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Prevalence and trends of sensitization to aeroallergens in allergic rhinitis patients in Guangzhou, China

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ABSTRACT

Objective: To investigate the prevalence and trends of sensitization to common aeroallergens among outpatients with allergic rhinitis (AR) in Guangzhou, China over the past decade.

Design: A retrospective study; Linear-by-linear association and simple linear regression were used to determine the trends in the prevalence of allergen sensitization.

Setting: One Grade-A hospital in Guangzhou, the largest city in southern China.

Participants: 5,486 patients with nasal hyper-reactivity symptoms were enrolled between 2005 and 2014. The inclusion criteria for study population was positive sIgE reactivity to at

least one aeroallergen component. Thus, of the 5,486 samples, 4,085 (2,269 males and 1,816 females) were AR patients who constituted the main study population.

Outcome measures: The prevalence of allergen sensitization was the outcome of interest. It was defined as the positive sIgE reactivity to at least one aeroallergen component.

Results: The overall prevalence of sIgE to aeroallergens were as follows: 84.4% for house dust mites, 23.4% for pet allergens, 21.1% for cockroaches, 9.1% for mold allergens, 7.7% for tree pollens, and 6.0% for weed pollens. For each additional 10 years, occurrence of a positive sIgE result decreased by approximately 5.13% (95% confidence interval [CI]: -7.28, -2.98, $p < 0.01$). Within the past decade, the prevalence of sensitization to pet allergens increased at an annual rate of 1.3% (95% CI: 0.85, 1.67, $p < 0.001$).

Conclusions: House dust mites are the most common culprit allergen in Guangzhou, China. The prevalence of sensitization to at least one common aeroallergen decreased significantly with age. From 2005 to 2014, the prevalence of sensitization to pet allergens has steadily increased, suggesting the importance of introducing a specific immunotherapy for treating individuals with pet allergies.

Keywords: serum sIgE; HDM; pet allergens; allergic rhinitis

Strengths and limitations of this study

•This study is among the first carried out in Guangzhou, the largest city in southern China, investigating the trends in the prevalence of common aeroallergen sensitizations to allergic rhinitis patients over the last decade.

•The study was based on the results of serum specific-allergen IgE (sIgE) test, a measurement with a high specificity and sensitivity for the diagnosis of common aeroallergen sensitization.

•The study was conducted by retrospective collection and analysis of the results of sIgE test. It was difficult to offer any information on the severity of AR symptoms and the risk factors for exposure to common allergens. .

•The study was primarily a single-center study. The findings may not be representative of the general population.

INTRODUCTION

Allergic rhinitis (AR) is the most common allergic respiratory disease affecting 10-40% of individuals worldwide. AR can adversely affect the quality of life and impose a substantial burden on both patients and society.[1 2] AR is an immunoglobulin E (IgE)-mediated type I nasal allergic disorder characterized by nasal hyper-reactivity symptoms, including nasal pruritus, sneezing, airflow obstruction, and rhinorrhea.[3] It is crucial during diagnosis to distinguish the type of allergen causing AR to identify an effective therapy. Recent studies describing allergic sensitization in different countries and regions have had conflicting results. In the United Kingdom, grass pollen was the most common inhalant allergen, while cat allergens and cedar pollen were the most common allergen for AR in Sweden and Japan, respectively. [4-6] China is suffering from an increasing incidence of AR. A multicenter study performed by Li *et al.* found that the prevalence of sensitization to pollens and house dust mites (HDM) was higher in northern and southern regions, respectively. [7] Recently, the global

prevalence of AR has steadily increased, which may be attributed to urbanization, resulting in subsequent environmental and lifestyle changes due to economic development.[8-10] A study by Mehulic *et al*. reported a significant change in the sensitization to different aeroallergens in Croatia.[11] However, few similar studies have been performed in Guangzhou, the largest city in southern China. Thus, in this study we enrolled AR patients from 2005 to 2014 and retrospectively analyzed sera for the presence of specific-allergen IgE (sIgE). The results from our study enabled us to determine the prevalence and trends of sensitization to aeroallergens in Guangzhou, China over the last decade.

MATERIALS AND METHODS

Study design and subjects

We performed a retrospective study based on the presence of sIgE from 5,486 patients with nasal hyper-reactivity symptoms who attended the ear, nose, and throat (ENT) outpatient clinics at the Third Affiliated Hospital of Sun Yat-sen University in Guangzhou, China from January 2005 to December 2014. The inclusion criteria for AR subjects were as follows: (1) nasal hyper-reactivity symptoms, including sneezing and a runny, itchy, or blocked nose and (2) positive sIgE reactivity to at least one aeroallergen component. Thus, of the 5,486 samples, 4,085 were AR patients who constituted the main study population.

Patients covered a wide geographic area and came from the following districts in Guangzhou: Tianhe (n = 1,496, 36.6%), Yuexiu (n = 751, 18.4%), Haizhu (n = 642, 15.7%), Liwan (n = 509, 12.5%), Baiyun (n = 371,9.1%), and Conghua and Zengcheng (n = 316,

7.7%).

Ethics statement

This study was approved by the Third Affiliated Hospital of Sun Yat-Sen University Ethics Committee in Guangzhou, China. In addition, all adult participants aged ≥ 18 years old and the guardians on behalf of their minor participants aged < 18 years old signed informed consent forms.

sIgE measurements

German AllergyScreen (Mediwiss Analytic GmbH, Moers, Germany) was used to measure serum allergen sIgE levels. The following six types of common aeroallergens were detected: house dust mites (*Dermatophagoides pteronyssinus*, Der p), pet allergens (combination of dog hair and cat dander), cockroaches, molds (mixture of *Penicillium notatum,* branch spore mildew, *Aspergilus fumigates*, and *Alternaria*), tree pollens (combination of cypress, elm, phoenix tree, willow, and cottonwood), and weed pollens (combination of short ragweed, mugwort, *Humulus scandens*, and pigweed). The sIgE levels were calculated using a calibration curve and expressed as a concentration of international units per milliliter (IU/mL). The concentrations of sIgE were quantitatively ranked as follows: class 0, < 0.35 IU/mL; class 1, ≥ 0.35-0.70 IU/mL; class 2, ≥ 0.70-3.5 IU/mL; class 3, ≥ 3.5-17.5 IU/mL; class 4, ≥ 17.5-50 IU/mL; class 5, ≥ 50-100 IU/mL; class 6, ≥ 100 IU/mL. Serum sIgE levels of ≥ 0.35 IU/mL (class 1 or above) were considered positive.

Statistical analysis

The IBM-SPSS (ver. 20; SPSS Inc., Chicago, IL, USA) statistical software package was used for data processing and analysis. Linear-by-linear association was used to investigate whether or not the changing prevalence of allergen sensitization was characterized by a significant Linear-by-linear association with years or increasing ages. And the simple linear regression was used to analyze how the overall trends in the prevalence of the sensitization to allergens occurred among age groups or year groups on the premise of the significant Linear-by-linear association. Due to the ages not being normally distributed, we used a Mann-Whitney U test to compare the age difference between genders. A $p < 0.05$ was considered statistically significant.

RESULTS

Demographic data

In total, 4,085 AR patients were enrolled in this study, consisting of 2,269 males (55.5%) and 1,816 females (44.5%). The study population was between the ages of 1-79 years (median age = 23.0 years, interquartile range [IQR]: 10.0, 32.0). The median ages were 19.0 (IQR: 8.5, 30.0) for males and 26.0 (IQR: 15.0, 33.0) for females. The age of sensitization to aeroallergen in males was significantly younger than in females ($p < 0.001$).

Prevalence of sensitization to aeroallergens in Guangzhou

As shown in Figure 1, the prevalence of sensitization to aeroallergens were as follows: 84.4% for HDM, 23.4% for pet allergens (combination of dog hair and cat dander), 21.1% for cockroaches, 9.1% for mold allergens, 7.7% for mixed tree pollens, and 6.0% for mixed weed pollens.

Allergen sensitization by age group

To further assess the correlation between the prevalence of sensitization to aeroallergens and age, we stratified AR patients into the following seven age groups: 1-9, 10-19, 20-29, 30-39, 40-49, 50-59, and ≥ 60 years. The prevalence of sensitization to allergens for each age group is shown in Figure 2. The prevalence was highest in the 10-19 years age group (86.6%) and the lowest in the ≥ 60 years age group (52.6%). Allergen-sIgE reactivity decreased as age increased, and for each additional 10 years the prevalence decreased by 5.13% (95% CI: -7.28, -2.98, $p < 0.01$).

Prevalence of sensitization to HDM was highest for the 10-19 years age group (91.4%) and decreased with age ($p < 0.001$). The rates decreased by 3.0% every 10 years after the age of 19 years (95% CI: -5.6, -0.45, $p < 0.05$). Sensitization to pet allergens was most common among young AR patients (30.2%). The prevalence of sensitization to weed pollens increased on average by 2.09% for every 10 years (95% CI: 1.28, 2.90, $p < 0.05$). Similarly, the prevalence of sensitization to tree pollens showed an upward trend, increasing with age ($p < 0.001$) at a rate of 1.36% every 10 years (95% CI: 0.17, 2.56, $p < 0.05$) (table 1).

