0.35-0.69 IU/mL; level 2: 0.7-3.49 IU/mL; level 3: 3.50-17.49 IU/mL; level 4: 17.50-49.99 IU/mL; level 5: 50.00-100.00 IU/mL; level 6: >100.00 IU/mL.

Questionnaire

The questionnaire was designed by the authors of the study and included questions regarding age; gender; maternal gestational weeks; birth order; feeding pattern; family history of allergies; history of allergies within 6 months of birth; duration of symptoms; nasal symptoms; results of the sIgE test; co-morbidities such as asthma, cough, allergic conjunctivitis, tympanitis, and eczema; impairments of daily life such as those of sleep, daily activities, leisure, sport, and school; and medical treatments.

Breastfeeding for more than 4 months after birth was defined as breastfeeding. Passive smoking was defined as exposure to parental smoking or any other second-hand smoke for more than 6 months at home. A family history of allergies was defined as having parents with

AR, allergic conjunctivitis, asthma, and/or eczema.

The severity of AR symptoms was classified as intermittent mild (IM), intermittent moderate-severe (IMS), persistent mild (PM), or persistent moderate-severe (PMS) according to the ARIA guidelines (Bousquet et al., 2001). Intermittent symptoms indicate those occurring <4 days/week or <4 weeks/year, whereas persistent symptoms represent those occurring ≥4 days/week and ≥4 weeks/year. Mild indicates that no impairment of daily activities or sleep resulted from nasal symptoms, and moderate-severe indicates that an impairment of daily activities or sleep was caused by nasal symptoms.

Statistical analysis

All statistical analyses were performed using the SAS version 9.1.3 software (SAS Institute Inc., Cary, NC, USA). Descriptive parameters are reported as means ± SD. Comparison between groups for each variable and the correlation between different AR classifications and related influencing factors were assessed by chi-square tests. The distribution of sIgE in response to *D. pteronyssinus* in different age groups was assessed by the chi-square test, the Cochran-Mantel-Haenszel chi-square test, and Spearman's analysis. $P < 0.05$ was considered statistically significant.

RESULTS

Patient characteristics

From January 2011 to December 2014, the Otorhinolaryngology Department of Shanghai Children's Medical Center, affiliated to Shanghai Jiao Tong University School of Medicine, admitted a total of 3474 patients presenting AR symptoms. Based on the results of sIgE tests, 2713 patients with ages ranging between 2-15 years old were diagnosed with AR. The average patient age was 6.2 ± 2.4 years. In total, 1821 patients (67.1%) were males and 892 (32.9%) were females. The mean duration of AR was 3.4 ± 2.6 years.

Sensitized allergens

The percentage of patients testing positive for sIgE antibodies was 78.1%. The sensitized allergens of the AR patients are summarized in Table 1. The most common offending inhalant allergen was *D. pteronyssinus*, with positive test results in 76.7% of cases. This was followed by dog dander (28.2%), mixed mold (26.1%), and house dust (19.5%). The most common food allergens were milk (26.7%), egg white (15.6%), beef (9.6%), and crab (6.8%). Of the 2713 patients tested, 1170 (43.1%) were sensitive to one allergen, 631 (23.3%) were sensitive to two allergens, and 912 (33.6%) were sensitive to three or more allergens. The percentage of patients positive for total food allergen-specific IgE was 39.5%. The percentage of patients positive for inhalant and food allergens was 32.7%. Food allergies accounted for 6.8% of cases. The percent of those positive for sIgE against house dust, cat dander, cockroach, mixed grass pollen, mixed tree pollen, and pineapple was higher in females. The percent of those positive for sIgE against *Amaranthus retroflexus* was the same in male and female subjects. The results of sIgE in response to mussels were negative in all children. We found no significant differences in gender distribution among the study groups ($P > 0.05$).

Table 1. Distribution of the 19 common allergens in 2713 children with AR.

