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ORIGINAL ARTICLE

Analysis of Aeroallergens in Sichuan Province after the COVID-19 Epidemic

Menglan Zhang [1, 2], Lingyi Yan [1, 2], Leiwen Peng [1, 2], Yongmei Jiang [1, 2]

[1] *Department of Laboratory Medicine, West China Second University Hospital, Sichuan University, Chengdu, China*
[2] *Key Laboratory of Birth Defects and Related Diseases of Women and Children, Ministry of Education, Sichuan University, Chengdu, China*

SUMMARY

Background: **Identifying the distribution and pattern of specific aeroallergens in Sichuan, China, after the coronavirus disease (COVID-19) epidemic and to provide a basis for future prevention and clinical treatment.**
Methods: **Serological tests for 10 types of aeroallergens were performed on 10,036 participants attending the West China Second University Hospital from January 2020 to January 2021. SPSS23.0 was used to statistically analyze their specific immunoglobulin E (sIgE) grades in different genders, various age groups, and different diseases.**
Results: **Of the 10,036 participants, 4,578 (45.62%) were allergic to at least one allergen. House dust had the highest sensitization rate (2,974, 29.63%), followed by Dermatophagoides farina (2,717, 27.07%) and Dermatophagoides pteronyssinus (2,611, 26.02%). Male and female participants had no significant difference in overall sensitization distributions. The prevalence differences between 0 - 3, 4 - 6, 7 - 9, 10 - 12, 13 - 15, and over 16-year-old age groups were statistically significant ($p < 0.05$), and the highest incidence age for children to be sensitive to aeroallergens was 4 - 6 years, respectively. Sensitization to D. pteronyssinus, D. farina, house dust, dog epithelium, and Alternaria alternata was more common in patients with rhinitis and asthma compared with bronchitis.**
Conclusions: **Aeroallergens are important causes of respiratory-related allergic diseases, and the characteristics of allergen sensitization discovered in this study could help with inhalant allergy disease prevention, diagnosis, and management in the post-epidemic era.**
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Correspondence:
Dr. Yongmei Jiang
Department of Laboratory Medicine
West China Second University Hospital of Sichuan University
No. 20 Renmin South Road
Chengdu 610041
Sichuan
China
Phone: +86 28 85501635
Fax: +86 28 85501635
Email: jiangyongmeiwst@163.com

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INTRODUCTION

Allergy-related disorders are a significant public health issue on a global scale. Simultaneously, for more than 50 years, the prevalence of allergic diseases has continued to rise in the industrialized world [1,2]. According to a survey, approximately 30% of the population will have at least one allergic reaction during their lifetime, and the rate of occurrence continues to rise each year. Variations in genetic susceptibility, environmental exposure, and socioeconomic status vary by region.
Allergic reactions are frequently used to refer to type I hypersensitivity reactions, which typically manifest

symptoms within 30 minutes and frequently result in allergic rhinitis, conjunctivitis, urticaria, asthma, and other serious allergic conditions [3]. Allergic disorders are most frequently caused by an atopic constitution and triggered by environmental factors. The majority of allergens that cause type I hypersensitivity are naturally occurring proteins, such as dust mites, animal hair, and plant pollen. Due to the fact that type I hypersensitivity reactions are defined by the presence of allergens and specific immunoglobulin E (sIgE), detecting sIgE has become critical for diagnosing allergic disorders [4]. Specific IgE antibodies are widely recognized as an objective marker of allergic reactions both at home and abroad, and they aid in illness prediction and therapy [5].

The novel coronavirus pneumonia epidemic outbreak in late 2019 has had a big effect on the health and lives of everyone across the country [6,7]. There was a new emphasis on self-protection against respiratory diseases, such as keeping social distance, wearing masks in public places, and paying attention to respiratory and hand hygiene. With changes in the environment and society, these lifestyle and routine measures have also played an important role in reducing the number of respiratory infections and inhalation allergies [7]. For patients with inhaled allergic diseases, the most important part of daily protection is to avoid contact with allergens as much as possible [8]. However, there is limited evidence about whether the distribution of aeroallergens changed with reduced exposure to sensitizing factors in patients following the COVID-19 outbreak. Due to the fact that aeroallergens vary between individuals and communities, it is critical to understand the distribution of environmental aeroallergens associated with clinical disease in order to adequately explain symptoms and implement effective integrated interventions. Analysis of aeroallergens is helpful to understand the impact of epidemic prevention and control measures on the prevalence of common respiratory diseases other than COVID-19.

