

Prevalence of food allergen and aeroallergen sensitization among children in Sichuan province

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Abstract

Food allergen and aeroallergen sensitization are common allergic diseases worldwide, with widely varying estimates of prevalence in children. Our study investigated the characteristics of ingestion and inhalation allergy among children from Sichuan province in Southwest China, so as to get public awareness of these disorders.

A total of 1722 children between 0 and 14 years' old were enrolled in this study. They were outpatients in the West China Second University Hospital during June 2019 to September 2019. Serum specific IgE specific to 10 types of food allergen and 10 types of aeroallergen were estimated. Nutrition indicators were tested by electrochemical luminescence.

59.70% children were allergic to at least 1 allergen, comprising 24.90% to aeroallergen and 38.81% to food allergen, respectively, whereas 36.28% children were allergic to both aeroallergen and food allergen. Milk was the most common food allergen, and egg came in second place. With regard to aeroallergen, house dust mite held the maximum proportion (65.02%), whereas dust mite followed behind. Inhalation allergy was more commonly seen in boys than girls. Bronchitis was the most common symptom of both allergies. In addition, the highest incidence age for children to be sensitive to food allergen and aeroallergen were 0~2 years' old and 3~5 years' old, respectively. It is worth mentioning that there was no significant difference in nutritional status between children with or without allergic diseases.

Our findings reveal that milk, egg, house dust mite, and dust mite are the most common allergens among children in Sichuan province. Boys are more susceptible to aeroallergen than girls. Furthermore, the prevalence of ingestion and inhalation allergy varies from different age groups, and has no correlation with nutritional status. In brief, the analysis of the pattern of food allergen and aeroallergen sensitization is invaluable to effective diagnosis and treatment of allergic diseases.

Abbreviations: Alb = albumin, Ca = calcium, ECRHS = European Community Respiratory Health Survey, Hb = hemoglobin, RDA = recommended dietary allowances, sIgE = specific IgE, TP = total protein, Vit D = vitamin D.

Keywords: food allergen sensitization, aeroallergen sensitization, prevalence, gender, age, nutritional status

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TL and S-YL contributed equally to this study.

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1. Introduction

Allergic disease refers to the human body inhaling, ingesting, injecting or contacting certain substances containing allergens, which in turn triggers the body to produce excessive amounts of immunoglobulin E.^[1,2] Allergy disease can cause various functional disorders or tissue damages, and sometimes it can even cause death.^[3-6] Allergic inflammation and reactions to allergen challenge can be local (within the target organ), as is the case for allergic rhinitis and allergic asthma, or systemic, as is the case for anaphylaxis.^[7] Different systemic allergic symptoms can occur at the same time and can be complex, requiring experienced and comprehensive diagnosis. In most of the European Union (EU) countries, allergic diseases are the most common chronic illnesses of childhood, affecting >1 child in 4 in some countries.^[4] Between 1997 and 2007, the self-reported prevalence of food allergy in children younger than 18 years in the United States increased by 18% to an estimated prevalence of 3.9%,^[8] and prevalence had reached ~5% by 2011.^[9] Therefore, allergy has become a global problem that endangers children's health.^[10]

Allergens mainly include food allergen and aeroallergen, such as egg, milk, peanut, aquatic animal products, pollen, dust, and animal dander, and so on. Generally, staying away from certain allergens is the most effective way to avoid allergies. A report suggested that avoidance of important allergens seems not only to result in clinical remissions but in many cases also reduce bronchial hyper-reactivity.^[11] The long-term solution to the asthma epidemic is thought to be prevention, but not treatment of

established disease.^[12] Infants of allergic parents were either subjected to an allergen-avoidance regimen from birth for 6 months or managed conventionally. As a result the experimental group had less eczema at 6 months and 1 year than did the control group.^[13] Notably, the use of medications such as steroids, antihistamines, and adrenaline is the main treatment for allergies.^[14] However, currently available pharmaceuticals only control the symptoms of allergy, and they do not address the underlying immune disorder.^[15] Allergen immunotherapy is useful for some types of allergies such as hay fever and reactions to insect bites, but it is less effective in asthma.^[16] Furthermore, the course of treatment is too long (>2~3 years) and improper use can cause serious adverse reactions. For these reasons, allergen isolation is the most efficient, economical, and convenient means to prevent allergic diseases. It is of great clinical significance to understand the allergen types of children in specific areas.

