

The prevalence and sex difference of allergen sensitization among adult patients with allergic diseases in Shanghai, China

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Abstract

Background: The worldwide prevalence of allergic diseases has increased during the last few decades, but it is not well known about the sensitization profiles of adult patients in Shanghai.

Objective: This study aimed to identify the prevalence and sex difference of allergen sensitization among adult with allergic diseases in Shanghai.

Methods: The sensitization profiles of 7,996 patients (18–60 yrs old) with allergic diseases at our center were retrospectively analyzed, based on the results of skin prick tests. The prevalence of various allergen, age and sex difference of allergen sensitization were investigated.

Results: The most common allergens were *Dermatophagoides farinae* (73.10%), *Dermatophagoides pteronyssinus* (72.21%) and *Blomia tropicalis* (53.10%), followed by *Blattella germanica* (31.18%), *Periplaneta americana* (27.75%), dog dander (24.96%), mixed molds (17.56%), and shrimp (17.02%). For the patients aged 18–30 yrs, mites and animal dander were most common allergen, whereas cockroaches and mixed molds for those aged over 40 yrs old. As for sex difference, males were more sensitive to *Blomia tropicalis*, cockroaches and mixed molds. Females were more sensitive to *Dermatophagoides farinae* and animal dander.

Conclusions: The most common allergen in Shanghai are mites, cockroaches, and dog dander. There are sex and age difference on profiles of allergen sensitization.

Key words: allergic disease; allergen; the skin prick test; sensitization; sex difference

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Introduction

The worldwide prevalence of allergic diseases has increased during the past few decades.^{1–2} In China, the prevalence of allergic rhinitis also changed rapidly from 5% in 1998 to 49.7% in 2008 among 13–14 years old children.^{1,3} The causes for such significant increase in allergic conditions include the changes of the environment, life style, nutrition state, and health awareness. Exposing to allergen is a critical trigger factor in the development of allergic diseases. Identifying allergen sensitization is essential for the diagnosis and personal specific immune therapy.⁴ For a long time, the skin prick test (SPT) was widely used as the standard method for identifying IgE-mediated sensitization to inhalant allergens.⁵

The profiles of allergen sensitization varies among different

regions and population. In China, although a multi-center study found that mites were the most prevalent allergens among patients with asthma and/or rhinitis based on the results of SPT, there is little epidemiology data about the sensitization rate of the common allergen in Shanghai.⁶ Thus, we aimed to investigate the profiles of allergen sensitization among adult patients with allergic diseases.

Materials and Methods

Study population and definitions

The study enrolled the outpatients who underwent a routine SPT (at Department of Allergy, Renji Hospital) due to present or former allergic symptoms during 2007–2016. The diagnosis

included rhinitis, asthma, atopic dermatitis, and food allergy. The diagnosis were based on the ARIA guidelines (rhinitis),⁷ GINA criteria (asthma), Williams' criteria (atopic dermatitis).⁸⁻⁹ Food allergy were defined by a history of ingestion symptoms, skin symptoms, or anaphylaxis when eating the specific food.¹⁰ The exclusion criteria included, patients with unclear demographic data, patients who accepted the immunotherapy, e.g. subcutaneous injection immunotherapy (SCIT) and sublingual immunotherapy (SLIT), etc.

The study was approved by the ethics committee of the Shanghai Jiao Tong University School of Medicine at Renji Hospital. Written informed consent were obtained from all participants.

The SPT

The protocol of SPT was referred to Li et al.⁶ Allergen extracts and control solutions were supplied by ALK (Horsholm, Denmark). Histamine (10 mg/mL) and control solutions were used as the positive and negative controls. Before the SPT, the administration of anti-histaminic drugs or glucocorticoid discontinued at least ≥ 1 week.

The SPT testing investigated six groups of allergen, i.e. food allergens (milk and shrimp), mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, and *Blomia tropicalis*), animal dander (dog dander and cat dander), cockroaches (*Blattella germanica* and *Periplaneta americana*), pollens (*Artemisia vulgaris* and *Ambrosia artemisiifolia*), mixed grasses (including *Poa pratensis*, *Dactylis glomerata*, *Lolium perenne*, *Phleum pratense*, *Festuca pratensis*, and *Helictotrichon pratensis*), mixed trees

(including *Platanus*, *Populus*, *Salix*, and *Ulmus*), and mixed molds (*Alternaria*, *Chaetomium*, *Cladosporium*, *Fusarium* and *Penicillium*).

