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ORIGINAL RESEARCH

Distributional Characteristics Analysis of Allergens in Patients with Allergic Rhinitis in Southern Fujian Province, China

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Background: Allergic rhinitis (AR) is a chronic inflammatory disease of the nasal mucosa. However, few studies focus on the distributional characteristics of allergens in AR patients in Southern Fujian Province, China.

Methods: A skin prick test (SPT) was performed and eight common allergens including *Dermatophagoides farinae* (*Df*), *Dermatophagoides pteronyssinus* (*Dpt*), weeds, animal dander, molds, cockroaches, and mangoes were chosen.

Results: The positive reactions rate to the allergens was 65.79% in 6689 patients in Southern Fujian Province. Positive reactions to *Df* and *Dpt* had a negative association with age, whereas positive reactions to cockroach and weed had a positive association with age. A linear trend analysis demonstrated a significant positive relationship between positive reactions to various allergens from 2016 to 2019. Positive reactions to *Df* and *Dpt* were both correlated with the season. Positive reactions to *Df, Dpt*, cockroach and weed were related to disease duration and positive reactions to cockroach were correlated with city residence. Multivariate analysis revealed that male positive reactions gradually decreased with age (≤ 60), in contrast to female (≤ 60) positive reactions. Statistical difference was observed between the genders with regard to AR incidence from 2016 to 2019. The positive rate of skin tests was highest in summer in men, whereas in women it was lowest in summer. The gender composition ratios of positive cases in Xiamen, Zhangzhou, and Quanzhou cities differed significantly. The proportion of patients with positive reactions to the allergens in the three cities decreased with age. The highest proportions of patients with positive reactions all occurred during summer in the three cities. Furthermore, there were statistically significant differences in the age composition ratios across the seasons.

Conclusion: This study analyzed the distributional characteristics of AR allergens in Southern Fujian Province, China. These findings will inform specific immunotherapy for AR patients.

Keywords: allergic rhinitis, allergen, skin prick test, Southern Fujian Province in China

Introduction

Allergic rhinitis (AR), which is a chronic inflammatory disease of the nasal mucosa, is mediated by allergen-specific immunoglobulin E (IgE) after exposure of atopic individuals to allergens. The prevalence rate in the general population is 10–25%, and it is increasing each year.[1–5] The prevalence of self-reported AR is approximately 15% in Southeast China.[6] Members of the order Blattodea (eg, cockroaches), and marine crabs and lobsters produce the most important allergens in Quanzhou, which is a city in Southern Fujian Province, China.[7] The species that produce the most common AR allergens, such as dust mites and cockroaches, prefer warm and humid environments. The south of Fujian Province has a warm and humid sub-tropical maritime climate. Consequently, the incidence of AR is high in that region. In fact, AR allergens have obvious regional characteristics. An important tenet of AR treatment is that exposure to allergens should be avoided.

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Therefore, analysis of the common AR allergens present in a particular setting has practical significance for the prevention and treatment of AR. In the present study, the region of interest, ie, Minnan, is located in the south of Fujian Province in China, and includes the cities of Xiamen, Quanzhou, and Zhangzhou. Minnan region is situated within one of the most dynamic economic regions in eastern China, the so-called "Golden Triangle of Southern Fujian". The population of Southern Fujian is homogenous, and shares the same dialect, customs, food, and culture. However, there have been few studies or reviews detailing the distributional characteristics of allergens in this region. To address this deficiency, we examined multiple allergens that affect AR patients between January 2016 and December 2019 in the Minnan region of China. The present study provided multiple complex analysis data about the distributional characteristics of allergens that affect AR patients in Southeast China.

Materials and Methods

Research Objective

The present study was retrospective. All persons provided informed consent prior to inclusion and a parent of participants under 18 years of age also provided informed consent. The study was reviewed by the Medical Ethics Committee of the First Affiliated Hospital of Xiamen University (2022–029), and was conducted in accordance with the ethical standards laid down in an appropriate version of the 1964 Declaration of Helsinki. We included 6689 outpatients that had been admitted to the Department of Otolaryngology Head and Neck Surgery of the First Affiliated Hospital of Xiamen University between January 2016 and December 2019. AR patients who had discontinued oral antihistamines for < 1 week were excluded from the study. The diagnostic criteria were as follows: (1) at least two clinical symptoms such as sneezing, watery nose, nasal congestion, or nasal itching, with symptoms lasting (continuously or accumulatively) for more than 1 h every day and accompanied by itching, tears, conjunctival congestion, or other optical symptoms; (2) clinical signs such as pale nasal mucosa, edema, or watery nasal secretions; and (3) at least one positive skin prick test (SPT) reaction to an allergen.[8] All patients were diagnosed by an otorhinolaryngologist, and all patients were subjected to an anterior rhinoscopy examination or a nasal endoscope examination. All 6689 cases presented with at least two of the following symptoms: nasal obstruction, watery nose, nasal itching, or sneezing. In all cases, a physical examination revealed pale nasal mucosa edema and watery nasal secretions, which were consistent with AR. Of the included cases, 4401 patients tested positive for an allergen and were diagnosed with AR. All patients were from Southern Fujian province, China (5039 in Xiamen, 881 in Zhangzhou, and 769 in Quanzhou), and had lived locally for at least 1 year (in cases of children ≤ 2 years old, their parents had lived locally for at least 1 year).