Allergen	Male (N = 1821) (%)	Female (N = 892) (%)	Total (%)
D. pteronyssinus	1398 (76.8)	684 (76.7)	2082 (76.7)
House dust	530 (29.1)	342 (38.3)	530 (19.5)
Mulberry	30 (1.6)	8 (0.9)	38 (1.4)
Cat dander	122 (6.7)	66 (7.4)	188 (6.9)
Dog dander	516 (28.3)	250 (28.0)	766 (28.2)
Cockroach	30 (1.6)	20 (2.2)	50 (1.8)
A. retroflexus	22 (1.2)	12 (1.3)	34 (1.3)
Mixed mold	482 (26.5)	226 (25.3)	708 (26.1)
Mixed grass pollen	10 (0.5)	10 (1.1)	20 (0.7)
Mixed tree pollen	44 (2.4)	44 (4.9)	88 (3.2)
Egg white	308 (16.9)	116 (13.0)	424 (15.6)
Milk	514 (28.2)	210 (23.5)	724 (26.7)
Shrimp	82 (4.5)	14 (1.6)	96 (3.5)
Beef	196 (10.8)	64 (7.2)	260 (9.6)
Mussel	0	0	0
Crab	142 (7.8)	42 (4.7)	184 (6.8)
Mango	26 (1.4)	6 (0.7)	32 (1.2)
Cashew nut	98 (5.4)	32 (3.6)	130 (4.8)
Pineapple	0	2 (0.2)	2 (0.1)

Data are reported as N (%).

Differences in allergen distribution among different age groups

We analyzed common allergens and sIgE concentrations in all patients divided into the following different age groups: 2-3 years, 3-4 years, 4-5 years, 5-6 years, 6-8 years, and 8-15 years old. Positive results of sIgE against *D. pteronyssinus* were the highest in each age group. The results of sIgE against the different allergens in all age groups are shown in Table 2. The differences in IgE reactivity against *D. pteronyssinus*, house dust, cat dander, mixed mold, egg white, shrimp, and crab were statistically significant ($P < 0.05$) among the different age groups. Additionally, our results revealed that the type of sensitized allergens differed according to age. For example, the percent of those positive for sIgE against inhalant allergens significantly increased with increasing age (Figure 1), whereas the percent of those with sIgE reactivity against food allergens significantly decreased with increasing age (Figure 2).

Allergic grades of sIgE to *D. pteronyssinus*

The most common offending allergen was *D. pteronyssinus*, with positive results in 76.7% of cases among the 2713 patients tested. We subsequently analyzed the distribution of the allergic grades of sIgE (based on sIgE concentration as defined above) against *D. pteronyssinus* in the different age groups. Our results revealed that the proportion of those with high allergic grades (i.e., levels 4, 5, or 6) increased with increasing age. In contrast, the proportion of those with low allergic grades (i.e., levels 1, 2, or 3) was decreased with increased age (Figure 3). Furthermore, a positive correlation was found between age and allergic grades of sIgE in response to *D. pteronyssinus* (Spearman $r = 0.255$, $P < 0.001$).

AR classification and influencing factors

All AR patients were classified into the IM, IMS, PM, and PMS groups based on the ARIA guidelines. In total, 233 (8.6%) patients were classified as IM, 114 (4.2%) were PM, 1099 (40.5%) were IMS, and 1267 (46.7%) were PMS. The percentages of patients experiencing different nasal symptoms are shown in Figure 4. Nasal obstruction was the most common nasal symptom. Of the 2713 AR patients, 1424 (52.5%) had allergic conjunctivitis, which was the most common co-morbidity.

Table 2. Comparison of reactions against 19 common allergens according to age groups.

Allergen	2-3 years (N = 238) (%)	3-4 years (N = 433) (%)	4-5 years (N = 472) (%)	5-6 years (N = 410) (%)	6-8 years (N = 537) (%)	8-15 years (N = 623) (%)
*D. pteronyssinus***	134 (56.3)	278 (64.2)	330 (69.9)	302 (73.3)	470 (87.5)	568 (91.2)
House dust**	22 (9.2)	64 (14.8)	56 (11.9)	66 (16.1)	138 (25.7)	184 (29.5)
Mulberry	6 (2.5)	4 (0.9)	4 (0.8)	6 (1.5)	10 (1.9)	8 (1.3)
Cat dander*	22 (9.2)	30 (6.9)	14 (3.0)	14 (3.4)	44 (8.2)	64 (10.2)
Dog dander	74 (31.1)	106 (24.5)	120 (25.4)	108 (26.3)	158 (29.4)	200 (32.1)
Cockroach	2 (0.8)	6 (1.4)	4 (0.8)	6 (1.5)	14 (2.6)	18 (2.9)
A. retroflexus	4 (1.7)	8 (1.8)	2 (0.4)	2 (0.5)	8 (1.5)	10 (1.6)
Mixed mold**	28 (11.8)	84 (19.4)	88 (18.6)	114 (27.8)	170 (31.7)	224 (36.0)
Mixed grass pollen	2 (0.8)	6 (1.4)	2 (0.4)	0	0	10 (1.6)
Mixed tree pollen	6 (2.5)	22 (5.1)	14 (3.0)	10 (2.4)	20 (3.7)	16 (2.6)
Egg white**	72 (30.3)	126 (29.1)	90 (19.1)	50 (12.2)	48 (8.9)	38 (6.1)
Milk**	102 (42.9)	148 (34.1)	134 (28.4)	102 (24.9)	110 (20.5)	128 (20.5)
Shrimp*	16 (6.7)	24 (5.5)	12 (2.5)	12 (2.9)	14 (2.6)	18 (2.9)
Beef	18 (7.6)	56 (12.9)	50 (10.6)	42 (10.2)	38 (7.1)	56 (9.0)
Mussel	0	0	0	0	0	0
Crab**	42 (17.6)	48 (11.1)	30 (6.4)	12 (2.9)	22 (4.1)	30 (4.8)
Mango	8 (3.4)	4 (0.9)	6 (1.3)	4 (1.0)	4 (0.7)	6 (1.0)
Cashew nut	8 (3.4)	34 (7.9)	30 (6.4)	14 (3.4)	26 (4.8)	18 (2.9)
Pineapple	0	2 (0.5)	0	0	0	0

