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ORIGINAL RESEARCH

Sensitization to Furry Animals in Patients with Suspected Allergic Disease in China: A Multicenter Study

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Purpose: An objective of this study was to investigate the allergen sensitization characteristics of cat, dog and horse dander in patients with suspected allergic diseases in different geographical regions of Chinese mainland.

Patients and Methods: We invited 2377 patients aged 0–86 years with suspected allergic diseases to participate in a cross-sectional survey in 11 provinces in China. Combined with the questionnaires and animal-specific IgE levels, we analyzed the epidemiological characteristics and risk factors of furry animal sensitization in different regions and populations of Chinese Mainland.

Results: Among the 2377 patients with suspected allergic diseases, 14.9% were sensitized to cat dander, 9.3% to dog dander and 5.5% to horse dander. Animal allergens mainly cause low-level sensitization (class 1–3). There was a significant correlation between cat, dog and horse dander allergen sIgE, with correlation coefficients (r_s) all greater than 0.750. The majority (46.5%) of sIgE-positive patients were sensitized to at least two animal allergens simultaneously. The prevalence of these animals all showed a trend of increasing first and then decreasing with age, and all reached the peak in young adolescence. As for the geographical factors, the sensitization rate of cats and dogs in Western was significantly higher than that in Eastern (cat: 18.4% vs 9.2%, dog: 11.6% vs 5.5%, all $P < 0.001$), however, no significant differences were found in horses. Aged ≤6 years, living in Western, and high animal allergen exposure elevated the risk of cat or dog sensitization. Living on a lower floor (aOR: 0.56) was a protective factor for horse sensitization.

Conclusion: In this representative sample of Chinese patients with suspected allergic diseases, there was an apparent geographic variation in sensitization to cats and dogs. Age factor and living in Western also had a significant impact on animal allergen sensitization rate.

Keywords: animal allergen, specific immunoglobulin E, cross-sectional survey, suspected allergic patient

Introduction

Immunoglobulin E (IgE) - associated allergy is the most frequent immunologically mediated hypersensitivity disease. Allergic patients suffer from a variety of clinical symptoms which include hay fever (ie, rhinitis, conjunctivitis), asthma, skin inflammation (eg, urticaria, atopic dermatitis), gastrointestinal allergy (eg, oral allergy syndrome-OAS, vomiting, diarrhea) and life-threatening systemic anaphylactic shock.[1] Allergic disease is a common and frequently occurring disease in clinic. In recent years, allergic diseases have affected nearly 30% of the world's population, and the incidence rate is still rising worldwide, which has become a public health problem that requires attention.[2] While seriously affecting the work and life of

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patients, it also brings a greater economic burden to society.[3,4] Allergic diseases mainly include atopic dermatitis, food allergy, eosinophilic esophagitis, asthma and allergic rhinitis. Different allergic diseases are usually found in the same person, for instance, asthma often accompanied by allergic rhinitis (AR).[5,6] Therefore, physicians and patients must have a more comprehensive understanding of the potential causes of allergies.

Pets, especially mammalian furry pets, are a major source of indoor inhalant allergens. Sensitization to animal allergens is considered a risk factor for the occurrence and development of respiratory allergic diseases. Studies have pointed out that the prevalence of sensitization to pet allergens in patients with AR increased at an annual rate of 1.3%.[7] More than half of the world's population keep pets at home. According to an international survey of more than 27,000 participants from 22 countries, it is estimated that 57% of people have at least one pet at home, most commonly dogs (33%) and cats (23%).[8] In China, 25% and 10% of people own dogs and cats, respectively.[8] With the rapid development of the national economy and the acceleration of urbanization, more and more people keep various pets at home and report pet allergies.[9] Animal allergens are present in saliva, urine and dander, and they spread to the environment through sticking to animal hair and dander, making them ubiquitous. Even in families without owing a pet, animal allergen levels in the environment may be high enough to sensitize people.[10]

The incidence and prevalence of cat and dog allergies vary in different countries and regions.[11] The knowledge regarding animal allergies remains fragmented. The Nordic countries have higher sensitization rates to furry animals, which are a significant contributor to the local burden of allergic rhinitis and asthma.[12,13] However, many previous studies on the distribution characteristics and sensitization patterns of inhalant allergens in China were mostly limited to a specific region such as in a province or a hospital. For example, Wang et al reported that the prevalence of pet allergens in AR patients in Guangzhou was 23.4% and showed an increasing trend over years,[7] while a hospital in Sichuan Province reported that the sensitization rates of cat hair and dog dander were 0.89% and 0.73%, respectively, among 14,030 people who received routine medical examinations.[14] These results indicated that some studies cannot compare well with the distribution differences between the vast areas of China. At present, there is a lack of large-scale epidemiological studies on the sensitization of cats, dogs and other furry animals in China.

Large-scale epidemiological studies to assess the true burden of allergic diseases are necessary to increase the expertise of allergists and to raise public awareness of allergy prevention. There are two primary aims of this study: 1. To investigate the allergen sensitization characteristics of cat, dog and horse dander in patients with suspected allergic diseases in different geographical regions of Chinese mainland. 2. To analyze the differences in pet allergen sensitization rates by gender, age, and region, and to explore the effects of parental allergy history, delivery mode, passive smoking and living environment on pet allergen sensitization rates, as well as the cross-sensitization among cat, dog and horse dander allergens.