The positive control was defined as a wheal size of ≥ 3 mm, after subtracting the negative control value. The skin index (SI = mean size of the allergen weal/mean size of a histamine wheal) was also used for presentation of the SPT results. Four levels based on the SI: level 1 (SI: 0.25–0.49), level 2 (SI: 0.50–0.99), level 3 (SI: 1.0–1.99), and level 4 (SI: >2.00).

Statistical analysis

All data were analyzed using SPSS software (version 13.0; SPSS Inc., Chicago, IL, USA). Demographic variables (age group and sex group) were defined as categorical variables, and Chi-square test was used to compare the difference among groups. A *p*-value of < 0.05 was considered statistically significant.

Results

Demographic characteristics

Among the 13,538 patients with positive SPT results during 2006–2016, 5,542 patients were excluded (**Figure 1**). Finally, 7,996 patients (3,244 males and 4,752 females) were enrolled in the analysis, with mean age of 36.38 yrs (range: 18–60 yrs, interquartile range: 24.99–47.77 yrs). The diagnosis included rhinitis (3,010 cases), asthma (2,409 cases), combining diagnosis of rhinitis and asthma (1,611 cases), and other allergic diseases (atopic dermatitis, and food allergies, 966 cases) (**Table 1**).

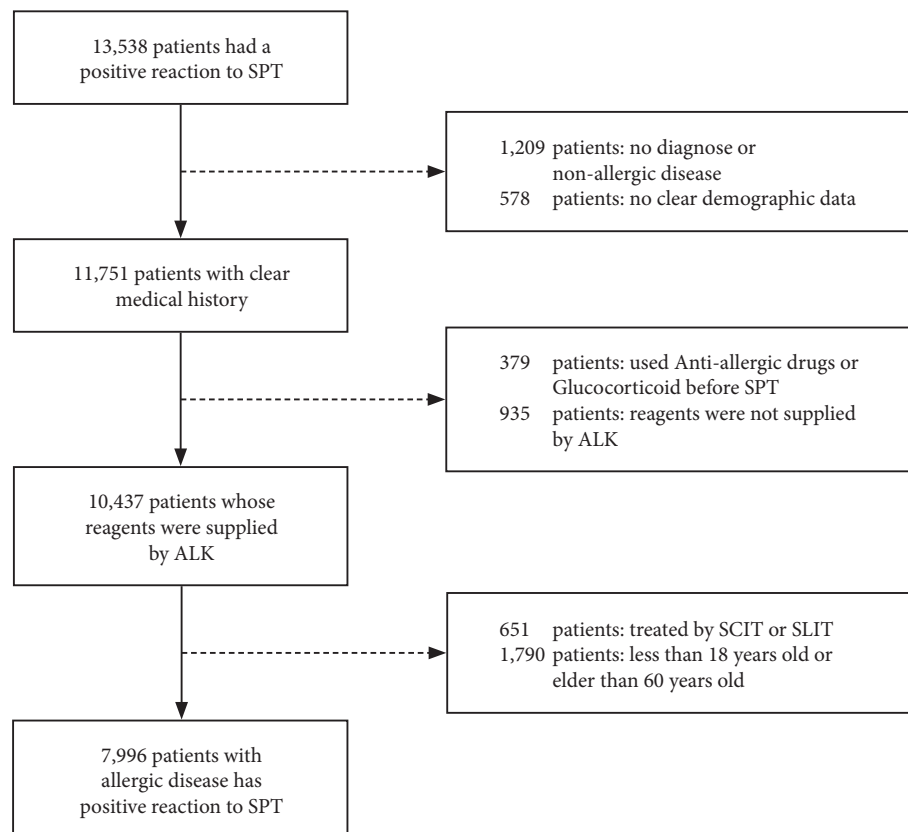


Figure 1. Flow chart for the present study.

Table 1. The Demographic characteristics

	N	18–30 yrs	31–40 yrs	41–50 yrs	51–60 yrs
N	7996	3129	2230	1346	1291
Male/Female	3244/4752	1355/1774	963/1267	479/867	447/844
Diagnose					
Rhinitis	3010	1203	945	534	328
Asthma	2409	938	648	506	317
Asthma accompanied with rhinitis	1611	510	503	378	220
Other allergic diseases*	966	137	156	382	291

*other allergic diseases: atopic dermatitis and food allergy.

