Serum allergen spectrum and prevalence of allergic disease in Shenzhen, China

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Research

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Abstract

Purpose: Allergen sensitization are common allergic diseases worldwide, with widely varying estimates of prevalence in the population. The characteristics and prevalence of allergens and diseases in Shenzhen.

Patients and methods: Allergen-specific IgE results were investigated among 20483 subjects from January 2016 to June 2020 based on by Western blotting, and statistical analysis was performed on sIgE and related diseases in patients with different ages, genders, months, mixed allergens and grade.

Results: Among 20483 subjects, 13149 (64.19%) were clinically positive for at least single allergen. Single allergen positive rate (35.42%), double allergen positive rate (23.96%), triple allergen positive rate (16.04%). The positive rate of sIgE in male was higher than that in female (69.15% and 60. 02% respectively, P<0.01). Allergen detection rate varies with age (P<0.05). The cumulative positive results were 35083, grade 1: 16705 items, 47.61%; grade 2: 8003 items, 22.81%; grade 5: 3840 items, 10.94%. The positive rate of sIgE in March was the highest (82.20%), which was statistically significant compared with other months (P<0.05). The probability of cockroach allergen causing atopic dermatitis/urticaria was 67%, and asthma in just 4%.

Conclusion: Our findings reveal that the positive rate of allergens was high in Shenzhen. Dust mite was the main allergen. There were differences in age, gender and month, and the probability of allergic diseases such as atopic dermatitis/urticaria aznd rhinitis/sinusitis is high.

Introduction

With the progress of society and the global flow of production factors, people are exposed to more and more allergens, and various allergic diseases follow.[1,2,3] Allergic diseases can occur in all ages, and the incidence rate is high. In the literature, about 1/3 of people have had allergic diseases in their lifetime, which seriously affect the quality of life of patients.[4,5] Allergic diseases caused by allergens are mainly allergic asthma and allergic rhinitis, with a clinical incidence of 10% and 20%, while the incidence of other allergic diseases is usually low, for example, the incidence of food allergy is about 4%. In addition, the economic effect of allergic disease is often underestimated as indirect costs are substantial, such as allergic rhinitis. The effect of allergic rhinitis on work productivity is estimated to cost €30 billion to €50 billion per year in the EU.[6,7]

Changes in people's living conditions, food nutrition and health concepts and awareness also promote the occurrence of allergic diseases. Although allergic diseases have become commonplace and common, they still cause physical and psychological troubles to patients as well as the socioeconomic problems mentioned above.[8] Since, entering the 21st century, allergic diseases have become one of the most common global diseases.[9] Therefore, for the prevention and treatment of allergic diseases, the type and distribution of allergens, as well as the correlation between allergic diseases caused by allergens, should be identified first. Allergic characteristics vary in age, gender, between children and adults and between men and women due to differences in immune systems and lifestyle habits. Based on the quantitative results of allergen, this study analyzed the serum allergen spectrum and prevalence of allergic disease in Shenzhen, combined with relevant data, to guide the early prevention, early diagnosis and early treatment of allergic diseases.

Materials And Methods

Study population

A total of 20483 suspected allergic patients including 9364 males and 11119 females between 0 and 97 years were enrolled in this study, and the youngest is just born, 55.3% are children. Their specimens were tested in Shenzhen Luohu hospital group during January 2016 to June 2020. Informed consents were obtained from their guardians before serum IgE analysis. The subjects were divided into six age groups (years old):0-2, 3-5, 6-15, 16-30, 31-50, ≥ 51. There were significant differences among the age groups ($\chi^2=2000.623, P=0.000$), gender and age were stratified (Table 1).

Instruments and reagents

EUROBlot Master (EUROIMMUN Medizinische Labordiagnostika AG, Hangzhou, China), Beckman table centrifuge SX4750A (BECKMAN COULTER, America); EUROLINE Atopy China (IgE) (EUROIMMUN Medizinische Labordiagnostika AG, Hangzhou, China).