Trends in the prevalence of sensitization to aeroallergens over the past decade

The prevalence of sensitization to aeroallergens from 2005 to 2014 was as follows: 69.7% (2005), 73.6% (2006), 75.1% (2007), 72.0% (2008), 75.7% (2009), 76.6% (2010), 74.1% (2011), 75.8% (2012), 75.9% (2013), and 74.0% (2014). During those 10 years, we did not observe a significant trend among the prevalence rates ($p > 0.05$). Figure 3A shows the specific type of aeroallergen and the respective prevalence rates. There were no significant differences in the prevalence of sensitization to HDM, cockroaches, weed pollens, tree pollens, and mold allergens over the past decade. However, the prevalence of pet allergens increased from 16.5% to 28.6%, showing an upward trend with an average annual rate increase of 1.3% (95% CI: 0.85, 1.67, $p < 0.001$) (figure3B).

DISCUSSION

The production of sIgE is a hallmark of AR and sIgE testing for allergens and has been widely utilized to determine sensitization to specific allergens. In this study, we collected sIgE test results from 4,085 AR outpatients within the last 10 years in Guangzhou, the largest city in southern China, to determine the prevalence and trends of sensitization to aeroallergens between 2005 and 2014.

In this study we observed the following prevalence rates of sensitization to aeroallergens: 84.4% HDM, 23.4% pet allergens (combination of dog hair and cat dander), 21.1% cockroaches, 9.1% mold allergens, 7.7% tree pollens, and 6.0% weed pollens. HDM were the predominant allergen in Guangzhou, which was consistent with previously published studies.

[7 12] High humidity and ambient temperatures have been reported as optimal conditions for HDM propagation.[13] Guangzhou is located in the subtropical region with high temperature, high humidity, and rainy weather, and where there is little difference in the perennial temperature. The characteristics of the local climate in Guangzhou are optimal for HDM propagation, which is in accordance with our results in which we observed a high prevalence of sensitization to HDM in this region.

Lifestyle may be another potential contributor to the high prevalence of sensitization to HDM. In Guangzhou, residents in the municipality spend a majority of time indoors, especially in environments with air conditioning. The major sources of HDM are bed sheets, carpets, and pillows. A previous study confirmed the presence of high concentrations of Der p in air conditioning filters.[14] Long durations in environments with poor ventilation increases the chance of exposure to house dust mites.[13] Another study showed that residing in homes with mechanical ventilation instead of air-conditioning can reduce house dust mite exposure, leading to overall clinical improvement for HDM-sensitized patients.[15]

In this study, we observed that the prevalence of sensitization to aeroallergens was higher among the younger age groups (1-9 and 10-19 years). In addition, we further analyzed the relationship between the prevalence of sIgE and age group. For each additional 10 years, the prevalence of sIgE decreased by 5.13% (95% CI: -7.28, -2.98, $p < 0.01$). These results suggest that sensitization to allergens was most prevalent among younger patients, which was consistent with previously published studies. [16] However, the exact reasons for the higher prevalence of sIgE observed in young AR patients are unknown. One explanation may be

immunosenescence, which reduces innate and adaptive immune responses, resulting in an attenuated response to foreign antigens and subsequently decreased sIgE production. [17 18] De Amici *et al*. reported that the sIgE levels for several aeroallergens decreased significantly with increasing age. [19] Further studies will be necessary to determine the relationship between sIgE levels and the high prevalence of sIgE.

To the best of our knowledge, this is the first study to determine the prevalence and describe the trends in the sensitization to aeroallergens in Guangzhou within the last 10 years. The increasing incidence of AR and changes in aeroallergen sensitization have been attributed to urbanization, resulting in subsequent alterations to the environment and lifestyle. [11 20] Within the last 10 years, Guangzhou has undergone rapid changes towards urbanization and western lifestyle. Thus, this study retrospectively analyzed the data on allergic sensitization between 2005 and 2014 to investigate the changing prevalence and trends of aeroallergen sensitization.

In this study, the prevalence of sensitization to aeroallergens, as reflected by a positive sIgE test, was within the range of 69.7-76.6% from 2005 to 2014. From our results, we did not observe a significant change within the last 10 years, which was in accordance with studies performed by Jarvis *et al*[21] In addition, there were no significant differences in the prevalence of sensitization to HDM, cockroaches, mold, weed pollens, and tree pollens between 2005 and 2014. In this study, we observed an upward trend in the sensitization to pet allergens (dog hair and cat dander), rising from 16.5% to 28.6% at an average annual rate of 1.3% (95% CI: 0.85, 1.67, $p < 0.001$). These results indicate that over the last 10 years an

increasing number of AR patients have become sensitized to pet allergens in Guangzhou.

The results from a cross-sectional questionnaire found that exposure to pets was a risk factor for respiratory diseases.[22] Given the improvement in living standards in Guangzhou, an increasing number of people in the municipality keep cats and dogs as indoor pets, increasing the concentration of dog hair and cat dander, as well as the chance of exposure to these allergens. It was reported that long-term exposure to animal allergens may cause respiratory hyper-reactivity and accelerate the development of asthma and AR.[23] The increasing prevalence of sensitization to pet allergens within the past 10 years has indicated the importance of therapy for AR patients with pet allergies. However, pet allergens were found not only in families with pets, but also in those without pets or in public places, including communities and schools. [24] Thus, the exact allergen that should be avoided was difficult to identify. Specific immunotherapy (SIT) is the only treatment for AR,[25] and previous studies have reported that this treatment is clinically effective in desensitization to pet allergens. [26 27] However, SIT for cat and dog allergens is still not available in China. Thus, this study further supports the importance for Chinese health authorities and research institutions to introduce pet allergen immunotherapy, allowing AR patients and pets to cohabitate

This study is among the first carried out in Guangzhou, the largest city in southern China, investigating the trends in the prevalence of common aeroallergen sensitizations to allergic rhinitis patients over the last decade. The study was based on the results of serum specific-allergen IgE (sIgE) test, a measurement with a high specificity and sensitivity for the diagnosis of common aeroallergen sensitization. However, this study has several limitations.

The study was conducted by retrospective collection and analysis of the results of sIgE test. It was difficult to offer any information on the severity of AR symptoms and the risk factors for exposure to common allergens. For example, although we found that an increasing number of AR patients had been sensitized to pet allergens, we still have no idea about the details on pets keeping among those patients. Moreover, although all 4,085 AR patients were from the majority of the districts in Guangzhou, this study was primarily a single-center study; however, to some extent, the results from this study describe the prevalence and trends of sensitization to aeroallergens within the past 10 years. From our results, we recommend that additional, multi-center studies are needed to reach a more accurate and generalized conclusion.

CONCLUSION

This study demonstrated that HDM were the most common aeroallergens in Guangzhou. The prevalence of sensitization to inhalant allergens decreased with increasing age. Between 2005 and 2014 the prevalence of sensitization to pet allergens revealed an upward trend, suggesting the importance in introducing SIT for individuals with pet allergies.

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Abbreviations AR, allergic rhinitis; sIgE, specific immunoglobulin E; HDM, house dust mite ENT, the clinic of Ear, Nose, Throat

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Competing interests None.

Contributors QY conceptualized the study, designed the protocol, analyzed the data and drafted the manuscript. WW, XH collected the data, analyzed the data and drafted the manuscript. ZC, RZ, YC, GZ participated in administrative and technical support.

Patient consent Obtained.

Ethics approval Obtained.

Data sharing statement No additional data are available.

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Table

Table 1 The positive rates of sensitization to each kind of aeroallergens in age groups.

