



Prevalence and risk factors of allergic rhinitis and asthma in the southern edge of the plateau grassland region of northern China: A cross-sectional study

Tingting Ma^a, Yanlei Chen^a, Yaojun Pang^b, Xiangdong Wang^c, Deqing Dai^b, Yan Zhuang^a, Haiyun Shi^a, Ming Zheng^c, Ruijuan Zhang^b, Weiting Jin^b, Xiaomei Yang^b, Ye Wang^d, Guangliang Shan^d, Yong Yan^e, Deyun Wang^f, Xiaoyan Wang^a, Qingyu Wei^g, Jinshu Yin^{h***}, Xueyan Wang^{a**} and Luo Zhang^{c*}

ABSTRACT

Background: The prevalence rates of allergic rhinitis (AR) and asthma in the border region of China may be different from those in the central region of plateau grasslands. A survey was performed to investigate the prevalence and risk factors for AR, asthma, and AR combined with asthma among adults (age ≥ 20 years) residing in the southern border of plateau grasslands in northern China.

Methods: From May to August 2018, a cross-sectional survey was completed by subjects that were selected using a cluster random sampling method. The subjects completed a questionnaire and were administered skin prick tests (SPTs). Risk factors for AR, asthma, and AR combined with asthma were examined by multivariate logistic regression analyses.

Results: A total of 1815 adult subjects in the selected region completed study. The prevalence rates of physician-diagnosed AR, asthma, and AR combined with asthma were 13.9% (253), 9.8% (177), and 2.9% (52), respectively. Among the patients with AR, 20.6% were found to have concurrent asthma; among the patients with asthma, 29.4% were found to have concurrent AR. *Artemisia* and *Humulus* pollen were the most common sensitizing pollen types. Approximately 70% of subjects with AR and $<30\%$ of asthma patients were sensitized to *Artemisia* and *Humulus* pollen. Symptoms of AR and asthma mainly appeared during August. A multivariable logistic regression analysis identified sensitization pollen as an independent risk factor for both AR and AR combined with asthma (AR: OR = 16.23, 95% CI: 10.15–25.96; AR combined with asthma: OR = 6.16, 95% CI: 1.28–29.66). An age >40 years old, family history of asthma, moderate-to-severe AR, adverse food reactions, and mold allergies were independent risk factors for AR combined with asthma.

^aDepartment of Allergy, Beijing Shijitan Hospital, Capital Medical University, Beijing, China

*Corresponding author. Department of Otolaryngology Head and Neck Surgery, Beijing TongRen Hospital, Capital Medical University Beijing Key Laboratory of Nasal Diseases Beijing, Institute of Otolaryngology, No. 17, Hou Gou Hu Tong, Dong Cheng District, Beijing, 100005, China. E-mail: dr.luozhang@139.com

**Corresponding author. Department of Allergy, Beijing Shijitan Hospital, Capital Medical University, No.10, Tieyi Road, Haidian District, Beijing, 100038, China. Email: wangxueyan2018@163.com

***Corresponding author. Department of Otorhinolaryngology Head and Neck Surgery, Beijing Shijitan Hospital, Capital Medical University No.10,

Tieyi Road, Haidian District, Beijing, 100038, China. Email: yinjinshu55@aliyun.com

Full list of author information is available at the end of the article.

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Conclusions: This study identified the prevalence rates of AR and asthma in the southern borders of the plateau grassland in northern China (>1500 m above sea level). Sensitization pollen is an independent risk factor for AR and AR combined with asthma.

Keywords: Allergic rhinitis, Prevalence, Asthma, Pollen, Risk factors

INTRODUCTION

Allergic respiratory diseases such as allergic rhinitis and asthma are among the most frequent diseases worldwide.¹⁻³ It has been estimated that 6.0%-12.0% of adults in developed countries have asthma.⁴ Approximately 20%-30% of adults in both the United States and Europe have allergic rhinitis (AR).⁵ The presence of AR, which shares common pathophysiological characteristics with asthma,^{6,7} is a recognized risk factor for adult onset asthma, and its co-existence with asthma is usually associated with poor disease control.⁸

Allergic diseases are considered to arise through complex interactions between genetic susceptibility and environmental exposures. Classically, outdoor pollen allergens are a major cause of AR and asthma.^{9,10} Hence, regions rich in vegetation, such as grasslands, are important locations for preventing and treating AR and asthma.¹¹ A previous study reported that high altitude reduced the allergen concentrations, and consequently, the incidence of allergic airway disease. Furthermore, high altitude was shown to be inversely correlated with asthma and allergic airway diseases.¹² It is speculated that major variations in temperature and humidity over a 24-hour period may lead to differences in the incidence of asthma and AR, and that altitude and geographical location indirectly affect the incidence of asthma and AR by influencing those variables. However, few studies have investigated that possibility.