Of the 6689 patients included, 3976 were male and 2713 were female. The age range of the cohort was 1–87 years, with a median age of 15 years. In total, there were 3568 minors (≤ 17 years old) and 3121 adults (≥ 18 years old). The patients were divided into four groups according to age: ≤ 17 years old (3568 cases); 18–39 years old (2354 cases); 40–59 years old (695 cases); and ≥ 60 years old (72 cases). In addition, the juvenile group (≤ 17 years old) was further divided into two subgroups: 1–6 years old (the preschool subgroup); and 7–17 years old (the school-age subgroup). The seasons were defined as spring (March to May), summer (June to August), autumn (September to November), and winter (December to February). Among all the cases, 1604 patients had family histories, clinical symptoms, and disease duration data. These cases were divided into four groups based on disease duration: ≤ 1 year; 1–5 years; 5–10 years; and > 10 years. Allergen SPTs were performed on all patients. The research flow chart is presented in Figure 1.

Skin Prick Test (SPT)

Allergen extract skin test detection reagents were provided by Zhejiang Wowu Biotechnology Co. LTD (CN). Each patient was tested for eight common allergens, ie, from: *Dermatophagoides farinae* (Df*); Dermatophagoides pteronyssinus* (*Dpt*); weeds (mugwort, long leaf nettle, dandelion, and plantain); animal dander (hamster, dog, rabbit, cat, and guinea pig epithelia); type I molds (crosslinking spore fungus, *Botrytis*, the polymajor mycospora genus, crescent bending spore fungus, beaded *Fusarium oxysporum*, and *Helminthosporium*); type II molds (smoke *Aspergillus*, bee *Mucor*, specific *Penicillium, Pullularia, Rhizopus*, immortal bacteria); cockroaches; and mangos. Antihistamines were discontinued for at least 7 days prior to the test, and systemic glucocorticoids were not applied. The results were evaluated by measuring the orthogonal diameters of the wheal

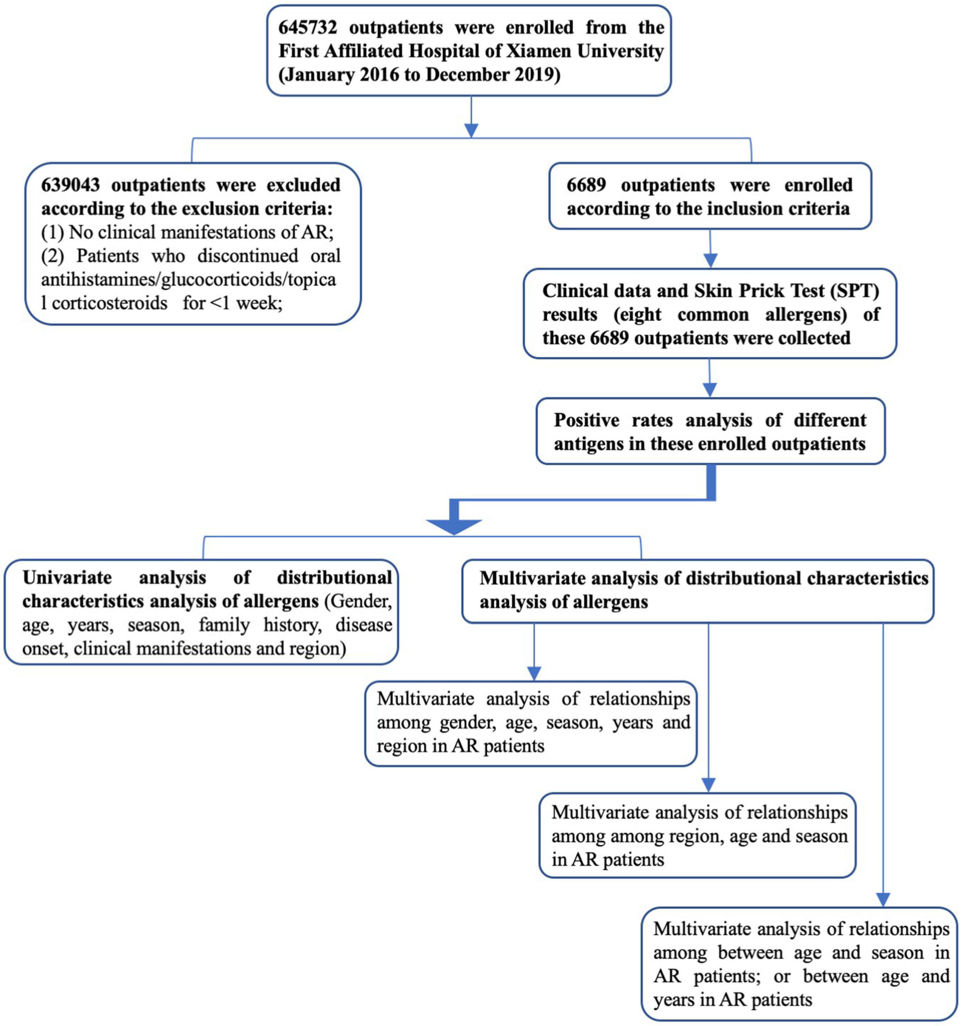

Figure 1 Schematic diagram of this study. 645,732 outpatients from January 2016 to December 2019 were enrolled from the First Affiliated Hospital of Xiamen University. Among these outpatients, 639,043 cases were excluded according to the exclusion criteria. 6689 outpatients were enrolled and clinical data/Skin Prick Test (SPT) results (eight common allergens) were collected and analysed. Subsequently, univariate analysis and multivariate analysis of distributional characteristics analysis of allergens in these patients were performed to illustrated the distributional characteristics of allergens in AR patients in Southern Fujian Province, China.

and taking the mean, in mm, with the presence of erythema. The results were as follows: negative (-), the area of the wound mass caused by allergenic spines was 0%–25% of that caused by the positive control; "+", the wind mass was 26–50% that of the positive control; "++", the wind mass was 51–100% that of the positive control; "+++", the wind mass was 101–200% that of the positive control; and "++++", the wind mass was more than twice that of the positive control.

