

Prevalence of uncontrolled allergic rhinitis in Wuhan, China: A prospective cohort study

Youna Wang, Ph.D.,^{1,2,3} Rongfei Zhu, M.D.,¹ Guanghui Liu, M.D.,¹ Wenjing Li, M.D.,¹ Hao Chen, Ph.D.,¹ Jean-Pierre Daurès, Ph.D.,³ Anca Mirela Chiriac, M.D.,^{2,4} and Pascal Demoly, M.D., Ph.D.^{2,3,4}

ABSTRACT

Background: Allergic rhinitis (AR) is a highly prevalent disease that affects the quality of life, especially in the “severe chronic upper airway disease” (SCUAD) group of patients who still have severe symptoms after adequate treatment. This study investigated the prevalence of uncontrolled AR and SCUAD consulting in the Allergy Department of Tongji Hospital, Wuhan, China.

Methods: In this prospective cohort study, all patients consulting for AR were prospectively assessed using visual analog scale (VAS) and Allergic Rhinitis Control Test (ARCT) and put on standardized treatment based on the Allergic Rhinitis and Its Impact on Asthma (ARIA) guidelines. After 15 days, they were reevaluated by a telephone interview using a numerical scale (NS) and ARCT. A score of ARCT of <20 defined uncontrolled AR and a score of NS of ≥ 5 at day 15 defined SCUAD patients.

Results: A total of 252 patients were included. Moderate/severe AR (VAS ≥ 5) was diagnosed in 82.9% of the patients which had an impact on sleep (86.9%), work life (84.9%), social activities (81%), and physical activities (90.1%). Patients with uncontrolled AR (27.7%) at day 15 more frequently presented a higher weight ($p = 0.042$), history of ear, nose, and throat (ENT) infection or antibiotics intake for respiratory infection in the last 12 months (62.3% versus 45.6%; $p = 0.018$), smoking (15.9% versus 6.7%; $p = 0.024$), and smell disturbance (26.1% versus 11.7%; $p = 0.005$). Patients with SCUAD (24.5%) more frequently presented a history of ENT infection or antibiotics intake for respiratory infection in the last 12 months (63.9% versus 45.7%; $p = 0.014$) and smell disturbance (27.9% versus 11.7%; $p = 0.003$), and less commonly had atopic dermatitis (13.1% versus 28.2%; $p = 0.017$).

Conclusion: Uncontrolled AR and SCUAD patients are numerous. VAS and ARCT are simple and quantitative methods and self-completion questionnaires that can be used for a global evaluation of the severity and control of AR.

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Allergic rhinitis (AR) is a common disease worldwide affecting up to 40% of the population in young adults in Europe and its prevalence is increasing.¹ In China, its prevalence was shown to vary from 8.7 to 24.1% according to a cross-sectional, population-based study in 11 major cities.²

Although AR is not a severe disease, it substantially affects work and school productivity, social functioning, and the quality of sleep besides the classic symptoms of sneezing, rhinorrhea, and nasal obstruction.^{3–5} The majority of patients suffering from AR consult their general practitioner first.^{6–7} In China, patients are allowed to consult the specialist directly.

The treatment of AR is now well established^{3,8} and most patients respond well to the treatment. However, some do not, leading to the concept of severe chronic upper airway disease (SCUAD).⁹ These patients have uncontrolled AR despite optimal maximum treatment. Severity can be measured in treatment-naïve patients as proposed by the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines³ but, by definition, the concept of disease control is only applicable in treated patients.¹⁰ The Allergic Rhinitis Control Test (ARCT) can be used to evaluate the control level of AR.^{11,12} In the national French survey validating the ARCT instrument, 14.9% of the 902 AR patients were not controlled after 15 days of treatment.¹¹ Poor disease control may be related to suboptimal treatment, poor treatment compliance, and psychosocial factors and treatment-resistant AR. Both severity and control can be measured in different ways, with both objective and subjective

measurements and patient-reported outcomes versus physician-reported outcomes. Patients with SCUAD often present uncontrolled nasal and/or ocular symptoms and impaired quality of life. In a randomized European trial, it was found that 10–20% of patients with AR consulting a specialist have SCUAD.¹⁰ In China, there are insufficient epidemiological data regarding uncontrolled AR and SCUAD.