Allergen detection, including *in vivo* test and *in vitro* test, is a basic method to determine whether it is allergic disease and also identify allergens. Briefly, *in vitro* tests were performed to detect total IgE and specific IgE (sIgE) in peripheral blood.^[17-19] *In vitro* test includes prick test and intradermal test, both of which reflect type I rapid allergic reaction, mainly targeting macromolecular allergens. Serum sIgE analysis can detect hundreds of allergen at the same time with high stability and specificity. It is especially suitable for severe dermatitis or skin scratch patients, poor skin response of the elderly and children younger than 3 years. It can be used in people who need to assess the severity of allergies and who are planning specific immunotherapy. In this study, serum sIgE analysis was used for safe and accurate allergen detection in children.

Due to the distinctions of immune system and living habit, the prevalence and characteristics of allergies are different between children and adults. So far the studies on the prevalence of allergies for children in Chinese Mainland are rare. Our study probed into allergies in children from Sichuan province, an area located in Southwest China with a basin climate region. Enzyme-linked immunosorbent assay was performed to detect serum IgE specific to 20 common allergens including 10 kinds of food allergen and 10 kinds of aeroallergen. Statistical analysis was used to study the differences of allergy in different sex and age groups. Our study may provide references and recommendations for the diagnosis as well as the treatment of allergic diseases.

2. Materials and Methods

2.1. Study population

A total of 1722 children including 1033 boys and 689 girls between 0 and 14 years were enrolled in this study. They were outpatients in the West China Second University Hospital during June 2019 to September 2019. This study was approved by Ethics Committee of West China Second Hospital of Sichuan University. Informed consents were obtained from their guardians before serum IgE analysis. This study excluded children from remote rural areas, and focused on Chinese Han children from urban areas in Sichuan province, Southwest China.

2.2. Serum sIgE analysis

Serum samples from each participant were collected and then tested by Uranus AE-65 Automatic Elisa Analyzer (AIKANG MEDTECH, Shenzhen, China) with allergen testing kit purchased

from Fooke (HOB-biotech, Suzhou, China) following standard operating procedure. Serum IgE for 10 food allergens (milk, egg, crab, beef, wheat, shrimp, peanut, codfish, mutton and soybean) and 10 aeroallergens (house dust mite, dust mite, dust, alternaria, cockroach, willow, cat hair, artemisia vulgaris, dog dander, and artemisiifolia) were detected in this study; 0.35 IU/mL was used as the cutoff point of IgE value between normal and abnormal. Based on the level of serum sIgE, we classified the allergy intensity into levels 0, 1, 2, 3, 4, 5, and 6 (0, <0.35 IU/mL; 1, 0.35~0.7 IU/mL; 2, 0.7~3.5 IU/mL; 3, 3.5~17.5 IU/mL; 4, 17.5~50 IU/ml; 5, 50~100 IU/mL; 6, >100 IU/mL). The total score for allergy intensity is the sum of the intensity score of different allergens.

2.3. Nutrition indicators analysis

Levels of several nutrition indicators such as total protein (TP), albumin (Alb), hemoglobin (Hb), calcium (Ca), and vitamin D (Vit D) were tested by electrochemical luminescence (Siemens, Germany).

2.4. Statistical analysis

For continuous variables, the results were shown as mean \pm SEM. Analysis of variance (ANOVA) test was used to determine the significance of different age group differences. χ^2 test was used for comparison of rates or constituent ratios. All statistical analyses were performed on SPSS 19.0 (SPSS Inc, Chicago, IL). $P < .05$ was considered statistically significant.

3. Results

3.1. General situation of children's allergy in Sichuan province

The characteristics of the children included in this study are summarized in Table 1. Of the 1722 children we studied, 59.70% (1028/1722) were allergic to at least 1 allergen (Fig. 1A). For those 1028 children, more than one-third (36.28%) children were hypersensitive to both aeroallergen and food allergen (Fig. 1B); 24.90% children were hypersensitive to aeroallergen alone, whereas 38.81% children were hypersensitive to food allergen alone (Fig. 1B). Bronchitis (18.29%), cough (16.93%), and rash (13.13%) were the top 3 allergy symptoms (Fig. 1C). For food allergens, milk and egg were the most important food allergens, causing 73.96% and 54.79% allergies, respectively (Fig. 1D). As for aeroallergen, house dust mite (65.02%) and dust mite (63.12%) lead to most of the allergies, followed by

Table 1
Characteristics of included children.