Sensitization profiles

Sensitization to various allergens are listed in **table 2**. The most common allergens in Shanghai were mites (*Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, and *Blomia tropicalis*), cockroaches (*Blattella germanica* and *Periplaneta americana*), followed by dog dander, mixed molds, and shrimp. The prevalence was 73.10% for *Dermatophagoides farinae*, 72.21% for *Dermatophagoides pteronyssinus*, 53.10% for *Blomia*

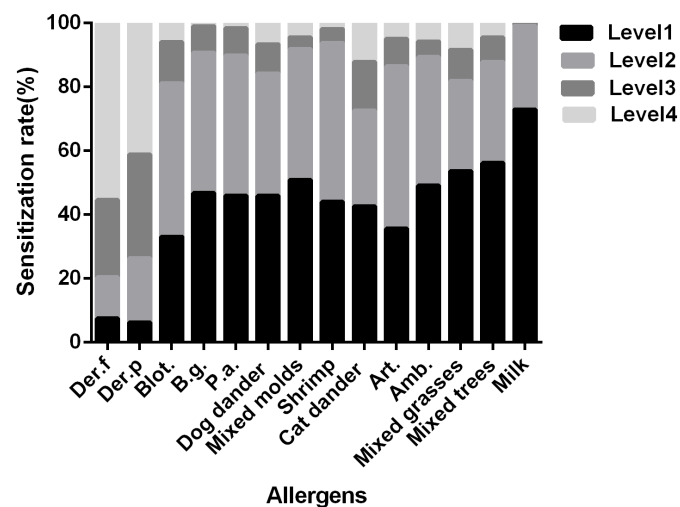
tropicalis, 31.18% for *Blattella germanica*, 27.75% for *Periplaneta americana*, 24.96% for dog dander, 17.56% for mixed molds and 17.02% for shrimp. Approximately 90% patients were co-sensitization to *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*. Less common allergens included cat dander, pollens and milk.

We also found that *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* frequently elicited a strong positive skin reaction (levels 3–4), and that the other allergens generally elicited a weaker positive reaction (levels 1–2) (**Figure 2**).

Table 2. Positive rate and skin index levels among 7,996 adults with allergic diseases.

Allergen	Positive	Skin index level (%of the positive)			
	n (%)	Level 1	Level 2	Level 3	Level 4
Mites					
<i>Der.f</i>	5,845 (73.10)	7.53	12.85	24.21	55.41
<i>Der.p</i>	5,774 (72.21)	6.18	20.21	32.47	41.14
<i>Blot.</i>	4,246 (53.10)	33.06	48.16	12.83	5.95
Cockroaches					
<i>Blattella germanica</i>	2,493 (31.18)	46.81	43.92	8.30	0.97
<i>Periplaneta americana</i>	2,219 (27.75)	45.97	43.95	8.47	1.61
Animal dander					
Dog dander	1,996 (24.96)	45.87	38.35	9.13	6.65
Cat dander	1,358 (16.98)	42.65	30.03	15.14	12.18
Mixed molds	1,404 (17.56)	50.88	40.95	3.73	4.44
Pollen					
<i>Artemisia vulgaris</i>	1,016 (12.71)	35.65	50.80	8.57	4.98
<i>Ambrosia artemisiifolia</i>	968 (12.11)	49.11	40.31	4.85	5.73
Mixed grasses	650 (8.13)	53.58	28.24	9.78	8.40
Mixed trees	576 (7.20)	56.20	31.69	7.58	4.53
Food					
Shrimp	1,361 (17.02)	44.01	49.82	4.34	1.83
Milk	449 (5.62)	72.95	26.23	0.82	0.00

Abbreviations: *Der.f*, *Dermatophagoides farinae*; *Der.p*, *Dermatophagoides pteronyssinus*; *Blot.*, *Blomia tropicalis*.



Abbreviations: *Der.f*, *Dermatophagoides farinae*; *Der.p*, *Dermatophagoides pteronyssinus*; *Blot.*, *Blomia tropicalis*; *B.g.*, *Blattella germanica*; *P.a.*, *Periplaneta americana*; *Art.*, *Artemisia vulgaris*; *Amb.*, *Ambrosia artemisiifolia*.