The present prospective study, therefore, aimed to assess the prevalence and the characteristics of patients with uncontrolled AR and SCUAD in a university hospital allergy unit in Wuhan, China.

METHODS

Patients

A total of 252 patients aged 18–75 years were consecutively included in the study after written informed consent was obtained and after approval of the Ethics Committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, China. Y. Wang and R. Zhu contributed equally to this work. All patients fulfilled the following inclusion criteria: (1) patients had a history of AR for at least the past 2 years and presented at least two clinical symptoms of AR (rhinorrhea, nasal congestion, sneezing, and/or nasal itching) at inclusion, (2) patients had positive skin-prick tests to aeroallergens and/or serum-specific IgE levels (Thermo Fisher Scientific Phadia CAP System, phadiaAB, Uppsala, Sweden), (3) patients should not have received allergen immunotherapy or been treated with antihistamines during the last week, (4) patients should not have an infection of the upper airway and have finished necessary antibiotics intake in >14 days or a viral infection of >7 days, and (5) patients should not have chronic sinusitis and purulent discharge. Patients were categorized as having intermittent, persistent, mild, or moderate-to-severe AR according to the ARIA classification.^{3,8}

Study Design

This epidemiological study was a prospective cohort study designed to investigate the prevalence of uncontrolled AR and SCUAD

From the ¹Department of Allergy, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, ²Allergy Unit, Hôpital Arnaud de Villeneuve, University Hospital of Montpellier, Montpellier, France, ³Laboratoire de Biostatistique, d'Epidémiologie et de Santé Publique, IURC, EA2415, Montpellier, France, and ⁴EPAR-IPLESP, Sorbonne Universités, Paris, France

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Address correspondence Pascal Demoly, M.D., Ph.D., Hôpital Arnaud de Villeneuve, University Hospital of Montpellier and Sorbonne Universités, IPLESP EPAR-UPMC, UMR-S 1136, Paris, 34295 Montpellier Cedex 5, France

E-mail address: pascal.demoly@inserm.fr

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in the Allergy Department of Tongji University Hospital of Wuhan, China, and to describe their characteristics. The patients were enrolled during 1 year (August 2011 to July 2012). Physicians completed a general questionnaire on the consultation day including contact information, sociodemographic data, rhinitis symptoms, diagnostic history, concomitant diagnosed pathologies (such as asthma, upper respiratory tract infections, sinusitis, and nasal polyps), and AR treatments. For each patient, symptoms of AR and their impacts were scored by visual analog scale (VAS) levels and AR control by treatment measured by the ARCT.¹¹ Scores were assessed before and at the end of the 2-week treatment period. Physicians followed a simple treatment based on the ARIA guidelines³ using a VAS score to assess severity.

Outcome Measures

Visual Analog Scale. The severity of all combined symptoms was assessed using a VAS ranged from 0 (no symptoms) to 10 cm (maximal imaginable symptoms).¹² Patients were asked to mark the line at the location that they found appropriate to best describe the severity of the symptoms they experienced at baseline. Patients were also asked to rate the severity of their symptoms by a telephone interview using a numeric scale (NS) ranging from “0” (no symptoms) to “10” (maximum imaginable symptoms) after 15 days of treatment. Patients with a baseline VAS level of <5 cm were considered as having “mild” AR, whereas a VAS level of ≥ 5 cm was equated with “moderate-to-severe” AR.¹³

Allergic Rhinitis Control Test. ARCT is a self-completion questionnaire on the control of AR validated by Demoly *et al.*¹¹ It is made up of five questions ranging from 1 to 5, and these scores were then added up to obtain a score ranging from 5 to 25 (best score). A Chinese version of ARCT was obtained after a translation-back translation process.¹⁴

Uncontrolled AR. Uncontrolled AR was defined by the score of ARCT after 15 days of treatment. Patients with a score of ARCT of <20 were considered as having uncontrolled AR at day 15.¹¹

Significant Improvement in Symptoms. A change between VAS (day 0) and NS (day 15) of ≥ 2.5 was considered a significant improvement in symptoms.^{11,15,16} Patients whose initial VAS score was ≤ 2 were considered as having a significant improvement in symptoms if they had an NS score equal to 0 at day 15.