In this paper, we retrospectively analyzed the results of 10,036 patients who were tested for 10 inhaled allergen-specific IgE antibodies in Sichuan after the COVID-19 epidemic, in an attempt to understand the distribution characteristics and patterns of aeroallergens in this region and to provide epidemiological information and a clinical diagnostic basis for the prevention and management of allergic diseases in the post-epidemic era.

MATERIALS AND METHODS

Subjects

In this retrospective study, 10,036 patients who sought medical care at West China Second University Hospital between January 2020 and January 2021 were analyzed. This study was approved by the Ethics Committee of West China Second Hospital of Sichuan University. Patients ranging from 14 days to 64 years of age were classified into 6 groups according to age. The majority of patients came from the Department of Pediatrics. Clinical diagnosis mainly covered bronchitis, allergic rhinitis, allergic asthma, and urticaria. None of the 10,036 patients was diagnosed with a corona-virus infection.

Methods

Common inhaled allergen-specific IgE antibodies (sIgE) were measured by capture enzyme-linked immunosorbent assay (ELISA), Fooke™ system (HOB Biotech Group Corp., Ltd.) according to the manufacturers' recommendations. A total of 10 types of aeroallergens were analyzed, including Dermatophagoides pteronyssinus, Dermatophagoides farina, house dust, mugwort, ragweed, willow, dog epithelium, cat epithelium, cockroach, and Alternaria alternata. According to the results from this system, sIgE are graded and interpreted according to international standards: 0.35 - 0.7 IU/mL for grade 1; 0.7 - 3.5 IU/mL for grade 2; 3.5 - 27.5 IU/mL for grade 3; 27.5 - 50 IU/mL for grade 4; 50 - 100 IU/mL for grade 5; > 100 IU/mL for grade 6. A test result in grade 1 or above was considered positive.

Statistical analysis

The test results were statistically analyzed using the Statistical Package for Social Sciences version 23.0 (IBM SPSS Statistics for Windows; IBM Corp., Armonk, NY, USA). For categorical values, the chi-squared test or Fisher's exact probability method was used. $p < 0.05$ was considered statistically significant.

RESULTS

Characteristics of the study population

The study population consisted of 5,870 males (58.49%) and 4,166 females (41.51%). The age of the patients ranged from 14 days to 64 years, with an average of 3.64 ± 4.45 (mean ± SD) years. Six age groups were used to categorize the subjects: 0 - 3 years, 4 - 6 years, 7 - 9 years, 10 - 12 years, 13 - 15 years, and over 16 years (Table 1).

Overall allergen sensitization

Of the 10,036 patients, 4,578 tested positive for at least one allergen, a prevalence of 45.62%. Among the 10 aeroallergens evaluated, house dust was the most commonly positive for sIgE (29.63%), followed by D. farina (27.07%) and D. pteronyssinus (26.02%). The sensitization difference was statistically significant (χ^2 = 15,930.72, $p < 0.05$). With the exception of mites, the majority of aeroallergens (> 80%) were linked to low-grade allergic reactions (grade 1 or 2, corresponding to a sIgE level of 0.35 to 3.5 IU/mL). In this study, the only case of an extremely high-grade response to house dust was also sensitized to D. pteronyssinus and D. farina (at grade 6). None of the ragweed, willow, or cockroach were related to the occurrence of allergic reactions above grade 5 (Table 2).

Table 1. Gender and age groups for the 10,036 patients.