China has the most abundant grassland resources in the world, covering an area of nearly 400 million hectares, or 40% of the total Chinese land area. The grasslands are characterized by an abundance and wide diversity of grass pollen species. In our previous cross-sectional study, AR prevalence was measured and risk factors were

assessed in the central regions of Inner Mongolia grasslands, where the altitudes are <1000 m.¹³ We did not assess the prevalence of AR and asthma or identify their associated risk factors in grassland plateau areas at different altitudes.

The Zhangbei grassland located at the southern edge of the plateau grassland region of northern China runs from 114° 10' to 115° 27' E in longitude, 40° 57' to 41° 34' N in latitude, and covers an area of 4185 km². The region selected for this study is a wide area located far from the ocean and at a high altitude above sea level in the southern edge of northern China. The elevation in the region varies from 1500 to 2128 m, the mean annual temperature is 3.2 °C (range, -8 °C to 27 °C), and the mean annual precipitation is 300 mm.¹⁴ The present study was conducted to investigate the prevalence and risk factors for AR, asthma, and AR combined with asthma among adults in this high altitude grassland plateau area.

METHODS

Subjects and ethics

From May to August 2018, the survey was completed by 1902 individuals residing in the Zhangbei grasslands of the Mongolia plateau grassland region of China, which is representative of the plateau hilly region in terms of climate and vegetation composition. Inhabitants ≥ 20 years of age who had been residing in the area for at least 2 years based on the local household register were recruited for the survey. Adults who spoke incoherently or did not cooperate with the study were excluded.

The study protocol was approved by the Ethics Committees of Beijing Shijitan Hospital and Zhangbei Hospital. All subjects provided their written informed consent for study participation.

Study design

The present population-based cross-sectional survey was conducted by using a multistage, stratified, clustered, and randomized sampling design. Among 18 towns, 4 towns (2 villages and 2 communities) were sampled using a random sampling method. Each village or community was designated as a cluster sampling unit, and all eligible inhabitants in each village or community were included in the sampling process. The total population in the study region was approximately 141 617 individuals (based on data obtained from the 2010 nationwide population census). The sample size calculation was based on an estimated AR prevalence of 20% to reach a significance level (α) of 0.05 and error tolerance of 0.10 p. The estimated minimum sample size was 1585. An additional 20% was added to the minimum sample size after factoring in possible noncompliance and attrition rates. Finally, 1902 subjects of the same gender and age range were targeted for enrollment. The study was conducted in 2 stages. In the first stage, consenting residents in the study areas completed a questionnaire during a face-to-face interview. In the second stage, all subjects who had completed the questionnaire were asked to undergo skin prick tests (SPTs) performed by medical specialists (Fig S1). All study investigators were medical professionals who had been trained and evaluated for the data collection process to ensure consistency.

Data collection

Demographic data such as gender, age, height, weight, and annual family income were collected from the study subjects. Other relevant information such as nasal symptoms (itchy nose, sneezing, nasal discharge, and nasal congestion) on a month-to-month basis during the past 12 months, respiratory symptoms (wheezing, cough, shortness of breath, and chest tightness) during the past 12 months, time duration of the symptoms (seasonal or perennial), AR or asthma severity, disease course, self-reported adverse allergic reactions to drugs or foods, and other miscellaneous factors such as a family history of AR or asthma, smoking status, or pet raising history were also recorded.

Definitions of diagnoses

AR was diagnosed according to criteria proposed by the Allergic Rhinitis and its Impact on Asthma (ARIA) document (2016).¹⁵ Each survey subject was asked the following question (in the questionnaire): Have you had any of the following symptoms in the past 12 months after exposure to pollens, house dust mites, or other allergens? (i) Itchy nose, (ii) Sneezing, (iii) Nasal discharge, (iv) Nasal congestion. If the subject answered "yes," and had 2 or more of the above symptoms, they were diagnosed with self-reported AR. When a subject with self-reported AR showed a positive SPT to at least 1 of the allergens in the local region, they were diagnosed with physician-diagnosed AR.

Asthma was diagnosed by asking the following 2 questions: Question (1): Did you once have physician-diagnosed asthma? If the answer was "yes," the respondent was required to answer question #2, which had 4 parts: (i) Have you had this wheezing or whistling when you did not have a cold in the past 12 months? (ii) Have you woken up with a feeling of tightness in your chest at any time in the last 12 months? (iii) Have you been woken up by a bout of shortness of breath at any time in the last 12 months? (iv) Have you been woken up by a coughing bout at any time in the last 12 months? If the respondent answered "yes" to the first question and had experienced at least 1 of the 4 symptoms described in question 2, he or she was diagnosed with asthma.¹⁶

Seasonal AR was evaluated by asking the following question: "Do you have any nasal allergies including "seasonal allergic rhinitis"?"¹⁷ Perennial AR was evaluated by asking the question "Do you have any nasal allergies including "perennial rhinitis"?" AR severity was classified as mild or moderate-severe on the basis of symptoms as well as the subject's quality of life. Mild AR was defined as AR with normal sleep, no impairment of daily activities, sports or leisure, normal work and school, and no troublesome symptoms. Moderate-severe AR was defined as AR with one or more items of abnormal sleep, impairment of daily activities, sports or leisure,