	HDM	Pet allergens	Cockroaches	Mixed mold	Weed pollens	Tree pollens
1-9 years	788(83.1%)	286(30.2%)	110(11.6%)	105(11.1%)	23(2.4%)	44(4.6%)
10-19 years	729(91.4%)	200(25.1%)	148(18.5%)	71(8.9%)	30(3.8%)	41(5.1%)
20-29 years	909(84.2%)	224(20.8%)	303(28.1%)	83(7.7%)	86(8%)	96(8.9%)
30-39 years	650(82.7%)	144(18.3%)	195(24.8%)	65(8.3%)	49(6.2%)	78(9.9%)

40-49 years	262(83.2%)	61(19.4%)	73(23.2%)	28(8.9%)	33(10.5%)	32(10.2%)
50-59 years	74(68.5%)	28(25.9%)	21(19.4%)	10(9.3%)	16(14.8%)	17(15.7%)
≥60 years	36(70.6%)	11(21.6%)	11(21.6%)	8(15.7%)	7(13.7%)	5(9.8%)
$p^{※}$	< 0.001	< 0.001	< 0.001	0.181	< 0.001	< 0.001
$P^{△}$	0.027	0.298	0.396	0.306	0.001	0.033

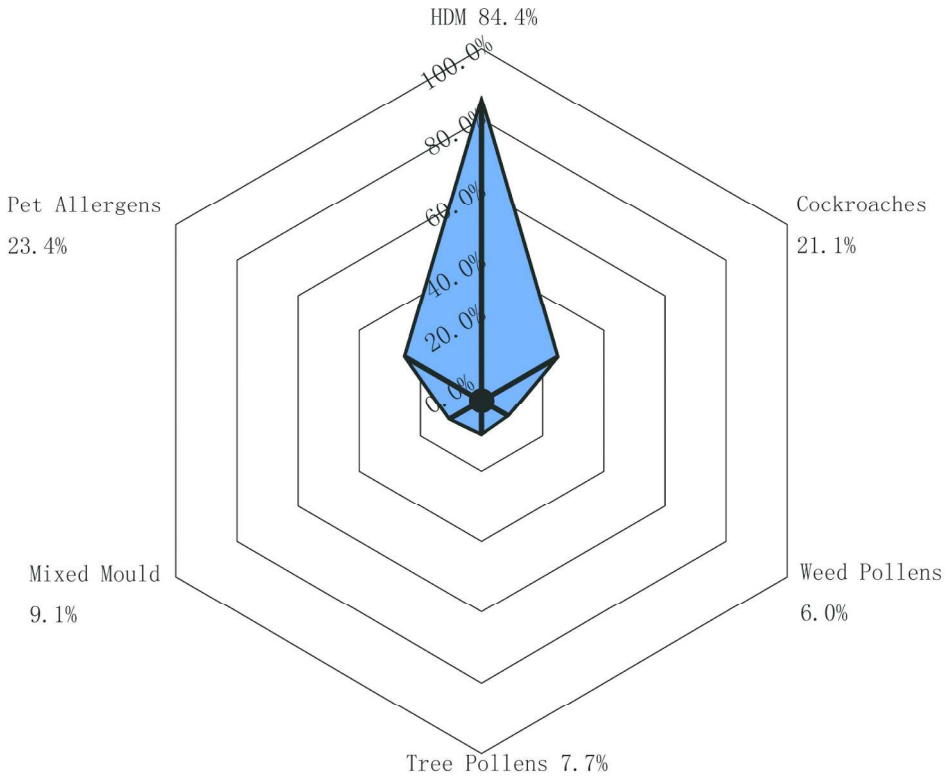
Abbreviation: HDM, house dust mite

Figure legends

Figure 1 The overall prevalence of sensitization to common inhalant allergens in Guangzhou.

Figure 2 Age differences in the sIgE positive rates of sensitization to at least one aeroallergens.

Figure 3 Trends of aeroallergen sensitization prevalence. **(A)**The changing prevalence of sensitization to each kind of aeroallergens. **(B)**The significant uptrend of the prevalence of sensitization to pet allergens from 2005 to 2014.



The overall prevalence of sensitization to common inhalant allergens in Guangzhou
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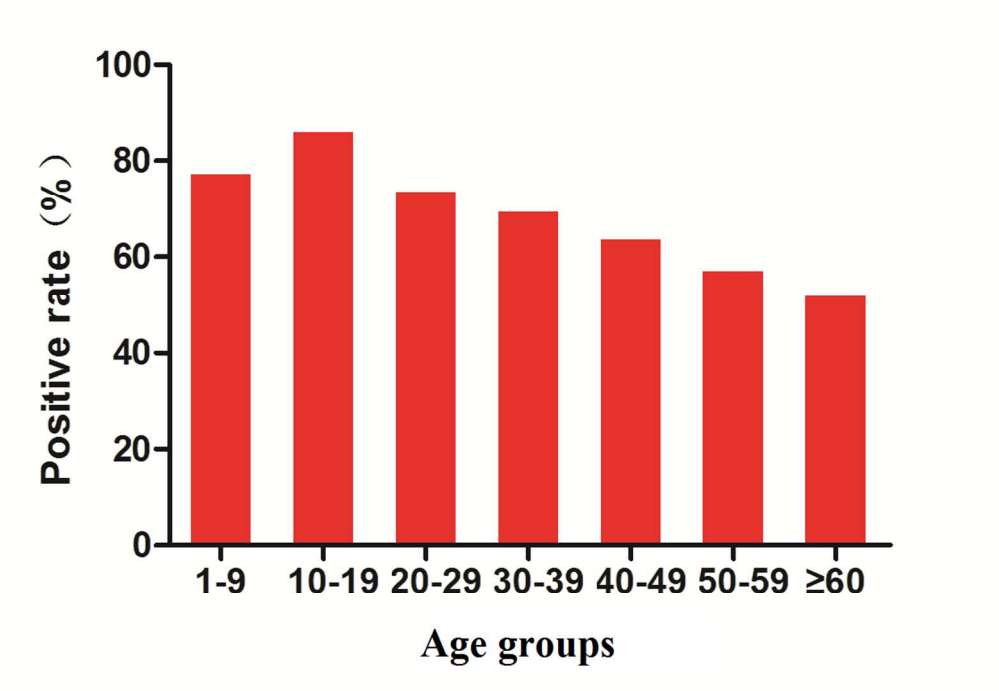
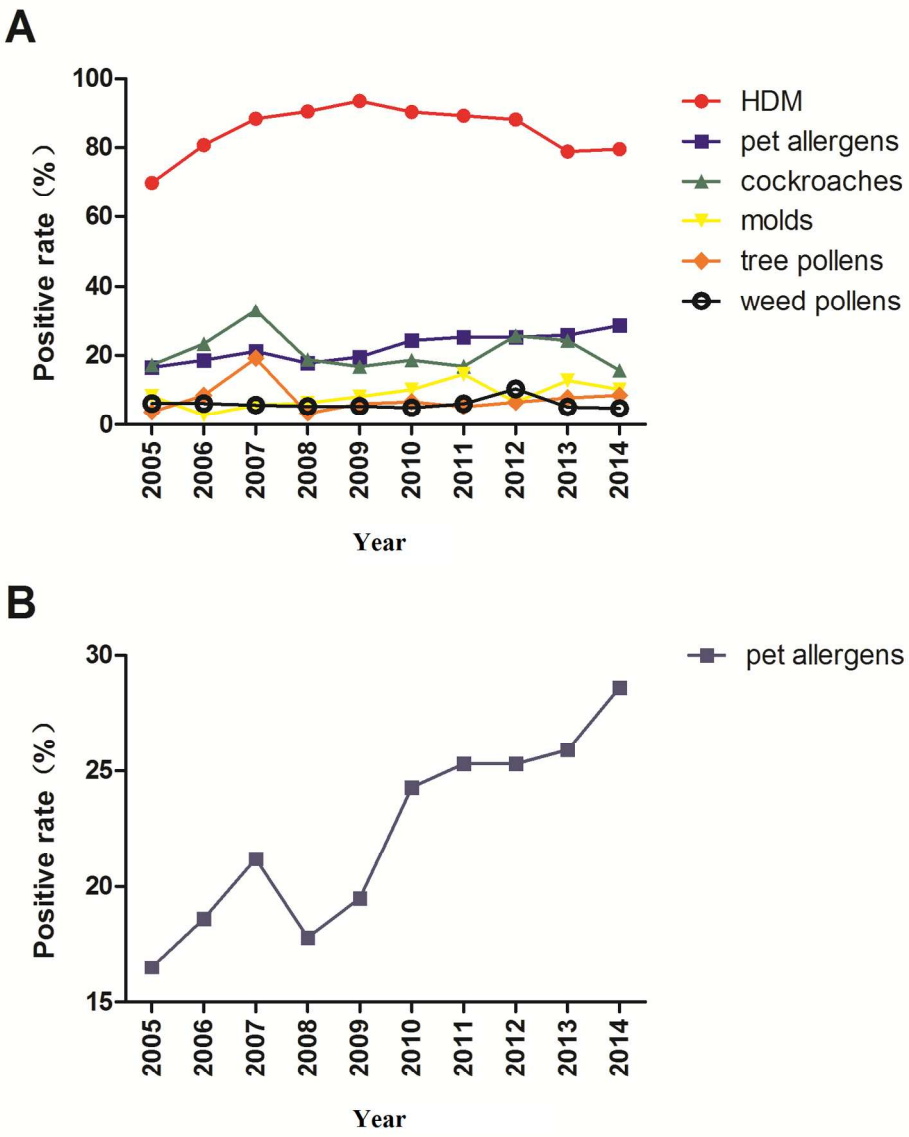


Age differences in the sIgE positive rates of sensitization to at least one aeroallergens
105x73mm (300 x 300 DPI)



Trends of aeroallergen sensitization prevalence. (A)The changing prevalence of sensitization to each kind of aeroallergens. (B)The significant uptrend of the prevalence of sensitization to pet allergens from 2005 to 2014.
153x189mm (300 x 300 DPI)

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Prevalence and trends of sensitization to aeroallergens in allergic rhinitis patients in Guangzhou, China: A 10-year retrospective study

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Prevalence and trends of sensitization to aeroallergens in allergic rhinitis patients in Guangzhou, China: A 10-year retrospective study

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Keywords: allergic rhinitis; serum sIgE; house dust mite; pet allergens

Word Count: 2150 words

ABSTRACT

Objective: To investigate the prevalence and trends of sensitization to common aeroallergens among outpatients with allergic rhinitis (AR) in Guangzhou, China over the past decade.

