

A multicenter study of the clinical features of allergic rhinitis in central China

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ABSTRACT

Background: Several epidemiological surveys of allergic rhinitis (AR) have been conducted in China. However, the clinical features of AR are still not clear enough. The aim of the current study was to perform a multicenter investigation to evaluate the clinical features of AR in China.

Methods: A multicenter investigation was performed in 13 allergy centers in central China. A disease-related questionnaire was completed by each patient themselves or with guardian assistance after the diagnosis of AR. The clinical features of AR and allergen profile were analyzed.

Results: Eleven thousand four patients who were diagnosed with AR were recruited in this study. The percentages of classification of AR according to the Allergic Rhinitis and Its Impact on Asthma guidelines were 9.7% intermittent mild (IM), 3.1% persistent mild (PM), 33.9% intermittent moderate-severe (IMS), and 53.3% persistent moderate-severe (PMS). There were 61.6 and 42.2% AR patients who had concomitant ocular or lower respiratory symptoms in clinic. The occurrence of ocular and lower respiratory symptoms was found to be gradually increased from IM, PM, and IMS to PMS. Cold air and temperature change were the two most common factors triggering the nasal symptoms. *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* were the most important allergens of central China.

Conclusions: This study has contributed to a better understanding of clinical features of AR in China.

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Allergic rhinitis (AR) is a common disease with prevalence of 10–25% around the world. AR can affect the daily life of the patients and cause huge social-economic burdens. It has been reported that AR has a close relationship with ocular and lower respiratory symptoms.^{1–3} In China, several epidemiological surveys of AR had been conducted recently.^{4–7} However, the clinical features of AR are still not clear enough.

The aim of the current study was to perform a multicenter investigation to evaluate the clinical features of AR in China, particularly for the subgroups of AR according to the Allergic Rhinitis and Its Impact on Asthma (ARIA) guidelines; occurrence of ocular and lower respiratory symptoms in AR patients; the seasonal features; triggers of nasal symptoms; and the distribution of sensitized allergens.

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MATERIALS AND METHODS

Study Design

The study was approved by the Ethics Committee of Huazhong University of Science and Technology (Wuhan, China). Informed consent forms were obtained from all patients (patients <14 years old were assisted by their guardians) before the investigation.

This study was conducted from January 2010 to December 2010 in 13 allergic centers of central China. The diagnostic criteria, skin-prick test (SPT), and questionnaire were standardized for all centers before the study. The same history record sheets and data management software were used. All physicians and nurses were trained together before the project. The data of each patient were verified by the center supervisor and double checked by the principal investigator before analysis.

Patients

All patients with hyperreactive nasal symptoms (at least two symptoms from nasal obstruction, nasal itching, sneezing, and rhinorrhea) were included. Patients with nasal infections or tumors were excluded by examination. SPT was then conducted. Patients ≤14 years old were classified into the children group, and the others were classified into the adult group. A detailed questionnaire was completed by the patients themselves (>14 years old) or assisted by their guardians (≤14 years old).

Skin-Prick Test

Common aeroallergens of the local area were tested with SPTs. Standardized allergen extracts and control solutions were obtained from ALK (Hørsholm, Denmark), including mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, and *Blomia tropicalis*), dog dander (*Canis familiaris*), cat dander (*Felis domesticus*), cockroach (American cockroach and *Blattella germanica*), pollen (mugwort, ragweed, mixed grasses, and mixed trees), and a mixture of molds. Histamine (10 mg/mL) and saline were used as positive and negative controls,

respectively. Antihistaminics were suspended for at least 7 days before the SPTs. The results of the test were shown as skin index (SI; SI = mean size of allergen wheal/mean size of histamine wheal, given a negative reaction to saline). A positive SPT was defined as SI ≥ 0.5 against one or more allergens.

Questionnaire

The questionnaire designed by the authors in the study included questions for the AR patients, such as their nasal symptoms, concomitant eye and lower respiratory symptoms, visual analog scale (VAS), impairment of daily life (sleep, daily activities, leisure, sport, school, and work), seasonal features of nasal symptoms attack, triggers, etc. of AR.

Some Definitions

The diagnostic criteria of AR were positive nasal symptoms and positive SPT for one or more allergens.

VAS scores were assessed; "0" stands for nasal symptom free, whereas "100" represents the worst possible nasal symptoms.