Severe Chronic Upper Airway Disease. SCUAD defines those patients who have poor control of symptoms despite adequate guideline-directed pharmacotherapy.⁹ For this study, patients who presented an NS score at day 15 of ≥ 5 were considered SCUAD patients.

Statistical Analysis

Qualitative variables such as demographic data and symptoms were expressed in percentages and frequencies. Quantitative data were expressed as means and SDs. Medians and 25th–75th percentiles defined quantitative not normally distributed data. Comparisons for the qualitative data such as patient characteristics were performed between groups by using χ^2 . Comparisons of quantitative variables were made by using nonparametric Mann–Whitney *U* test and Wilcoxon test. Correlations between ARCT and VAS were examined using Spearman’s rank test. A binary logistic regression was performed to evaluate possible risk factors for SCUAD, uncontrolled AR, and insignificant improvement in symptoms. Only factors associated ($p < 0.15$) with the outcome were included in this model. The analysis was performed with SPSS Version 11.5 software (SPSS, Inc., Chicago, IL) with the significance level set at 5% (0.05). Based on published data,² we expected a prevalence of AR in Wuhan of around 20%. Considering that only 10% of patients with AR would be uncontrolled, with a margin of error of 5% and a confidence interval of 95%, a sample of at least 126 participants was required. To account for an adjustment of 10% for nonresponse, a minimum of 139 participants was finally estimated.

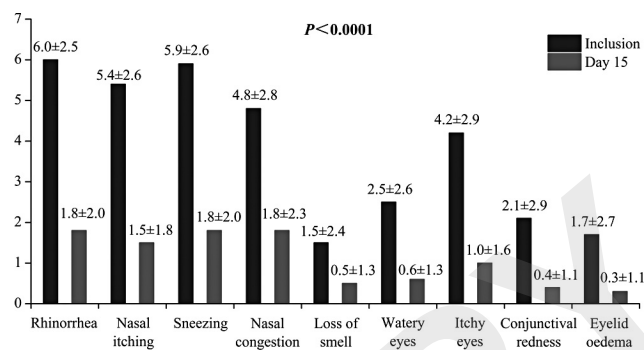


Figure 1. Improvement of nasal and ocular symptoms (mean $\pm$ SD).

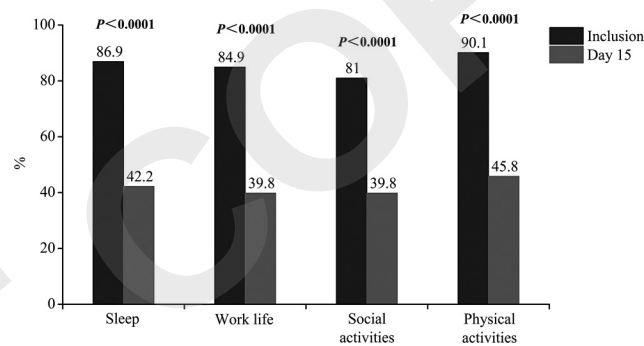


Figure 2. Improvement of impact of allergic rhinitis on sleep, work life, and social and physical activities.