Age groups, years	Male, n	Female, n	Total, n (%)
0 - 3	3,344	2,379	5,723 (57.02)
4 - 6	1,548	1,073	2,621 (26.12)
7 - 9	608	400	1,008 (10.04)
10 - 12	265	187	452 (4.50)
13 - 15	71	53	124 (1.24)
≥ 16	34	74	108 (1.08)
total	5,870	4,166	10,036 (100.00)

Table 2. Overall prevalence of 10 aeroallergens.

Allergen	grade 1	grade 2	grade 3	grade 4	grade 5	grade 6	Total, n (%)
D. pteronyssinus	235	553	781	536	274	232	2,611 (26.02)
D. farina	238	518	730	474	274	483	2,717 (27.07)
house dust	1,342	1,444	175	10	2	1	2,974 (29.63)
mugwort	11	37	19	2	2	1	72 (0.72)
ragweed	58	30	7	0	0	0	95 (0.95)
willow	53	30	4	1	0	0	88 (0.88)
dog epithelium	136	97	41	10	4	3	291 (2.90)
cat epithelium	68	134	77	16	7	14	316 (3.15)
cockroach	36	28	2	0	0	0	66 (0.66)
Alternaria alternata	50	135	167	109	41	16	518 (5.16)

Table 3. Comparison of prevalence in male and female.

Allergen	Male (n)	%	Female (n)	%	Chi-square (χ^2)	p-value
D. pteronyssinus	1,644	28.01	967	23.21	29.108	0.000
D. farina	1,709	29.11	1,008	24.20	29.854	0.000
house dust	1,801	30.68	1,173	28.16	7.450	0.006
mugwort	49	0.83	23	0.55	2.733	0.098
ragweed	56	0.95	37	0.89	0.115	0.734
willow	54	0.92	34	0.82	0.302	0.583
dog epithelium	175	2.98	116	2.78	0.335	0.563
cat epithelium	187	3.19	129	3.10	0.064	0.801
cockroach	45	0.77	21	0.50	2.571	0.109
Alternaria alternata	321	5.47	197	4.73	2.724	0.099

Allergen sensitization in different gender groups

The overall male to female ratio was 1.41. Of the male participants, 45.71% (2,683/5,870) were positive for at least one allergen, compared to 45.49% (1,895/4,166) in females. As a result, there was no significant difference in the overall prevalence of inhalation allergy in different genders ($\chi^2 = 0.047$, $p > 0.05$). As shown in Figure 2, sensitization against D. pteronyssinus, D. farina, and house dust was more common in males than in females. Other distributions of allergens listed did not differ significantly (Table 3).

Table 4. Comparison of prevalence in different age groups.

Allergen	0 - 3 years	4 - 6 years	7 - 9 years	10 - 12 years	13 - 15 years	≥ 16 years	Chi-squared (χ^2)	p-value
Number of patients	5,723	2,621	1,008	452	124	108		
D. pteronyssinus	884 (15.45)	1,046 (39.91)	424 (42.06)	176 (38.94)	52 (41.94)	29 (26.85)	785.42	0.000
D. farina	921 (16.09)	1,089 (41.55)	430 (42.66)	191 (42.26)	54 (43.55)	32 (29.63)	821.87	0.000
house dust	1,581 (27.63)	903 (34.45)	325 (32.24)	127 (28.10)	27 (21.77)	11 (10.19)	67.32	0.000
mugwort	16 (0.28)	26 (0.99)	13 (1.29)	12 (2.65)	1 (0.81)	4 (3.70)	50.37△	0.000
ragweed	43 (0.75)	34 (1.30)	9 (0.89)	8 (1.77)	0 (0.00)	1 (0.93)	9.42△	0.072
willow	36 (0.63)	32 (1.22)	14 (1.39)	5 (1.11)	1 (0.81)	0 (0.00)	11.45△	0.031
dog epithelium	157 (2.74)	64 (2.44)	41 (4.07)	21 (4.65)	3 (2.42)	5 (4.63)	13.48	0.022
cat epithelium	164 (2.87)	97 (3.70)	36 (3.57)	10 (2.21)	4 (3.23)	5 (4.63)	6.79	0.236
cockroach	19 (0.33)	22 (0.84)	7 (0.69)	8 (1.77)	8 (6.45)	2 (1.85)	46.61 △	0.000
Alternaria alternata	144 (2.52)	232 (8.85)	100 (9.92)	32 (7.08)	8 (6.45)	2 (1.85)	207.60	0.000