Data are reported as N (%). *$0.001 < P < 0.01$; **$P < 0.001$.

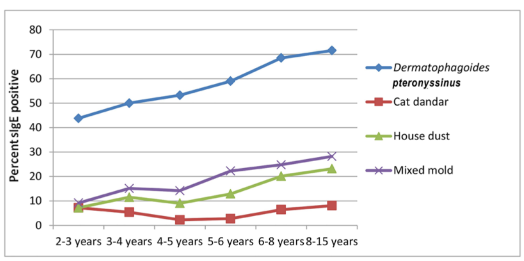

Figure 1. Distribution of inhalant allergens in different age groups. The type of sensitized allergens differed according to age. The percentage of patients with positive sIgE test results to inhalant allergens was significantly increased as age increased.

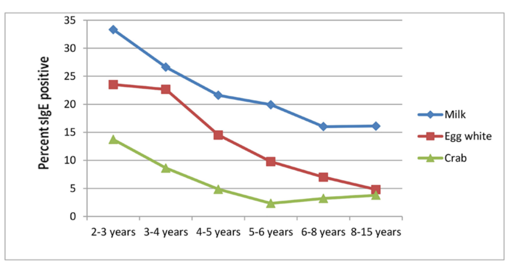

Figure 2. Distribution of food allergens in different age groups. The percentage of patients with IgE against food allergens was significantly decreased as age increased.

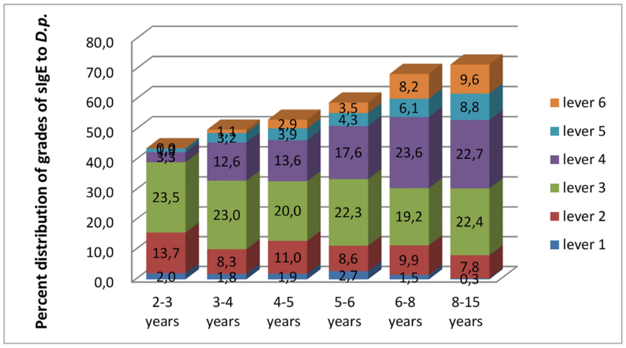

Figure 3. Distribution of allergic grades of sIgE to *Dermatophagoides pteronyssinus* (*D.p.*) in different age groups. The proportion of patients with high allergic grades based on sIgE concentrations (such as levels 4, 5, or 6) was increased as age increased. In contrast, the proportion of patients with low allergic grades (such as levels 1, 2, or 3) was decreased. A positive correlation was found between the age and the allergic grades of sIgE to *D.p.* (Spearman $r = 0.255$, $P < 0.001$).

Additionally, 1114 (41.1%) patients had cough, 894 (33.0%) had tympanitis, 401 (14.8%) had asthma, and 192 (7.1%) had eczema. The factors affecting the different AR symptom classifications are shown in Table 3. The duration and severity of AR were not associated with birth order, maternal gestational weeks, breastfeeding patterns, passive smoking, or pet ownership (P > 0.05). A family history of allergies and patient history of allergies within 6 months of birth were found to be significant influencing factors (P < 0.001). The occurrence of co-morbidities such as allergic conjunctivitis, cough, and asthma gradually increased from IM, PM, and IMS to PMS (P < 0.001).