The severity of AR symptoms can be classified as intermittent mild (IM), intermittent moderate-severe (IMS), persistent mild (PM), persistent moderate-severe (PMS) according to the ARIA guidelines.¹ "Intermittent" stands for symptoms that occurred "<4 days/wk" or "<4 wk/yr," whereas "persistent" represents symptoms that occurred " ≥ 4 days/wk" and " ≥ 4 wk/yr." "Mild" indicates no impairment of daily activities or sleep was caused because of nasal symptoms, and "moderate-severe" indicates impairment of daily activities or sleep was caused by nasal symptoms.¹

Statistical Analysis

The statistical analysis was performed by the Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL) for Microsoft Windows, Version 17.0 (Microsoft Corp., Redmond, WA). For all analyses, $p < 0.05$ was considered statistically significant. Descriptive parameters were shown in the result as mean $\pm$ SD. The Student's t -test and one-way ANOVA were used to compare clinical characteristics between the children and adults. Wilcoxon rank sum test was conducted when data were not normally distributed. In addition, Spearman's analysis was used to measure the correlation between the different classes of AR patients and their VAS scores.

RESULTS

Patients

Eleven thousand four patients were diagnosed with AR from the 13 centers during the study period. The ratio of male/female in the patients was 1.25:1 (6114:4890), and the ratio of children/adults was 0.56:1 (3950:7054). The percentage of male patients in the children group was larger than the adults group (68.9% versus 48.1%; $p < 0.001$). The distribution of age and gender in all AR patients is shown in Fig. 1.

Classification

The classification of AR patients according to ARIA guideline is shown in Table 1. The percentage of IMS and PMS were found much higher than the IM and PM in the clinic. In addition, the tendency was similar between the adults and children.

VAS Score

The average VAS score of all subjects in the study was 60.97 ± 22.11 (mean $\pm$ SD). No significant difference was found in terms of the VAS scores between the male and female population (60.40 ± 21.72 versus 61.68 ± 22.58 ; $p = 0.173$). Although VAS scores of the children group was significantly lower than the adults group, the difference was mild (59.85 ± 21.52 versus 61.59 ± 22.42 ; $p < 0.05$). The VAS scores of the

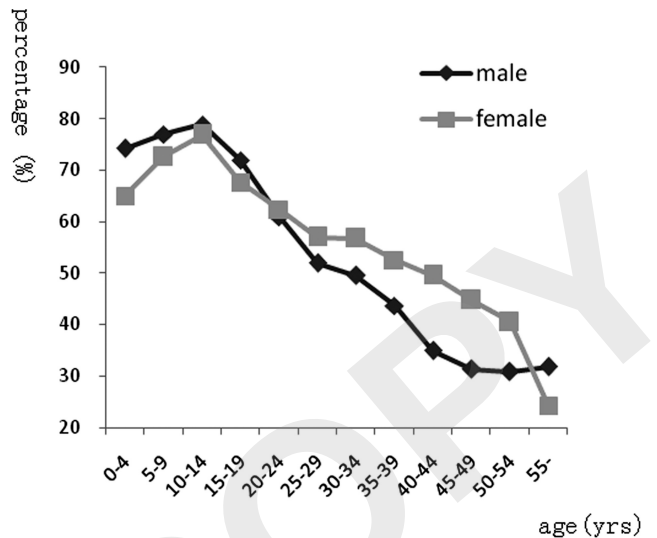


Figure 1. Distribution of age and gender in allergic rhinitis (AR) patients

Subdivision	Children (n = 3950) (%)	Adults (n = 7054) (%)	Total (n = 11,004) (%)
IM	339 (8.6)	451 (6.4)	790 (7.2)
PM	181 (4.6)	148 (2.1)	329 (3.0)
IMS	1655 (41.9)	2927 (41.5)	4582 (41.6)
PMS	1775 (45.0)	3528 (50.0)	5303 (48.2)

AR = allergic rhinitis; IM = intermittent mild; PM = persistent mild; IMS = intermittent mild-severe; PMS = persistent mild-severe.

	Children (n = 3950) (%)	Adults (n = 7054) (%)	Total (n = 11004) (%)
Nasal symptoms			
Nasal obstruction	3650 (92.4)	6511 (92.3)	10161 (92.3)
Nasal itching*	3243 (82.1)	6052 (85.8)	9295 (84.5)
Sneezing**	3559 (90.1)	6666 (94.5)	10225 (92.9)
Rhinorrhea**	3523 (89.2)	6574 (93.2)	10097 (91.8)
Ocular symptoms			
Eye itching*	2009 (50.9)	3850 (54.6)	5859 (53.2)
Eye congestion***	636 (16.1)	1728 (24.5)	2364 (21.5)
Eye swelling***	561 (14.2)	1665 (23.6)	2226 (20.2)
Dacryorrhea***	1090 (27.6)	2821 (40.0)	3911 (35.5)
Bronchial symptoms			
Tightness of breath***	612 (15.5)	1644 (23.3)	2256 (20.5)
Wheezing*	490 (12.4)	1093 (15.5)	1583 (14.4)
Cough***	1441 (36.5)	1974 (28.0)	3415 (31.0)
Chest distress***	407 (10.3)	1291 (18.3)	1698 (15.5)

Comparison of each symptom between children and adults.