△ **Fisher's exact probability method. Bold values represent significant values. $p < 0.05$.**

Table 5. Comparison of prevalence in patients with different types of disease.

	rhinitis	asthma	bronchitis	Chi-squared (χ^2)	p-value
Number of patients	897	749	1,259		
D. pteronyssinus	370 (41.25)	388 (51.80)	329 (26.13)	140.29	**0.000**
D. farina	385 (42.92)	395 (52.74)	346 (27.48)	135.65	**0.000**
house dust	388 (43.26)	331 (44.19)	389 (30.90)	49.57	**0.000**
mugwort	12 (1.34)	9 (1.20)	7 (0.56)	3.95	0.139
ragweed	9 (1.00)	9 (1.20)	10 (0.79)	0.84	0.658
willow	7 (0.78)	10 (1.34)	11 (0.87)	1.51	0.471
dog epithelium	47 (5.24)	27 (3.60)	34 (2.70)	9.47	**0.009**
cat epithelium	26 (2.90)	23 (3.07)	41 (3.26)	0.23	0.893
cockroach	5 (0.56)	6 (0.80)	8 (0.64)	0.39	0.825
Alternaria alternata	88 (9.81)	61 (8.14)	64 (5.08)	18.21	**0.000**

Underlined values represent significant values.

Allergen sensitization in different age groups

Aeroallergen sensitization varied significantly across age groups, including those aged 0 - 3 years, 4 - 6 years, 7 - 9 years, 10 - 12 years, 13 - 15 years, and > 16 years, and was 37.97% (2,173/5,723), 57.80% (1,515/2621), 54.86% (553/1,008), 51.99% (235/452), 48.39% (60/124), and 37.04% (40/108), respectively (χ^2 =337.53, $p < 0.05$), with patients aged 4 - 6 years having the highest overall positive rate to allergen. In the age group of 0 - 3 years, the positive rate of sIgE to house dust was higher than to other allergens, whereas the positive rate of D. farina was the highest in the other age groups

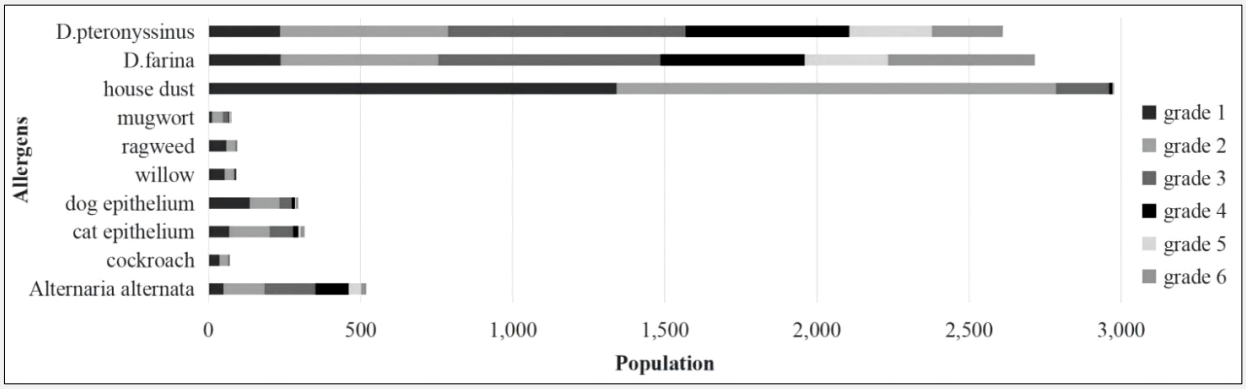

Figure 1. Overall prevalence of 10 aeroallergens. 0.35 - 0.7 IU/mL for grade 1; 0.7 - 3.5 IU/mL for grade 2; 3.5 - 27.5 IU/mL for grade 3; 27.5 - 50 IU/mL for grade 4; 50 - 100 IU/mL for grade 5; > 100 IU/mL for grade 6.