Design: A retrospective study; Linear-by-linear association and simple linear regression were used to determine the trends in the prevalence of aeroallergen sensitization.

Setting: One Grade-A hospital in Guangzhou, the largest city in southern China.

Participants: 5486 patients (2,297 males and 2,489 females) who visited the Ear, Nose and Throat Outpatient Clinic between January 2005 and December 2014 were enrolled. All the patients met the inclusion criteria: patients who presented nasal hyper-reactivity symptoms and had completed the test of allergen-specific IgE (sIgE) in serum. Among them, 4085 subjects (2,269 males and 1,816 females) were diagnosed as AR patients.

Outcome measures: Prevalence and trends of sensitization to various types of aeroallergens were assessed.

Results: The overall prevalence of sIgE-mediated sensitization to aeroallergens in these AR patients were as follows: 84.4% for house dust mites, 23.4% for pet allergens, 21.1% for cockroaches, 9.1% for mold allergens, 7.7% for tree pollens, and 6.0% for weed pollens. With 10 years old increasing, the sIgE positive rates decreased by approximately 5.13% (95% confidence interval [CI]: -7.28, -2.98, $p < 0.01$). Within the past decade, the prevalence of sensitization to pet allergens increased at an annual rate of 1.3% (95% CI: 0.85, 1.67, $p < 0.01$).

Conclusions: This study demonstrated that HDM was the most common aeroallergen in

Guangzhou. The prevalence of sensitization to aeroallergens decreased with increasing age. During the past decade, the prevalence of sensitization to pet allergens showed an upward trend, suggesting an urgent need for its prevention and treatment.

Keywords: allergic rhinitis; serum sIgE; house dust mite; pet allergens

Strengths and limitations of this study

- This is the first study investigating the trends in the prevalence over the last decade and sIgE-mediated sensitization profiles in patients with AR in Guangzhou, China.
- The study has been conducted based on the results of serum sIgE test, a standard diagnostic test with high sensitivity and specificity for the common aeroallergens.
- This is a retrospective clinical study. The patients' history records on the severity of AR symptoms and on the potential risk factors in association with allergen exposure are uncompleted.
- The study was primarily a single-center study. The prevalence and pattern of allergen sensitization profile in the general population in Guangzhou remain unknown.

INTRODUCTION

Allergic rhinitis (AR) is the most common allergic respiratory disease affecting 10-40% of individuals worldwide. AR can adversely affect the quality of life and impose a substantial burden on both patients and society.[1 2] AR is an immunoglobulin E (IgE)-mediated type I nasal allergic disorder characterized by nasal hyper-reactivity symptoms, including nasal

pruritus, sneezing, airflow obstruction, and rhinorrhea.[3] It is crucial during diagnosis to distinguish the type of allergen causing AR symptoms and to identify an effective therapy. From the literature, the pattern of allergic sensitization profiles differs in different countries or regions. In the United Kingdom, grass pollen was the most common aeroallergen, while cat allergens and cedar pollen were the most common aeroallergen for AR in Sweden and Japan, respectively.[4-6] China is suffering from an increasing incidence of AR. A multicenter study performed by Li *et al*. found that the prevalence of sensitization to pollens and house dust mites (HDM) was higher in northern and southern regions, respectively.[7] Recently, the global prevalence of AR has steadily increased, which may be attributed to urbanization, resulting in subsequent environmental and lifestyle changes due to economic development.[8-10] A study by Mehulic *et al*. reported a significant change in the sensitization to different aeroallergens in Croatia.[11] However, there is a lack of such data in Guangzhou, the largest city in southern China. Thus, the aim of this study was to investigate the prevalence and trends of allergic sensitization to common aeroallergens in patients with AR in Guangzhou over the past decade.

MATERIALS AND METHODS

Study design and subjects

We performed a retrospective study based on the results of serum specific IgE (sIgE) test from 5,486 patients with nasal hyper-reactivity symptoms who attended the Ear, Nose, and Throat (ENT) outpatient clinics at the Third Affiliated Hospital of Sun Yat-sen University in

Guangzhou, China from January 2005 to December 2014. The inclusion criteria for enrolled subjects were as follows: (1) presence of nasal hyper-reactivity symptoms, including sneezing and a runny, itchy, or blocked nose and (2) completed the serum sIgE test for common aeroallergens. Therefore, all the patients with nasal hyper-reactivity symptoms were included in this study and 4,085 AR patients met the diagnostic criteria.[12]

The study patients were from a wide-range of geographic area and came from the following districts in Guangzhou: Tianhe (n = 2,269, 41.4%), Yuexiu (n = 1,048, 19.1%), Haizhu (n = 735, 13.4%), Liwan (n = 623, 11.4%), Baiyun (n = 438, 8.0%), and Conghua and Zengcheng (n = 373, 6.8%).

Ethics statement

This study was approved by the Third Affiliated Hospital of Sun Yat-Sen University Ethics Committee in Guangzhou, China. In addition, all participants signed informed consent forms.

sIgE measurements

German AllergyScreen (Mediwiss Analytic GmbH, Moers, Germany) was used to measure serum sIgE levels to common aeroallergens. The following six types of common aeroallergens were detected: house dust mites (*Dermatophagoides pteronyssinus*, Der p), pet allergens (combination of dog hair and cat dander), cockroaches, molds (mixture of *Penicillium notatum,* branch spore mildew, *Aspergilus fumigates*, and *Alternaria*), tree pollens (combination of cypress, elm, phoenix tree, willow, and cottonwood), and weed

pollens (combination of short ragweed, mugwort, *Humulus scandens*, and pigweed). The serum sIgE levels were calculated using a calibration curve and expressed as a concentration of international units per milliliter (IU/mL). In accordance with the manufacturer's protocols, the concentrations of sIgE were quantitatively ranked as follows: class 0, < 0.35 IU/mL; class 1, ≥ 0.35-0.70 IU/mL; class 2, ≥ 0.70-3.5 IU/mL; class 3, ≥ 3.5-17.5 IU/mL; class 4, ≥ 17.5-50 IU/mL; class 5, ≥ 50-100 IU/mL; class 6, ≥ 100 IU/mL. Serum sIgE levels of ≥ 0.35 IU/mL (class 1 or above) were considered positive.

Statistical analysis

The IBM-SPSS (ver. 20; SPSS Inc., Chicago, IL, USA) statistical software package was used for data processing and analysis. Linear-by-linear association was used to investigate whether or not the changing prevalence of aeroallergen sensitization was characterized by a significant Linear-by-linear association with years or increasing ages. And the simple linear regression was used to analyze how the overall trends in the prevalence of the sensitization to aeroallergens occurred among age groups or year groups on the premise of the significant Linear-by-linear association. Due to the ages not being normally distributed, we used a Mann-Whitney U test to compare the age difference between genders. A $p < 0.05$ was considered statistically significant.

RESULTS

Demographic data

Among the 5,486 patients, 4,085 subjects were diagnosed as AR, 2,269 males (55.5%) and 1,816 females (44.5%), aged between 1 and 79 years old (median age = 23.0 years, interquartile range [IQR]: 10.0, 32.0). The median ages were 19.0 (IQR: 8.5, 30.0) for males and 26.0 (IQR: 15.0, 33.0) for females. The age of sensitization to aeroallergen in males was significantly younger than in females ($p < 0.01$).

Prevalence of sensitization to aeroallergens in Guangzhou

Among the 4,085 AR patients, the prevalence of sensitization to aeroallergens were as follows: 84.4% for HDM, 23.4% for pet allergens (combination of dog hair and cat dander), 21.1% for cockroaches, 9.1% for mold allergens, 7.7% for mixed tree pollens, and 6.0% for mixed weed pollens.

Allergen sensitization by age group

To further assess the impact of age on the prevalence of allergic sensitization in AR patients among the patients with nasal hyper-reactivity symptoms, we have grouped them into the following age groups: 1-9, 10-19, 20-29, 30-39, 40-49, 50-59, and ≥ 60 years. The prevalence of allergic sensitization to aeroallergens for each age group is shown in Figure 1. The prevalence was the highest in the 10-19 years old group (86.6%) and the lowest in the ≥ 60 years old group (52.6%). The sIgE reactivity decreased as age increased, and with 10 years old increasing the prevalence decreased by 5.13% (95% CI: -7.28, -2.98, $p < 0.01$).