Statistical Analysis

The $\chi 2$ test was used to compare two or more sample rates. If the theoretical frequency was too small, the likelihood ratio $\chi 2$ test was used. The linear trend test (linear-by-linear association) was used to determine whether there was a linear correlation between a categorical variable and a rank variable. SPSS 20.0 statistical software was used for all statistical analyses. The count data are represented by the number of cases or as a percentage. A Chi-squared test was used to compare rates between each group. When the theoretical frequency was too small, a likelihood ratio Chi-squared test was used. A difference with a $P < 0.05$ was considered statistically significant.

Results

Distribution of Positive Reactions to Various Allergens Detected by SPTs in AR Patients

Among the 6689 subjects, 4401 tested positive for at least one allergen, and there was an overall positive test rate of 65.79%. The overall positive test rates of the allergens from high to low were: Df (63.93%); *Dpt* (63.33%); cockroach (22.35%); animal dander (1.99%); weed (0.64%); mold I (0.31%); mold II (0.22%); and mango (0.07%). The eight allergens are discussed below in the same order. The strongly positive results ("+++" and "++++") of the allergens from high to low were: Df (59.01%); *Dpt* (55.93%); cockroach (13.35%); animal dander (0.37%); weed (0.09%); mold I and mold II (0.03%); and mango (0%) (Table 1).

The SPT was suitable for multiple antigens. Of the 6689 subjects, 1495 (22.35%) had a positive reaction to cockroach allergen, and 59.73% (893/1495) had a strong positive reaction. Of the 1495 patients allergic to cockroach allergen, 92.11% (1377/1495) patients were allergic to both Df and *Dpt*. Of those 1377 cases, 763 patients (51.04%, 763/1495) had strong positive reactions to cockroach, Df, and *Dpt* allergens. We found that 133 cases (1.99%) reacted positively to animal dander, and of those, 18.80% reacted strongly. Furthermore, 126 (94.74%, 126/133) of the 133 patients that were allergic to animal dander were also allergic to both Df and *Dpt*. Only 22 patients (16.54%, 22/133) were strongly allergic to all three. In addition, 67 patients were allergic to animal dander, Df, *Dpt*, and cockroach allergens, accounting for 50.38% (67/133) (Table 1).

Overall, 4276 patients were allergic to Df: the rate of positive reaction was 63.93%. Of these, 4230 patients (98.92%) were allergic to *Dpt* (46 cases were negative). Similarly, 4236 patients were allergic to *Dpt*: the rate of positive reaction was 63.33%. Of these patients, 4230 patients were simultaneously allergic to Df, equal to 99.86% (six cases were negative). There were positive reactions to both Df and *Dpt* in 4230 cases (63.24%), accounting for 96.11% (4230/4401) of all the allergen-positive patients (Table 1).

The rate of positive reaction to the allergens was statistically correlated with the type of allergens (X^2 = 24,585.249; P = 0.000). The linear trend test demonstrated statistical significance (X^2 = 17,743.547; P = 0.000), indicating that the rates of positive reaction to the eight allergens exhibited a decreasing trend (Table S1). Multiple comparisons revealed that the rates of positive reaction were highest with regard to Df and *Dpt* allergens (but with no statistical difference), and were different from the rates of reaction to the other six allergens. The rates of positive reaction to cockroach or animal dander were also statistically different from those of reaction to the other seven allergens.

Determination of Single Factors That Affect a Positive Reaction to Various Allergens

Of the 6689 subjects, 4401 patients tested positive for allergens. This included 2628 males (66.10%, 2628/3976) and 1773 females (65.35%, 1773/2713). There was no significant difference in the rate of positive reactions to the allergens between males and females (X^2 = 0.397; P = 0.529) (Tables 2 and 3).

Table 1 Positive Rates and Distribution of Various Allergens in Skin Prick Test in Allergic Rhinitis Patients (n=6689)

Allergen Types	Skin Prick Test					Positive Number (%)	Strong Positive Number (%)
	–	+	++	+++	++++		
Df	2413	57	272	2311	1636	4276 (63.93%)	3947 (59.01%)
Dpt	2453	53	442	2325	1416	4236 (63.33%)	3741 (55.93%)
Cockroach	5194	41	561	854	39	1495 (22.35%)	893 (13.35%)
Animal dander	6556	30	78	23	2	133 (1.99%)	25 (0.37%)
Weed	6646	8	29	6	0	43 (0.64%)	6 (0.09%)
Mold I	6668	8	11	2	0	21 (0.31%)	2 (0.03%)
Mold II	6674	6	7	2	0	15 (0.22%)	2 (0.03%)
Mango	6684	3	2	0	0	5 (0.07%)	0 (0%)

Notes: Dermatophagoides farinae (Df); Dermatophagoides pteronyssinus (Dpt); mold I (cross-linking spore fungus, botrytis, polymajor mycospora genus, crescent bending spore, beaded fusarium oxysporum, helminthosporium); mold II (smoke aspergillus, bee mucor, specific penicillium, pullularia, rhizopus, Immortal bacteria).