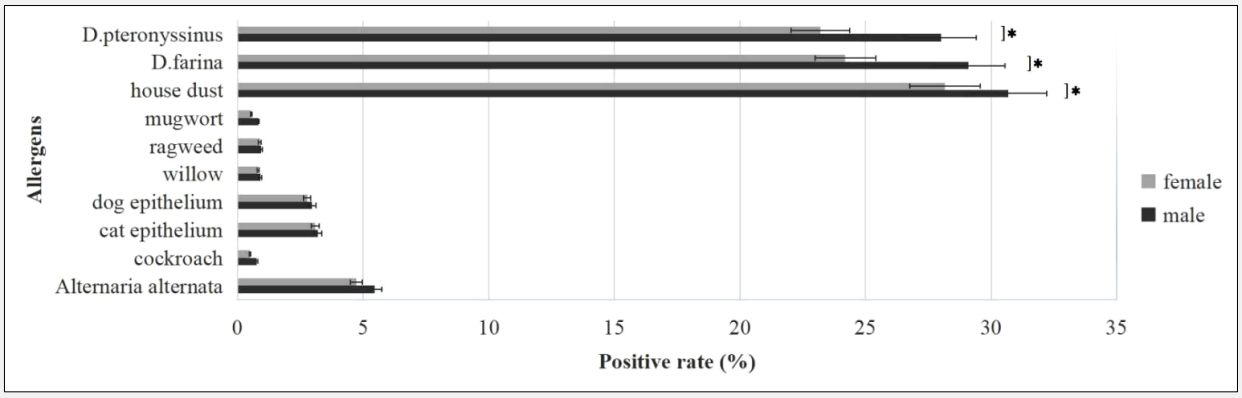

Figure 2. Allergen sensitization in different gender groups. * $p < 0.05$, male vs. female.

studied (Table 4). Sensitization to D. pteronyssinus and D. farina was comparable between each other in all age groups (Figure 3).

Allergen sensitization in patients with different disease types

Patients with rhinitis, asthma, and bronchitis had sIgE positive rates of 62.43% (560/897), 67.56% (506/749), and 46.62% (587/1,259), respectively, with the highest in patients with asthma and the lowest in patients with bronchitis ($\chi^2 = 100.08$, $p < 0.05$). Among the 10 allergens, D. pteronyssinus, D. farina, and house dust were the major ones leading to allergies. A correlation between disease types and the sIgE sensitization for D. pteronyssinus, D. farina, house dust, and Alternaria alternata was observed ($p < 0.05$) (Figure 4). Patients with rhinitis, asthma, and bronchitis all tested sensitive to house dust allergies at a higher rate (Table 5).

DISCUSSION

Sensitization to allergens has been identified as the major risk factor for allergy diseases, which are becoming more common around the world. There are many different types of allergens that can cause allergic diseases,