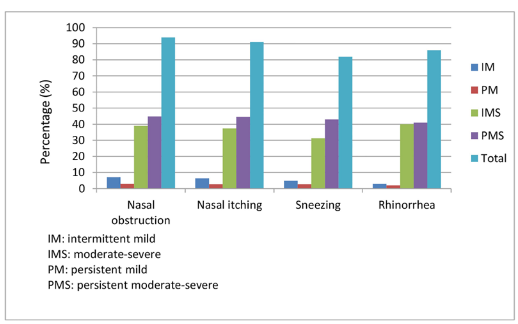

Figure 4. Occurrence of nasal symptoms in different AR groups. The most common nasal symptom was nasal obstruction.

Drug use

The most frequently used drugs were topical corticosteroids (2352 patients, 86.7%), followed by oral antihistamines (2143 patients, 79.0%), topical antihistamines (1331 patients, 49.1%), anti-leukotrienes (929 patients, 34.2%), nasal decongestants (104 patients, 3.8%), Chinese patent medicine (968 patients, 35.7%), and allergen-specific immunotherapy (174 patients, 6.4%). Additionally, irregular drugs, such as anti-inflammatory, antipyretic, analgesics, and antibiotics, were used in 19 patients (0.7%).

Table 3. AR symptom classifications and influencing factors.

		IM (N = 233) (%)	PM (N = 114) (%)	IMS (N = 1099) (%)	PMS (N = 1267) (%)
First born		199 (85.4)	92 (80.7)	940 (85.5)	1073 (84.7)
Partus maturus		218 (93.6)	101 (88.6)	1004 (91.4)	1142 (90.1)
Breastfeeding		110 (47.2)	51 (44.7)	509 (46.3)	532 (42.0)
Parental family history of allergies*		76 (32.6)	18 (15.8)	497 (45.2)	841 (66.4)
Passive smoking		114 (48.9)	61 (53.5)	482 (43.9)	555 (43.8)
History of allergies within 6 months of birth*		57 (24.5)	21 (18.4)	552 (50.2)	924 (72.9)
Pet ownership		30 (12.9)	12 (10.5)	144 (13.1)	112 (8.8)
Co-morbidities	Allergic conjunctivitis*	44 (18.9)	28 (24.6)	489 (44.5)	863 (68.1)
	Cough*	12 (5.2)	21 (18.4)	452 (41.1)	629 (49.6)
	Tympanitis	86 (36.9)	31 (27.2)	384 (34.9)	393 (31.0)
	Asthma*	6 (2.6)	4 (3.5)	154 (14.0)	237 (18.7)
	Eczema	9 (3.9)	11 (9.6)	78 (7.1)	94 (7.4)

Data are reported as N (%). *P < 0.001.

DISCUSSION

Studies investigating the main offending allergens in AR are essential for its treatment. Offending allergens change regularly with the surrounding atmosphere, and their distributions differ by region. Therefore, the investigation and monitoring of offending allergens is a prerequisite for effectively treating AR. The sIgE test for trigger allergens, which can be performed *in vitro*, prevents the risk of inducing severe allergic reactions in the tested patients. In the 2713 AR patients studied herein, the most common offending inhalant allergen was *D. pteronyssinus*, with positive results in 76.7% of cases, and this was followed by dog dander (28.2%), mixed mold (26.1%), and house dust (19.5%). The most common food allergens were milk, egg white, beef, and crab with positive results observed in 26.7, 15.6, 9.6, and 6.8% of patients, respectively. We found that most children were sensitized to indoor aeroallergens such as house dust mites and animal dander. The proportion of children sensitized to pollens was significantly lower than that reported for children in European countries (Zureik et al., 2002). *D. pteronyssinus* was observed to be the most common allergen, and the percentage of patients sensitized to *D. pteronyssinus* was 76.7%, which was much higher than that for other allergens. This suggests that there is a strong relationship between this allergen and the climate of Shanghai, which is warm, humid, and rainy due to its location. It was previously reported by Park et al. (2014) that the percent of patients sensitized to mixed tree pollen was 18.0% in Seoul, a similar Asian city in South Korea, whereas only 3.2% of patients were found to be sensitized to this allergen in the current study. Different geo-climatic conditions may have caused variations in the prevalence of aeroallergen reactivity in these different regions. The adaptation of specific microbiological flora and fauna to specific climatic conditions also adds to the variation in allergens. In the current study, the percent of those positive for total food allergen-specific IgE was 39.5%. However, most of these patients (32.7% total) were allergic to both inhalant and food allergens. IgE-associated food allergies have severe effects on the daily life of patients as their reactions manifest not only in the gastrointestinal tract, but also in other organ systems. IgE cross-reactivity often occurs between allergenic molecules in closely related species or between well-conserved molecules in the same protein family with similar functions that are present in different species (Propescu, 2015). Some food allergens are more heat-labile and susceptible to digestion, and therefore do not cause gastrointestinal sensitization, but rather provoke allergic reactions in patients already sensitized to cross-reactive aeroallergens through the respiratory route (Melioli et al., 2014), such as in patients with AR.