Table 2 Different Allergen Positive Rates in Patients with Positive Skin Tests

Parameters	Allergen Positive Rate (%)							
	Df	Dpt	Cockroach	Animal Dander	Weed	Mold I	Mold II	Mango
Gender								
Male	64.08	63.71	22.36	1.81	0.68	0.38	0.23	0.13
Female	63.69	62.77	22.34	2.25	0.59	0.22	0.22	0
Age								
≤ 17	68.97	68.53	19.37	1.96	0.36	0.39	0.22	0.08
18~39	63.55	62.70	28.42	2.34	0.93	0.25	0.21	0.04
40~59	42.88	42.30	18.56	0.86	1.01	0.14	0.29	0.14
≥ 60	29.17	29.17	8.33	2.78	1.39	0	0	0
Year								
2016	56.17	55.89	23.49	3.61	1.52	1.01	0.62	0.28
2017	64.54	64.43	27.85	1.01	0.10	0.05	0.05	0
2018	63.30	62.35	17.33	0.48	0.82	0.07	0.07	0
2019	73.05	71.77	18.62	2.84	0.14	0.07	0.14	0
Seasons								
Spring	60.08	59.08	20.43	2.27	0.67	0.20	0.27	0
Summer	67.05	66.54	22.62	1.91	0.89	0.47	0.30	0.17
Autumn	62.19	61.77	23.05	1.46	0.42	0.14	0.07	0.07
Winter	64.58	64.08	23.24	2.35	0.43	0.36	0.21	0
Family history								
AR	73.02	73.81	9.52	1.59	0	0	0	0
None	73.09	71.85	14.32	1.36	0.74	0.37	0	0
Disease onset								
≤ 1 year	64.75	62.97	15.84	2.77	0	0	0.19	0
1~5 years	77.17	76.50	18.83	1.87	0	0	0	0.13
5~10 years	77.45	75.49	24.51	2.94	0.98	0	0	0
>10 years	68.49	66.44	14.38	4.11	0	0.68	0	0
Clinical manifestations								
Nasal congestion	72.79	71.42	18.02	2.75	0.14	0.07	0.07	0.07
Sneezing	75.17	73.89	18.90	2.55	0.15	0.08	0.08	0.08
Runny nose	73.36	72.08	18.64	2.64	0.15	0.08	0.08	0.08
Nasal itching	73.86	72.71	17.52	2.64	0	0.09	0	0.09
Region								
Zhangzhou	62.88	62.54	18.27	1.93	0.34	0.45	0.23	0
Quanzhou	65.54	65.02	21.59	3.12	0.65	0.26	0.39	0.13
Xiamen	63.86	63.21	23.18	1.83	0.69	0.30	0.20	0.08

The data reveal that positive reactions to the Df, *Dpt*, cockroach, and weed allergens were related to age. Linear trend analysis confirmed that these relationships were statistically significant (X^2 = 178.752, 181.594, 6.020, and 8.353, respectively; with *P* values of 0.000, 0.000, 0.014, and 0.004, respectively). The rates of positive reaction to Df and *Dpt* decreased with age, as directly reflected in the observation that the rates of reaction to Df and *Dpt* decreased from 68.97% and 68.53% in the ≤ 17 years of age group to 29.17% in the ≥ 60 years of age group. However, the rate of positive reaction to weed allergens increased with age, ie, from 0.36% in the ≤ 17 years of age group to 1.39% in the ≥ 60 years of age group. The rate of positive reaction to cockroach allergens was highest in the 18–39 years of age group (28.42%); the other three age groups did not demonstrate statistical differences. The rates of positive reaction to animal dander, mold I, mold II, and mango allergens were not related to age. The rate of positive reaction to Df was highest in the ≤ 17 years of age group (68.97%), and the rates of positive reaction to mold I, mold II, and mango were lowest in the ≥ 60 years of age group (0%) (Tables 2 and 3).

Table 3 Univariate Analysis of Risk Factors in Patients with Positive Skin Tests

Parameters	Relationship Between Allergen Positive Rate and Various Risk Factors															
	Df		Dpt		Cockroach		Animal Dander		Weed		Mold I		Mold II		Mango	
	χ2	P	χ2	P	χ2	P	χ2	P	χ2	P	χ2	P	χ2	P	χ2	P
Gender	0.107	0.744	0.608	0.436	0.000	0.983	1.584	0.208	0.201	0.654	1.256	0.262	0.002	0.965	**1.93**	0.164
Age	210.816	<0.001	210.386	<0.001	82.170	<0.001	6.221	0.101	9.590	0.022	2.188	0.534	0.453	0.929	0.886	0.829
Year	100.239	<0.001	89.256	<0.001	68.909	<0.001	56.126	<0.001	37.144	<0.001	32.563	<0.001	15.031	0.002	13.277	0.004
Seasons	21.698	<0.001	23.932	<0.001	4.329	0.228	3.667	0.300	4.472	0.215	4.100	0.251	2.740	0.433	6.439	0.092
Family history	0.000	1.000	0.208	0.749	2.126	0.164	0.042	0.691	1.741	1.000	0.869	1.000	0.052	1.000	0.052	1.000
Disease onset	27.083	<0.001	30.391	<0.001	8.965	0.030	2.944	0.400	8.266	0.041	4.800	0.187	2.313	0.510	1.524	0.677
Clinical manifestations	2.150	0.542	2.255	0.521	0.968	0.809	0.105	0.991	2.977	0.395	0.022	0.999	1.488	0.685	0.022	0.999
Region	1.293	0.524	1.213	0.545	10.686	0.005	5.761	0.056	1.729	0.421	0.604	0.739	0.929	0.628	1.589	0.452