Materials and Methods

Study Design and Participants

This study was based on a multicenter epidemiological survey of allergic diseases, which was conducted in mainland China. The study was conducted in 14 clinical centers from October 2019 to October 2021, including 11 provinces and cities from eastern and western China: Gansu, Inner Mongolia, Ningxia, Shaanxi, Sichuan, Yunnan, Beijing, Guangdong, Hebei, Jiangsu and Shandong. A total of 2377 patients with suspected allergic diseases were included in this study. Patients who reported previous allergic diseases or current allergic symptoms such as respiratory allergy (itchy nose, nasal obstruction, paroxysmal sneezing, runny nose, coughing, wheezing and chest distress, dyspnea), skin allergy (itching, swelling, papules, blisters, wheals, eczema after exposure to certain allergens), ocular allergy (itchy eyes, conjunctival congestion, streaming eyes and swollen eyelids), food allergy (skin rash, throat tightness, abdominal pain, diarrhea, vomiting, oral allergy syndrome) during the visits to outpatient departments of respiratory, pediatrics, dermatology, otolaryngology and allergy, were invited to participate in the survey. First, clinicians introduced the purpose and significance of this study to the patients, then patients who agreed to participate in the study needed to sign the informed consent form (The informed consent of subjects under the age of 18 was signed by the guardian).

All subjects participating in the study need to fill in a questionnaire and collect blood samples to measure allergen-specific IgE levels. The inclusion criteria of the subjects are as follows: 1) Patients who visited the departments of

respiratory, pediatrics, dermatology, otolaryngology and allergy in 14 centers mentioned above from October 2019 to October 2021; 2) Reported allergic symptoms or diseases, such as allergic rhinitis, asthma, eczema, conjunctivitis, etc.; 3) all ages and genders were enrolled. The exclusion criteria were 1) history of specific allergen immunotherapy, 2) patients with incomplete medical records, 3) failed to provide informed consent, 4) obvious hemolysis, lipids (chyle), or coagulation (turbidity) in serum samples. Five milliliters of venous blood were collected from each patient, the blood was centrifuged at 1000 xg for 10 min, and the serum was stored at −80°C until use.

Questionnaires

This is a standardized questionnaire (Figure S1) for allergic diseases patient in Chinese population. The questionnaire included demographic characteristics such as age and gender, delivery mode, residence and living environment, parent allergy history, tobacco exposure, animal exposure and related symptoms. The questionnaire was completed by patients under the face-to-face guidance of a specialist or a trained nurse.

Detection of Animal Allergen Specific IgE

All patients specific IgE concentrations of cat, dog and horse dander allergens were measured using the ALLEOS 2000 system (HYCOR Biomedical, US) according to the manufacturer's instructions. The system uses fluorescent magnetic bead chemiluminescence technology. The principle is that horseradish peroxidase (HPR) is directly labeled on the anti-human IgE antibody as a marker, reacts with biotinylated antigen/antibody and streptavidin-coated magnetic beads, and after the antigen-antibody reaction, the streptavidin-biotin system forms an immune complex. The immune complex reacts with the substrate and produces a luminescent signal, the intensity of which is proportional to the concentration of specific IgE in the serum sample. Specific IgE levels were expressed in kilo units antibody per liter (kU_A/L) with the following range: 0.10–100 kU_A/L. Tests with sIgE levels greater than or equal to 0.35 kU_A/L were defined as sIgE-positive, and lower than 0.35 kU_A/L were defined as negative (class 0). Specific IgE-positive tests were categorized into the following 6 classes: class 1 (≥ 0.35 to < 0.70 kU_A/L), class 2 (≥ 0.70 to < 3.50 kU_A/L), class 3 (≥ 3.50 to < 17.50 kU_A/L), class 4 (≥ 17.50 to < 50 kU_A/L), class 5 (≥ 50 to < 100 kU_A/L), and class 6 (≥ 100 kU_A/L).

Statistical Analysis

Descriptive parameters such as means and standard deviations (SDs) for normally distributed continuous data and frequencies and percentages for categorical data were calculated. Nonnormally distributed data were expressed as medians and 25–75% interquartile ranges. The *t*-test or Mann–Whitney *U*-test was used to compare the difference of numerical data distribution between two groups. The Chi-square (χ^2) test was used to compare differences of allergen distribution among groups (Fisher's exact test was used when the expected count is less than 5), and the Spearman rank correlation analysis was used to evaluate the correlation between allergens. Histograms and Venn diagrams were used to show the distribution of positive rates and the cross-sensitization among multiple allergens. The binary logistic regression was used to analyze the risk factors of allergen sensitization in three kinds of animals, and forest map was used to show the risk ratio. The odds ratio (OR) value and 95% confidence interval (CI) were calculated. P values below 0.05 were considered statistically significant. All statistical analyses were performed using Excel 2019 (Microsoft® Excel® 2019), Statistical Package for the Social Sciences 25.0 (International Business Machines Corporation Corp., Armonk, NY), and GraphPad Prism 8 (GraphPad Software, inc.).