Figure 2 The positive skin reactions to 14 kinds of allergens.

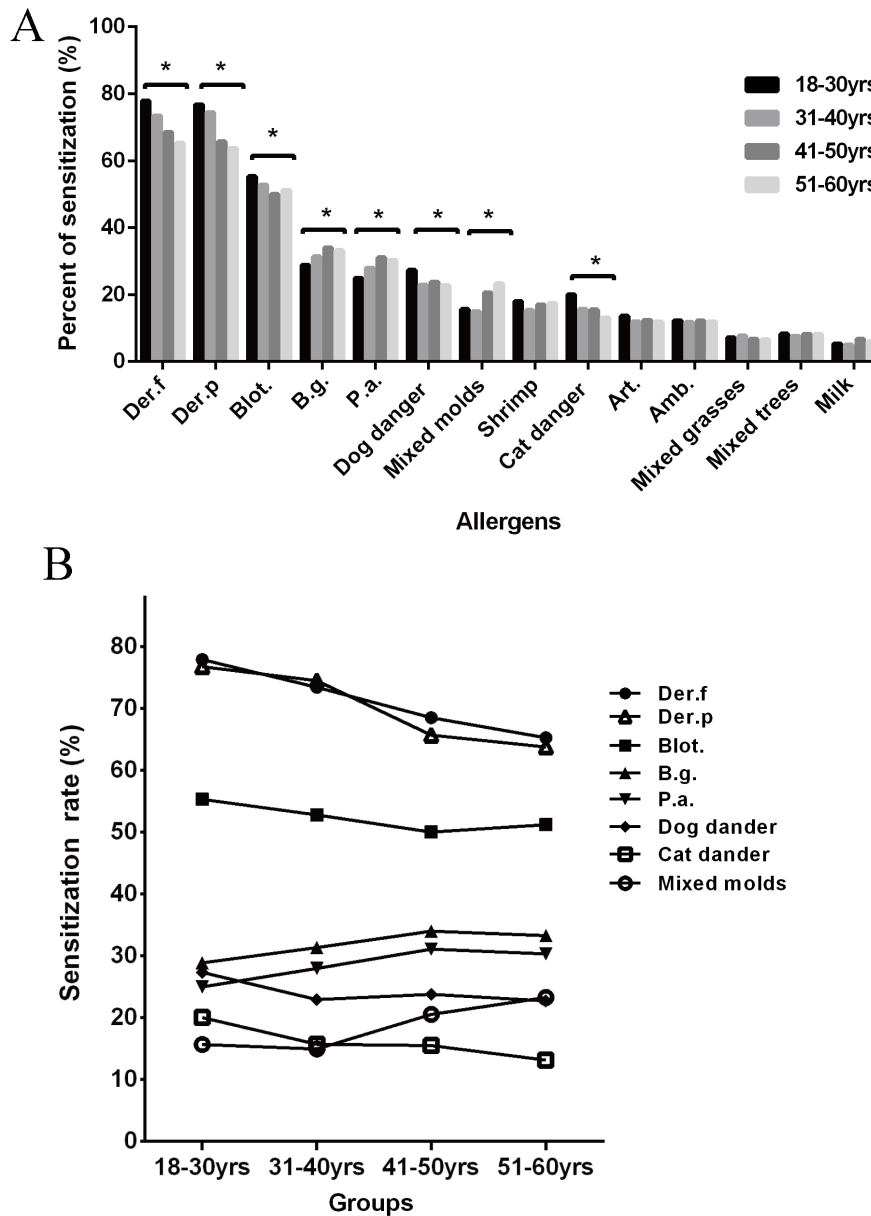
Dermatophagoides farinae and *Dermatophagoides pteronyssinus* frequently elicited a strong positive reaction (levels 3 and level 4, $P < 0.01$), and that the other allergens generally elicited a weaker positive reaction (levels 1 and level 2, $P < 0.01$).

Level 1 ($0.25 < SI < 0.49$), level 2 ($0.50 < SI < 0.99$), level 3 ($1.0 < SI < 1.99$), and level 4 ($SI \geq 2.0$).