Notes: (1) The underlined character are indicates statistically significant ($P < 0.05$). (2) The red characters indicate that Chi-squared test (Likelihood ratio) was used to compare rates between each group (Number of theoretical frequency are more than five (T<5)). (3) The blue characters indicate that Chi-squared test (continuity correction) was used to compare rates between each group. (4) The black characters indicate that Pearson Chi-squared test was used to compare rates between each group (Number of theoretical frequency are more than five (T>5)).

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The top three rankings of positive reactions to allergens in all four age groups were: Df, *Dpt*, and cockroach. Animal dander and weed allergens ranked 4th and 5th, respectively, except in 2018, when animal dander ranked 5th and weeds ranked 6th. Mold I and mold II ranked 6th and 7th place, respectively; the positive reaction rates of these allergens were roughly the same, with occasionally slight fluctuations (for example, in 2019, the positive reaction rate of mold II exceeded that of mold I). The bottom ranking place (8th) was always mango. A linear trend analysis demonstrated that these differences were statistically significant (X^2 = 84.876, 71.554, 68.909, 56.126, 15.149, 21.412, 7.851, and 8.042, respectively; with *P* values of 0.000, 0.000, 0.000, 0.042, 0.000, 0.000, 0.002, and 0.004, respectively). Overall, the rates of positive reaction to Df and *Dpt* allergens demonstrated an approximate upward trend over the 4 years, peaking at 73.05% and 71.77%, respectively, in 2019 (Tables 2 and 3).

The changes in the rates of positive reaction to allergens across spring (March to May), summer (June to August), autumn (September to November), and winter (December to February) were also analyzed. The rates of positive reaction to Df and *Dpt* allergens were both correlated with season (X^2 = 21.698 and 23.932, respectively; P = 0.000 and P = 0.000, respectively). The rates of positive reaction to Df and *Dpt* were both highest in the summer, reaching 67.05% and 66.54%, respectively. In contrast, the rates of positive reaction to cockroach, animal dander, weed, mold I, mold II, and mango allergens were not correlated with season (X^2 = 4.329, 3.667, 4.472, 4.100, 2.740, and 6.439, respectively; all P values > 0.05) (Tables 2 and 3).

In total, 4401 cases (of the 6689 included) tested positive for an allergen. Of these, 592 patients (13.45%) had a family history of AR. The rates of positive reaction to Df, *Dpt*, cockroach, animal dander, weed, and mold I allergens were not correlated with family history (X^2 = 0.000, 0.208, 2.126, 0.000, 1.741, 0.869, 0.052, and 0.052, respectively; P = 1.000, 0.749, 0.164, 0.691, 1.000, 1.000, 1.000, and 1.000, respectively) (Tables 2 and 3).

The disease onset ranged from 10 days to 40 years. The rates of positive reaction to Df, *Dpt*, cockroach, and weed allergens were related to the duration of disease. A linear trend analysis demonstrated that the differences in the rates of reaction to Df and *Dpt* were statistically significant (X^2 = 5.460 and 4.996, respectively; P = 0.019 and 0.025, respectively). As shown in Table 3, whereas the rates of positive reaction to Df and *Dpt* were dependent on disease onset, differences in these rates occurred mainly between the ≤ 1 year duration group and the 1–5 years duration group. Multiple comparisons demonstrated that the rates of positive reaction to Df and *Dpt* were lowest in the ≤ 1 year duration group (64.75% and 62.97%, respectively). No significant differences in the rates of positive reaction to Df and *Dpt* were observed across the 1–5 years, 5–10 years, and >10 years duration groups (Tables 2 and 3).

The rate of positive reaction to cockroach allergen was correlated with city residence (X^2 = 10.686; P=0.005). Therefore, the rates of positive reaction to cockroach allergen increased in Zhangzhou, Quanzhou, and Xiamen cities. Although there was a significant difference in the rate of positive reaction to cockroach allergen between Xiamen and Zhangzhou cities, no such difference in the rate of positive reaction existed between Quanzhou and the other two cities. The rates of positive reaction to Df, *Dpt*, animal dander, weeds, mold I, mold II, and mango allergens were not correlated with city residence (X^2 = 1.293, 1.213, 5.761, 1.729, 0.604, 0.929, and 1.589, respectively; all P values > 0.05) (Tables 2 and 3).