RESULTS

Patient Characteristics

Two hundred fifty-two patients were recruited by eight allergists from the Allergy Department of Tongji Hospital. Three patients could not be contacted by telephone after 15 days and, therefore, 249 patients were analyzed at day 15. Of these patients, the mean (SD) age was 32 ± 18 years; 103 (41%) were men and the mean (SD) age was 30 ± 10.9 years. Mean weight, height, and body mass index, respectively, were 58 ± 13 kg, 164 ± 10 cm, and 21.3 ± 3.1 kg/m². Twenty patients (7.9%) had postgraduate degrees, 95 patients (37.7%) had bachelor degrees, and 137 patients (54.4%) had undergraduate degrees. Among them, 191 (75.8%) lived in the city, 47 (18.7%) in the suburbs, and 14 (5.6%) in a mountainous area. Twenty-four patients (9.5%) were smokers. All patients had a diagnosis of sensitization to aeroallergens determined by skin-prick tests (96% of patients with a documented diagnosis) and/or serum allergen-specific IgE (53.6% of patients with a documented diagnosis). The first symptoms of their rhinitis appeared at a mean of 17 years before the consultation; 38.1% presented a family history of atopy, rhinitis for 27.8%, asthma for 11.5%, and atopic dermatitis for 5.2%. Similarly, 43.7% had personal history of atopic dermatitis (24.6%) and asthma (24.2%). One-half of them (50%) had a history of ear, nose, and throat (ENT) infection or antibiotics intake for respiratory infection in the last 12 months. Sneezing (99.2%), rhinorrhea (98.9%), nasal itching (96.8%), nasal congestion (92.9%), and itchy eyes (88.9%) commonly presented. Ocular symptoms were also commonly presented by most patients (65.9%), followed by nasal deformity (31.7%), rhinosinusitis (21.4%), and smell disturbance (15.9%). AR affected sleep in 86.9% of patients, work life in 84.9%, social activities in 81%, and physical activities in 90.1%. Mild intermittent rhinitis (according to ARIA) was diagnosed in 6 patients (2.4%), mild persistent rhinitis was diagnosed in 7 (2.8%), moderate/severe intermittent rhinitis was diagnosed in 35 (13.9%), and moderate/severe persistent rhinitis was diagnosed in 204 (81%).

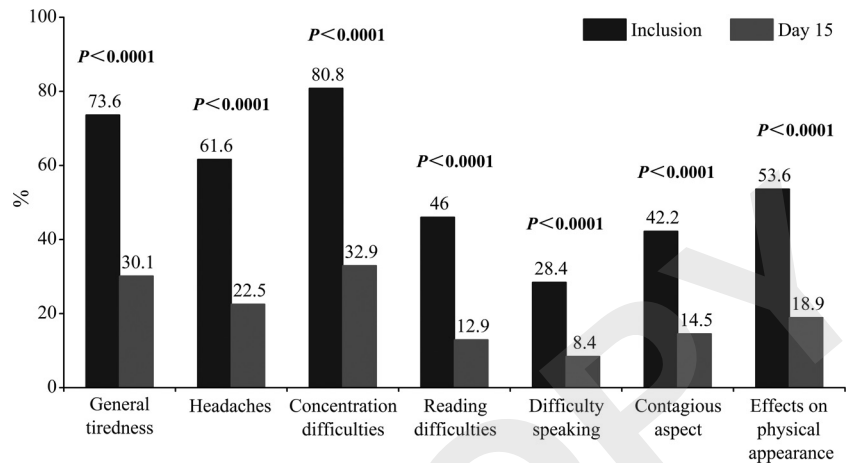


Figure 3. Improvement of impact of allergic rhinitis on overall discomfort.

patients. On the consultation day, all 249 patients were receiving H₁-antihistamines (87.6% of cases were oral administration, 1.6% were nasal administration, and 10.8% were both routes of administration); 210 patients (84.3%) were receiving corticosteroids (97.6% nasal and 2.4% oral); 156 patients (62.7%) were being treated with ocular antihistamines, 74 patients (29.7%) with an antileukotriene, and 28 patients (11.2%) with other treatments.

Evolution of Patients under Treatment

Patients received treatment as an oral antihistamine in 98.4% of cases, in association with local corticosteroids in 81.1% of cases.

Assessed on VAS at inclusion and NS on the 15th day, all nasal and ocular symptoms were reduced dramatically ($p < 0.0001$; Fig. 1). This reduction in symptomatology was accompanied by a very important improvement of impact of AR on sleep, work life, and social and physical activities (Fig. 2), as well as on the overall discomfort (Fig. 3).