Variable	Total (n = 1815)	AR with Asthma (n = 52)	AR alone (n = 201)	Asthma alone (n = 125)	P value*	P value†
Gender, n (%)				0.3125	0.9236	
Male	901 (49.6)	26 (50.0)	99 (49.3)	52 (41.6)		
Female	914 (50.4)	26 (50.0)	102 (50.7)	73 (58.4)		
Age (y), mean ± SD	49.1 ± 15.9	44.6 ± 11.6	39.5 ± 12.3	53.4 ± 13.9	<.0001	0.0068
Age group					<.0001	0.0241
20-29	271 (14.9)	3 (5.8)	48 (23.9)	9 (7.2)		
30-39	280 (15.4)	16 (30.8)	68 (33.8)	13 (10.4)		
40-49	351 (19.3)	16 (30.8)	42 (20.9)	23 (18.4)		
50-59	391 (21.6)	12 (23.2)	27 (13.4)	34 (27.2)		
≥60	522 (28.8)	5 (9.6)	16 (8.0)	46 (36.8)		
Smoking					0.0365	0.5648
Never	1233 (67.9)	38 (73.1)	145 (72.1)	91 (72.8)		
Current	508 (28.0)	11 (21.1)	50 (24.9)	24 (19.2)		
Ever	74 (4.1)	3 (5.8)	6 (3.0)	10 (8.0)		
Annual family income (CNY, ×10 ⁴ , mean ± SD)	4.9 ± 4.1	5.6 ± 3.6	6.6 ± 4.2	4.2 ± 3.5	<.0001	0.1428
Type of AR				-	0.3614	
Seasonal	-	29 (55.8)	126 (62.7)			
Perennial	-	23 (44.2)	75 (37.3)			
Severity of AR or Asthma					0.5605	0.0103
Mild	-	21 (40.4)	121 (60.2)	54 (43.2)		
Moderate-Severe	-	31 (59.6)	80 (39.8)	71 (56.8)		
Course of AR or Asthma (years)					-	-
≤ 1	-	-	9 (4.5)	6 (4.8)		
1-3	-	-	66 (32.8)	37 (29.6)		
4-5	-	-	49 (24.4)	33 (26.4)		
6-10	-	-	37 (18.4)	18 (14.4)		
≥ 10	-	-	40 (19.9)	31 (24.8)		
Family history					-	-
AR	144 (7.9)	10 (19.2)	40 (19.9)	11 (8.8)	<.0001	0.9139
Asthma	80 (4.4)	7 (13.5)	8 (4.0)	20 (16.0)	<.0001	0.0099
Pets	259 (14.3)	3 (5.8)	23 (11.4)	19 (15.2)	0.1772	0.2298
Adverse food reactions	195 (10.7)	18 (34.6)	39 (19.4)	14 (11.2)	<.0001	0.0193
Adverse drug reactions	326 (18.0)	15 (28.9)	34 (16.9)	37 (29.6)	0.0006	0.0523

Table 1. Characteristics of the study subjects. P value*: differences between AR with Asthma and Asthma alone; P value†: differences between AR with Asthma and AR alone

abnormal work and school, and troublesome symptoms.¹⁸ An adverse food or drug reaction was defined as a self-reported adverse food (including allergic reactions to food and food intolerance) or adverse drug reaction.^{19,20}

Skin prick tests

SPTs were performed using a standard SPT kit (Beijing Macro-Union Pharmaceutical Limited Corporation, Batch number: 03026, License code:

S20130002). SPTs were performed for 7 common inhaled allergens in the northern grasslands, namely *Dermatophagoides pteronyssinus* (Dp), *Dermatophagoides farinae* (Df), *Artemisia* (Ar), *Humulus scandens* (Hu), *Salix* (Sa), *Ulmus pumila* (Ul), and *Alternaria* (Al). Histamine in phosphate acid (5 mg/mL) and normal saline were used as negative and positive controls, respectively. SPTs were performed by nurses in the unilateral flexed forearm, and results were observed after 15 min. A positive reaction was defined as a wheal with a diameter >3 mm after subtracting the negative control.²¹

Pollen collection and pollen count

Pollen-monitoring stations were established in the study areas starting in January 2017, and were used to monitor the daily pollen counts in the regions. The pollen counts were measured with a Durham pollen sampler (gravity sedimentation) that was valid for a perimeter of 33 m above the ground. The monitoring stations had abundant ventilation, and were placed in locations that avoided surrounding obstacles. Each slide was placed daily at 8:00 a.m., collected 24 hours later, and then mounted immediately after collection. Each slide was examined and counted by 2 trained examiners in a blinded manner. Results were reported as the daily total number of pollen grains per 1000 mm².

Statistical analyses

All statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc. Cary, NC, USA). Categorical data are presented as

numbers and percentages. Continuous data are presented as the mean value \pm standard deviation or median value with an interquartile range (IQR). Between-group differences in subject characteristics were tested by using the *t*-test/Wilcoxon rank-sum test for continuous variables and chi-square/Fisher exact test for categorical variables. A multivariate regression analysis was performed to explore the risk factors for AR combined with asthma and estimate odds ratios. All tests were two-sided, and a *P*-value \leq 0.05 was considered to be statistically significant.