Multiple-Factor Analysis Was Used to Determine Factors That Affect Rates of Positive Reaction to Various Allergens

There were statistical differences in the gender composition ratio between the various age groups (X^2 = 385.604; P = 0.000), as shown in Table 4. A linear trend analysis revealed that the proportion of males gradually decreased with age (X^2 = 283.618; P = 0.000). However, in the ≥ 60 years of age group, the proportion of males gradually increased. This trend was reversed for the female ratio (Table 4).

In the years from 2016 to 2019 (inclusive), there were 1094, 1139, 905, and 838 male patients in the various age groups described above, respectively. Over the same period, there were 681, 832, 579, and 621 female patients, respectively. There were statistically significant differences in gender with regard to the incidence of AR during the four years (X^2 = 9.671; P = 0.022) (Table 4).

The gender composition ratio of patients was also correlated with the season (X^2 = 23.020; P = 0.000). Multiple comparisons demonstrated that the gender composition ratio in summer was statistically different from that in spring,

Table 4 Multivariate Analysis of Relationships Among Gender, Age, Season, Years and Region in AR Patients

	Gender		Chi-Square test (χ2)	P-value
	Male (59.44%) (Composition Ratio %)	Female (40.56%) (Composition Ratio %)		
Age			385.604	<0.001
≤ 17	70.35	29.65		
18~39	47.07	52.93		
40~59	45.04	54.96		
≥ 60	62.50	37.50		
Year			9.671	0.022
2016	61.63	38.37		
2017	57.79	42.21		
2018	60.98	39.02		
2019	57.44	42.56		
Seasons			23.029	<0.001
Spring	56.94	43.06		
Summer	63.27	36.73		
Autumn	56.75	43.25		
Winter	58.45	41.55		
Region			12.217	0.002
Zhangzhou	60.61	39.39		
Quanzhou	64.89	35.11		
Xiamen	58.40	41.60		

Notes: The underlined character are indicates statistically significant (P < 0.05). P < 0.001 represents an extremely low P value.

autumn, and winter. The proportion of male patients was highest in the summer, rising to 63.27%. Conversely, the proportion of female patients was lowest in summer, dropping to 36.73% (Table 4).

There were significant differences in the gender composition ratio in the three cities in Southern Fujian (X^2 = 12.217; P = 0.002). In Xiamen, Zhangzhou, and Quanzhou cities, the proportion of male patients increased from 58.40% (Xiamen) to 64.89% (Quanzhou), whereas the proportion of female patients decreased from 41.60% (Xiamen) to 35.11% (Quanzhou) (Table 4).

There were significant differences in the age composition ratio in the three cities in Southern Fujian (X^2 = 31.360; P = 0.000). As demonstrated in Table 5, the number and proportion of patients in the three cities in Southern Fujian decreased with age (Table 5).

Table 5 Multivariate Analysis of Relationships Among Region, Age and Season in AR Patients

	Region			Chi-Square Test (χ2)	P-value
	Zhangzhou (%)	Quanzhou (%)	Xiamen (%)		
Age				31.360	<0.001
≤ 17	56.75	55.79	52.37		
18~39	30.65	30.95	36.63		
40~59	11.46	13.13	9.78		
≥ 60	1.14	0.13	1.21		
Seasons				37.717	<0.001
Spring	23.95	24.97	21.95		
Summer	36.55	41.61	33.94		
Autumn	19.07	18.47	22.21		
Winter	20.43	14.95	21.91		

Notes: The underlined character are indicates statistically significant (P < 0.05). P < 0.001 represents an extremely low P value.

Table 6 Multivariate Analysis of Relationships Between Age and Season in AR Patients

	Age (Composition Ratio %)				Chi-Square Test (χ^2)	P-value
	≤ 17	18~39	40~59	≥ 60		
Seasons					127.802	<0.001
Spring	20.32	23.53	27.34	40.28		
Summer	40.22	30.29	26.62	26.39		
Autumn	18.11	25.53	25.04	20.83		
Winter	21.36	20.65	21.01	12.50		

Notes: The underlined character are indicates statistically significant (P < 0.05). P < 0.001 represents an extremely low P value.

There were statistically significant differences in the constituent ratios of patients between the three cities in Southern Fujian across the four seasons (X^2 = 37.717; *P* = 0.000). Xiamen, Zhangzhou, and Quanzhou cities had the highest number and proportion of patients in summer (33.94%, 36.55%, and 41.61%, respectively); in all three cities, the numbers and proportions of patients were significantly higher in summer than in the other three seasons. Xiamen and Quanzhou had the lowest number and proportion of patients in winter (21.91% and 14.95%, respectively), whereas Zhangzhou had the lowest number and proportion of patients in autumn (19.07%) (Table 5).

The proportion of patients was highest in summer (35.16%), followed by spring (22.56%), and autumn (21.36%). The proportion of patients was lowest in winter (20.91%). From 2016 to 2019, there were statistically significant differences in the constituent ratios of patients across the four seasons in Southern Fujian (X^2 = 41.634; *P* = 0.000) (Table 5).

Among the four age groups, the proportion of patients was highest in the ≤ 17 years old group (53.34%). The proportion of patients was lowest in the ≥ 60 years of age group (1.08%). There was no statistically significant difference in the constituent ratios of patients across the four age groups (X^2 = 15.182; *P* = 0.086) (Table 6). There were statistically significant differences in the age composition ratio across the seasons (X^2 = 127.802; *P* = 0.000) (Table 6).