Age difference of sensitization profiles

We compared the difference of allergen sensitization in various age groups. The patients aged 18–30 yrs had significantly higher sensitization rates to mites (*Dermatophagoides farinae* 77.98% vs. 65.30%, *Dermatophagoides pteronyssinus* 76.80% vs. 63.83%, *Blomia tropicalis* 55.35% vs. 50.07%, $p < 0.05$) and animal dander (dog dander 27.36% vs. 22.77%, cat dander 20.07% vs. 13.17%, $p < 0.05$) than 41–50 yrs or 51–60 yrs old ones.

The 41–50 yrs old patients had significantly higher sensitization to cockroaches than 18–30 yrs old ones (*Blattella germanica*, 34.03% vs. 28.92%, *Periplaneta americana* 31.13% vs. 25.02%, $p < 0.05$). As for molds, patients aged 51–60 yrs had higher sensitization rates than 18–30 yrs old ones (23.32% vs. 15.72%, $p < 0.05$). No significant difference for sensitization rates of shrimp, pollen and milk were found among groups (Figure 3).



Abbreviations: *Der.f*, *Dermatophagoides farinae*; *Der.p*, *Dermatophagoides pteronyssinus*; *Blot.*, *Blomia tropicalis*; *B.g.*, *Blattella germanica*; *P.a.*, *Periplaneta americana*; *Art.*, *Artemisia vulgaris*; *Amb.*, *Ambrosia artemisiifolia*.

Figure 3. Age difference of allergic sensitization.

A: age difference of all allergen; B: allergen of different positive rate in four age groups.

Chi-square test was used to compare the difference among groups.

The 18–30 yrs old patients exhibited the highest sensitization rates to mites and animal dander; The 41–50 yrs old patients exhibited significantly higher sensitization to *Blattella germanica* and *Periplaneta americana*; The 51–60 yrs patients exhibited significantly higher sensitization rates for mixed molds (all $p < 0.05$).

Table 3. Sex and age difference of sensitization rates (%).

Allergen			18–30 yrs		31–40 yrs		41–50 yrs		51–60 yrs	
	M	F	M	F	M	F	M	F	M	F
Mites										
<i>Der. f</i>	70.84	74.64*	77.08	78.69	73.02	75.34	64.92	70.59*	57.94	69.19*
<i>Der. p</i>	71.76	72.52	77.05	76.61	74.97	74.19	62.00	67.82	60.28	66.23
<i>Blot.</i>	54.84	51.91*	56.83	54.23	55.97	50.43*	49.90	50.17	51.68	51.07
Cockroaches										
<i>Blattella germanica</i>	35.88	27.97*	32.69	26.04*	36.34	27.62*	40.29	30.57*	39.82	29.88*
<i>Periplaneta americana</i>	33.17	24.05*	29.74	21.42*	33.96	23.53*	38.62	26.99*	36.02	27.37*
Animal dander										
Dog dander	22.69	26.52*	27.01	27.62	23.63	25.49	19.83	27.57*	19.24	24.65*
Cat dander	16.47	18.13*	18.45	21.31	14.64	16.57	16.94	16.96	10.96	14.34*
Mixed molds	19.42	16.29*	15.64	14.26	16.41	13.89	24.63	18.34*	25.73	20.04*
Pollen										
<i>Artemisia vulgaris</i>	12.78	13.34	13.65	13.70	10.59	13.02	11.04	13.14	12.40	13.27
<i>Ambrosia artemisiifolia</i>	12.15	12.08	13.13	11.67	11.94	11.68	10.86	13.03	10.96	12.56
Mixed grasses	6.75	7.51	7.16	7.21	7.48	7.97	5.22	7.73	5.59	7.23
Mixed trees	8.45	7.91	8.19	8.46	8.31	7.26	8.77	7.96	9.17	7.70
Food										
Shrimp	16.95	17.07	17.65	18.26	15.26	15.47	17.54	16.84	17.90	17.18
Milk	5.15	5.93	5.24	5.52	5.03	5.93	6.68	6.81	6.26	5.92

Abbreviations: M, Males; F, Females; *Der.f*, *Dermatophagoides farinae*; *Der.p*, *Dermatophagoides pteronyssinus*; *Blot.*, *Blomia tropicalis*.

Sex difference of sensitization profiles

Males were more sensitive than the females to *Blomia tropicalis* (54.84% vs. 51.91%), cockroaches (*Blattella germanica* 35.88% vs. 27.97%, *Periplaneta americana* 33.17% vs. 24.05%, respectively) and mixed molds (19.42% vs. 16.29%). Comparing with the males, females were more sensitive to *Dermatophagoides farinae* (74.64% vs. 70.84%) and animal dander (dog dander 26.52% vs. 22.69%, cat dander 18.13% vs. 16.47%, respectively, all $p < 0.05$).