The highest prevalence of allergic sensitization to HDM in AR patients was in the age

group of 10-19 years (91.4%) and decreased with age (p <0.01). It decreased by 3.0% every 10 years old after the age of 19 years (95% CI: -5.6, -0.45, p < 0.05). Sensitization to pet allergens was higher in 1-9 year age group (30.2%) than other age groups. The prevalence of sensitization to weed pollens increased on average by 2.09% for every 10 years (95% CI: 1.28, 2.90, p < 0.05). Similarly, the prevalence of sensitization to tree pollens showed an upward trend, increasing with age (p < 0.001) at a rate of 1.36% every 10 years (95% CI: 0.17, 2.56, p < 0.05) (Table 1).

Trends in the prevalence of sensitization to aeroallergens over the past decade

The prevalence of sensitization to at least one aeroallergens from 2005 to 2014 were 69.7% (2005), 73.6% (2006), 75.1% (2007), 72.0% (2008), 75.7% (2009), 76.6% (2010), 74.1% (2011), 75.8% (2012), 75.9% (2013), and 74.0% (2014). During these 10 years, we did not observe a significant trend among the prevalence rates (p > 0.05). There were no significant differences in the prevalence of sensitization to HDM, cockroaches, weed pollens, tree pollens, and mold allergens over the past decade. However, the prevalence of pet allergens increased from 16.5% to 28.6%, showing a significant upward trend with an average annual rate increase of 1.3% (95% CI: 0.85, 1.67, p < 0.01) (Figure 2).

DISCUSSION

The production of sIgE is a hallmark of allergic sensitization and measurement of serum sIgE to common local aeroallergens has been widely utilized as a standard diagnostic tool for AR.

In this study, we retrospectively analyzed sIgE testing results from 5,486 outpatients with nasal hyper-reactivity symptoms during the past 10 years in Guangzhou. This is in order to study the prevalence and trends of allergic sensitization to common aeroallergens in Guangzhou.

The data from this study showed that HDM were the predominant aeroallergen in Guangzhou, which was consistent with previously published studies. [7 13] High humidity and ambient temperatures have been reported as optimal conditions for HDM propagation.[14] Guangzhou is located in the subtropical region with high temperature, high humidity, and rainy weather, and where there is little difference in the perennial temperature. The characteristics of the local climate in Guangzhou are optimal for HDM propagation, which is in accordance with our results in which we observed a high prevalence of sensitization to HDM in this region.

Lifestyle may be another potential contributor to the high prevalence of sensitization to HDM. In Guangzhou, residents in the municipality spend a majority of time indoors, especially in environments with air conditioning. The major sources of HDM are bed sheets, carpets, and pillows. A previous study confirmed the presence of high concentrations of Der p in air conditioning filters.[15] Long durations in environments with poor ventilation increases the chance of exposure to HDMs.[14] Another study showed that residing in homes with mechanical ventilation instead of air-conditioning can reduce house dust mite exposure, leading to overall clinical improvement for HDM-sensitized patients.[16]

In this study, the prevalence of sensitization to at least one aeroallergens was higher among

the younger age groups (10-19 years). With 10 years old increasing, the prevalence of sIgE decreased by 5.13%. These results suggest that sensitization to allergens was most prevalent among younger patients, which was consistent with previously published studies. [17] However, the exact reasons for the higher prevalence of sIgE observed in young AR patients are unknown. One explanation may be immunosenescence, which reduces innate and adaptive immune responses, resulting in an attenuated response to foreign antigens and subsequently decreased sIgE production. [18,19] De Amici *et al*. reported that the sIgE levels for several aeroallergens decreased significantly with increasing age. [20] Further studies will be necessary to determine the impact of age on the positive rate of serum sIgE test.

In this study, the prevalence of sensitization to aeroallergens was within the range of 69.7%-76.6% from 2005 to 2014. We did not observe a significant change in sensitization rate within the last 10 years, which was in accordance with studies performed by Jarvis *et al*[21] However we observed an upward trend in the sensitization to pet allergens (dog hair and cat dander), rising from 16.5% to 28.6% at an average annual rate of 1.3%. These results indicate that over the last 10 years an increasing number of AR patients have become sensitized to pet allergens in Guangzhou.

The results from a cross-sectional questionnaire found that exposure to pets was a risk factor for respiratory diseases.[22] Given the improvement in living standards in Guangzhou, an increasing number of people in the municipality keep cats and dogs as indoor pets, increasing the concentration of dog hair and cat dander, as well as the chance of exposure to these allergens. It was reported that long-term exposure to animal allergens may cause respiratory

hyper-reactivity and accelerate the development of asthma and AR.[23] The increasing prevalence of sensitization to pet allergens within the past 10 years has indicated the importance of therapy for AR patients with pet allergies. However, pet allergens were found not only in families with pets, but also in those without pets or in public places, including communities and schools.[24] Thus, the exact aeroallergen that should be avoided was difficult to identify. Specific immunotherapy (SIT) is the only disease-modifying treatment for AR,[25] and previous studies have reported that this treatment is clinically effective in desensitization to pet allergens.[26 27] However, SIT for cat and dog allergens is still not available in China. Thus, this study further supports the importance for Chinese health authorities and research institutions to introduce pet SIT, allowing AR patients and pets to cohabitate.

This study is the first study on the trends in the prevalence of common aeroallergen sensitizations to AR patients over the last decade in Guangzhou. The study was based on the results of serum sIgE test, a measurement with a high specificity and sensitivity for the diagnosis of common aeroallergen sensitization. However, there are several limitations in this study. The study was conducted by retrospective analysis of the results of serum sIgE test. It was difficult to offer any information on the severity of AR symptoms and the risk factors for aeroallergen exposure. For example, although we found that an increasing number of AR patients had been sensitized to pet allergens, we still have no idea about the details on pets keeping among those patients. Moreover, although all patients were from the majority of the districts in Guangzhou, this study was primarily a single-center study. In addition, the sIgE results were obtained from the population of patients with nasal hypersensitivity, which may

not be applicable to the general population in Guangzhou. From our results, we recommend that additional, multi-center studies are needed to gain more accurate and generalized conclusion.

CONCLUSION

This study demonstrated that HDM was the most common aeroallergens in Guangzhou. The prevalence of sensitization to aeroallergens decreased with increasing age. From 2005 to 2014 the prevalence of allergic sensitization to pets has increased significantly, suggesting the importance in introducing more effective measures for its prevention and treatment in Guangzhou.

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Abbreviations AR, allergic rhinitis; sIgE, specific immunoglobulin E; HDM, house dust mite ENT, the clinic of Ear, Nose, Throat

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Competing interests None.

Contributors QY conceptualized the study, designed the protocol, analyzed the data and drafted the manuscript. WW, XH collected the data, analyzed the data and drafted the manuscript. ZC, RZ, YC, GZ participated in administrative and technical support.

Patient consent Obtained.

Ethics approval Obtained.

Data sharing statement No additional data are available.

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Table

Table 1 The prevalence of sensitization to each kind of aeroallergens in age groups.

	HDM	Pet allergens	Cockroaches	Mixed mold	Weed pollens	Tree pollens
1-9 years(n=948)	83.1%(788/948)	30.2%(286/948)	11.6%(110/948)	11.1%(105/948)	2.4%(23/948)	4.6%(44/948)
10-19 years(n=798)	91.4%(729/798)	25.1%(200/798)	18.5%(148/798)	8.9%(71/798)	3.8%(30/798)	5.1%(41/798)
20-29 years(n=1079)	84.2%(909/1079)	20.8%(224/1079)	28.1%(303/1079)	7.7%(83/1079)	8.0%(86/1079)	8.9%(96/1079)
30-39 years(n=786)	82.7%(650/786)	18.3%(144/786)	24.8%(195/786)	8.3%(65/786)	6.2%(49/786)	9.9%(78/786)
40-49 years(n=315)	83.2%(262/315)	19.4%(61/315)	23.2%(73/315)	8.9%(28/315)	10.5%(33/315)	10.2%(32/315)
50-59 years(n=108)	68.5%(74/108)	25.9%(28/108)	19.4%(21/108)	9.3%(10/108)	14.8%(16/108)	15.7%(17/108)
≥60 years(n=51)	70.6%(36/51)	21.6%(11/51)	21.6%(11/51)	15.7%(8/51)	13.7%(7/51)	9.8%(5/51)
$p^{※}$	< 0.05	< 0.05	< 0.05	0.18	< 0.05	< 0.05
$P^{△}$	< 0.01	0.30	0.40	0.31	< 0.01	< 0.05

Abbreviation: HDM, house dust mite

※ Linear-by-linear association; △ Simple linear regression

Figure legends

Figure 1 Age differences in the sIgE positive rates of sensitization to at least one aeroallergens.

Figure 2 The significant uptrend of the prevalence of sensitization to pet allergens in AR patients from 2005 to 2014.