Discussion

AR is one of the most common clinical diseases, and its incidence is increasing year by year. It affects 500 million people around the world, and is now the main chronic inflammatory disease of the respiratory tract. AR seriously affects patient quality of life and imposes a huge economic burden.[9–13] The current recommendation is that patients should avoid contact with allergens during treatment. This is commonly instigated after completion of an allergen skin prick test (SPT).[14–17] The SPT (which involves a reaction between an antigen and an antibody on the body surface) is highly sensitive and specific. Moreover, there are no age restrictions on its use. The SPT is the recommended examination method for clinical allergen detection because it is safe, simple, quick, and cheap.

The top four AR allergen-positive rates in Southern Fujian were Df (63.93%), *Dpt* (63.33%), cockroach (22.35%), and animal dander (1.99%). These four allergens are all present indoors, and cause perennial AR. Therefore, the AR cases encountered in Southern Fujian are mainly perennial. Three outdoor allergens, ie, from weeds and molds were ranked from 5th to 7th place, and had positive reaction rates of 0.64%–0.22%. These outdoor allergens mainly cause seasonal AR, which occurs at a much lower rate than perennial AR. Mango allergen, which is ingested, ranked last, with a positive reaction rate of only 0.07%. The positive reaction rates of the Df and *Dpt* allergens (~63%), and the positive reaction rate of the cockroach allergen (~22%) were far higher than the positive rates of the other five allergens. The observed rates were also higher than the positive reaction rates of Df, *Dpt*, and cockroach allergens reported in the literature.[18] This discrepancy may be explained by the use of different detection methods. In addition, because the patient populations reported in the literature were only from Xiamen or Quanzhou, the overall distribution of AR patients across Southern Fujian was not fully reflected.

According to the medical literature (both domestic and foreign), there has been an increase in the incidence of AR patients with allergies to pet hairs, especially those of cats and dogs.[19,20] It has been reported that the sensitization rate in

Guangzhou, China, is increasing by 1.3% per year. In the present study, the rate of positive reaction to animal dander was mainly "++", and the strong positive reaction rate was only 18.8%. Approximately 95% of the animal dander-positive patients also had concurrent Df and *Dpt* allergies, and approximately 50% had concurrent Df, *Dpt*, and cockroach allergies. Therefore, it is much more likely that patients in this region are highly sensitized to house dust mite allergens owing to the hot and humid climate, and the vast majority of patients (whether sensitized to animal dander or not) would also be sensitized to house dust mite allergens. Moreover, cockroaches breed more and are more difficult to control when pets are present. Consequently, indoor pets cause more severe AR allergy symptoms, which are also more difficult to control. In the present study, we observed that the number of AR patients in Southern Fujian was lowest in winter. The number of patients then gradually increased in spring (with the increase in temperature), spiking in the hot summer. The number of AR patients then gradually decreased during the cool autumn, and eventually returned to a winter minimum. The Southern Fujian province has a subtropical maritime monsoon climate, with sunshine throughout the year and an average annual temperature of 20–28°C. Overall, the climate is warm and humid. Summer in Southern Fujian (June to September) is dominated by high-temperature weather systems, and local thunderstorms and typhoon activity are more frequent. The average temperature is 30°C (usually within the 26–34°C range), the wind is southerly, and the rainfall is abundant. This warm and humid environment is ideal for the growth and reproduction of dust mites and cockroaches, which therefore thrive in Southern Fujian during summer. Consequently, dust mite and cockroach allergens are common, and the incidence of AR is high.

In winter, the average temperature in Southern Fujian is 16°C, and there is little rainfall. Because these are not ideal living conditions for dust mites and cockroaches, the number of AR patients was lowest in winter, which accounted for only 1/5 of the total annual AR patients. However, climate change may modulate weather conditions, potentially increasing allergic respiratory system disease development.[21–24] According to the scientific literature,[25] higher temperatures, rain, and southerly winds may increase the incidence of AR and exacerbate its severity. The changes in AR incidence with temperature and humidity are consistent with the results presented in the present paper. However, information about the correlation between AR incidence and wind direction, and the reason for this correlation, is limited, and further research is required.

The majority of suspected AR patients in Southern Fujian were male (~60%). However, the proportion of male to female patients varied significantly over the four-year period from 2016 to 2019. In approximately 65% of the 6689 cases, we were able to detect a specific allergen, and the rate of positive reaction to allergens (response intensity) was independent of gender. Among all the age groups, the incidence of AR was highest in the juvenile group (≤ 17 years of age), which accounted for more than half of the patients (~53%). The incidence of AR then gradually decreased with age, until the elderly group (≥ 60 years of age), which accounted for only 1%. These results suggest that approximately half of all AR patients will develop the disease as juveniles, and the rest as young or middle-aged adults (the incidence was very low in old age).

In the juvenile group, the rate of positive reaction to indoor allergens (Df, *Dpt*, cockroach, and animal dander) in the 7–17 school age group was higher than that in the 1–6 preschool age group. School-age minors spend more time inside during their studies, and are therefore more likely to contact indoor allergens. Consequently, the rate of positive reaction to indoor allergens is higher in school-age minors than in preschool children. In contrast, the rate of positive reaction to mold, which is an outdoor allergen, was lowest in the elderly group (≥ 60 years of age). The elderly are less involved in outdoor activities (compared to those in the other age groups). Therefore, they experience less exposure to mold.