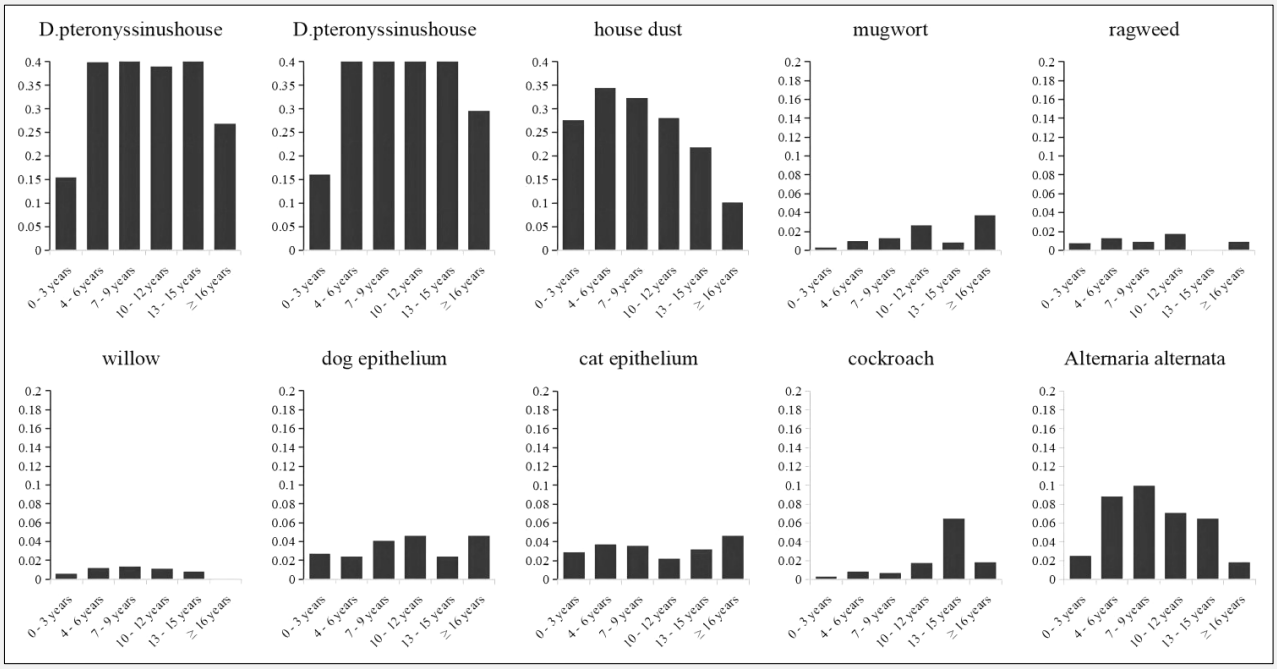

Figure 3. Sensitization to aeroallergens in different age groups.

The total number of cases in each age group: 0 - 3 years (n = 5,723), 4 - 6 years (n = 2,621), 7 - 9 years (n = 1,008), 10 - 12 years (n = 452), 13 - 15 years (n = 124), and 16 years and above (n = 108).

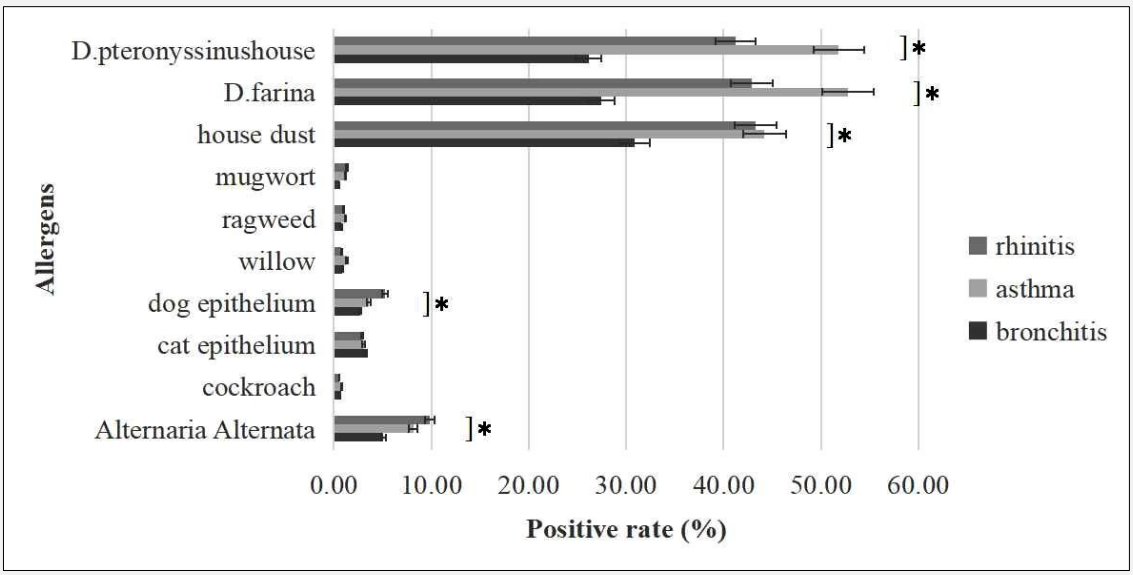

Figure 4. Allergen sensitization in different disease groups. * p < 0.05.

and the distribution of pathogenic allergens varies greatly in different regions due to differences in geography, vegetation types, climate, customs, dietary structure, and economic development [9-11]. To our knowledge, this is the first study to investigate the prevalence of aeroallergen sensitization after the pandemic in Sichuan Province, southwest China.

