

Investigation of self-reported chronic urticaria among adults in grasslands of northern China

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Abstract

The clinical epidemiological characteristics of chronic urticaria (CU) in different populations were not completely consistent, and the epidemiological characteristics of CU were very complex. At present, there were some patient-based studies on CU, but few natural population-based studies in the world.

This study aimed to analyze the prevalence of self-reported CU among adults in grasslands of northern China and its closely related factors.

A multistage and proportionately stratified random sampling with a field interviewer-administered survey study was performed together with skin prick tests (SPT) and measurements of the daily pollen count.

A total of 3406 subjects completed the study. The prevalence of self-reported CU was 5.61% (n=191), which was higher in women than that of men (6.91% vs 4.08%, $\chi^2=12.785$, $P<.001$). Seasonal or seasonal aggravation CU accounted for 110 (57.59%) patients. Pollen dispersal season was basically consistent with the peak season of CU, but there was no significant difference in the positive rate of pollen SPT between CU with seasonal or seasonal aggravation symptom and CU with free of symptom ($\chi^2=0.425$, $P=.51$), as well as between CU with seasonal or seasonal aggravation symptom and perennial CU ($\chi^2=0.439$, $P=.51$). Eczema (odds ratio [OR]=2.807, $P<.001$), chronic diarrhea (OR=2.486, $P<.01$), food allergy history (OR=1.890, $P<.01$), history of family allergy (OR=1.800, $P<.001$), and conjunctivitis (OR=1.749, $P<.01$) were closely related to CU.

This investigation provided the factors closely related to CU, and provided certain ideas for further research on the etiology and prevention of CU.

Abbreviations: AR = allergic rhinitis, Ar = artemisia, Be = betula, Ch = chenopodium, CU = chronic urticaria, Hu = humulus scandens, Ju = juniperus chinensis var. chinensis, Po = populus, Sa = salix, SPT = skin prick test, Ul = ulmus pumila, Ze = zea mays.

Keywords: chronic urticaria, investigation, pollen allergen, prevalence, skin prick test

1. Introduction

Urticaria is a common, mast-cell-driven disease, characterized clinically by the development of wheals; it can be divided into

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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acute urticaria wherein wheals last less than 6 weeks versus chronic urticaria (CU) wherein wheals last >6 weeks.^[1–3] Although often self-limited and benign, CU is easy to relapse and delay.^[2] CU is disabling, impairs quality of life and affects performance at work and school.^[3]

Due to the crowd of different countries, different regions in life style, living environment, immunogenetics, and social economic structure differences, a certain differences of the crowd clinical epidemiological features in different patients with urticaria will exist.^[4,5] There were some patient-based studies on CU but few natural population-based studies all over the world.^[5–9] This survey mainly investigated the epidemiological characteristics of allergic diseases of 3600 natural population-based adult residents in grasslands of northern China, and the prevalence of urticaria was also involved. We analyzed the epidemiological characteristics of self-reported CU in grasslands of northern China which would provide important reference for the causes, effective management, and prevention of CU in this region and beyond.

2. Methods

2.1. Ethics approval

Ethical approval for this study ([2015] Ethics Quick Trial No. 3) was provided by the Ethical Committee of Beijing Shijitan Hospital, the affiliated hospital of the Beijing Capital Medical University on May 15, 2015. All respondents signed informed consent.

2.2. Study region

This study was conducted in the region of Xilingol and Horqin grasslands, located in the eastern and middle part of the Inner Mongolia Autonomous Region, China. The region was representative of the Eurasian steppe in terms of climate and vegetation composition. A total of 6 municipality's areas were included, such as Erenhot, Xilinhot, Duolun, Jarud, Kailu, and Tongliao. Daily pollen count throughout a year was available for all these cities.