Results

Demographic Characteristics of the Study Population

A total of 2377 patients with suspected allergic diseases were included, of which 1561 (65.7%) were children. There were 1360 males (57.2%) and 1017 females (42.8%), with a median age of 10 (6, 28) years. Table 1 shows the demographic characteristics of the total study population. Most of the patients (91.2%) were Han people, and 62.5% were came from Western China. In the studied population, 59.6% patients delivered vaginally, and 47.1% reported second-hand smoke exposure. Besides, 30.0% and 9.6% of patients reported that one or both parents had a history of allergic

Table 1 The Demographic and Allergy Sensitization Characteristics of the Participants

Variables	Total	Cat Dander		*P* value*	Dog Dander		*P* value†	Horse Dander		*P* value‡
	n=2377(%)	n	Po%		n	Po%		n	Po%	
Age										
<18 years	1561 (65.7)	295	18.9	**<0.001**	170	10.9	**<0.001**	115	7.4	**<0.000**
≥18 years	816 (34.3)	60	7.4		52	6.4		16	2.0	
Median(P_{25}, P_{75})	10 (6, 28)	9 (7, 13)			10 (6, 15)			9 (6, 12)		
Gender										
Male	1360 (57.2)	234	17.2	**<0.001**	139	10.2	0.088	76	5.6	0.849
Female	1017 (42.8)	121	11.9		83	8.2		55	5.4	
Ethnic groups										
Han	2168 (91.2)	310	14.3	**0.005**	194	8.9	**0.035**	117	5.4	0.431
Others	209 (8.8)	45	21.5		28	13.4		14	6.7	
Family history										
One of the parents	712 (30.0)	120	16.9	**0.016**	73	10.3	**0.018**	45	6.3	0.274
Both of the parents	229 (9.6)	45	19.7		32	14.0		18	7.9	
None	1101 (46.3)	146	13.3		90	8.2		58	5.3	
Region										
Western	1486 (62.52)	273	18.4	**<0.001**	173	11.6	**<0.001**	81	5.5	0.868
Eastern	891 (37.48)	82	9.2		49	5.5		50	5.6	
Living location										
Downtown	1505 (63.3)	242	16.1	0.115	165	11.0	**0.001**	93	6.2	0.161
Urban	358 (15.0)	51	14.2		25	7.0		23	6.4	
Rural	205 (8.6)	22	10.7		8	3.9		6	2.9	
Delivery mode										
Vaginal delivery	1417 (59.61)	197	13.9	**0.002**	138	9.7	0.931	76	5.4	0.105
Cesarean delivery	655 (27.56)	126	19.2		63	9.6		47	7.2	
Passive smoking										
Yes	1119 (47.1)	191	17.1	**0.025**	115	10.3	0.212	62	5.5	0.465
No	969 (40.8)	131	13.5		84	8.7		61	6.3	
Using air conditioner										
Yes	1249 (52.5)	157	12.6	**<0.001**	102	8.2	**0.013**	70	5.6	0.532
No	814 (34.2)	158	19.4		93	11.4		51	6.3	
Using mattress										
Yes	1851 (77.9)	293	15.8	**0.048**	177	9.6	0.902	116	6.3	**0.041**
No	215 (9.0)	23	10.7		20	9.3		6	2.8	

Notes: Chi-square test was used to compare differences in the positive rate of animal allergens between different groups (Fisher's exact test was used when the expected count is less than 5). If the difference between groups is statistically significant, use bold fonts. n - Number of patients with positive results; Po% - Prevalence of animal sensitization. *P value of sensitization rates in cats grouped by different variables; †P value of sensitization rates in dogs grouped by different variables; ‡P values of sensitization rates in horses grouped by different variables.

diseases, respectively. We also analyzed the characteristics of the patient's living environment and indoor environment (using air conditioning and cotton quilts).

The results showed that sensitization to cat, dog, and horse dander was more popular in the <18 years age group (all $P < 0.001$). Among cat-sensitized patients, the prevalence of cat dander sensitization was significantly higher in males than in females (17.2% vs 11.9%, $P < 0.001$), while this gender difference was not significant in dog and horse-sensitized patients (all $P > 0.05$). Among cat-sensitized and dog-sensitized patients, sensitization rates were significantly higher in patients with allergy history in one or both parents than in those without family history of allergic disease ($P = 0.016$ and

0.018, respectively); besides, the sensitization rate was significantly higher in Western than in Eastern (All $P < 0.001$). Among dog-sensitized patients, the positivity rate was significantly lower in rural/suburb residents than in downtown residents ($P = 0.001$). Additionally, among cat-sensitized patients, the positive rate was also higher in cesareans and passive smokers ($P = 0.002$, 0.025, respectively). The positive rate of other environmental exposure factors such as the use of air conditioning and mattress among animal-sensitized patients are shown in Table 1.