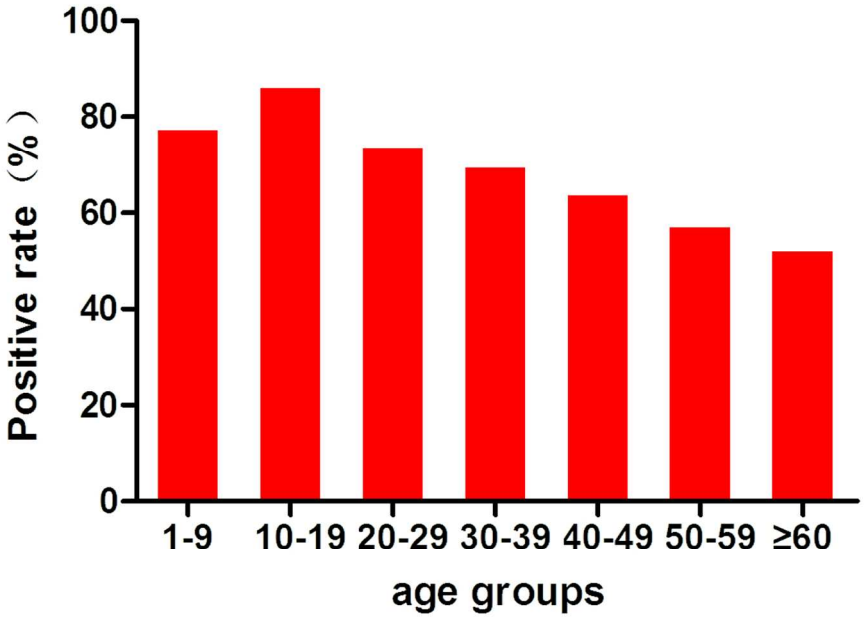

Figure 1 Age differences in the sIgE positive rates of sensitization to at least one aeroallergens.
105x73mm (300 x 300 DPI)

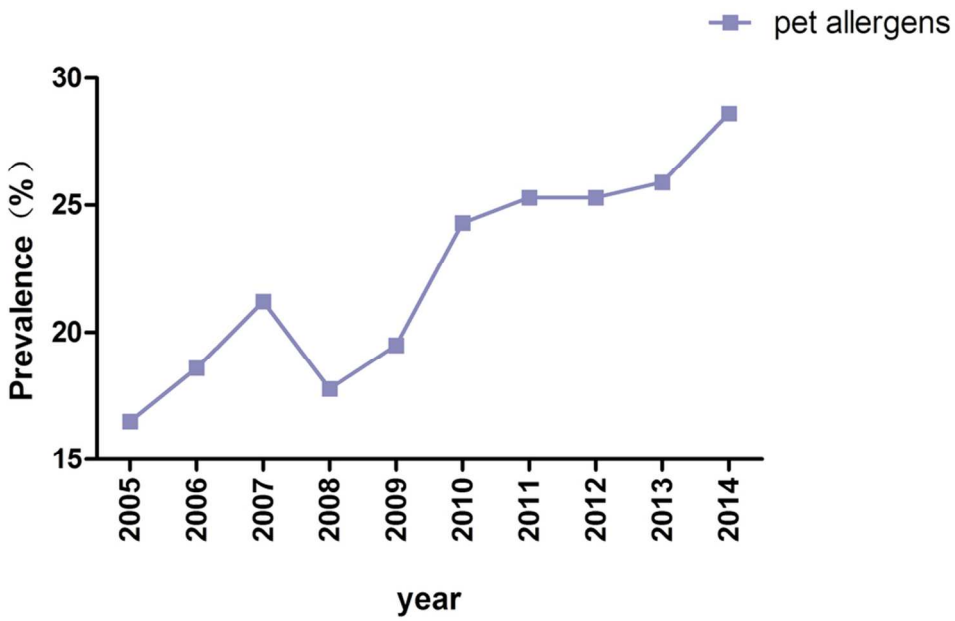

Figure 2 The significant uptrend of the prevalence of sensitization to pet allergens in AR patients from 2005 to 2014.
88x58mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Report 4ed on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4
Methods			
Study design	4	Present key elements of study design early in the paper	Page 4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Page 5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 5-6
Bias	9	Describe any efforts to address potential sources of bias	Page 5
Study size	10	Explain how the study size was arrived at	Page 4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 6
		(*b*) Describe any methods used to examine subgroups and interactions	None
		(*c*) Explain how missing data were addressed	None
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	None
		(*e*) Describe any sensitivity analyses	None
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 7-8
		(b) Give reasons for non-participation at each stage	None
		(c) Consider use of a flow diagram	None
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page7
		(b) Indicate number of participants with missing data for each variable of interest	None
Outcome data	15*	Report numbers of outcome events or summary measures	Page7-8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 7-8
		(*b*) Report category boundaries when continuous variables were categorized	None
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	None
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	None
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 9-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 9-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 12-13

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prevalence and trends of sensitization to aeroallergens in allergic rhinitis patients in Guangzhou, China: A 10-year retrospective study

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Prevalence and trends of sensitization to aeroallergens in allergic rhinitis patients in Guangzhou, China: A 10-year retrospective study

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Keywords: allergic rhinitis; serum sIgE; house dust mite; pet allergens

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ABSTRACT

Objective: To investigate the prevalence and trends of sensitization to common aeroallergens among outpatients with allergic rhinitis (AR) in Guangzhou, China over the past decade.

Design: A retrospective study; Linear-by-linear association and simple linear regression were used to determine the trends in the prevalence of aeroallergen sensitization.

Setting: One Grade-A hospital in Guangzhou, the largest city in southern China.

Participants: 5486 patients (2,297 males and 2,489 females) who visited the Ear, Nose and Throat Outpatient Clinic between January 2005 and December 2014 were enrolled. All patients who presented with nasal hyper-reactive symptoms completed serological allergy testing, measuring soluble IgE in the serum (sIgE) were included. Among them, 4085 subjects (2,269 males and 1,816 females) were diagnosed as AR patients.

Outcome measures: Prevalence and trends of sensitization to various types of aeroallergens were assessed.

Results: The overall prevalence of sIgE-mediated sensitization to aeroallergens in these AR patients were as follows: 84.4% for house dust mites, 23.4% for pet allergens, 21.1% for cockroaches, 9.1% for mold allergens, 7.7% for tree pollens, and 6.0% for weed pollens. When all patients with nasal hyper-reactivity were stratified by decade of age, increasing age was associated with a decrease in sIgE positivity by approximately 5.13% (95% confidence interval [CI]: -7.28, -2.98, $p < 0.01$). Within the past decade, the prevalence of sensitization to pet allergens in AR patients increased at an annual rate of 1.3% (95% CI: 0.85, 1.67, $p < 0.01$).

Conclusions: This study demonstrated that HDM was the most common aeroallergen in Guangzhou. The prevalence of sensitization to aeroallergens decreased with increasing age. During the past decade, the prevalence of sensitization to pet allergens showed an upward trend, suggesting an urgent need for its prevention and treatment.

Keywords: allergic rhinitis; serum sIgE; house dust mite; pet allergens

Strengths and limitations of this study

- This is the first study investigating the trends in the prevalence over the last decade and sIgE-mediated sensitization profiles in patients with AR in Guangzhou, China.
- The study has been conducted based on the results of serum sIgE test, a standard diagnostic test with high sensitivity and specificity for the common aeroallergens.
- This is a retrospective clinical study. The patients' history records on the severity of AR symptoms and on the potential risk factors in association with allergen exposure are uncompleted.
- The study was primarily a single-center study. The prevalence and pattern of allergen sensitization profile in the general population in Guangzhou remain unknown.

INTRODUCTION

Allergic rhinitis (AR) is the most common allergic respiratory disease affecting 10-40% of individuals worldwide. AR can adversely affect the quality of life and impose a substantial burden on both patients and society.[1 2] AR is an immunoglobulin E (IgE)-mediated type I

nasal allergic disorder characterized by nasal hyper-reactivity symptoms, including nasal pruritus, sneezing, airflow obstruction, and rhinorrhea.[3] It is crucial during diagnosis to distinguish the type of allergen causing AR symptoms and to identify an effective therapy. From the literature, the pattern of allergic sensitization profiles differs in different countries or regions. In the United Kingdom, grass pollen was the most common aeroallergen, while cat allergens and cedar pollen were the most common aeroallergen for AR in Sweden and Japan, respectively.[4-6] China is suffering from an increasing incidence of AR. A multicenter study performed by Li *et al*. found that the prevalence of sensitization to pollens and house dust mites (HDM) was higher in northern and southern regions, respectively.[7] Recently, the global prevalence of AR has steadily increased, which may be attributed to urbanization, resulting in subsequent environmental and lifestyle changes due to economic development.[8-10] A study by Mehulic *et al*. reported a significant change in the sensitization to different aeroallergens in Croatia.[11] However, there is a lack of such data in Guangzhou, the largest city in southern China. Thus, the aim of this study was to investigate the prevalence and trends of allergic sensitization to common aeroallergens in patients with AR in Guangzhou over the past decade.