RESULTS

Characteristics of the study subjects

A total of 1815 subjects (901 [49.6%] males and 914 [50.4%] females) completed the questionnaire and SPTs. The mean age of the subjects was 49.1 ± 15.9 years (range, 20–88 years). Among the subjects, 28% were current tobacco smokers and 7.9% and 4.0% of the subjects had a family history of AR or asthma, respectively (Table 1). Among the subjects with AR alone, 126 (62.7%) were diagnosed with seasonal rhinitis. The proportions of subjects with moderate-severe AR alone, asthma alone, and AR combined with asthma were 39.8% (80/201), 56.8% (71/125), and 59.6% (31/52), respectively (Table 1).

Prevalence of allergic rhinitis and asthma

The proportions of subjects with physician-diagnosed AR, asthma, and AR combined with asthma were 13.9% (253), 9.8% (177), and 2.9% (52), respectively (Fig. 1A). The prevalence of AR

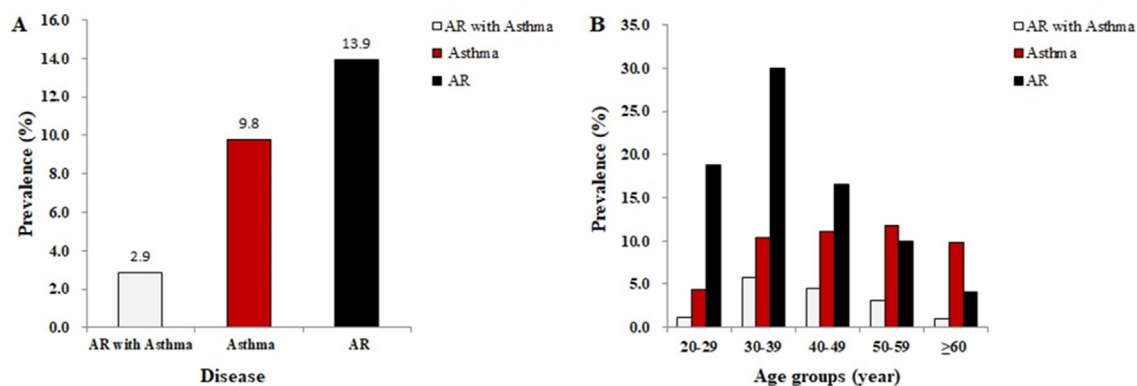


Fig. 1 The prevalence of physician-diagnosed AR, asthma, and AR combined with asthma (A). Age group distribution in the physician-diagnosed AR, asthma, and AR combined with asthma groups (B)

Variable	Total	AR with Asthma		AR alone		Asthma alone	
	n	n	Prevalence (%)	n	Prevalence (%)	n	Prevalence (%)
Total	1815	52	2.9	201	11.1	125	6.9
Gender							
Male	901	26	2.9	99	11.0	52	5.8
Female	914	26	2.8	102	11.2	73	8.1
Age group (years)							
20-29	271	3	1.1	48	17.7	9	3.3
30-39	280	16	5.7	68	24.3	13	4.6
40-49	351	16	4.6	42	12.0	23	6.6
50-59	391	12	3.1	27	6.9	34	8.7
≥60	522	5	1.0	16	3.1	46	8.8
Annual family income							
<5	857	17	2.0	58	6.8	58	6.8
≥5	958	35	3.7	143	14.9	67	7.0
Smoking							
Never	1233	38	3.1	145	11.8	91	7.4
Current	508	11	2.2	50	9.8	24	4.7
Ever	74	3	4.1	6	8.1	10	13.5
Family history of AR							
Yes	144	10	6.9	40	27.8	11	7.6
No	1671	42	2.5	161	9.6	114	6.8
Family history of asthma							
Yes	80	7	8.8	8	10.0	20	25.0
No	1735	45	2.6	193	11.1	105	6.1
Pets							
Yes	259	3	1.2	23	8.9	19	7.3
No	1556	49	3.2	178	11.4	106	6.8
Food allergy							
Yes	195	18	9.2	39	20.0	14	7.2
No	1620	34	2.1	162	10.0	111	6.9
Drug allergy							
Yes	326	15	4.6	34	10.4	37	11.3
No	1489	37	2.5	167	11.2	88	5.9

Table 2. The prevalence rates of AR with asthma, AR alone, and asthma alone in the plateau grassland of China

alone was 11.1% (201), and asthma alone was 6.9% (125). Concurrent asthma was diagnosed in 20.6% of the 253 subjects with AR, whereas concurrent AR was diagnosed in 29.4% of the 177 subjects with asthma (Table 2).