2.3. Survey method

This study which was a multistage and proportionately stratified random sample study was conducted in grasslands of northern China. The study was organized together with the local healthcare authorities and hospitals. The interviewers consisted of physicians and nursing staff. The survey manager prepared a standard procedure flowchart for the fieldwork at each investigational site. Two weeks before the study, a letter of introduction was sent to the study subjects to explain the purpose of the study, together with the proposed survey date. It was then followed by telephone call or a verbal reminder that was done by the study coordinator or local healthcare officers. In the selected clusters (e.g., street districts from rural areas and villages from urban areas), all members aged 18 to 80 from a household were invited to participate in this study. All subjects were investigated using an interviewer-administered questionnaire and the skin prick test (SPT) was performed at the same time (SPT allergen was summer autumn and spring pollen allergens: artemisia (Ar); betula (Be) *chenopodium* (Ch); *humulus scandens* (Hu); *salix* (Sa); *zea mays* (Ze); *juniperus chinensis var. chinensis* (Ju); *ulmus pumila* (Ul); *populus* (Po).) at a medical center or hospital near their home. While investigating urticaria, we also showed photos representing wheals to all subjects and asked them if the photos were applicable to their symptoms. If there were any missing information in the survey questionnaire, it will be completed immediately by the survey manager with the subject.

2.4. Questionnaire and field interview

The following information was collected in questionnaire on allergic diseases (including CU), including demographic data (age, sex, ethnic group, place of residence); skin symptoms in the past 12 months (wheals), allergic disorders, and comorbidities/complications, family history of allergy, risk factors (heating ways, outdoor activity time, smoking, and pet keeping), allergic reactions to drugs and/or foods, etc (Supplemental Digital Content, <http://links.lww.com/MD/F210>).

2.5. Study population

Based on data obtained from the 2010 Chinese nationwide population census, the population aged 18 to 80 in the study region was 1.42 million (urban: 594,684; rural: 830,726). The sample calculation was based on an estimated prevalence of 15% for allergy-related diseases, to reach a significance level (α) of 0.05 and error tolerance 0.10p, the estimated sample size was 3600 with equal distribution in urban and rural areas, and with the same sex and age stratification. From May to August 2015 in the grasslands of northern China, 3600 adults aged 18 and above were surveyed, and 3565 valid questionnaires (effective 99.03%)

were conducted. When analyzing the risk factors of CU, 159 patients with acute urticaria were excluded to prevent confounding factors. Finally, there were 3406 valid questionnaires (94.6%) including 1568 men and 1838 women.

2.6. Definitions used in this study

CU: It was diagnosed on the basis of positive answers to the written question: "Wheal occurs twice a week at least, and disappears within 24 hours, lasting at least six weeks" during the past year.^[10]

Allergic rhinitis (AR): The subjects with at least 2 of the 4 symptoms suggestive of allergic rhinitis (itchy nose, sneezing, runny, and blocked nose) for at least 1 hour on most days during the past year.^[11]

Conjunctivitis: We estimated conjunctivitis symptoms on the basis of positive answers to the written question: "Have you had itchy or red or watery eyes during the past year?"^[12]

Seasonal aggravation: Symptoms of the disease exist throughout the year, but worsen in spring, summer, and/or autumn.

2.7. Statistical analyses

The patient enumeration data were tested using Chi-square/Fisher exact test (the tests were 2-sided with a significant level of <0.05) or Partitions of chi-square method (the tests were two-sided with a significant level of <0.0167). Multivariate logistic regression analysis was performed to explore the risk factors related to CU and estimate their odds ratio (OR) (the tests were 2-sided with a significant level of <0.05). All of the analyses were performed using IBM SPSS STATISTICS 22.0 (IBM Corp., Armonk, NY).