MATERIALS AND METHODS

Study design and subjects

We performed a retrospective study based on the results of serum specific IgE (sIgE) test from 5,486 patients with nasal hyper-reactivity symptoms who attended the Ear, Nose, and

Throat (ENT) outpatient clinics at the Third Affiliated Hospital of Sun Yat-sen University in Guangzhou, China from January 2005 to December 2014. The inclusion criteria for enrolled subjects were as follows: (1) presence of nasal hyper-reactivity symptoms, including sneezing and a runny, itchy, or blocked nose and (2) completed the serum sIgE test for common aeroallergens. Therefore, all the patients with nasal hyper-reactivity symptoms were included in this study and 4,085 AR patients met the diagnostic criteria. [12]

The study patients were from a wide-range of geographic area and came from the following districts in Guangzhou: Tianhe (n = 2,269, 41.4%), Yuexiu (n = 1,048, 19.1%), Haizhu (n = 735, 13.4%), Liwan (n = 623, 11.4%), Baiyun (n = 438, 8.0%), and Conghua and Zengcheng (n = 373, 6.8%).

Ethics statement

This study was approved by the Third Affiliated Hospital of Sun Yat-Sen University Ethics Committee in Guangzhou, China. In addition, all participants signed informed consent forms.

sIgE measurements

German AllergyScreen (Mediwiss Analytic GmbH, Moers, Germany) was used to measure serum sIgE levels to common aeroallergens. The following six types of common aeroallergens were detected: house dust mites (*Dermatophagoides pteronyssinus*, Der p), pet allergens (combination of dog hair and cat dander), cockroaches, molds (mixture of *Penicillium notatum,* branch spore mildew, *Aspergilus fumigates*, and *Alternaria*), tree

pollens (combination of cypress, elm, phoenix tree, willow, and cottonwood), and weed pollens (combination of short ragweed, mugwort, *Humulus scandens*, and pigweed). The serum sIgE levels were calculated using a calibration curve and expressed as a concentration of international units per milliliter (IU/mL). In accordance with the manufacturer's protocols, the concentrations of sIgE were quantitatively ranked as follows: class 0, < 0.35 IU/mL; class 1, ≥ 0.35-0.70 IU/mL; class 2, ≥ 0.70-3.5 IU/mL; class 3, ≥ 3.5-17.5 IU/mL; class 4, ≥ 17.5-50 IU/mL; class 5, ≥ 50-100 IU/mL; class 6, ≥ 100 IU/mL. Serum sIgE levels of ≥ 0.35 IU/mL (class 1 or above) were considered positive.

Statistical analysis

The IBM-SPSS (ver. 20; SPSS Inc., Chicago, IL, USA) statistical software package was used for data processing and analysis. Linear-by-linear association was used to investigate whether or not the changing prevalence of aeroallergen sensitization was characterized by a significant Linear-by-linear association with years or increasing ages. And the simple linear regression was used to analyze how the overall trends in the prevalence of the sensitization to aeroallergens occurred among age groups or year groups on the premise of the significant Linear-by-linear association. Due to the ages not being normally distributed, we used a Mann-Whitney U test to compare the age difference between genders. A $p < 0.05$ was considered statistically significant.

RESULTS

Demographic data

Among the 5,486 patients, 4,085 subjects were diagnosed as AR, 2,269 males (55.5%) and 1,816 females (44.5%), aged between 1 and 79 years old (median age = 23.0 years, interquartile range [IQR]: 10.0, 32.0). The median ages were 19.0 (IQR: 8.5, 30.0) for males and 26.0 (IQR: 15.0, 33.0) for females. The age of sensitization to aeroallergen in males was significantly younger than in females ($p < 0.01$).

Prevalence of sensitization to aeroallergens in Guangzhou

Among the 4,085 AR patients, the prevalence of sensitization to aeroallergens were as follows: 84.4% for HDM, 23.4% for pet allergens (combination of dog hair and cat dander), 21.1% for cockroaches, 9.1% for mold allergens, 7.7% for mixed tree pollens, and 6.0% for mixed weed pollens.

Allergen sensitization by age group

To further assess the impact of age on the prevalence of allergic sensitization among the patients with nasal hyper-reactivity symptoms, we have grouped them into the following age groups: 1-9, 10-19, 20-29, 30-39, 40-49, 50-59, and ≥ 60 years. The prevalence of allergic sensitization to aeroallergens for each age group is shown in Figure 1. The prevalence was the highest in the 10-19 years old group (86.6%) and the lowest in the ≥ 60 years old group (52.6%). The sIgE reactivity decreased as age increased, and with 10 years old increasing the prevalence decreased by 5.13% (95% CI: -7.28, -2.98, $p < 0.01$).

The highest prevalence of allergic sensitization to HDM in AR patients was in the age group of 10-19 years (91.4%) and decreased with age (p <0.01). It decreased by 3.0% every 10 years old after the age of 19 years (95% CI: -5.6, -0.45, p < 0.05). Sensitization to pet allergens was higher in 1-9 year age group (30.2%) than other age groups. The prevalence of sensitization to weed pollens increased on average by 2.09% for every 10 years (95% CI: 1.28, 2.90, p < 0.05). Similarly, the prevalence of sensitization to tree pollens showed an upward trend, increasing with age (p < 0.001) at a rate of 1.36% every 10 years (95% CI: 0.17, 2.56, p < 0.05) (Table 1).

Trends in the prevalence of sensitization to aeroallergens over the past decade

The prevalence of sensitization to at least one aeroallergens from 2005 to 2014 were 69.7% (2005), 73.6% (2006), 75.1% (2007), 72.0% (2008), 75.7% (2009), 76.6% (2010), 74.1% (2011), 75.8% (2012), 75.9% (2013), and 74.0% (2014). During these 10 years, we did not observe a significant trend among the prevalence rates (p > 0.05). There were no significant differences in the prevalence of sensitization to HDM, cockroaches, weed pollens, tree pollens, and mold allergens over the past decade. However, the prevalence of pet allergens increased from 16.5% to 28.6%, showing a significant upward trend with an average annual rate increase of 1.3% (95% CI: 0.85, 1.67, p < 0.01) (Figure 2).

DISCUSSION

The production of sIgE is a hallmark of allergic sensitization and measurement of serum sIgE

to common local aeroallergens has been widely utilized as a standard diagnostic tool for AR. In this study, we retrospectively analyzed sIgE testing results from 5,486 outpatients with nasal hyper-reactivity symptoms during the past 10 years in Guangzhou. This is in order to study the prevalence and trends of allergic sensitization to common aeroallergens in Guangzhou.

The data from this study showed that HDM were the predominant aeroallergen in Guangzhou, which was consistent with previously published studies. [7 13] High humidity and ambient temperatures have been reported as optimal conditions for HDM propagation.[14] Guangzhou is located in the subtropical region with high temperature, high humidity, and rainy weather, and where there is little difference in the perennial temperature. The characteristics of the local climate in Guangzhou are optimal for HDM propagation, which is in accordance with our results in which we observed a high prevalence of sensitization to HDM in this region.

Lifestyle may be another potential contributor to the high prevalence of sensitization to HDM. In Guangzhou, residents in the municipality spend a majority of time indoors, especially in environments with air conditioning. The major sources of HDM are bed sheets, carpets, and pillows. A previous study confirmed the presence of high concentrations of Der p in air conditioning filters.[15] Long durations in environments with poor ventilation increases the chance of exposure to HDMs.[14] Another study showed that residing in homes with mechanical ventilation instead of air-conditioning can reduce house dust mite exposure, leading to overall clinical improvement for HDM-sensitized patients.[16]

In this study, the prevalence of sensitization to at least one aeroallergens was higher among the younger age groups (10-19 years). With 10 years old increasing, the prevalence of sIgE decreased by 5.13%. These results suggest that sensitization to allergens was most prevalent among younger patients, which was consistent with previously published studies. [17] However, the exact reasons for the higher prevalence of sIgE observed in young AR patients are unknown. One explanation may be immunosenescence, which reduces innate and adaptive immune responses, resulting in an attenuated response to foreign antigens and subsequently decreased sIgE production. [18,19] De Amici *et al*. reported that the sIgE levels for several aeroallergens decreased significantly with increasing age. [20] Further studies will be necessary to determine the impact of age on the positive rate of serum sIgE test.

In this study, the prevalence of sensitization to aeroallergens was within the range of 69.7%-76.6% from 2005 to 2014. We did not observe a significant change in sensitization rate within the last 10 years, which was in accordance with studies performed by Jarvis *et al*[21] However we observed an upward trend in the sensitization to pet allergens (dog hair and cat dander), rising from 16.5% to 28.6% at an average annual rate of 1.3%. These results indicate that over the last 10 years an increasing number of AR patients have become sensitized to pet allergens in Guangzhou.

The results from a cross-sectional questionnaire found that exposure to pets was a risk factor for respiratory diseases.[22] Given the improvement in living standards in Guangzhou, an increasing number of people in the municipality keep cats and dogs as indoor pets, increasing the concentration of dog hair and cat dander, as well as the chance of exposure to these

allergens. It was reported that long-term exposure to animal allergens may cause respiratory hyper-reactivity and accelerate the development of asthma and AR.[23] The increasing prevalence of sensitization to pet allergens within the past 10 years has indicated the importance of therapy for AR patients with pet allergies. However, pet allergens were found not only in families with pets, but also in those without pets or in public places, including communities and schools. [24] Thus, the exact aeroallergen that should be avoided was difficult to identify. Specific immunotherapy (SIT) is the only disease-modifying treatment for AR,[25] and previous studies have reported that this treatment is clinically effective in desensitization to pet allergens. [26 27] However, SIT for cat and dog allergens is still not available in China. Thus, this study further supports the importance for Chinese health authorities and research institutions to introduce pet SIT, allowing AR patients and pets to cohabitate.