Prevalence of Sensitization and sIgE Levels of Furry Animals in the Study Population

Of the 2377 patients recruited with suspected allergic disease, cat dander allergen had the highest positive rate of 14.9%, followed by dog dander (9.3%) and horse dander (5.5%), Cat sensitization rates were significantly higher than those of dogs and horses (all $P < 0.001$) (Figure 1A). A total of 81.3% (1932/2377) of the patients were not sensitized to any of the allergens studied. As for the severity of individual sIgE reactivity, sensitization to these animal allergens were usually mild in most of the subjects. For example, 88.2% and 88.7% of cat and dog positive subjects caused only low-level sIgE reactivity (class 1–3), respectively; and low sIgE level of horse allergen (class 1–2) accounted for 94.7% of the positive results (Figure 1A). Patients sensitized to cats and dogs had significantly higher sIgE levels than those sensitized to horse dander [cats 2.05 (0.78, 6.75) vs. horses 0.67 (0.48, 1.25); dogs 1.17 (0.58, 4.54) vs. 0.67 (0.48, 1.25), all $P < 0.001$]; in addition, the sIgE levels were significantly higher in cat sensitized patients than those sensitized to dog (2.05 (0.78, 6.75) vs.1.17 (0.58, 4.54), $P < 0.001$) (Figure 1B).

Correlation Analysis and Cross Sensitization of Furry Animal Allergen sIgE

Spearman's rank correlation analysis of sIgE levels in furry animals was performed to explore the potential association between animal allergens. Correlation analysis results (Table S1) showed that there was a strong correlation between cat, dog and horse allergens, and the Spearman correlation coefficients (r_s) among them was all greater than 0.75, with the strongest correlation between cat and dog allergens (r_s=0.834). Based on the potentially high correlation between animal allergens, a Venn diagram was drawn to analyze the potential cross-reactivity between furry animal allergens. The Venn diagram in Figure 2 showed that 12.6% (56/445) of the samples were positive to all 3 furry animal allergens, and 46.5% (207/445) of the samples were positive to at least 2 animal allergens.

Distribution of Furry Animal Allergens in Different Age-Groups

For investigating the distribution trends of animal allergens in different age groups, participants (range 1 month to 86 years old) were divided into eight age-groups: 0–6 years old (710, 29.9%), 7–12 years old (716, 30.1%), 13–18 years old

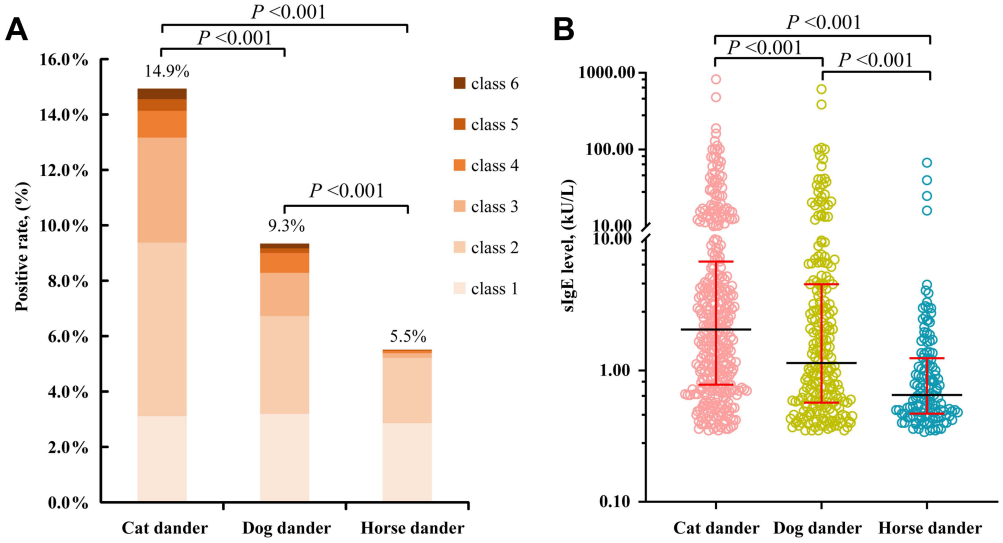


Figure 1 Distribution of positive rates (**A**) and specific IgE levels (**B**) of cat, dog and horse dander allergens in 2377 subjects with suspected atopy.