In Southern Fujian, 13.45% of AR patients had a family history of AR. The most common three clinical symptoms were nasal obstruction (86.16%), sneezing (83.10%), and watery nasal discharge (82.61%). The next most common clinical symptom was nasal itching (70.82%). All four clinical manifestations were independent of the allergen species. In addition, the rate of positive reaction to dust mite allergens increased with disease onset, with a time node of one year. The lowest rate of positive reaction to *Dermatophagoides* was 63%–65%, when the disease onset was less than 1 year. After more than 1 year, the rates of positive reaction to Df and *Dpt* increased, fluctuating at approximately 66%–77%. However, there were no significant differences in the rates of positive reaction to Df and *Dpt* between disease onsets of 1–5 years, 5–10 years, and > 10 years.

Owing to their geographical proximity, the three cities of Xiamen, Zhangzhou, and Quanzhou in Southern Fujian share a similar environment, climate, living habits, and eating habits. Consequently, the characteristics of AR in these three cities share several similarities, including a high proportion of male AR patients and a peak in AR cases during summer. Across

Southern Fujian, there were no significant differences in the rates of positive reaction to dust mite, animal dander, weed, mold, or mango allergens. In addition, as patient age increased, there was a downward trend in the number of patients. Therefore, most patients were ≤ 17 years of age (~52%), followed by young adults in the 18–39 age range (30%). The number of patients was lowest in the elderly patient group (≥ 60 years old). However, several characteristics of AR allergens were different in the three cities. For example, whereas Xiamen and Quanzhou had the lowest incidences of AR in winter, Zhangzhou had the lowest incidence in autumn. Furthermore, the rates of positive reaction to cockroach allergens differed between Xiamen and Zhangzhou (Zhangzhou had the lowest and Xiamen the highest rate).

In most cases, 2–3 allergens elicited a positive reaction in the AR patients (representing 94.38% of the patients that reacted to at least one allergen). In contrast, patients that reacted to one allergen accounted for only 3.52% and patients that reacted to four allergens accounted for only 1.86% (of patients that reacted to at least one allergen. Reaction to ≥ 5 allergens was extremely rare (0.09%). In general, most of the double-allergen cases were simultaneously allergic to Df and *Dpt*; 90.73% of the reaction intensity was the same, and 88.25% was strongly positive.

The rate of positive reaction to cockroach allergens in AR patients in Southern Fujian was 22.35%, which was second only to the rate of positive reaction to dust mite allergens. The rate of positive reaction was mainly "+++", and the strong rate of positive reaction reached ~60%. Interestingly, 92% of the cockroach allergen-positive patients were Df- and *Dpt*-positive, and more than half of the patients reacted strongly to all three allergens. This grouping may be related to the phenomenon of antigen crossing.[26] The cockroach-positive rate of AR patients in China is highest in the south,[27] followed by the east (the cockroach-positive rate of AR was lowest in the north). The reported overall positive rate was 19.37%, which is similar to that reported here. However, most of the cockroach-positive cases reported in the previous study were "+" or "++", which is inconsistent with the strong positive rate reported here. One explanation for this is that the distribution of AR patients in China has gradually changed over recent years.

Currently, allergen-specific immunotherapy is the only causative treatment for AR, and allergen-specific immunotherapy is the first-line treatment recommended by the guidelines for the diagnosis and treatment of AR.[28] Allergen vaccines currently available for clinical use are mainly suitable for dust mite allergy. In view of the high rate of positive reaction to cockroach allergen in southern China, a vaccine against cockroach allergens should be developed. Such a vaccine would have wide application prospects in Southern Fujian. Several authors have suggested that air pollution aggravates AR.[29–32] For perennial AR patients, indoor environmental pollution should be controlled as much as possible. Important measures include avoiding pets, maintaining indoor hygiene and cleanliness, drying clothes, changing bedding frequently, and cleaning air conditioning filters regularly. In addition, patients with perennial AR should stay away from outdoor environmental pollution. It has been reported[33–35] that $PM_{2.5}$ (particulate matter defined as particles having an aerodynamic diameter of less than 2.5 μm) is deposited across the whole respiratory tract, directly damaging the human body. Because $PM_{2.5}$ can absorb allergens and microorganisms, sensitization and allergic symptoms may accompany $PM_{2.5}$ deposition.

Conclusions

In our analysis of AR patients in Southern Fujian province, China, we have summarized the distribution, age, gender, seasonal, clinical, and overall trend characteristics of AR patients in recent years. Our findings, which further support existing theories and data, indicate the high prevalence of sensitization to specific allergens such as those generated by dust mites (Df and *Dpt*) and cockroaches. Interestingly, AR allergens across the three cities were summarized and compared to dynamically adjust the type of allergen test required for AR patients in the Southern Fujian region. We hope that our findings will inform the development of an inexpensive personalized plan that ameliorates the rate of positive reaction to each allergen. There are clear differences in susceptibility to allergens among the various demographic groups in the Southern Fujian region of China. This information may inform the further testing and treatment of certain allergens. In a subsequent study, we will conduct an analysis of the allergens in various geographic settings or larger populations in Fujian region. This may provide more potential interventions for AR treatment in Southern Fujian region.

Data Sharing Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethics Approval and Informed Consent

This study was approved by Medical Ethics Committee of the First Affiliated hospital of Xiamen University (code 2022-029). Written informed consent was obtained from all participants.

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Disclosure

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