The prevalence of both AR alone and AR combined with asthma gradually increased starting at the age of 20 years, peaked at 30-39 years, and then gradually decreased after 40 years of age. The prevalence of asthma alone gradually

increased starting at the age 20 years, peaked at 50-59 years, and gradually decreased after 60 years of age (Fig. 1B, Table 2).

SPT results

SPTs were performed on 1815 individuals. The single allergen sensitivity of patients with AR combined with asthma was higher than that of patients with AR or asthma alone. The top 3 allergens were *Ar* pollen, *Hu* pollen, and dust mites.

Among the total number of patients with AR combined with asthma, 84.6% exhibited a positive SPT for *Ar* pollen and 73.1% tested positive for *Hu* pollen. Among the subjects with AR combined with asthma, pollen sensitization was exhibited in 83.3% of patients, and pollen combined with dust mite sensitization was observed in 60.0% of patients (Fig. 2A and B).

Clinical symptoms and peak presence of symptoms

The main clinical symptoms of AR were sneezing (97.6%) and runny nose (92.1%). Olfactory dysfunction was observed in 43.9% of patients with AR. The main clinical symptoms of asthma were wheezing (29.4%) and shortness of breath (26.0%). Tables S1 and S2 show the specific frequency of occurrence of various symptoms.

Fig. 3 shows the sum of the mean total monthly pollen counts and the presence of AR, asthma, and AR combined with asthma symptoms during a 12 month period (2018). The trend shows a typical two-peak phenomenon of total pollen count with a spring peak (April-May) and summer/autumn peak (July-September). The highest mean monthly pollen count in August was 13,335 grains/1000 mm², and in April it was 5456 grains/1000 mm². The *Ar* pollen count reached 9362 grain/1000 mm². Similarly, the frequency of symptoms of AR, asthma, and AR combined with asthma also peaked in August (Fig. 3).

Risk factors

Results of a multivariable logistic regression analysis revealed pollen to be an independent risk

factor for both AR and AR combined with asthma (AR: OR = 16.23, 95% CI: 10.15-25.96; AR combined with asthma: OR = 6.16, 95% CI: 1.28-29.66). Patients ≥ 40 years of age were 1.79-fold and 3.16-fold more likely to have asthma and AR combined with asthma, respectively, than patients <40 years of age (asthma: OR = 1.78, 95% CI: 1.06-3.00, $P = 0.0308$; AR combined with asthma: OR = 2.69, 95% CI: 1.24-5.86, $P = 0.0126$). Patients with moderate to severe AR were at a 2.30-fold higher risk of having co-existing asthma than patients with a mild case of AR (OR = 2.30, 95% CI: 1.09-4.86, $P = 0.0285$). Patients with adverse food reactions were at a 2.79-fold greater risk than patients with no adverse food reactions of having AR combined with asthma (OR = 2.79, 95% CI: 1.24-6.25, $P = 0.0129$). Mold allergy was an independent risk factor for both AR and AR combined with asthma among adults (AR: OR = 3.84, 95% CI: 1.56-9.45, $P = 0.0034$; AR combined with asthma: OR = 2.48; 95% CI: 1.05-5.85, $P = 0.0378$) (Table 3).

DISCUSSION

To our knowledge, this is the first epidemiological survey to examine the prevalence of AR, asthma, and AR with asthma among adults in the southern border of the plateau grassland region of northern China. In the present study, we found that the prevalence of physician-diagnosed AR was 13.9%, which was higher than the prevalence (6.2%) reported by Zheng et al²² in 2008 in Beijing, China. However, it was lower than the prevalence (21.8%) observed in the grasslands of Inner Mongolia of China in our previous study in 2015.¹³ The prevalence of asthma (9.8%) among

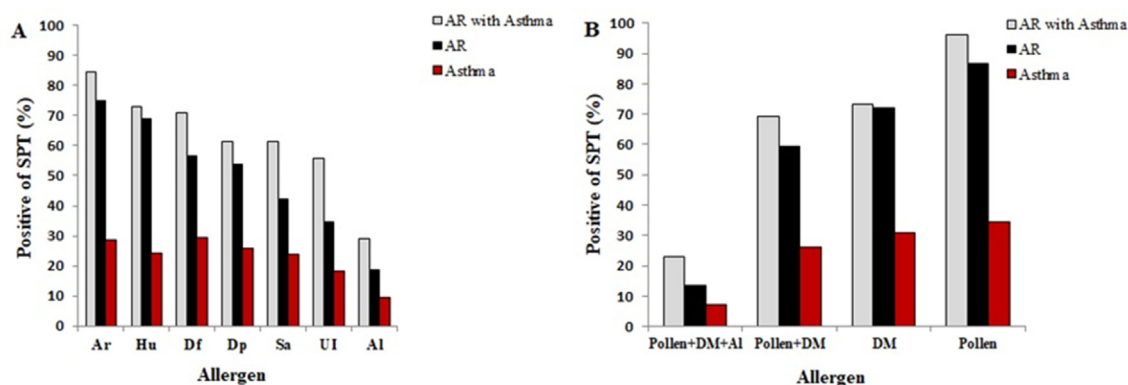


Fig. 2 The aeroallergen sensitization of AR, asthma, and AR combined with asthma. *Ar*, *Artemisia species*; *Dp*, *Dermatophagoides pteronyssinus*; *Df*, *Dermatophagoides farinae*; *Hu*, *Humulus scandens*; *Sa*, *Salix*; *UI*, *Ulmus pumila*; *Al*, *Alternaria*; *DM*, Dust mite