Characteristics	Value
Age, y, n (%)	
0-2	752 (43.67%)
3-5	613 (35.60%)
6-8	236 (13.70%)
9-11years	76 (4.41%)
12-14	45 (2.61%)
Sex, n (%)	
Male	689 (40.01%)
Female	1033 (59.99%)
Ethnicity (Han Chinese), n (%)	1722 (100%)
Residence (Urban areas), n (%)	1722 (100%)

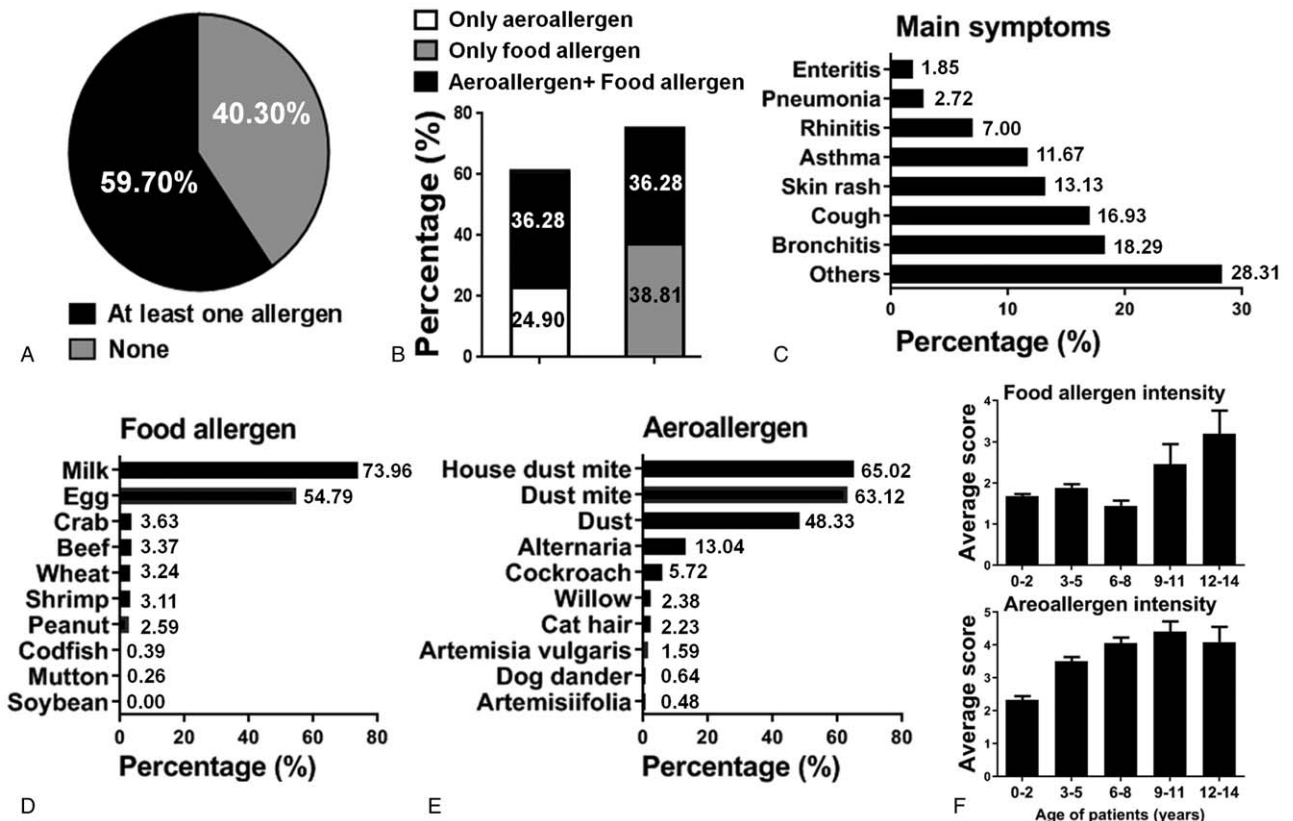


Figure 1. General situation of children's allergy in Sichuan province. (A) 59.70% (1028/1722) children in Sichuan province were allergic to at least 1 allergen. (B) For those children with allergies, 36.28% were hypersensitive to both aeroallergen and food allergen. 24.90% children were hypersensitive to aeroallergen alone, whereas 38.81% children were hypersensitive to food allergen alone. (C) Bronchitis (18.29%), cough (16.93%), and rash (13.13%) were the top 3 allergy symptoms. (D) For food allergens, milk and egg were the most important food allergens, causing 73.96% and 54.79% allergies, respectively. (E) As for aeroallergen, house dust mite (65.02%) and dust mite (63.12%) lead to most of the allergies, followed by house dust (48.33%) inducing nearly half of the allergies. (F) The average food allergen intensity scores for 0~2, 3~5, 6~8, 9~11, and 12~14 years' age group were 2.33 ± 0.12 , 3.51 ± 0.13 , 4.06 ± 0.17 , 4.40 ± 0.32 , and 4.10 ± 0.46 , respectively. Although the average aeroallergen intensity score for 0~2, 3~5, 6~8, 9~11, and 12~14 years' age group were 1.69 ± 0.05 , 1.90 ± 0.08 , 1.46 ± 0.12 , 2.47 ± 0.49 , and 2.06 ± 0.55 , respectively. Data presented are the mean \pm SEM (analysis of variance, $P < .001$). These results show that allergies to food allergen and aeroallergen are common among