3. Results

3.1. Demographic characteristics and prevalence of self-reported CU in the survey population

Of the 3406 subjects analyzed, 1568 men and 1838 women, age 43.8 ± 14.7 years (mean \pm SD). 191 (5.61%) were diagnosed as self-reported CU (Table 1). Among CU patients, 64 (4.09%) were men and 127 (6.91%) were women. 110 (57.59%) patients had shown seasonal occurrence or persistent diseases with seasonal increased in severity of CU (Table 2). The prevalence rate of self-reported CU in women was significantly higher than that of men (4.08% vs 6.91%, $P < .001$). There was no significant difference in the seasonal prevalence rate of self-reported CU (women 57.81% vs men 57.48, $P = .97$) and the positive rate of skin prick test (SPT) (women 51.35% vs men 43.84, $P = .46$) between different sexes.

3.2. The relationship between self-reported CU and seasons

3.2.1. Onset of self-reported CU and pollen count in seasons. The results showed that there were 2 peaks of pollen dispersal in grasslands of northern China: April and August; the 2 peaks of CU were in April to May and July to August (Fig. 1) or (Supplemental Digital Content: Table S1, <http://links.lww.com/MD/F210>).

3.2.2. Comparison of the positive rate of pollen SPT. The positive rate of pollen SPT in CU with seasonal or seasonal aggravation of symptoms (seasonal or seasonal aggravation) was

Table 1
Characteristics of the study subjects.

Characteristic	Total	Chronic urticaria		P value
		Yes	No	
	3406	191(5.61)	3215 (94.39)	
Gender, n (%)				
Male	1568	64 (4.08)	1504 (95.92)	<.001
Female	1838	127 (6.91)	1711 (93.09)	
Age, n (%)				
18–39	1418	85 (5.99)	1333 (94.01)	.13
40–59	1475	87 (5.90)	1388 (94.10)	
≥60	513	19 (3.70)	494 (96.30)	
Race, n (%)				
Han	1969	109 (5.54)	1860 (94.46)	.95
Mongolian	1305	74 (5.67)	1231 (94.33)	
Others	132	8 (6.06)	124 (93.94)	
Degree of education				
Below primary school	199	5 (2.51)	194 (97.49)	<.01
Primary school	521	25 (4.80)	496 (95.20)	
Middle school	1436	70 (4.87)	1366 (95.13)	
University degree or above	1250	91 (7.28)	1159 (92.72)	
Area of residence, n (%)				
Urban	1644	112 (6.81)	1532 (93.19)	<.01
Rural	1762	79 (4.48)	1683 (95.52)	
Family allergy history, n (%)				
Yes	1063	98 (9.22)	965 (90.78)	<.001
No	2240	88 (3.93)	2152 (96.07)	
Unknown	103	5 (4.85)	98 (95.15)	

Chi-square test was performed in this table.

44.55%, and that of in CU free of symptom was 41.43%, and there was no significant difference ($P = .51$). There was also no significant difference between seasonal or seasonal aggravation CU and CU without seasonal aggravation symptoms (Perennial) (44.55% vs 49.38%, $P = .51$) (Table 3).

3.3. Analysis of suspected risk factors of self-reported CU

For investigation of potential risk factors, 29 independent variables were selected and the independent variables without significant role were excluded (factors that had no significant include age, race, heating ways, pet keeping, history of previous surgery, vaccination allergy history, multiple use of antibiotics, hypertension, heart disease, diabetes, apoplexy, asthma, etc) (Supplemental Digital Content: Table S2, <http://links.lww.com/>

Table 2
Comparison of the prevalence of chronic urticaria in different gender.

Gender	Male	Female	χ^2 value	P value
CU, n (%)				
Yes	64 (4.08)	127 (6.91)	12.785	<.001
No	1504 (95.92)	1711 (93.09)		
CU with seasonal or seasonal aggravation of symptoms, n (%)				
Yes	37 (57.81)	73 (57.48)	0.002	.97
No	27 (42.19)	54 (42.52)		
CU with seasonal or seasonal aggravation of symptoms, n (%)				
Positive skin prick test	19 (51.35)	32 (43.84)	0.558	.46
Negative skin prick test	18 (48.65)	41 (56.16)		

Chi-square test was performed in this table.

CU = chronic urticaria.