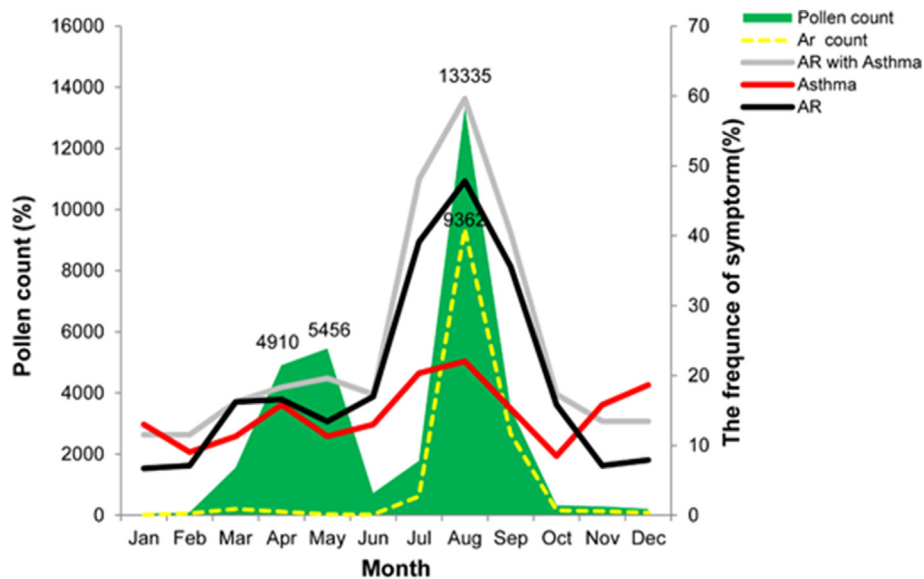


Fig. 3 The presence of AR, asthma, and AR combined with asthma symptoms over 12 months (2018) and the mean total monthly pollen count in the study area. The peak number represents the pollen count

adults in our study was higher than the 8.6% prevalence reported in a cross-sectional study conducted in 70 countries worldwide.²³ It is also higher than the asthma prevalence in China in 2012–2015 (4.2%) reported by Huang et al²⁴ in a population of patients aged > 20 years. However, the prevalence of AR combined with asthma (2.9%) in our study was much lower than that (7.06%) reported in a previous study conducted in Guangdong, China.⁷ This difference may be due to climatic factors and the pollen counts in the area. Previous studies found that AR was positively correlated with pollen counts, temperature, and precipitation, while wind speed was negatively correlated with AR.¹¹ Compared with the central Inner Mongolia grassland, the wind speed in the Zhangbei grassland is higher (4.1 m/s vs. 3.4 m/s), while the pollen concentration (32,219 grains/1000 m² vs. 36,209 grains/1000 m²), temperature (3.2 °C vs. 6.0 °C) and precipitation (300 mm vs. 400 mm) are relatively low. The high prevalence rate of asthma in this area may be related to the changeable weather, large temperature difference from morning to night within a 24-hour period, and the susceptibility to respiratory tract infections in this area.

The present study indicated that AR and AR combined with asthma both developed mainly

between 30 and 39 years of age. Our results are in agreement with those of other studies which reported that the prevalence of AR was highest in the age group of 20–44 years, and then declined in both men and women starting at the age of 45 years.²⁵ In this study, we found that age (>40 years) was a risk factor for both the incidence of asthma and AR developing into asthma. This finding is essentially similar to that previously reported by Guerra et al,²⁶ who found that rhinitis was associated with a higher risk for asthma among subjects older than 50 years than among subjects younger than 50 years, indicating that age is a vital factor for the development of asthma in individuals with AR. Huang et al²⁴ found that the prevalence of asthma among an elderly population (≥age 60 years) in China was 6.0%, and 7.4% among individuals aged 70 years and above. In our study, the prevalence of asthma patients >60 years old was 8.8%, which is similar to the percentage reported by Huang et al. The reason may be that older patients with asthma more often have an airflow limitation. Asthma with airflow limitation is likely to represent the overlap phenotype of asthma and chronic obstructive pulmonary disease, and possibly an early form of the latter. Limited airflow might also be attributed to under-treatment of asthma, such as the insufficient use of inhaled corticosteroids.