Comparison of Patients with Mild versus Moderate/Severe AR According to VAS

At inclusion, the comparisons of patients with mild (VAS score of <5) and moderate/severe (VAS score of ≥ 5) AR are presented in Table 1. No difference was found for age, gender, height, weight, education, residential area, or smoking. There was, however, greater moderate/severe persistent AR according to the ARIA in the moderate/severe (VAS score of ≥ 5) group (87.6% versus 48.8%; $p < 0.001$) and, in this group, allergic conjunctivitis and the most impacts of AR, such as sleep, work life, social activities, and physical activities were significantly more common ($p < 0.001$). Treatment with nasal corticosteroid was more frequent and the number of SCUAD was significantly greater in patients with moderate/severe AR at inclusion ($p < 0.001$). Patients receiving nasal antihistamines were more common in the mild (VAS score of <5) group (46.3 versus 5.8%; $p < 0.001$).

Prevalence and Characteristics of SCUAD Patients

Twenty-four and one-half percent of the patients had SCUAD ($n = 61/249$). A history of ENT infection or antibiotics intake for respiratory infection in the last 12 months; smell disturbance; and impact of AR on sleep, work life, social activities, and physical activities were more frequently present in patients with SCUAD, whereas history of atopic dermatitis was less common ($p < 0.05$; Table 2). Patients with SCUAD were less frequently treated with antileukotriene (4.9% versus 37.8%; $p < 0.001$), and nasal corticosteroid and other drugs were more frequently received (93.4% versus 78.7%; $p = 0.009$). Almost all of them had uncontrolled AR according to ARCT at day 15 (Table 2). In the multivariate analysis, treatment with oral corticosteroid, treat-

ment with "others," and smell disturbance were positively associated with SCUAD (Table 3).

Characteristics of Patients According to ARCT

The mean ARCTs were 14 ± 3.3 and 21 ± 4.0 at days 0 and 15, respectively. ARCT of ≥ 20 patients at inclusion were 4.8 and 72.3% after 15 days of treatment (Table 2). Correlations between ARCT and VAS (Table 4) were poor on the consultation day ($r = -0.482$; $p < 0.001$) but significantly stronger after 15 days of treatment ($r = -0.884$; $p < 0.001$). Similar findings were observed for the change between consultation day and day 15 ($r = 0.588$; $p < 0.001$). At day 15, patients with uncontrolled AR had higher weight ($p = 0.042$) and were more often smokers (15.9% versus 7.0%; $p = 0.024$); they frequently presented a smell disturbance; moderate/severe persistent rhinitis according to ARIA; history of ENT infection or antibiotics intake for respiratory infection in the last 12 months and impact of their AR on sleep, work life, social activities, and physical activities ($p < 0.05$; Table 2). Patients with uncontrolled AR more frequently received other drugs (27.5% versus 5.0%; $p < 0.001$), but fewer were being treated with antileukotriene than patients with controlled AR (7.2% versus 38.3%; $p < 0.001$). The number of SCUAD was significantly greater in patients with uncontrolled AR (84.1% versus 1.7%; $p < 0.001$). Impact of AR on work life (odds ratio [OR] = 9.409), treatment with oral corticosteroid (OR = 15.772), and treatment with "others" (OR = 6.826) were significant risk factors for uncontrolled AR (Table 3).

Characteristics of Patients According to Clinically Significant versus Insignificant Improvement of Symptoms

Thirty-four and one-half percent of the patients had insignificant improvement in symptoms at day 15. Most of them had postgraduate degrees (12.8% versus 5.54%; $p = 0.045$), whereas less of them had bachelor degrees (29.1% versus 42.3%; $p = 0.040$). Moreover, they frequently presented a smell disturbance (22.1% versus 12.3%; $p = 0.043$) and were more frequently treated with other drugs (20.9% versus 6.1%; $p < 0.001$), and less of them received antileukotrienes (4.7% versus 42.9%; $p < 0.001$). The number of controlled AR at day 15 was significantly less (32.6% versus 93.3%; $p < 0.001$). In the multivariate analysis, treatment with "others" presented the strong association with patients who had significant improvement in symptoms (Table 3).