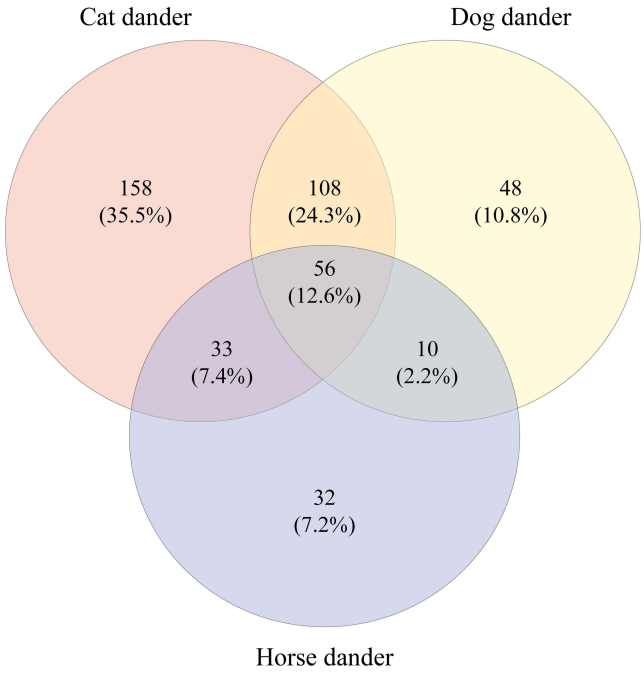
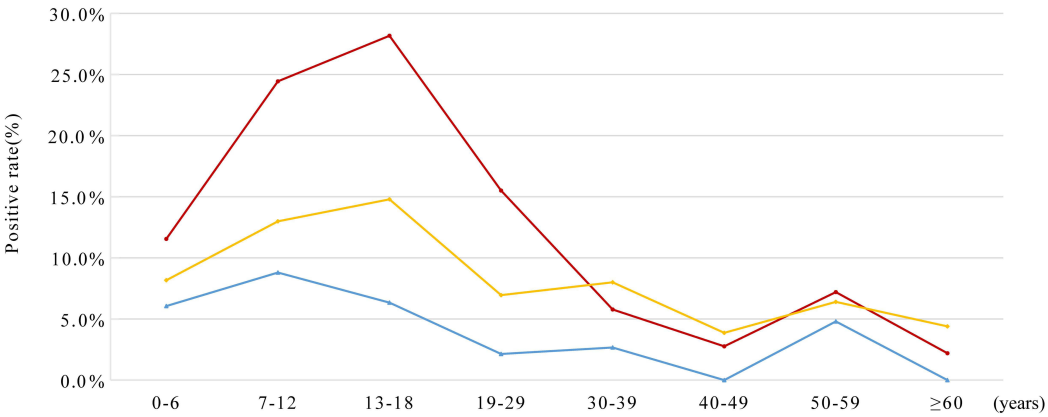


Figure 2 The co-sensitization between cat, dog and horse dander. The Venn Diagram shows the number of patients what were co-sensitized.

(142, 6.0%), 19–29 years old (187, 7.9%), 30–39 years old (225, 9.5%), 40–49 years old (181, 7.6%), 50–59 years old (125, 5.3%), and ≥60 years old (91, 3.8%). As shown in Figure 3, analysis of distribution of cat, dog and horse dander in different age-group indicated cat was the most popular animal allergens in patients aged 0–29 years old. In general, sensitivity to furry animal allergens showed a trend of increasing first and then decreasing with the increasing age. All three animal allergens showed peaks of sensitization in the young adolescence. In this study, cat and dog reached the highest sensitization rate in 13–18 age-group with 28.2% and 14.8%, respectively. Notably, horse reached a peak of sensitization (8.8%) in 7–12 age-group.



	0-6	7-12	13-18	19-29	30-39	40-49	50-59	≥60
n	710	716	142	187	225	181	125	91
Cat dander	11.5%	24.4%	28.2%	15.5%	5.8%	2.8%	7.2%	2.2%
Dog dander	8.2%	13.0%	14.8%	7.0%	8.0%	3.9%	6.4%	4.4%
Horse dander	6.1%	8.8%	6.3%	2.1%	2.7%	0.0%	4.8%	0.0%

Figure 3 Distribution of furry animals sensitization rate in different age-groups. n - Total number of subjects in each age group.

Geographical Distribution of Furry Animal Sensitization Rate in China

We divide these 11 provinces (14 clinical centers) into Eastern and Western regions according to the level of economic development and difference of geographical location (Table 1). First of all, we compared the sensitization rates of furry animals in the Eastern and Western China. The results showed that the prevalence of sensitization to cat and dog dander was higher in the Western than Eastern (Cat: 18.4% vs 9.2%; Dog: 11.6% vs 5.5%. All $P < 0.001$) (Figure S2), while the prevalence of sensitization to horse was not significantly different between the Eastern and Western regions (5.6% vs 5.5%, $P = 0.868$). We plotted a heatmap (Figure 4) to compare the prevalence distribution of sIgE reactivity to animal allergens in different provinces in mainland China. Among the 11 provinces investigated, cat and dog sensitization were more prevalence in the Western, and the sensitization rates of cat and dog dander were significantly higher in both Yunnan and Gansu provinces than in other provinces (Figure 4A and B). With regard to horses, the highest sensitization rate of horse dander was found in Yunnan Province (16.9%) in the Western, while Hebei (10.3%) and Jiangsu Province (10.3%) in the Eastern also had a higher sensitization rate. The prevalence (%) and total number of each province are shown in Table S2.