Variable	AR ^a		Asthma ^b		AR with asthma ^c	
	Multivariable analysis		Multivariable analysis		Multivariable analysis	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Male (vs. Female)	0.93 (0.53, 1.62)	0.7860	0.82 (0.48, 1.40)	0.4675	1.08 (0.44, 2.65)	0.8654
Age (vs. 20-39 years) ≥40	0.66 (0.41, 1.05)	0.0772	1.78 (1.06, 3.00)	0.0308	2.69 (1.24, 5.86)	0.0126
Family income (CNY, ×10 ⁴ , vs. ≤3)						
≤6	1.59 (0.92, 2.75)	0.0991	1.41 (0.92, 2.18)	0.1192	0.93 (0.39, 2.24)	0.8699
>6	1.55 (0.87, 2.77)	0.1417	0.72 (0.40, 1.30)	0.2747	0.42 (0.15, 1.17)	0.0955
BMI (kg/m ² , vs. <24)						
24-27.9	1.11 (0.70, 1.77)	0.6551	0.98 (0.65, 1.47)	0.9173	1.33 (0.60, 2.93)	0.4874
≥28	1.13 (0.60, 2.11)	0.7051	0.88 (0.49, 1.60)	0.6780	1.19 (0.40, 3.53)	0.7572
Smoking (vs. no smoking)						
Current	0.84 (0.46, 1.53)	0.5644	0.82 (0.44, 1.53)	0.5396	1.30 (0.46, 3.73)	0.6222
Ever	1.38 (0.35, 5.44)	0.6481	2.20 (0.95, 5.08)	0.0660	1.03 (0.18, 5.88)	0.9730
Family history of AR (vs. no history)	2.21 (1.17, 4.18)	0.0143	-	-	-	-
Family history of asthma (vs. no history)			5.47 (2.99, 9.99)	<.0001	4.66 (1.23, 17.65)	0.0234
Pet (vs. no)	1.06 (0.57, 1.98)	0.8565	1.09 (0.64, 1.86)	0.7394	0.33 (0.08, 1.36)	0.1240
Course of AR (vs. <5 y)	-	-	-	-	1.94 (0.95, 3.93)	0.0674
Moderate-to-severe (vs. mild)	-	-	-	-	2.30 (1.09, 4.86)	0.0285
Type of AR (vs. seasonal)	-	-	-	-	1.34 (0.63, 2.84)	0.4468
Adverse food reactions (vs. none)	1.25 (0.71, 2.20)	0.4367	1.01 (0.53, 1.94)	0.9739	2.79 (1.24, 6.25)	0.0129
Adverse drug reactions (vs. none)	0.60 (0.34, 1.07)	0.0827	1.81 (1.17, 2.82)	0.0083	1.71 (0.73, 4.02)	0.2205
Pollen allergy (vs. no pollen allergy)	16.23 (10.15, 25.96)	<0.0001	0.65 (0.29, 1.44)	0.2868	6.16 (1.28, 29.66)	0.0235
DM allergy (vs. no DM allergy)	5.80 (3.73, 9.03)	<0.0001	1.55 (0.81, 2.99)	0.1882	0.94 (0.42, 2.12)	0.8881
Mold allergy (vs. no mold allergy)	3.84 (1.56, 9.45)	0.0034	2.04 (0.42, 9.98)	0.3810	2.48 (1.05, 5.85)	0.0378

Table 3. Risk factors and OR values (95% CI) for AR, asthma, and AR with asthma. a. Control: People without AR. b. Control: People without asthma. c. Control: Only AR without asthma; DM: Dust mite

Olfactory dysfunction is a key symptom in patients with AR. Our study found that olfactory dysfunction was present in 43.9% of all AR patients, including 56.1% of patients with perennial AR and 36.1% of patients with seasonal AR. Di Lorenzo et al²⁷ found that 24% of 1017 patients with AR reported olfactory dysfunction. In a larger sample (n = 5770), Binder et al²⁸ found that 41% of patients with perennial AR and 26% of patients with seasonal AR reported olfactory dysfunction. This was probably due to both a mechanical component (ie, blockage of the nasal airways via mucosal congestion) and an inflammatory component. Nasal allergies might be the single most common etiologic factor in olfactory dysfunction.

Several studies that investigated the causes of AR and asthma found that airborne pollen was the main cause as an outdoor allergen.²⁹⁻³¹ By combining pollen monitoring and SPT results in high altitude grassland regions, we found that most AR and asthma patients were sensitized to ragweed pollen (*Ar* and *Hu* pollen). Ragweed or grass pollen has been suggested as the major cause of hay fever in areas such as North America,³² Australia,³³ the United Kingdom,³⁴ and Sweden.³⁵ Peaks in airborne grass pollen that occur in late spring and early summer can exacerbate symptoms of allergic rhinitis,³⁶ allergic conjunctivitis, and asthma. For instance, a study in Australia found the levels of airborne grass pollen to be a strong independent nonlinear predictor of hospital admissions related to asthma.³⁷ In our study, we also found that symptoms of AR, asthma, and AR combined with asthma were all primarily associated with seasonal exacerbations. The frequency and occurrence of symptoms were most severe in August, with *Artemisia* and *Humulus* pollen counts being the highest in that month, and causing a high incidence of symptoms and outpatient visits. Moreover, our study results suggest that pollen sensitivity increases the risk for AR and AR combined with asthma. Further in-depth research will be required to identify a dose-response relationship between pollen counts and AR or AR combined with asthma.