We further explored the sex difference of allergen sensitization rate in various age groups. As showed in **table 3**, sex difference for *Dermatophagoides farinae*, animal dander and mixed molds was mainly found in 41–50 yrs old and 51–60 yrs old patients. As for *Blomia tropicalis*, the sex difference existed in 31–40 yrs old patients (all $p < 0.05$). (**Table 3**).

Discussion

The number of allergens and the allergenic pressure vary from countries and areas due to geographic factors. Northern and Eastern Europeans are most commonly sensitive to cat and dog dander, birch, hazel and alder pollen, whereas Western European and Mediterranean residents allergic to house dust mites, cockroaches, birch, olive, and grass pollen.⁴ Herein, we found that the most common allergen in Shanghai were mites, cockroaches, and dog dander.

Different from the western countries, the top three allergens in Shanghai were *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae* and *Blomia tropicalis* (73.10%, 72.21%, and 53.10%, respectively) and *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* elicited a strong positive skin reaction (levels 3–4), while other allergens elicited weaker positive skin reaction (levels 1–2). Li and colleagues found that severity of asthma was significantly correlated with skin index of reactivity to *Dermatophagoides farinae* and *Dermatophagoides*

pteronyssinus.⁶ In addition, approximately 90% patients were co-sensitized to *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*. The findings are consistent with previous studies.^{11–13} The co-sensitization might depend on the amino acid sequence homology within the allergens. There are 83% amino acid sequence homology between *Der p1* and *Der f1*, while 68% between *Der p2* and *Der f2*, also 68% between *Blo t4* and *Der p4*.^{14,15} Regarding the co-sensitization and amino acid sequence homology among different mites genus, it is suggested that a single mite extract or genetic recombinant could be used to treat mites allergic diseases.¹⁶

Cockroaches (*Blattella germanica*: 29.51%, *Periplaneta americana*: 26.23%) and dog dander (25.19%) were also common in Shanghai. We found some patients allergic to dog or cat dander (24.96% and 16.98%, respectively) had no history of contacting with pets. It is probably animal allergens carried with clothes or human hair.^{17–19} Arlian et al.²⁰ also found large amounts of dog and cat allergen that were located in carpets, upholstery, mattresses, and curtains, regardless of whether a pet was present in the home. Zhang et al.²¹ performed a survey of 107 houses and found that cockroach allergen were detected in 93% of the households, and that the allergen levels were higher in samples of living room, compared to that of bedding samples. Thus, it is essential for the patients to clean their indoor environment.

Mixed molds were also main allergen in Shanghai, which was probably related to the subtropical monsoon climate that features abundant precipitations and sunshine. Contrast to airborne pollens as important allergens in northwestern China,²² we found relatively low sensitization rates for *Artemisia vulgaris* (12.71%), *Ambrosia artemisiifolia* (12.11%), mixed grasses (8.13%) and mixed trees (7.20%) in Shanghai.

Further, the age and sex difference were analyzed. Firstly, compared with elderly patients, 18–30 yrs old patients were

more sensitive to mites and animal dander, which is consistent with the results in Northern Sweden study. The decrease of sensitization rates in the elderly could be related to the birth-cohort-effect.²³ Secondly, those aged 51–60 yrs were more sensitive to cockroaches and mixed molds than the youth, which may be due to the humid conditions in kitchens and bathrooms fostering molds and cockroaches,²¹ as elderly people are more likely to cook and clean in China.

As for the sex difference, males were more sensitive to *Blomia tropicalis*, cockroaches and mixed molds, while females were more sensitive to *Dermatophagoides farinae* and animal dander than males. The sex differences may related to following factors, such as the females were likely to have pets in China, and the males were less likely to keep indoor environment tidier than females.

Limitations of our study should be mentioned, such as not including the healthy asymptomatic controls and lack of inhibition test to determine the incidences of cross-reactivity or concomitant reactivity, etc.

Conclusion

The most common allergens in Shanghai were mites, cockroaches, and dog dander, with sex and age difference.

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Ya Ru Yan and Yan Hua Xu contributed equally and should be considered as co-first authors.

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