Risk Factors for Animal Allergen Sensitization

Analysis of the influencing factors of animal allergen sensitization showed that there were many confounding factors in the variables. In the univariate crude analysis (Figure 5A), age, gender, delivery mode, parental allergy history, cigarette smoking exposure, residential environment (region, urbanization and use of air conditioning), and animal exposure were all significantly associated with cat sensitization. Among them, the ≤6 years old, 7–12 years old and high-level animal allergen exposure pose a significant risk of cat sensitization, which ORs were 2.50 (1.87, 3.34), 2.96 (1.90, 4.60) and 3.30 (2.33, 4.67), respectively. After correcting for confounding factors, only age, residential environment and animal exposure were observed as risk factors for cat sensitization. Compared with patients ≥60 years old, patients ≤6 years old (aOR 2.54, (95% CI 1.80–3.60), P <0.001) and <12 years old (aOR 3.20, (95% CI 1.87–5.49), $P < 0.001$) had a two to three times the risk of being sensitized to cat. Living in western China (aOR 2.19, (95% CI 1.48–3.24), P <0.001) and high animal exposure levels (aOR 3.19, (95% CI 2.14–4.75), P <0.001) are still risk factors for cat sensitization (Figure 5B). Similar to the factors of cat sensitization, after adjusting for confounding factors, <6 years old (aOR 1.60, 95% CI 1.05–2.45), living in the western (aOR 2.14, 95% CI 1.33–3.43), and low (aOR 2.02, 95% CI 1.37–2.98) and high levels of animal exposure (aOR 3.61, 95% CI 2.27–5.74) were also significantly associated with dog dander sensitization (Figure 5C and D). One unanticipated finding was that residential floor was an influential factor only observed in the horse sensitization model. Living on lower floor was independently protective for horse sensitization (OR 0.55, 95% CI 0.38–0.80). Even after adjusting for confounding factors, it was still significant (aOR 0.56, 95% CI 0.37–0.85) (Figure 5E and F).

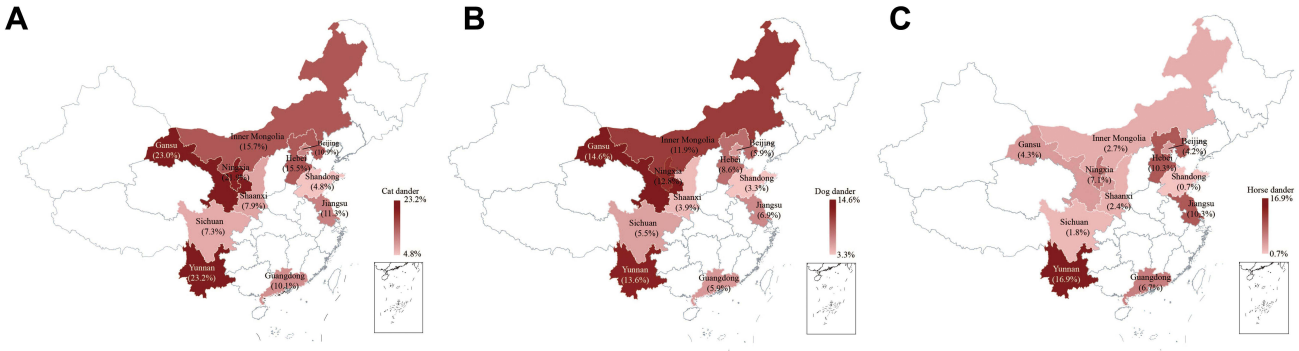


Figure 4 Heatmap for the prevalence of positive sIgE tests for cat dander (**A**), dog dander (**B**) and horse dander (**C**) in different regions. The prevalence (%) of each province were marked.