DISCUSSION

The prevalence of AR has increased in recent years worldwide. However, little epidemiological data have been published for AR in

Table 1 Characteristics of patients with mild and moderate/severe AR (as defined by VAS) at inclusion

	Mild AR (VAS <5)	Moderate/Severe AR (VAS ≥5)	p Value*
Number	43 (17.1)	209 (82.9)	
Age (yr)	30 ± 16.0	32 ± 18.0	0.729
Duration of the rhinitis (yr)	14 ± 11.0	16 ± 10.0	0.183
Height (cm)	163 ± 10.0	164 ± 10.0	0.863
Weight (kg)	58.5 ± 10.1	58 ± 13.0	0.834
Body mass index (kg/m ²)	21.3 ± 2.5	21.4 ± 3.0	0.821
Male gender	21 (48.8)	82 (39.2)	0.243
Education			
Postgraduate	4 (9.3)	16 (7.7)	0.957
Bachelor	15 (34.9)	80 (38.3)	0.676
Undergraduate	24 (55.8)	113 (54.1)	0.834
Residential area			
City	33 (76.7)	158 (75.6)	0.873
Suburbs	7 (16.3)	40 (19.1)	0.661
Mountainous area	3 (7.0)	11 (5.3)	0.935
Smoking	6 (14.0)	18 (8.6)	0.423
History of atopic dermatitis	12 (27.9)	50 (23.9)	0.581
Family history of allergic diseases	14 (32.6)	82 (39.2)	0.412
History of asthma	12 (27.9)	49 (23.4)	0.534
History of ENT infection or antibiotics intake for respiratory infection in the last 12 mo	20 (46.5)	106 (50.7)	0.615
Recurrent rhinosinusitis	12 (27.9)	42 (20.1)	0.256
Nasal deformities	9 (20.9)	71 (34)	0.094
Allergic conjunctivitis	18 (41.9)	148 (70.8)	<0.001
Smell disturbance	4 (9.3)	36 (17.2)	0.195
Rhinitis graded according to ARIA			
Mild intermittent	5 (11.6)	1 (0.5)	<0.001
Mild persistent	6 (14.0)	1 (0.5)	<0.001
Moderate/severe intermittent	11 (25.6)	24 (11.5)	0.015
Moderate/severe persistent	21 (48.8)	183 (87.6)	<0.001
Impact of AR on sleep	25 (58.1)	194 (92.8)	<0.001
Impact of AR on work life	22 (51.2)	192 (91.9)	<0.001
Impact of AR on social activities	25 (58.1)	179 (85.6)	<0.001
Impact of AR on physical activities	32 (74.4)	195 (93.3)	<0.001
Optimal treatment#§	36 (87.8)	194 (93.3)	0.377
Treatment at inclusion§			
Oral antihistamines	41 (100)	204 (98.1)	1.000
Nasal corticosteroid	5 (12.2)	200 (96.2)	<0.001
Ocular antihistamines	20 (48.8)	136 (65.4)	0.045
Antileukotrienes	14 (34.1)	60 (28.8)	0.497
Nasal antihistamines	19 (46.3)	12 (5.8)	<0.001
Oral corticosteroid	0 (0)	5 (2.4)	0.595
Others	1 (2.4)	27 (13.0)	0.092
Controlled at inclusion (day 0):			
According to ARCT	9 (20.9)	3 (1.4)	<0.001
Controlled at day 15§			
According to ARCT	37 (90.2)	143 (68.8)	0.005
SCUAD§	1 (2.4)	60 (28.8)	<0.001

Data are presented as number (percentage) or means ± SD, unless otherwise specified.

*The χ^2 and Wilcoxon–Mann–Whitney test were used for qualitative and quantitative variables.

#The treatment was considered as "optimal" if mild AR (VAS score at day 0, <5) received treatment with oral antihistamines and moderate-to-severe AR (VAS score at day 0, ≥5) received treatment with oral antihistamines and nasal corticosteroid.

§Three patients were lost for follow-up and therefore 249 patients were analyzed at day 15.

AR = allergic rhinitis; ARIA = Allergic Rhinitis and its Impact on Asthma; ARCT = Allergic Rhinitis Control Test; ENT = ear, nose, and throat; SCUAD = severe chronic upper airway disease; VAS = visual analog scale.