*0.01 < $p < 0.05$; **0.001 < $p < 0.01$; *** $p < 0.001$.

AR = allergic rhinitis.

four subgroups of AR symptoms were 33.89 ± 20.29 (IM), 40.75 ± 21.28 (PM), 51.61 ± 19.71 (IMS), and 65.77 ± 20.03 (PMS), respectively. A positive correlation was found between the grading of severity (IM, PM, and IMS to PMS) and the VAS scores (Spearman $r = 0.263$; $p < 0.001$).

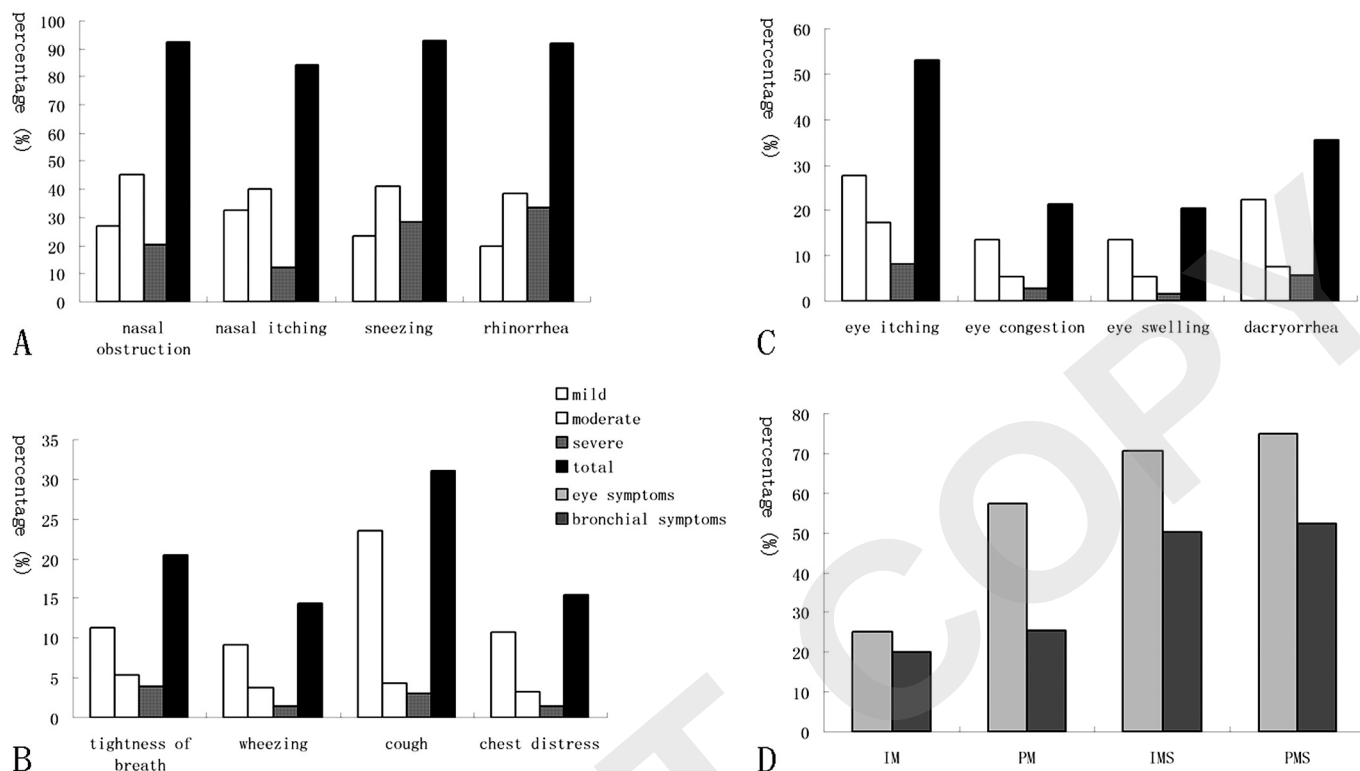


Figure 2. Severity of each symptom and occurrence of the ocular and lower respiratory symptoms in each allergic rhinitis (AR) subgroup. (A) Severity of each nasal symptom, (B) severity of each ocular symptom, (C) severity of each lower respiratory symptom, and (D) occurrence of the ocular and low respiratory symptoms in each AR subgroup.