children in Sichuan province. One child may be allergic to different allergens. Milk and egg are the most common food allergens. Besides house dust mite, dust mite and dust are the most common aeroallergens. The allergic intensity of aeroallergen is stronger than that of the food allergen.

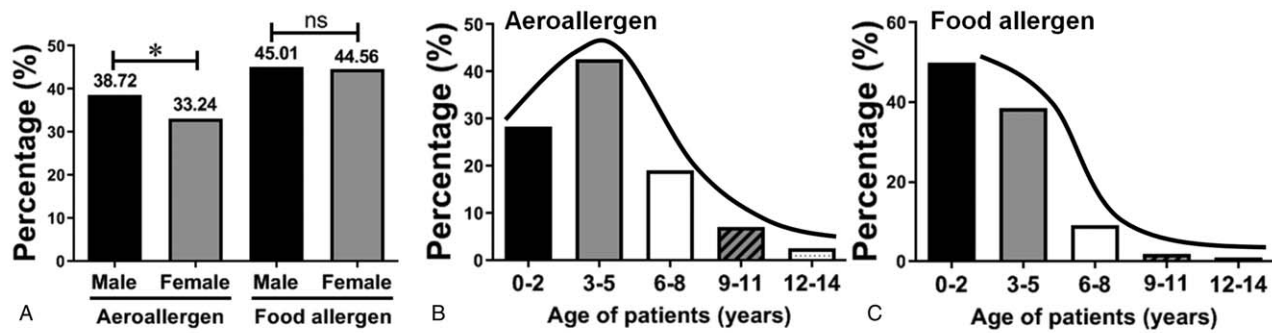
house dust (48.33%) inducing nearly half of the allergies (Fig. 1E). We classified the allergy intensity into levels 0, 1, 2, 3, 4, 5, and 6 (0, <0.35 IU/mL; 1, $0.35 \sim 0.7$ IU/mL; 2, $0.7 \sim 3.5$ IU/mL; 3, $3.5 \sim 17.5$ IU/mL; 4, $17.5 \sim 50$ IU/mL; 5, $50 \sim 100$ IU/mL; 6, >100 IU/mL). As we can see in Figure 1F, the average food allergen intensity scores for 0~2, 3~5, 6~8, 9~11, and 12~14 years' age group were 2.33 ± 0.12 , 3.51 ± 0.13 , 4.06 ± 0.17 , 4.40 ± 0.32 and 4.10 ± 0.46 , respectively (ANOVA, $P < .001$). These data indicated that the elder children aged from 9 to 14 years have more severe food allergies than younger children aged from 0 to 8 years. In addition, the average aeroallergen intensity scores for 0~2, 3~5, 6~8, 9~11, and 12~14 years age group were 1.69 ± 0.05 , 1.90 ± 0.08 , 1.46 ± 0.12 , 2.47 ± 0.49 , and 2.06 ± 0.55 , respectively (ANOVA, $P < .001$). Besides, we found that in children of the same age, aeroallergen intensity is stronger than food allergen intensity. These results show that allergies to food allergen and aeroallergen are common among children in Sichuan province. One child may be allergic to different allergens. Milk and egg are the most common food allergens. Besides house dust mite, dust mite and dust are the most common aeroallergens.