Epidemiological and pathophysiological studies have suggested that AR increases the risk for asthma development, based on the theme of "one

air-way, one disease."^{26,38} A previous study reported that AR significantly increased the risk for asthma in children.³⁹ In our study, patients with moderate-to-severe AR were at a 2.30-fold higher risk for developing concomitant asthma when compared to patients with mild AR. This finding was also reported by Jung et al,⁴⁰ who enrolled 606 children aged 7 years from the Panel Study of Korean Children. Those investigators found that children with moderate to severe AR were at a higher risk for developing concurrent asthma and bronchial hyper-responsiveness (BHR) when compared to children with mild AR (adjusted OR = 5.26; 95% CI: 1.77-15.62). It has been suggested that upper airway dysfunction might be a predictive factor for subsequent development of lower airway disease. Untreated or improperly managed AR can triple the risk for asthma attacks.^{8,41,42} Timely diagnosis and treatment of AR is crucial for preventing the development of asthma.

Smoking is one of the main causes of respiratory diseases. In our risk factor analysis, 21.1% of subjects in the asthma group were current smokers, and 24.9% of subjects in the AR alone group were smokers. In the multivariable analysis, the adjusted OR value of current smoking was 1.30 (0.46, 3.73). The *P*-value of current smoking was >0.05, indicating that current smoking had no a significant effect on asthma. A possible reason for that result is that our study was a cross-sectional survey, and changes in smoking behavior could not be observed. Furthermore, some people might have quit smoking because of respiratory diseases.

This study has some limitations that should be mentioned. First, the risk factor analysis was retrospective and we could not assess temporal relationships; this might have led to retrospective bias. Second, the subjects with asthma did not undergo lung function tests. Future studies will need to investigate larger cohorts using standardized survey forms and include a larger number of risk factors, (ie, endotoxins, parasites, and air pollution) in an attempt to better understand the prevalence, difference, and relationship between AR and asthma in the plateau grassland region of northern China.

Our current study provides epidemiological data concerning the prevalence of AR, asthma, and

AR combined with asthma in the high altitude (>1500 m) region of the plateau grasslands in northern China. Although hereditary factors are strongly associated with the development of AR and asthma, those diseases also occur due to age, the severity of AR, and high seasonal pollen exposure. Epidemiological data from this study will be very helpful for directing the development of healthcare policies and making plans for the appropriate use of healthcare resources.

Abbreviations

Al: Alternaria; Ar: Artemisia; AR: allergic rhinitis; ARIA: Allergic Rhinitis and its Impact on Asthma; BHR: Bronchial hyper-responsiveness; Df: Dermatophagoides farinae; Dp: Dermatophagoides pteronyssinus; Hu: Humulus scandens; IQR: Interquartile range; Sa: Salix; SPTs: Skin prick tests; Ul: Ulmus pumila

Consent for publication

All authors approved the publication of this work.

Availability of data and materials

Please contact corresponding author for primary data requests.

Author contributions

Luo Zhang, Xueyan Wang, Jinshu Yin, Yong Yan, Xiangdong Wang, Deyun Wang, Guangliang Shan, Qingyu Wei, Haiyun Shi, Yan Zhuang and Xiaoyan Wang conceived the study. Xueyan Wang, Tingting Ma, Yanlei Chen, Yaojun Pang, Deqing Dai, Ruijuan Zhang, Weiting Jin and Xiaomei Yang collected the data. Tingting Ma and Ye Wang analyzed and interpreted the data. Tingting Ma drafted the manuscript. Xueyan Wang, Luo Zhang, Deyun Wang, Xiangdong Wang and Ming Zheng edited the final approval of the manuscript.

Ethical approval

Prior to the study all the patients signed an informed consent approved for the Ethical Committee of Beijing Shijitan Hospital and Zhangbei Hospital.

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Declaration of competing interest

The authors declare no conflict of interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.waojou.2021.100537>.

Author details

^aDepartment of Allergy, Beijing Shijitan Hospital, Capital Medical University, Beijing, China. ^bDepartment of Allergy, Zhangbei Hospital, Hebei Province, China. ^cDepartment of Otolaryngology Head and Neck Surgery, Beijing TongRen Hospital, Capital Medical University, Beijing Key Laboratory of Nasal Diseases, Beijing Institute of Otolaryngology, Beijing, China. ^dDepartment of Epidemiology and Statistics, Institute of Basic Medical Sciences Chinese Academy of Medical Sciences, School of Basic Medicine Peking Union Medical College, Beijing, China. ^eDepartment of Urology, Beijing Shijitan Hospital, Capital Medical University, Beijing, China. ^fDepartment of Otolaryngology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore. ^gDepartment of Allergy, General Hospital of Northern Theater Command, Shenyang, Liao Ning Province, China. ^hDepartment of Otorhinolaryngology Head and Neck Surgery, Beijing Shijitan Hospital, Capital Medical University, Beijing, China.

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