China. Zhang *et al.*² reported the self-reported prevalence of AR in Wuhan (16- to 65-year-old general population) was 19.3%. Kong *et al.*¹⁷ reported the prevalence of AR in 3- to 6-year-old children in Wuhan was 24.1%, and 10.8% were confirmed by skin tests. Moreover, the prevalence of positive nasal symptoms was still high at 29.4% after

5-year follow-up.¹⁸ As a major industrial city of China with >8 million inhabitants, Wuhan has a high prevalence of AR and its impact on patient quality of life should be substantial but has never been evaluated.

AR has long been classified into intermittent and persistent rhinitis according to symptom duration and mild to moderate/severe rhinitis

Table 2 Characteristics of the patients in the different groups at day 15 (SCUAD vs non-SCUAD, controlled AR vs uncontrolled AR, significant improvement in symptoms vs insignificant improvement in symptoms)

	SCUAD	Non-SCUAD	p Value*	Controlled AR (ARCT ≥20)	Uncontrolled AR (ARCT <20)	p Value*	Significant Improvement in Symptoms	Insignificant Improvement in Symptoms	p Value*
Number	61 (24.5)	188 (75.5)	—	180 (72.3)	69 (27.7)	—	163 (65.5)	86 (34.5)	—
Age (yr)	32 ± 19.0	32 ± 18.0	0.664	32 ± 17.0	32 ± 18.0	0.799	32 ± 17.0	32 ± 17.0	0.660
Duration of the rhinitis (yr)	16 ± 10.5	16 ± 10.0	0.778	16 ± 10.0	16 ± 10.5	0.863	16 ± 9.0	15.5 ± 10.0	0.842
Height (cm)	165.4 ± 7.9	163.5 ± 10.0	0.813	163 ± 10.0	165 ± 11.5	0.403	164 ± 10.0	164.5 ± 12.0	0.443
Weight (kg)	60 ± 19.0	57.8 ± 14.0	0.248	57 ± 13.8	60 ± 17.0	0.042	58 ± 13.0	58 ± 17.0	0.657
Body mass index (kg/m ²)	21.6 ± 3.4	21.4 ± 2.7	0.435	21.3 ± 2.7	21.7 ± 3.4	0.093	21.4 ± 2.8	21.5 ± 3.1	0.418
Male gender	25 (41.0)	77 (41.0)	0.997	71 (39.4)	31 (44.9)	0.431	68 (41.7)	34 (39.5)	0.739
Education									
Postgraduate	8 (13.1)	12 (6.4)	0.159	11 (6.1)	9 (13.0)	0.072	9 (5.5)	11 (12.8)	0.045
Bachelor	20 (32.8)	74 (39.4)	0.357	70 (38.9)	24 (34.8)	0.550	69 (42.3)	25 (29.1)	0.040
Undergraduate	33 (54.1)	102 (54.3)	0.983	99 (55.0)	36 (52.2)	0.689	85 (52.1)	50 (58.1)	0.367
Residential area									
City	44 (72.1)	145 (77.1)	0.428	141 (78.3)	48 (69.6)	0.148	124 (76.1)	65 (75.6)	0.931
Suburbs	14 (23.0)	32 (17.0)	0.300	28 (15.6)	18 (26.1)	0.055	29 (17.8)	17 (19.8)	0.702
Mountainous area	3 (4.9)	11 (5.9)	1.000	11 (6.1)	3 (4.3)	0.816	10 (6.1)	4 (4.7)	0.846
Smoking	7 (11.5)	16 (8.5)	0.487	12 (6.7)	11 (15.9)	0.024	13 (8.0)	10 (11.6)	0.344
History of atopic dermatitis	8 (13.1)	53 (28.2)	0.017	48 (26.7)	13 (18.8)	0.199	42 (25.8)	19 (22.1)	0.522