The West China Second University Hospital of Sichuan University, is a tertiary comprehensive maternity and children's hospital in western China. Children make up the majority of patients. The results of this study showed that house dust and house dust mites (including D. pteronyssinus and D. farina) were the main allergens in patients with respiratory allergies, which is generally consistent with the major allergen types investigated in most other regions in China [12]. In a recent multicenter survey, Xue'an Wang et al. observed that mite mix was the most frequent allergen in southern China cities, with a prevalent sensitivity to one or more dust mite allergens of 19.82% among 55,432 participants [13]. The patients in this study were all from southwest China's Sichuan region, which has a subtropical monsoon climate. The environment of Sichuan is conducive to dust mite growth and reproduction, which explains the subjects' overall hypersensitivity to dust mite allergens. Of note, this study showed a comparable prevalence of sensitization to D. pteronyssinus and D. farina in all age groups, which may be explained by the potential cross-reactivity between them resulting from the presence of common epitopes among many allergens. This finding also suggests that clinics may choose only one of them when performing mass epidemiological screening. Furry pets are another important factor influencing the frequency, recurrence, and severity of allergic symptoms caused by an aeroallergen. According to Anders Bjerg et al., as mite allergy was uncommon, furry animals were the primary perennial sensitizers among schoolchildren in northern Sweden [14]. Among the 17,641 participants in a German population-based study (aged 3 - 17), 11.6% and 7.6% of boys were found to be allergic to dogs and cats, and 9.6% and 6.6% of girls, respectively [15]. It is observed that the pet population is increasing in towns in China, which results in an increase in exposure to allergens produced by furry animals.

By classifying sIgE reactivity, it was discovered that a large percentage of positive sIgE tests showed mild responses, which could be classified as weak or suspected positive results, and thus it should be considered with reference to clinical findings to diagnose allergy.

It is unidentified how gender influences the associations between allergen exposure and allergic disease in schoolchildren [16]. However, several studies indicate that male children and adults have higher levels of total and allergen-specific IgE than females [14,17]. We did not observe a significant difference in the overall rate of positive sIgE tests between male and female subjects in this study, which was similar to the study of Baoqing Sun et al. [18]. In this study, males were more likely than females to be allergic to D. pteronyssinus, D. farina, and house dust, which could be explained by the different genetic situations, physiological structures, hormone secretion grades, dietary habits, behavior, and interests, as well as the fact that males have more active places and are exposed to more allergens.

The discrepancies in sensitization to aeroallergens between ages may be due to developmental immaturity. The immune systems of school-age children are at a critical stage of development. The tonsils and adenoids begin to atrophy, leading to an increase in the incidence of this stage, and the incidence gradually decreases with age, which may be related to the body's long exposure to allergens to develop immune tolerance and a relatively stable living environment. The highest rate of aeroallergen positivity was found in children aged 4 - 6 years in this study, reaching 57.80%. Preschool children have an increased range of activity, but a lack of self-protection consciousness, and the influence of allergens in the external environment on the organism increases. Older children have a more mature respiratory tract and an increased ability to clear dust mites and other allergic substances, resulting in a lower incidence of dust mite allergic reactions compared to younger children. Most children have complex allergies that are not caused by a single factor. When performing allergen testing, clinical practice should fully consider the effects of the child's age and should also objectively analyze each of the complex allergens to reduce the risk of misdiagnosis and underdiagnosis.