Methods
The sample was centrifuged at 3000 rpm for 10 min and diluted (100μL sample + 1.0mL universal buffer), the concentration of allergen sIgE in serum was detected by Western blot, all tests were carried out the following standard operating procedure. The results are interpreted using the EUOrline Scan system, the threshold value is 0.35kU/L. The concentration of allergen sIgE was classified as grade 0 (<0.35 kU/L), grade 1 (0.35≤sIgE<0.7 kU/L), grade 2 (0.7≤sIgE<3.5 kU/L), grade 3 (3.5≤sIgE<17.5 kU/L), grade 4 (17.5≤sIgE<50 kU/L), grade 5 (50≤sIgE<100 kU/L) and grade 6 (≥100 kU/L).

Statistical analysis

All statistical analyses were performed on IBM SPSS 24.0. Chi-square test was used for comparison of rates or constituent ratios, P<0.05 was considered statistically significant.

Results

Serum allergen spectrum

The total positive rate of allergens sIgE in 20483 patients in Shenzhen was 64.19% (N=13149). The subjects were diagnosis with single allergen, double, three and above at 35.42%, 23.96%, 16.04%, 24.58%, respectively. Allergic kinds distribution showed dust mite (39.55%), house dust (11.40%) and cockroaches (10.33%) were the common inhaled allergens, and milk (17.91%), beef (12.82%), egg white (12.67%), soybean (11.53%) were the common food allergens. The most common double allergens were dust mite and house dust (23.03%), milk and beef (9.25%), dust mite and cockroaches (5.99%) followed. All the allergens have significant differences among different age groups (Fig. 1). Allergy in male was higher than that in female (69.15% and 60.02%, respectively, P<0.01). Except for the allergen including tree, ragweed, artemisia argyi, dog epithelium, cockroach, mould and soybean, 12 specific allergens showed a significant difference in gender (Fig. 1).

Age distribution of allergen

The prevalence showed an obvious difference at ages between inhaled allergens including dust mite, house dust and cockroach and food allergens including milk, beef, mutton and egg white. As shown in Fig. 2, the most prevalence the allergic in dust mites and house dust occurred at 6-15 years old (66.96%, 30.89%). Not the same as the first two, the highest sIgE positive rate of cockroach occurred at 16-30 years old (15.08%). There was no significant age change in sIgE positive rate of tree, artemisia argyi, cat hair, dog epithelium, ragweed, mould and humulus scandens. The positive rate of sIgE of four food allergens: showed a significant age change trend. The positive rates of all four allergens were the highest in infants aged 0-2 years (43.88%, 35.18%, 18.44%, 26.66%).

Concentration distribution of allergen

The concentration of sIgE was qualified and six grades was classified as the description (Table 2). The majority of the concentration was Grade 1 and 2, accounting for 47.61% and 22.81% in the whole prevalence. The proportion was observed a downside with the grade growing up unless grade 5 (10.94%). However, in the group of 0-2 years, the ratio of positive patients showed a decreasing trend with the increase of allergen grade including grade 5.

Temporal characteristics of allergy

The highest positive rate of allergen sIgE was detected in March (82.20%), followed by July (71.40%), which was statistically significant compared with other months (P<0.05) (Fig. 2).

Allergic disease

According to medical professionals, a percentage of 43.62% patients in 13149 allergen-positive subjects was eventually diagnosed with rhinitis/sinusitis, asthma, atopic dermatitis/urticaria and conjunctivitis. They were found to be allergic to dust mites, house dust and cockroaches (Fig. 3). Individuals allergic to dust mites and cockroaches were observed with a ratio of 51% and 67% suffering from atopic dermatitis/urticaria, respectively. A half of patients with house dust allergen occurred rhinitis/sinusitis. The prevalence of conjunctivitis with a combined-allergen was increased by approximately twice than single allergen.
Allergens sensitization are really common in Shenzhen. More than half of the subjects (64.19%) was diagnosis with at least single allergen, which was much higher than that in northern and western region of China, and was consistent with Wu et al’ report.\[2\] Allergic prevalence in males (69.15%) was higher than that in females (60.02%), probably deriving from differences in life habits, male tends to smoke and drink, and suffers from a lot of mental pressure. Besides, estrogen levels had an impact on the allergic disease. Previous studies proved a longer reproductive period was associated with a higher prevalence of rhinitis/sinusitis and inhaled allergens in the postmenopausal period.\[10,11\] Also, certain hormones before and after birth may be related to immune responses and the development of lifelong immune diseases.