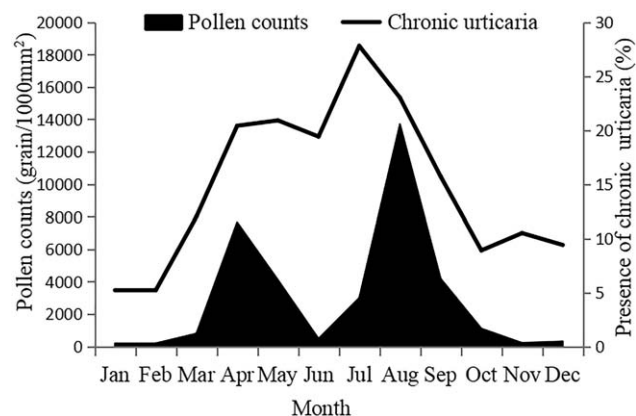


Figure 1. The prevalence of chronic urticaria and pollen counts in adults.

MD/F210). Logistic analysis was able to show 17 kinds of related factors of CU (sex, level of education, residence, outdoor activity time, smoking habit, family history, eczema, history of food allergy, history of drug allergy, AR, conjunctivitis, sleepiness, fatigue, oral ulcer, diarrhea, constipation, abdominal pain, etc) (Supplemental Digital Content: Table S3, <http://links.lww.com/MD/F210>), and 6 of them were further confirmed by multivariate logistic regression analysis (Table 4). The results showed that women had a higher risk of CU than men (OR = 1.511, 95% CI 1.098–2.080, $P = .01$); patients with family history of allergic diseases had higher risk of disease than those without family history (OR = 1.800, 95% CI 1.311–2.471, $P < .001$); the risk of chronic diarrhea was higher than that of non-diarrhoea (OR = 2.486, 95% CI 1.366–4.526, $P < .01$), and there was no difference between those who had diarrhea occasionally and those without diarrhea (OR = 1.540, 95% CI 0.974–2.433, $P = .07$); the risk of disease was increased in patients with food allergy (OR = 1.890, 95% CI 1.303–2.740, $P < .01$); the risk of conjunctivitis and eczema were higher than those without the disease (OR = 1.749, 95% CI 1.276–2.396, $P < .01$; OR = 2.807, 95% CI 1.933–4.076, $P < .001$) (Table 4).

4. Discussion

The prevalence rates of CU were different in different parts of the world. For example, the prevalence rate in Spain and Poland was 0.6%,^[13,14] that of Taiwan was 0.79%,^[6] and that of South Korea was 3.08%.^[7] The prevalence of self-reported CU in adults in this survey was 5.61% and the seasonal incidence was 57.59%. This survey found that women had a higher prevalence rate than men, with a risk of about 1.511 times as much as men, which was consistent with some reports.^[7,14,15] It was possible that CU was related to autoimmune mechanisms, and autoimmune diseases were frequently associated with women.

The etiology of CU was complicated, and pollen sensitization was determined as etiologic factors of CSU.^[16] In this study, the relationship between seasonal onset with CU and pollen quantity in different seasons showed that there were 2 peaks of pollen dispersal in April and August; the 2 peaks of CU were in April to May and July to August, and that was to say pollen dispersal season was basically consistent with the peak season of CU. It seemed that pollen allergen was the causative factor of CU. However, further analysis showed that there was no significant

Table 3
Comparison of the positive rate of pollen skin prick test.

CU	Pollen allergen positive SPT, n (%)	Pollen allergen negative SPT, n (%)	χ^2 value	P value
Seasonal or seasonal aggravation	49 (44.55)	61 (55.45)	0.425	.51
Free of symptom	1332 (41.43)	1883 (58.57)		
Perennial	40 (49.38)	41 (50.62)	2.056	.15
Free of symptom	1332 (41.43)	1883 (58.57)		
Seasonal or seasonal aggravation	49 (44.55)	61 (55.45)	0.439	.51
Perennial	40 (49.38)	41 (50.62)		

The analysis was performed based on partitions of chi-square method, $\alpha \leq 0.0167$.