In the current study, we showed that the type of sensitized allergens differed according to age. For example, the percent of patients with sIgE against inhalant allergens, such as *D. pteronyssinus*, house dust, and cat dander, significantly increased with increasing age (Figure 1). However, IgE reactivity against food allergens, such as milk and egg white, significantly decreased with increasing age (Figure 2). Sensitization to crab allergens decreased with age from 2 years to 5 years, and then increased progressively thereafter (Figure 2). This trend may be related to changes in eating habits undetected by the sIgE test, as toddlers rarely eat crab. Overall, the tolerance to foods gradually increased with increasing age and assumed continuous food intake. Thus, food allergies are frequently reported in the youngest patients. Food allergens are replaced by inhalant allergens as the main offending allergens as patient age increases.

As mentioned, the most common offending allergen observed herein was *D. pteronyssinus*, with positive results in 76.7% of cases among the 2713 patients tested. Therefore, we sought to determine whether the magnitude of the sIgE concentration against *D. pteronyssinus* provided additional prognostic information beyond that provided by a positive sIgE test result alone. To accomplish this, we analyzed the distribution of allergic grades of sIgE, which were based on sIgE concentrations as described above, against *D. pteronyssinus* in the different age groups. We found that the proportion of patients with high levels of sIgE against *D. pteronyssinus* increased with increasing age. Whether this trend was related to the maturity of the immune system of the included children was unclear. Additional studies are needed to determine the immunological and physiological mechanisms underlying these associations. A positive serum IgE result denotes a sensitized state. Thus, sIgE production may be considered as the hallmark of an allergy. Previous studies have generally supported the notion that increasingly strong sIgE test results correlate with an increasing likelihood of clinical reactivity, and particularly that high sIgE values indicate a high degree of likelihood of allergies (Bernstein et al., 2008; Burks et al., 2011). Additionally, the risk of an allergic response, which can be evaluated using serum sIgE tests, was greater when the levels of sIgE against mites were summed. Therefore, early intervention in children with positive sIgE results may be very important for treating AR.

The ARIA document introduced a new classification system for AR based on the duration and severity of symptoms. The document stated that AR phenotyping is very important, as phenotypization may greatly influence the choice of diagnostic tests, predict the response to specific treatments, and suggest long-term prognosis (Jáuregui et al., 2011). Additionally, the ARIA classification system is currently widely used because it was validated both in general and pediatric populations (Valero et al., 2012). In the current study, we analyzed various risk factors for AR duration and symptom severity based on ARIA classifications. We found that the symptoms of 2366 (87.2%) patients were classified as moderate-severe. Mild symptoms are often ignored by patients and physicians, and most affected individuals do not report their complaints or seek treatments, which likely led to this result.

AR is the result of interactions between genetic and environmental factors. A previous study in South Korea reported that 40.2% of perennial AR cases had a family history of allergies. Additionally, the incidence of AR in children with a family history of allergies was 1.3-fold higher than in children without a family history of allergies (Min et al., 2001). In the current study, we found that children with a parental history of allergies or a history of allergies within 6 months of birth had a higher frequency of moderate/severe AR as determined by the

Spearman test ($P < 0.001$). Inheritance plays an important role in the pathogenesis of AR. Atopy, defined as the genetic predisposition to develop sIgE to common allergens, is widely accepted as a major risk factor for developing allergic diseases later in life (Bottema et al., 2010). Based on our results, we hypothesize that children with an atopic constitution may develop severe AR in the future. Here, we found that children with a history of allergies within 6 months of birth had a higher frequency of moderate-severe AR ($P < 0.001$). Thus, we hypothesize that if a child presents allergies within 6 months of birth, it is possible to predict the tendency to develop respiratory or other allergies, and that the subsequent allergic symptoms will be more severe. As such, early diagnosis and effective treatment of AR are important. Together, these results indicate that the severity of AR is affected by both the patient's family history of allergies and the patient's own history of allergies.