3.2. Allergy characteristics of children in different sex and age groups

As shown in Figure 2A, the incidence of hypersensitive to aeroallergen in boys was 38.72%, which was greater than that of girls (33.24%) (χ^2 test, $P = .02$). However, the difference of the incidence of hypersensitive to food allergen was not statistically significant in different sexes. The incidence of inhalation allergy was highest and statistically significant in children aged 3 to 5 years (Fig. 2B). What's more, the ratio of ingestion allergy was highest in the 0~2 years' group and then decreased with age (Fig. 2C). TP, Alb, Hb, Ca, and vitamin D (VitD) were slightly higher in children with allergies than in healthy children, regardless of age 0~2 or 3~5, but the difference was not statistically significant (Fig. 2D). These results indicated that the nutritional status is not the cause of allergies affecting children in the Sichuan province.

4. Discussion

According to some epidemiological investigations abroad, the population accounts for 4% of the total population and 6%~7%



Nutritional status							
Age/years	Gender	Allergy	TP (g/L)	Alb (g/L)	Hb (g/L)	Ca (ng/ml)	VitD (ng/ml)
0-2	Male	(+)	68.09±1.04	42.79±0.90	121.19±0.84	2.44±0.03	39.36±1.46
		None	67.06±0.33	42.62±0.30	120.14±1.34	2.38±0.01	38.51±0.58
	Female	(+)	68.46±1.64	43.83±0.76	122.05±0.87	2.49±0.03	38.29±1.40
		None	66.93±0.36	42.31±0.38	120.63±0.84	2.36±0.01	38.47±0.56
3-5	Male	(+)	72.36±1.24	45.15±0.85	127.22±2.11	2.42±0.02	30.61±1.30
		None	69.22±0.40	44.83±0.33	124.11±0.21	2.38±0.01	30.57±0.51
	Female	(+)	74.08±1.82	45.27±0.72	127.15±1.11	2.43±0.06	29.28±1.82
		None	69.23±0.43	45.10±0.35	124.84±0.24	2.38±0.02	29.65±0.81

D TP, total protein; Alb, albumin; Hb, hemoglobin; Ca, calcium; VitD, vitamin D.

Figure 2. Allergy characteristics of children in different sex and age groups. (A) The incidence of hypersensitive to aeroallergen in boys was 38.72%, which was greater than that of girls (33.24%) (χ^2 test, $P=0.02$). However, the difference of the incidence of hypersensitive to food allergen was not statistically significant in different genders. (B) The incidence of inhalation allergy was highest and statistically significant in children aged 3 to 5 years. The line stands for the variation trend. (C) The ratio of ingestion allergy was highest in the 0~2 years' group and then decreased with age. The line stands for the variation trend. (D) Total protein (TP), albumin (Alb), hemoglobin (Hb), calcium (Ca), and vitamin D (VitD) were slightly higher in children with allergies than in healthy children, but the difference was not statistically significant. These results indicated that the nutritional status is not the cause of allergies affecting children in the Sichuan province. ($P < .05$, $**P < .01$ and $***P < .001$).

of infants younger than 3 years have allergies to certain foods.^[15] 63.6% children enrolled from pediatric clinics in New York reported perceived sensitization to one or more aeroallergen, with cat dander and dust being the most sensitive.^[20] In this study, we find that 59.70% children enrolled from West China Second University Hospital were allergic to at least 1 allergen. One child may be allergic to different allergens. And the allergic reaction intensity of aeroallergens was significantly higher than that of food allergens. Therefore, food allergen and aeroallergen sensitization are really common among children in Sichuan province, Southwest China.