CU=chronic urticaria, SPT=skin prick test; with seasonal or seasonal aggravation of symptoms, Seasonal or seasonal aggravation; with perennial and without seasonal aggravation symptoms, Perennial.

difference in the positive rate of pollen SPT between seasonal or seasonal aggravation and free of symptom in CU, as well as between seasonal or seasonal aggravation CU and perennial CU. So the association of onsets of CU and peaks of pollen counts in seasons did not necessarily mean a causative role of pollen allergy in the pathogenesis of CU, although there was a large variety of pollen in grasslands of northern China.^[17] The results again suggested that CU was not a typical type I allergy. Maurer's reported that the aggravating season of CU was in summer, followed by spring, considering the effect of temperature on mast cells.^[18]

At present, there was increasing evidence that CU was associated with chronic inflammatory processes.^[19] In addition, gastrointestinal disease was the most common comorbidity of CU in adults.^[20] This survey analysis found that the risk of CU in patients with chronic diarrhea was significantly higher than that of non-diarrhea (OR=2.486, $P < .01$), and there was no difference between occasional diarrhea and non-diarrhea (OR=1.540, $P = .07$), which further confirmed these points. This survey analysis also found that people with history of food allergies were 1.890 times as much as those without history of food allergy ($P < .01$), suggesting that screening and effective avoidance of food allergen in those with history of food allergies could help reduce the risk of CU; people with conjunctivitis and eczema both increased the risk of CU (OR=1.749, OR=2.807, $P < .01$), considering that there were the common allergens related to them^[21]; similar to many other allergic diseases, family history of allergy was still a risk factor for CU (OR=1.800, $P < .01$). An investigation based on a large community medical database showed a significant relationship between CU and hypertension or diabetes.^[19] Egeberg et al^[22]

found cardiovascular risk was not increased in patients with CU. In this survey based on natural populations in grasslands of northern China, whether in univariate analysis or multivariate analysis, no direct evidence of increased risk of CU was found in hypertension and diabetes, as well as heart and lung disease and stroke. The differences of results might be related to the difference in the survey population. This investigation was only a cross-sectional study currently, and the diagnosis of CU was based on questionnaires, which was retrospective and self-reported by respondents, therefore these results could be subject to recall and diagnosis bias. But the diagnosis of self-reported CU was made based on common symptoms, and the strict clinical diagnosis of CU also adopts symptom diagnosis. Therefore, although the diagnosis of CU in this study was biased, it was relatively small. Meanwhile, this study investigated the prevalence of CU in the past year, and the time span was not large, so the review bias of patients was small. What's more, the number of 3406 residents was still considerable, and it came from the natural population in grasslands of northern China, so the characteristics and regularity of the disease still had some reference value.

In summary, family allergy history, food allergy history, chronic diarrhea, conjunctivitis, and eczema were closely related to self-reported CU. As this survey was a cross-sectional study, the causal relationship between CU and them was still unclear and needed further study. However, no matter who was the cause or the effect, strengthening the prevention and treatment of chronic diarrhea, conjunctivitis and eczema in the crowd, as well as the detection of food allergens were undoubtedly of certain clinical significance to reduce and control the occurrence of CU symptoms.

Table 4
Multivariate logistic regression analysis of suspected risk factors of chronic urticaria.

Risk factors	P value	OR value	95% CI
Gender	.01	1.511	1.098–2.080
Diarrhea	<.01		
Occasional	.07	1.540	0.974–2.433
Chronic	<.01	2.486	1.366–4.526
Eczema	<.001	2.807	1.933–4.076
History of food allergy	<.01	1.890	1.303–2.740
Family allergy history	<.01		
Yes	<.001	1.800	1.311–2.471
Unknown	.82	1.114	0.436–2.844
Conjunctivitis	<.01	1.749	1.276–2.396

The analysis was performed based on logistic regression.

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