AR is also responsible for several co-morbidities, which were found to be more common in patients with moderate-severe AR in our study. The most common co-morbidity was conjunctivitis, which was present in 52.5% of cases, and this may explain why rhinoconjunctivitis was reported to occur very frequently in patients with AR (Rosario and Bielory, 2011). The other two most common co-morbidities were cough and tympanitis, which were observed in 41.1 and 31.0% of cases, respectively. The occurrence of allergic conjunctivitis, cough, and asthma gradually increased with increasing AR severity from IM, PM, and IMS to PMS ($P < 0.001$). Thus, allergic conjunctivitis, cough, and asthma are related to AR severity, whereby more severe symptoms are associated with a greater probability of these co-morbidities. This suggests that co-morbidity symptoms should be given more attention in AR patients, particularly in patients with IMS and PMS.

Whether or not breastfeeding is associated with allergic diseases remains controversial. Particularly, there are controversial reports regarding the protective effect of prolonged or exclusive breastfeeding against allergic diseases. For example, breastfeeding for less than 6 months was found to be a risk factor for physician-diagnosed AR (Morales et al., 2012). However, according to recent studies, there has been no consistently observed association between breastfeeding in the first year of life and either a history or current symptoms of allergic diseases in 6-7-year-old children (Björkstén et al., 2011). Interestingly, studies that have found breastfeeding to be protective have generally examined atopy during the first few years of life, whereas those finding no protective effect have typically examined AR later in childhood. In the current study, 44.3% of subjects were exclusively breastfed for more than 4 months after birth. However, there was no significant correlation between breastfeeding and AR severity. The protective effect of breastfeeding may be short-lived, and thus may not prevent the expression of atopy in later childhood. Additionally, the protective effect of breastfeeding may vary with maternal diet, maternal allergies, and the duration of breastfeeding.

Vlaski et al. (2011) conducted a random survey of 3026 children, and found that household tobacco smoking habits did not influence asthma, rhinitis, or eczema among 13-14-year-old adolescents. In agreement with these findings, we found no significant correlation between passive smoking and AR severity herein. Exposure to secondhand smoke is a common health problem worldwide, causing a substantial burden of disease for children and adults. Additionally, there are no adverse effects associated with smoking cessation or reducing the exposure to secondhand smoke. Therefore, children should avoid environmental tobacco smoke to reduce the risk of developing allergic diseases, such as AR, wheezing, and asthma.

Numerous recent studies have examined the associations between allergies and pets, but the conclusions have been inconsistent thus far. Specifically, while some studies have shown that exposure to pets within the first months or year of life increases the risk of subsequent allergic diseases, other studies have reported an inverse or no relationship between exposure to pets and risk of allergies (Chen et al., 2008; Wegienka et al., 2011; Lødrup Carlsen et al., 2012). In the current study, we found no significant correlation between pet ownership and AR severity. These discrepancies associated with allergies and pets may be attributed to the genetic makeup of both parents and children, extent of allergen exposure, housing conditions, and parental attitude towards pets. Therefore, the relationship between pet exposure and allergy symptoms is complex, and warrants further investigation.

In the treatment of AR, the most frequently used drugs include topical corticosteroids and oral antihistamines. This is in accordance with the ARIA guidelines, which describe the adequacy of these treatments based on evidence from controlled trials. In the current study, a total of 104 children, 64 of whom were less than 6 years old, used intranasal decongestants to control AR symptoms. The use of intranasal decongestants in children has a relatively high risk of serious adverse side effects compared to a relatively low potential benefit of reduced nasal blockage. Thus, the 2010 ARIA revision suggested that clinicians and parents should not administer intranasal decongestants to preschool children (Brozek et al., 2010). Moreover, clinical drug use for AR is not normative. Because of concerns regarding side effects, parents often stop drug administration, causing a lack of treatment. Additionally, irregular drugs, such as anti-inflammatory, antipyretic, analgesics, and antibiotics, were used for long periods in 19 patients (0.7%) in the current study to control AR symptoms. Ideally, effective treatments should limit adverse drug reactions, consider the consumption of medicines, and potentially involve personalized treatment plans. For the treatment of AR, additional thorough and systematic clinical studies are needed to determine the most effective treatment methods. Our results of this study advance the understanding of the clinical features of AR in children in Shanghai. However, this was a descriptive single-center study, and additional studies should examine other pediatric cases of AR in China. In the future, multicenter studies will be required to determine optimal management and prevention practices for pediatric AR.

Conflicts of interest

The authors declare no conflict of interest.

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