The general principles of the treatment of allergies include patient education, avoidance of environmental allergen exposure, standardized drug therapy, and allergen-specific immunotherapy.^[21-23] Avoiding allergen exposure is a key measure in the treatment of allergic diseases. Benefit from sIgE detection, both the avoidance of allergen and the allergen-specific immunotherapy can be implemented accurately and effectively. A meta-analysis showed milk and egg are the 2 most common food allergens in 15 countries of the ECRHS (European Community Respiratory Health Survey).^[24] As for aeroallergen, a survey from adult allergy clinic in the University of Wisconsin Hospital showed that tree, dust mite, and pet (cat and/or dog) are the most common sensitivities of allergens.^[25] Another study in New York revealed that tree pollen is the most commonly reported aeroallergen of children followed by dust.^[20] In our study, we

find that milk, egg, house dust mite, dust mite, and dust are the most common allergens among children in the Sichuan province. Accumulated studies found that most food reactions occur during the first year of life.^[26] Similar to this study, our results showed the incidence of food allergies was highest in the 0~2 years' age group, which declined with age. Before the age of 6, children are usually allergic to protein foods such as egg and milk. This is mainly due to the protective function of the baby's gastrointestinal mucosa is not mature enough, and the foreign protein is easy to pass through. With the increase of age, children's gastrointestinal system begins to accept a variety of food allergens, gastric acid secretion increases, gastrointestinal immune function matures, and intestinal protease gradually approaches adult level. Therefore, the rate of food allergy decreases as a result. Furthermore, our results showed that children aged 3~5 years had the highest incidence of inhalation allergy. This may be due to increased outdoor activity and underdeveloped immune systems in children of this age. Environmental exposures that occur during the first few months of life can influence the risk of allergy development in later childhood.^[27] It is interesting to note that the incidence of inhalation allergy in boys were significantly higher than that of girls in our study. The reason might be boys are usually more active than girls, so they get more chance to exposure to aeroallergens.

Allergy involves a wide range of clinical manifestations, including mucocutaneous, digestive, and respiratory symp-

toms,^[28–30] such as eczema, urticaria, vomiting, abdominal pain, bronchitis, cough, and asthma.^[15,31] Severe cases could lead to anaphylactic shock, which sometimes may be a life-threatening condition. Patients often choose long-term diet allergenic food to avoid the occurrence of allergy, which often leads to the lack of nutritional intake. A study found that parents of 9-year-old children with food hypersensitivity reported that their children had significantly worse physical functioning, more social limitations, and poorer general health than children with no allergic diseases. Those with high levels of food sIgE antibodies also had poorer mental health and general health.^[32] A study has shown that a group of children (aged 1–9 years) with known food allergies had very low intakes of nutrients including calcium, iron, vitamin D, vitamin E, and zinc, provided at <67% of the recommended dietary allowances.^[33] Children with serum vitamin D ≥ 75 nmol/L had significantly reduced odds of aeroallergen sensitization.^[34] However, another study suggested that neither vitamin D intake in pregnancy nor vitamin D supplementation in infancy were associated with risk of allergic rhinitis.^[34] The blood lipid profile is associated with asthma, airway obstruction, bronchial responsiveness, and aeroallergen sensitization in 7-year-old children.^[35] Our study paid close attention to the nutrition and lipid levels of TP, Alb, Hb, Ca, and Vit D, only to find no significant differences between children with allergies and a matched control group of children in 0~2 and 3~5 year' group. Children with allergies, especially food allergies, suffer from dystrophy because they avoid certain foods. Our results did not show malnutrition in children with allergies, possibly because modern families generally value the nutritional supply of children. Interestingly, some nutritional indicators in children with allergies group are slightly higher than control group, possibly due to the presence of allergy symptoms such as vomiting, diarrhea, and so on, leading to the higher serum concentrations.

Genetic factors certainly contribute to susceptibility to different allergic diseases, but genetics alone cannot explain the specificity of allergies. The researchers suggest that the nature of anaphylaxis may be caused by at least 2 factors: first, an accidental temporal association between a harmful irritant and a neutral antigen, leading to the development of anaphylaxis to the latter; second, the reason may be related to the different sensitivities of individuals to the harmful effects of allergens.^[34] For children with allergies, strict avoidance of allergens is the best precaution. Education of allergy sufferers is crucial. In a word, allergy is an objective natural phenomenon, which seriously affects the quality of life of some people and even endangers their lives, which deserves our attention. The detection of serum allergen-specific IgE is conducive to understanding the status of allergy, which can better provide help for identifying allergens and taking appropriate preventive measures to reduce the incidence of allergic diseases in children.

The present study has 3 limitations that should be mentioned. First, a small number of children is included in this study; thus, a larger study is needed. Second, limited by the type of the clinical detection kit, only 20 allergens were involved in this study. Third, because all the children in this study were outpatients, the proportion of children allergic to at least 1 allergen might be higher than that of the social average.

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