The low prevalence of inhalant allergens occurred in infants aged 0-2 with seldom exposed to broad allergens, it climbed to a peak value in the age group of 6-15 years. However, the highest food allergen was found in infants aged 0-2 years, and it decreased significantly with age increasing. The prevalence of food allergens prominently differed with inhalant ones at the same age. Inhaled allergy closely related with environmental exposure, while food allergy was related to the constitution of infants’ immune system dysfunction.\[12,13\] Chinese children started kindergartens at the age of 3 and primary education after the age of 6, increasing exposure opportunity to allergens. With growing up, immunity system has gradually developed mature and the tolerance to a variety food increases are beneficial for low risk of allergy.

The subjects were detected with a majority of allergen sIgE levels ranging from 0.35 kU/L to 3.5 kU/L (Grade 1 and 2). The less exposure contributed to a low concentration of allergen for infants aged 0-2. The specific allergen with the concentration at grade 5 was analyzed among different age groups. Dust mites were found to be the most common allergen (>80%) in all ages, which was closely related to the environment and climate in Shenzhen. March and July were the periods of high incidence of allergens in Shenzhen, which were mainly affected by such allergens as dust mites, consistent with the reported peak of dust mite breeding in February and June. Dust mite, house dust, cockroach were detected as the major inhaled allergens, likely due to the environment and circumstances exposure. Shenzhen belongs to the south-central coastal region of Guangdong Province in China, is located in the south of the Tropic of Cancer (113°46'E-114°37'E, 22°27'N-22°52'N). With a subtropical humid monsoon climate. Milk is the main food allergen, which is more common in infants and young children, which is inconsistent with previous reports that eggs are the main food allergen for children in southern cities.\[14,15\] This may be related to the diversified development of human diet. Milk is rich in minerals, such as calcium. Therefore, more and more families take milk as a necessary breakfast material. Shenzhen is a typical immigrant city with a high proportion of migrant population. According to the data released by the Shenzhen Bureau of Statistics, in 2019, the permanent resident population of Shenzhen was 13.44 million, among which the non-registered population was 8.49 million accounting for more than 63%. February and March are the time when the Spring Festival returns to its depths. Its large population circulation and reduced immunity to environmental changes may account for the extremely high rate of allergen positivity in March. In addition, Shenzhen is regarded as a subtropical humid monsoon climate zone, and generally enters the flood season from March, there is also concern about indoor mold growth in association with rising air moisture after extreme storms.\[16\] The life cycle time of dust mites depends on the temperature and relative humidity of the developing environment. The ideal development temperature and relative humidity are 20~25°C and 70~75%, respectively. Obviously, the climatic conditions in Shenzhen are fully conducive to the development of dust mites.

The dust mite, house dust and cockroach are important allergen to induce allergic diseases such as rhinitis/sinusitis and atopic dermatitis/urticaria in Shenzhen. In agreement with previous report, house dust mite allergy is present in up to 90% of Asian atopic patients.\[1\] There are many substances in household dust which can cause allergies in humans, including animal dander, insect parts (especially from cockroaches), mold spores and pollen. The house dust, a prominent factor on allergy, is mainly composed of powder, sand dust, dander, hair, dust mites, mold and other substances. The differences in results may be caused by allergic substances such as mold, pollen and spores. The most common allergenic components of house dust, are from house dust mites, Mite proteases have direct epithelial effects including the breaching of tight junctions and the stimulation of protease-activated receptors, the latter inducing pruritus, epithelial dysfunction, and cytokine release. Other components, including chitin, unmethylated mite and bacterial DNA, and endotoxin, activate pattern recognition receptors of the innate immune system and act as adjuvants promoting sensitization to mite and other allergens. In a sensitized person, mite allergens can provoke symptoms by direct external contact (conjunctivitis, eczema), inhalation (rhinitis, asthma, eczema), and ingestion (urticaria, anaphylaxis).\[17\] The above pathogenesis may explain the results of our data analysis.