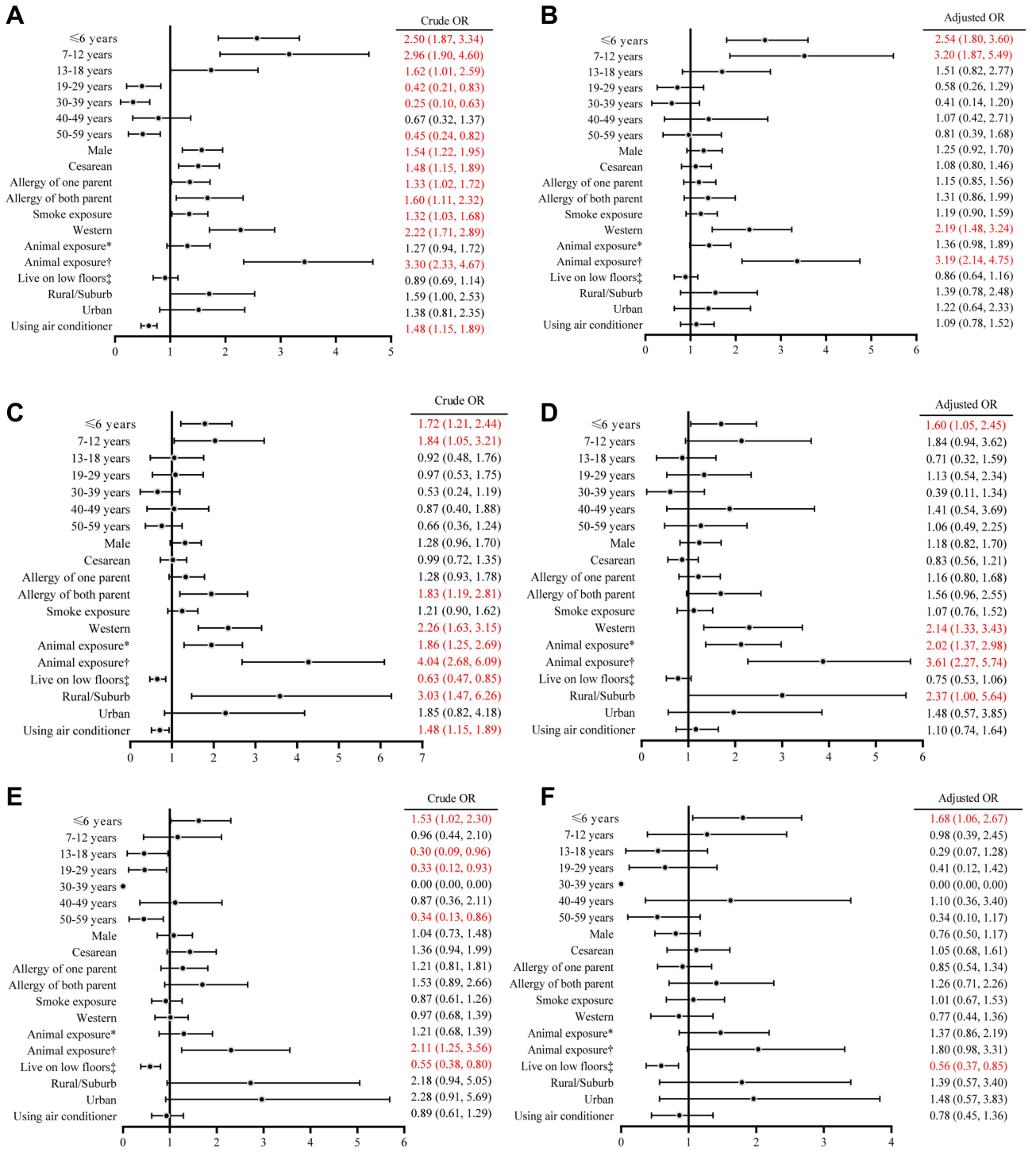


Figure 5 Risk factor analysis for animal allergen sensitization in patients with suspected allergic disease. Crude odds ratio and 95% CI of risk factors for cat sensitization (**A**), dog sensitization (**C**) and horse sensitization (**E**), adjusted odds ratio and 95% CI of risk factors for cat sensitization (**B**), dog sensitization (**D**) and horse sensitization (**F**). Multivariable-adjusted analysis included all factors in the univariate (crude) analysis. ORs of 1.00 indicate reference values. ORs associated with a *P* value of <0.05 are presented in red font. aOR - adjusted odds ratio. *No symptoms were reported after exposure to animal allergens. †Allergic symptoms were reported after exposure to animal allergens. ‡Patients living below the 9th floor.

Discussion

In recent years, the incidence of sensitization to furry animals has been increasing in China and abroad.[7,15,16] Mammalian furry animals have become the third largest category of inhalant allergens besides dust mites and pollen.[17] Identifying and proactively preventing diseases is the most economical and effective way to improve patients' health. Observing epidemic

characteristics of animal allergens in a wide geographical area is helpful to provide guidance for prevention and treatment strategies of animal-induced allergies.[16] In this study, a total of 2377 patients with suspected allergic diseases from 11 provinces in China were enrolled for full quantitative sIgE detection of furry animal allergen including cat, dog and horse.

Consistent with the literature,[15,18] this research found that cat dander was the predominant furry animal allergen in patients with suspected allergic disease, followed by dog and horse dander. Despite a significant increase in the prevalence of animal allergy, the results of this study showed that patients were mainly at low levels of sensitization (class 1–3). It seems possible that these results may be due to the immunogenicity of animal allergen proteins and the selection of study population.[19] Dust mites are the most popular inhalant allergen causing allergic diseases in the vast area of China.[14,20,21] Due to the lack of information on the severity of patient's symptoms in this study, it was difficult for us to assess the relationship between the level of animal sensitization and the severity of allergy.

The sensitization rate and sIgE levels were significantly lower in horses than in cat and dog dander. We could find from further correlation analysis that there is a strong correlation between cat, dog and horse dander. Among all animal sensitizers, 46.5% showed positive reaction to at least two allergens. Moreover, co-sensitization to all three animal extracts was also common (12.6%). This finding is consistent with that reported by Bjerg et al who found that of 259 school-aged children sensitized to animals (sIgE > 0.1 kU_A/L), more than half were sensitized to all three animals simultaneously.[22] A possible explanation for these results may be the extensive cross-reactivity induced by lipocalin and serum albumin between animals. Though serum albumin is a minor allergen, it is the main molecule causing allergic cross-reactivity in animals of different species.[23,24]