Symptoms

The numbers of AR patients who showed concomitant ocular and bronchial symptoms were 6778 (61.6%) and 4644 (42.2%), respectively. The occurrence of each symptom was shown in Table 2. Eye itching (53.2%) was found to be the most common ocular symptom, and cough (31.0%) was the most common bronchial symptom. The incidence of all combined symptoms was higher in the adult patients than in the children, apart from cough.

The severity of each symptom and the occurrence of the concomitant eye or lower respiratory symptoms in each subgroup of AR are shown in Fig. 2. We combined the data of the children group and the adult group, because the tendency between the two groups was similar. It was found that the occurrence of ocular and lower respiratory symptoms were gradually increased, as the upgrading of severity from IM, PM, and IMS to PMS.

Seasonal Features and Triggers of Nasal Symptoms

Seasonal features and triggers of nasal symptoms are summarized and shown in Table 3. The majority of AR patients turned out to have perennial rhinitis with or without seasonal aggravation (34.4 and 28.1%, respectively). Only 16.4% patients had symptoms in the identical season every year; these patients may be pure seasonal AR patients. Cold air and temperature change were shown to be the two most common factors triggering nasal symptoms. The tendency in terms of the seasonal features and triggers was similar between the children and the adult patients, although significant differences in some factors were found.

Sensitized Allergens

The sensitized allergens of AR patients are summarized in Table 4. *D. pteronyssinus* and *D. farinae* were detected as the two most impor-

Table 3 Seasonal feature and triggers of nasal symptoms

	Children (n = 3950) (%)	Adults (n = 7054) (%)	Total (n = 11,004) (%)
Seasonal features			
Perennial with seasonal aggravation*	1248 (31.6)	2532 (35.9)	3780 (34.4)
Perennial without seasonal aggravation	1059 (26.8)	2032 (28.8)	3091 (28.1)
In the identical season every year*	549 (13.9)	1256 (17.8)	1805 (16.4)
When season change	284 (7.2)	585 (8.3)	869 (7.9)
No regularity**	814 (20.6)	642 (9.1)	1456 (13.2)
Triggers			
Cold air	1987 (50.3)	3710 (52.6)	5697 (51.8)
Temperature change**	1639 (41.5)	3478 (49.3)	5117 (46.5)
Dust**	944 (23.9)	2645 (37.5)	3589 (32.6)
Stimulating odor**	498 (12.6)	1771 (25.1)	2269 (20.6)
Cotton fiber**	581 (14.7)	1686 (23.9)	2267 (20.6)
Pollen**	288 (7.3)	832 (11.8)	1120 (10.2)
Smoke in kitchen**	150 (3.8)	748 (10.6)	898 (8.2)
Cigarette**	111 (2.8)	663 (9.4)	774 (7.0)
Pet	146 (3.7)	261 (3.7)	407 (3.7)
Psychological pressure	36 (0.9)	134 (1.9)	170 (1.5)
Drink	0 (0)	176 (2.5)	176 (1.6)
Others	4 (0.1)	14 (0.2)	18 (0.2)
Unknown**	1276 (32.3)	1764 (25)	3040 (27.6)

Comparison of each factor between child and adult patients.

*0.01 < p < 0.05; **p < 0.001.

Table 4 Allergen sensitization profile

	Children (n = 3950) (%)	Adults (n = 7054) (%)	Total (n = 11,004) (%)
<i>Dermatophagoides pteronyssinus</i> **	3685 (93.3)	6342 (89.9)	10027 (91.1)
<i>Dermatophagoides farinae</i> **	3626 (91.8)	6158 (87.3)	9784 (88.9)
<i>Blomia tropicalis</i>	1201 (30.4)	2208 (31.3)	3409 (31.0)
Dog	257 (6.5)	394 (5.6)	651 (5.9)
Cat	273 (6.9)	397 (5.6)	670 (6.1)
Mixed mold**	229 (5.8)	240 (3.4)	469 (4.3)
<i>B. germanica</i> ***	174 (4.4)	882 (12.5)	1056 (9.6)
American cockroach	16 (0.4)	28 (0.4)	44 (0.4)
Mugwort***	115 (2.9)	670 (9.5)	785 (7.1)
Ragweed***	75 (1.9)	416 (5.9)	491 (4.5)
Mixed grass pollen*	64 (1.6)	212 (3.0)	276 (2.5)
Mixed tree pollen**	62 (1.6)	247 (3.5)	309 (2.8)

Comparison of the positivity of each allergen between children and adults.