This study is the first study on the trends in the prevalence of common aeroallergen sensitizations to AR patients over the last decade in Guangzhou. The study was based on the results of serum sIgE test, a measurement with a high specificity and sensitivity for the diagnosis of common aeroallergen sensitization. However, there are several limitations in this study. The study was conducted by retrospective analysis of the results of serum sIgE test. It was difficult to offer any information on the severity of AR symptoms and the risk factors for aeroallergen exposure. For example, although we found that an increasing number of AR patients had been sensitized to pet allergens, we still have no idea about the details on pets keeping among those patients. Moreover, although all patients were from the majority of the districts in Guangzhou, this study was primarily a single-center study. In addition, the sIgE

results were obtained from the population of patients with nasal hypersensitivity, which may not be applicable to the general population in Guangzhou. From our results, we recommend that additional, multi-center studies are needed to gain more accurate and generalized conclusion.

CONCLUSION

This study demonstrated that HDM was the most common aeroallergens in Guangzhou. The prevalence of sensitization to aeroallergens decreased with increasing age. From 2005 to 2014 the prevalence of allergic sensitization to pets has increased significantly, suggesting the importance in introducing more effective measures for its prevention and treatment in Guangzhou.

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Abbreviations AR, allergic rhinitis; sIgE, specific immunoglobulin E; HDM, house dust mite ENT, the clinic of Ear, Nose, Throat

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Competing interests None.

Contributors QY conceptualized the study, designed the protocol, analyzed the data and drafted the manuscript. WW, XH collected the data, analyzed the data and drafted the manuscript. ZC, RZ, YC, GZ participated in administrative and technical support.

Patient consent Obtained.

Ethics approval Obtained.

Data sharing statement No additional data are available.

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Table

Table 1 The prevalence of sensitization to each kind of aeroallergens in age groups.

	HDM	Pet allergens	Cockroaches	Mixed mold	Weed pollens	Tree pollens
1-9 years(n=948)	83.1%(788/948)	30.2%(286/948)	11.6%(110/948)	11.1%(105/948)	2.4%(23/948)	4.6%(44/948)
10-19 years(n=798)	91.4%(729/798)	25.1%(200/798)	18.5%(148/798)	8.9%(71/798)	3.8%(30/798)	5.1%(41/798)
20-29 years(n=1079)	84.2%(909/1079)	20.8%(224/1079)	28.1%(303/1079)	7.7%(83/1079)	8.0%(86/1079)	8.9%(96/1079)
30-39 years(n=786)	82.7%(650/786)	18.3%(144/786)	24.8%(195/786)	8.3%(65/786)	6.2%(49/786)	9.9%(78/786)
40-49 years(n=315)	83.2%(262/315)	19.4%(61/315)	23.2%(73/315)	8.9%(28/315)	10.5%(33/315)	10.2%(32/315)
50-59 years(n=108)	68.5%(74/108)	25.9%(28/108)	19.4%(21/108)	9.3%(10/108)	14.8%(16/108)	15.7%(17/108)
≥60 years(n=51)	70.6%(36/51)	21.6%(11/51)	21.6%(11/51)	15.7%(8/51)	13.7%(7/51)	9.8%(5/51)
$p^{※}$	< 0.05	< 0.05	< 0.05	0.18	< 0.05	< 0.05
$P^{△}$	< 0.01	0.30	0.40	0.31	< 0.01	< 0.05

Abbreviation: HDM, house dust mite

※ Linear-by-linear association; △ Simple linear regression

Figure legends

Figure 1 Age differences in the sIgE positive rates of sensitization to at least one aeroallergens.

Figure 2 The significant uptrend of the prevalence of sensitization to pet allergens in AR patients from 2005 to 2014.

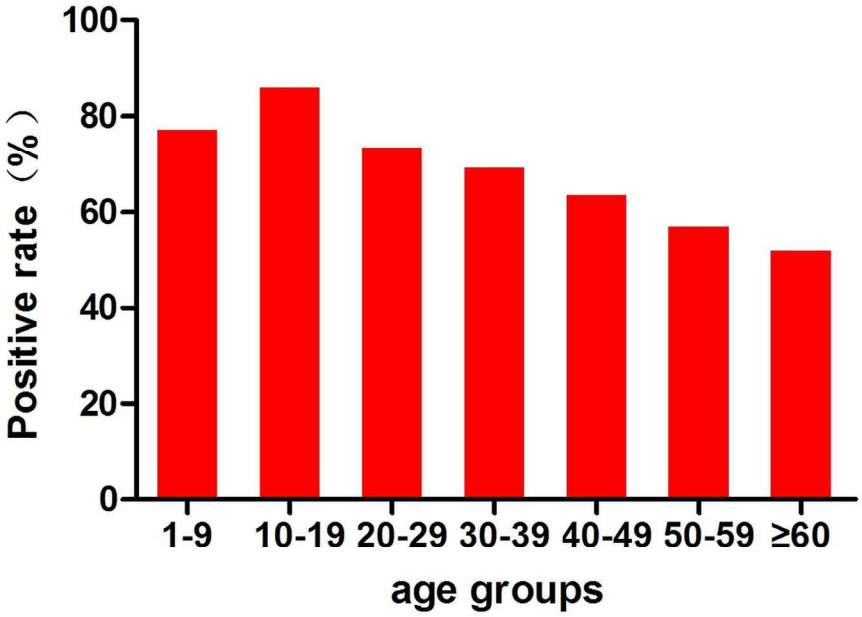

Figure 1 Age differences in the sIgE positive rates of sensitization to at least one aeroallergens.
129x90mm (300 x 300 DPI)

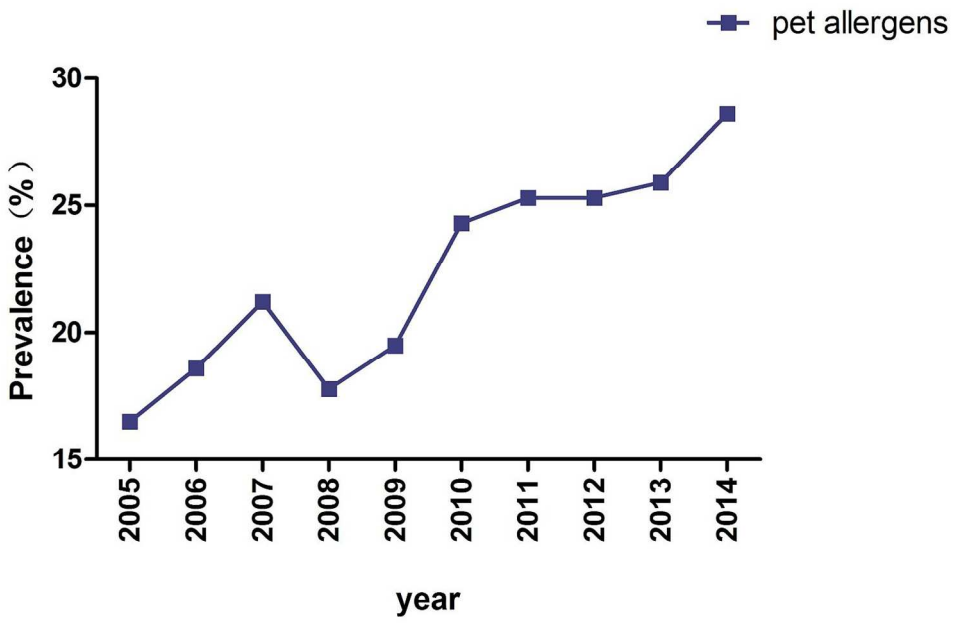

Figure 2 The significant uptrend of the prevalence of sensitization to pet allergens in AR patients from 2005 to 2014.
134x90mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Report 4ed on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4
Methods			
Study design	4	Present key elements of study design early in the paper	Page 4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Page 5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 5-6
Bias	9	Describe any efforts to address potential sources of bias	Page 5
Study size	10	Explain how the study size was arrived at	Page 4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 6
		(*b*) Describe any methods used to examine subgroups and interactions	None
		(*c*) Explain how missing data were addressed	None
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	None
		(*e*) Describe any sensitivity analyses	None
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 7-8
		(b) Give reasons for non-participation at each stage	None
		(c) Consider use of a flow diagram	None
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page7
		(b) Indicate number of participants with missing data for each variable of interest	None
Outcome data	15*	Report numbers of outcome events or summary measures	Page7-8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 7-8
		(*b*) Report category boundaries when continuous variables were categorized	None
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	None
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	None
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 9-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 9-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 12-13

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.