We also analyzed the distribution of animal allergen sensitization in different age groups. Sensitization to pet allergens appears to occur more frequently in children and adolescents. In line with those of previous studies, this research found that the prevalence of animal sensitization rises with age and peaks at adolescence.[25,26] The highest positive rate for cat and dog dander were found at 13–18 age-group, while horse was at 7–12 age-group, after which it gradually decreases. Studies showed that serum total IgE levels in elderly subjects are significantly lower than that in young subjects.[27–29] The decreasing trend in sensitization rates in all three animals then showed slight fluctuations in the age group of 50–59 years, but their sensitization rates were still much lower than those of the younger population. Some studies suggest that allergic inflammation may recede with age, and that westernization and modernization in recent decades may have increased the sensitization in population.[30]

Another important finding was that the prevalence of animal allergen sensitization is also associated with geographic environmental factors. For cat and dog dander, sensitization rates were significantly higher in Western than in Eastern, which also accords with our earlier observations.[18] However, the prevalence of horse sensitization appears to be slightly higher in the Eastern region than in Western, except in Yunnan Province, where the sensitization rate of the three animals was significantly higher than in the other provinces. The allergen sensitization pattern varies considerably in different countries and regions. China is a vast country with a complex and diverse climate, and a terrain high in the West and low in the East. There's an imbalance in economic development between the eastern and western regions, and people's lifestyles and living environments are changing due to differences in economic development levels. With the improvement of people's living standards, a growing number of people are keeping cats and dogs as pets in their homes, and therefore reports of pet allergies have increased. Frequent exposure and elevated concentrations of cat and dog allergens in the environment may lead to respiratory hyperreactivity in more patients.[22] However, previous studies have also demonstrated that exposure to high levels of pet allergens in early life may induce immune tolerance, thereby reducing the risk of allergy.[31] The rate of pet ownership is lower in the economically backward and low population density west than that in the economically advanced east. In contrast, horse ownership is significantly higher in the west than in the east, and recreational activities such as horseback riding are more popular in the west. People in the east develop better immune tolerance to cats and dogs after long-term exposure to them, while long-term exposure to horses helped people in the west induce tolerance to horse allergens, which reduced the risk of sensitization to these furry animals. Although we found differences in animal sensitization rates between the East and West, we lack precise information on pet ownership in these subjects.

We identified several influential factors associated with animal allergen sensitization. First, we found that children, especially those ≤6 years old, had a higher risk of sensitization to all three animal species compared to those ≥60 years old. In addition, gender, delivery mode, parental allergy history, tobacco exposure, residential environment (region,

urbanization and use of air conditioning) and animal exposure were the main influencing factors for cat sensitization. However, only age, residential area and level of animal allergen exposure were identified as risk factors for cat sensitization after correcting for confounding factors. These results were in agreement with Gabet S's findings.[32] The observed effect of age could be attributed to the frequency of exposure to animals in children and the immaturity of the immune system during childhood, while in adulthood, the immune system is gradually well-developed.[33] Additionally, living on lower floor may be a potential protective factor for horse sensitization.[34] The height of living floor is related to the level and types of allergens.[35,36] In this study, a history of allergic disease in both parents was found to pose a risk for allergen sensitization to cats and dogs; however, after adjusting for other variables, parental allergy history was not significantly associated with specific sensitization to any of these 3 animals. Unexpectedly, the findings of the current study do not support the previous research that family allergy history has a strong influence on allergy.[37]

Many previous studies were mostly limited to a specific region, which generally describe the local distribution of inhaled and food allergens. There were few multicenter researches focusing only on animal allergy characteristics prior to this study. This is a multicenter study conducted in Chinese Mainland. We describe in detail the sensitization characteristics of cats, dogs and horses based on participant characteristics according to the results of full quantitative serum sIgE test. However, there are still some limitations in this study. As mentioned above, based on the design of the questionnaire, we lack information on the subjects' pet ownership, severity of symptoms, etc., and therefore failed to further analyze the clinical correlation between animal sensitization and allergic diseases. Secondly, this study was conducted among participants attending outpatient clinics, which may have caused selection bias, because participants with more severe symptoms are more likely to seek medical care for their condition. Therefore, participants in this study may have a higher rate of pet sensitization than the general population. Thirdly, participants' assessments of animal exposure levels may be affected by recall bias. Finally, this study is unable to encompass the entire common inhalant and food allergens in different regions of China. Further studies, which take these variables into account, will need to be undertaken. Despite its limitations, this work has certainly added to our useful knowledge of the prevalence characteristics of animal allergies in various regions of China.

Conclusion

The investigation of patients with suspected allergic diseases has shown that cats were the most prevalent furry pet allergen. There were significant geographic differences in cat and dog sensitization rates, with significantly higher rates in the west than in the east. Age factor and living in Western also had a significant impact on animal allergen sensitization rate. Notwithstanding a limited number of pet species were investigated, this work offers valuable data for the management of animal allergy in China and provide useful guidance for the diagnosis, treatment and prevention of animal allergy.

Ethics and Consent Statement

This study and the use of human blood samples were approved by the Ethics Committee of The First Affiliated Hospital of Guangzhou Medical University (Ethical review of medical research -2018-93). It was conducted in accordance with the Declaration of Helsinki. All participants have given their written consent independently or through their parents (in the case of children).

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Disclosure

The authors report no conflicts of interest in this work.

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