*0.01 < p < 0.05; **0.001 < p < 0.01; ***p < 0.001.

tant allergens. The percentages of patients sensitized to *D. pteronyssinus* and *D. farinae* in the study were 91.1 and 89.9%, respectively. The number of children sensitized to pollens and *B. germanica* was significantly less than the adults, whereas the percentage of mold allergy was much higher in children than in the adult patients.

DISCUSSION

The current study was the first multicenter investigation of the clinical features of AR patients in central China. The percentage of male patients was found to be higher in children, and there was a gradual shift in gender after the age of 20–24 years old. Some other epidemiological investigations also found different prevalence of AR because of the factor of age and gender.^{8–11} An animal study has pointed out that androgen appeared to be involved in the production of specific IgE in male mice.¹² Furthermore, airway inflammation and remodeling were also shown to be different in male and female mice.¹³

All AR patients were classified into IM, IMS, PM, and PMS groups according to the ARIA guidelines. It was found that 89.8% patients were PMS or IMS in the clinic, and no significant difference was found in the tendency between the adults and children. The ratio between the subgroups in the clinic was different from other epidemiological study results, which showed a significantly lower percentage of moderate/severe AR patients.¹⁴ The majority of the AR patients with mild symptoms who choose not to go to the clinic could be the reason that led to the significant difference.

VAS is commonly used as a simple and subjective measurement in clinical practice. It had been proven that VAS positively correlates with the Rhinoconjunctivitis Quality of Life Questionnaire global score and could be used for the quantitative evaluation of the severity of AR.¹³ In this study, we found a statistically significant correlation between the grading of the severity (IM, PM, and IMS to PMS) and VAS scores (Spearman $r = 0.263$; $p < 0.001$). The results correspond to the findings that Bousquet reported previously.¹⁵

In this study, 61.6% of patients had shown ocular symptoms and 42.2% had shown bronchial symptoms; the number was similar as in other reports.^{16,17} In addition, the occurrence of ocular and lower respiratory symptoms was gradually increased from IM, PM, and IMS to PMS groups; 75.1 and 52.5% of PMS patients had ocular and lower respiratory symptoms, respectively. It is suggested that more attention of ocular and lower respiratory symptoms should be given in AR patients, especially for the patients with more severe nasal symptoms.

In this study, nasal symptoms occurred throughout each year in 83.6% of the patients (with or without seasonal aggravation). Prevalence of pure seasonal AR was relatively low (16.4%), which was in accordance with the major allergens distribution in central China. Cold air and temperature change were found to be the most common factors triggering nasal symptoms. The pathophysiological research revealed that cold dry air and sudden temperature change could lead to a pronounced nasal inflammation with the recruitment and activation of eosinophils.^{18,19} Because the location of central China is in the subtropical zone, large temperature variation can occur during different seasons and big temperature change can even take place in a single day. Consequently, cold air and temperature change may be the prominent factors inducing nasal symptoms in central China.

D. pteronyssinus and *D. farinae* were found to be the most important allergens in the current investigation; this conclusion corresponds with other epidemiological studies in China.^{20–22} The positive rate of *B. germanica* was much higher in adults than in children. Because of the quick economic development in China in recent years, young people in China usually choose to live in new houses once they get married. The likelihood of children exposed to *B. germanica* allergens was much lower than adults with middle age or elders, who often live in older buildings. Furthermore, pet allergy was commonly reported in most countries in Europe and America.²³ However, because keeping pets is not as popular in China, the occurrence of pet allergy was found to be relatively low in this study. Another study also showed that the positive rate of animal dander was only 6.3% in AR patients in Beijing (capital city of China).²⁴

In conclusion, the majority of the AR patients in this study were IMS or PMS in the clinic. The ocular and lower respiratory symptoms occurred frequently in AR patients, especially for the PMS patients. Most AR patients had nasal symptoms throughout the year. It is possible that cold air and temperature change were the two major factors that trigger nasal symptoms of the AR patients. In addition, dust mites were the most important allergens of AR in central China. The study has improved the understanding of the clinical features of AR in central China, and additional study is suggested in the clinic in terms of AR in the future.

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