Allergies can manifest clinically in a variety of ways, mainly including respiratory, mucocutaneous, and digestive symptoms such as coughing, bronchitis, asthma, urticaria, eczema, vomiting, and abdominal pain. Severe cases may result in anaphylactic shock, a potentially fatal condition [8]. Rhinitis, asthma, and bronchitis are some of the most common respiratory chronic diseases in children [19,20]. Sensitization to aeroallergens is generally considered to be the primary basis of allergic rhinitis and bronchial asthma. Indoor allergens such as animal dander and house dust mite (HDM) have been linked to an increased risk of asthma and rhinitis [21]. Analysis of the three different disease types included in the study revealed that the main allergens for rhinitis, asthma, and bronchitis were D. pteronyssinus, D. farina and house dust, which is also consistent with the overall distribution of aeroallergens in this area, but the positive rates for allergens in bronchitis were consistently lower than the others. Statistically significant differences were found in the sensitization rates of D. pteronyssinus, D. farina, house dust, dog epithelium, and Alternaria alternata in all three groups, which may be due to the population basis being larger than other items. For most common allergens, rhinitis and asthma groups had similar sensitization patterns, suggesting that allergic rhinitis and asthma are very similar in terms of etiology, immunology, and pathogenesis, and also have some similarity in allergen distribution [22].

Emine Vezir et al. reported that aeroallergen sensitization and allergic rhinitis in children may be associated with a milder course of COVID-19 [23]. Other studies found that environmental factors like aeroallergens and air pollution that have detrimental effects on respiratory illnesses also have an impact on COVID-19 [6,24]. Interestingly, according to a study by Wakabayashi et al., respiratory allergic diseases like asthma appear to have a protective effect against SARS-CoV-2 infection, but the underlying immune-molecular mechanisms were not fully established [25]. According to a previous study conducted by Liu Ting et al. [26], an analysis of aeroallergens in children in Sichuan from June to September 2019 revealed that 61.18% of children aged 0 - 14 years were allergic to at least one aeroallergen. The data from our study indicated that the overall sensitization was 45.62% between January 2020 and January 2021, with 9,915 children aged 0 - 14 years accounting for 98.79% of the total subjects studied, indicating that our findings largely reflect the distribution of aeroallergens among children in Sichuan following the COVID-19 outbreak. In comparison to the pre-epidemic period, allergy prevalence decreased significantly, regardless of health-care avoidance. It should be noted that, not only as stipulated by the laws and regulations of the National Health Commission of the People's Republic of China but also the community prevention guidance and epidemiological reports, all show that Chinese children were to some extent compliant in wearing masks during the epidemic and cooperated with home isolation and online distance learning models in order to control the spread of the coronavirus. Thus, the primary reason for the difference may be that the post-epidemic population avoided group gatherings, maintained a socially detached lifestyle, and protected themselves personally by paying attention to respiratory hygiene, all of which are critical for preventing respiratory allergy.

However, the current study has several limitations. To begin with, not all patients in this study had a definitive diagnosis of allergy, and thus the overall sensitization of 45.62% may be lower than the real data in patients with allergic diseases in this region. Second, despite the fact that the environment contains a large number of allergens, only 10 types of aeroallergens were tested for reactivity. Meanwhile, as information on the disease course of the patients was not collected, the severity of the disease and the pattern of sensitization of the patients could not be discussed jointly. Additionally, because this study is retrospective, there is a possibility of bias. Additional large-scale prospective studies should be conducted to determine the prevalence and incidence of allergen sensitization in the Sichuan area.

In conclusion, house dust and house dust mites (HDM) are the sources of the most important allergens associated with inhaled diseases in Sichuan, southwest China, and lead to the development of high-titer allergen-specific IgE. There was no significant difference in the overall sensitization distributions between males and females among the study population. The prevalence of inhalation allergy varies among different age groups. Patients with rhinitis and asthma were more sensitive to inhaled allergens than patients with bronchitis. These results reflect, to a certain extent, the characteristics and patterns of respiratory allergen distribution in Sichuan after the COVID-19 epidemic and provide epidemiological information and a clinical diagnostic basis for the prevention and treatment of allergic diseases.

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Declaration of Interest:
The authors declare no conflicts of interest.

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