Genetic factors certainly contribute to susceptibility to different allergic diseases,\[19,20\] but genetics alone cannot explain the specificity of allergies. The rising trend in allergies is associated with changes in lifestyle and the control of infections which, taken together, seem to result in an "under-challenged" immune system.\[18,19\] On the other hand, lifestyle changes and indoor and outdoor environmental pollutants are suspected to keep our immune system in a constant state of low-grade inflammation.\[20,21\]

In a word, allergy is an objective natural phenomenon, which seriously affects the quality of life of some people and even endangers their lives, which deserves our attention. Therefore, defining allergens and avoiding them effectively are effective prevention and treatment
measures for allergic diseases. Based on large data for the first time, this paper analyses and reports the distribution of allergens in Shenzhen, which provides convenience and reference for disease prevention and treatment in this region.

**Declarations**

**Ethics approval and informed consent**

After review by the Ethics Committee of the First Affiliated Hospital of Guangzhou Medical University (GYFY-2016-73). The use of human serum samples was in accordance of legislation in China and the wishes of donors, their legal guardians or next of kin, where applicable, who had offered written informed consent to using the serum samples for future unspecified research purposes.

**Consent for publication**

Written informed consent for publication was obtained from all participants.

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**Competing interests**

The authors state that there are no financial, personal, or professional conflicts of interests that may hinder this work.

**Authors' contributions**

Min Li, Rui Zheng, Enyun Wang contributed equally to this work in the design and write original draft; Min Li, Rui Zheng collected and analyzed the data; Dan Xiong, Baoqinq Sun performed the literature search and were responsible for data visualization; Xiaowen Dou, Xiuming Zhang conceived the study and contributed to the writing of the paper; All authors have read and approved the final manuscript.

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### Tables

**Table 1. 20438 cases of patients with age and group**

| Age group (years) | Male | Female | Total | Percentage (%) |
|-------------------|------|--------|-------|----------------|
| 0-2               | 2289 | 1540   | 3829  | 18.7           |
| 3-5               | 2236 | 1686   | 3922  | 19.1           |
| 6-15              | 2183 | 1397   | 3580  | 17.5           |
| 16-30             | 934  | 2953   | 3887  | 19.0           |
| 31-50             | 1152 | 2781   | 3933  | 19.2           |
| ≥51               | 570  | 762    | 1332  | 6.5            |
| Total             | 9364 | 11119  | 20483 | 100.0          |

**Table 2 The proportion of positive cases in different age group in different allergen grade**

| Parameter | 0-2 years | 3-5 years | 6-15 years | 16-30 years | 31-50 years | ≥51 years | Total     |
|-----------|-----------|-----------|------------|-------------|-------------|-----------|-----------|
| Grade 1   | 3827(49.70%) | 4425(51.32%) | 3130(40.71%) | 2434(46.42%) | 2167(48.97%) | 722(51.39%) | 16705(47.62%) |
| Grade 2   | 2122(27.56%) | 1947(22.58%) | 1437(18.69%) | 1151(21.95%) | 1006(22.73%) | 340(24.20%) | 8003(22.81%) |
| Grade 3   | 968(12.57%)  | 723(8.39%)  | 667(8.68%)  | 540(10.30%)  | 445(10.06%)  | 157(11.17%) | 3500(9.98%)  |
| Grade 4   | 504(6.55%)   | 561(6.51%)  | 633(8.23%)  | 398(7.59%)   | 325(7.34%)   | 72(5.12%)   | 2493(7.11%)  |
| Grade 5   | 270(3.51%)   | 863(10.01%) | 1518(19.75%)| 641(12.23%)  | 441(9.97%)   | 107(7.62%)  | 3840(10.95%) |
| Grade 6   | 9(0.12%)     | 103(1.19%)  | 303(3.94%)  | 79(1.51%)    | 41(0.93%)    | 7(0.50%)    | 542(1.54%)   |

### Figures
Figure 1

The allergen-positive rates of major food and inhalation allergens in 20483 patients were stratified by age (A, B), and gender analysis (C, D)

Note: Tree: willow, poplar, elm; Dust mite: house dust mite, dermatophagoides farinae; Mould: penicillium, mycosporum, aspergillus fumigatus, alternaria; Marine fish: cod, lobster, scallop; The same below. Two-sided P-values: chi square test for positive rates of allergens among six age groups * Six age groups P<0.05. The same below.
Figure 2

The age variation trend of the main food and inhalation allergens (A, B) and the monthly variation trend of the positive rate of allergens (C)
Figure 3

Allergens and related allergic disease