Family history of allergic diseases	28 (45.9)	67 (35.6)	0.152	66 (36.7)	29 (42.0)	0.436	56 (34.4)	39 (45.3)	0.090
History of asthma	14 (23.0)	45 (23.9)	0.875	46 (25.6)	13 (18.8)	0.265	39 (23.9)	20 (23.3)	0.906
History of ENT infection or antibiotics intake for respiratory infection in the last 12 mo	39 (63.9)	86 (45.7)	0.014	82 (45.6)	43 (62.3)	0.018	78 (47.9)	47 (54.7)	0.308
Recurrent rhinosinusitis	15 (24.6)	38 (20.2)	0.468	39 (21.7)	14 (20.3)	0.812	32 (19.6)	21 (24.4)	0.380
Nasal deformities	25 (41.0)	54 (28.7)	0.074	55 (30.6)	24 (34.8)	0.521	52 (31.9)	27 (31.4)	0.935
Allergic conjunctivitis	42 (68.9)	123 (65.4)	0.623	119 (66.1)	46 (66.7)	0.934	108 (66.3)	57 (66.3)	0.997
Smell disturbance	17 (27.9)	22 (11.7)	0.003	21 (11.7)	18 (26.1)	0.005	20 (12.3)	19 (22.1)	0.043
Rhinitis graded according to ARIA									
Mild intermittent	0 (0)	6 (3.2)	0.351	6 (3.3)	0 (0)	0.191	4 (2.5)	2 (2.3)	1.000
Mild persistent	0 (0)	7 (3.7)	0.279	7 (3.9)	0 (0)	0.217	5 (3.1)	2 (2.3)	1.000
Moderate/severe intermittent	4 (6.6)	31 (16.5)	0.052	30 (16.7)	5 (7.2)	0.056	27 (16.6)	8 (9.3)	0.117
Moderate/severe persistent	57 (93.4)	144 (76.6)	0.004	137 (76.1)	64 (92.8)	0.003	127 (77.9)	74 (86.0)	0.122
Impact of AR on sleep	58 (95.1)	158 (84.0)	0.027	151 (83.9)	65 (94.2)	0.032	141 (86.5)	75 (87.2)	0.876
Impact of AR on work life	61 (100)	150 (79.8)	<0.001	143 (79.4)	68 (98.6)	<0.001	134 (82.2)	77 (89.5)	0.126
Impact of AR on social activities	56 (91.8)	145 (77.1)	0.012	138 (76.7)	63 (91.3)	0.009	130 (79.8)	71 (82.6)	0.594
Impact of AR on physical activities	60 (98.4)	164 (87.2)	0.012	156 (86.7)	68 (98.6)	0.005	145 (89.0)	79 (91.9)	0.469
Optimal treatment	55 (90.2)	175 (93.1)	0.639	167 (92.8)	63 (91.3)	0.695	150 (92.0)	80 (93.0)	0.778
Classification of treatment									
Oral antihistamines	60 (98.4)	185 (98.4)	1.000	177 (98.3)	68 (98.6)	1.000	160 (98.2)	85 (98.8)	1.000
Nasal corticosteroid	57 (93.4)	148 (78.7)	0.009	143 (79.4)	62 (89.9)	0.054	141 (86.5)	64 (74.4)	0.017
Ocular antihistamines	43 (70.5)	113 (60.1)	0.145	110 (61.1)	46 (66.7)	0.417	105 (64.4)	51 (59.3)	0.428
Antileukotriene	3 (4.9)	71 (37.8)	<0.001	69 (38.3)	5 (7.2)	<0.001	70 (42.9)	4 (4.7)	<0.001
Nasal antihistamines	3 (4.9)	29 (15.4)	0.033	27 (15.0)	5 (7.2)	0.102	21 (12.9)	11 (12.8)	0.983
Oral corticosteroid	3 (4.9)	2 (1.1)	0.096	2 (1.1)	3 (4.3)	0.132	5 (3.1)	0 (0)	0.167
Others	18 (29.5)	10 (5.3)	<0.001	9 (5.0)	19 (27.5)	<0.001	10 (6.1)	18 (20.9)	<0.001
Controlled at inclusion (day 0)									
According to ARCT	0 (0)	12 (6.4)	0.093	—	—	—	10 (6.1)	2 (2.3)	0.306
Controlled at day 15									
According to ARCT	3 (4.9)	177 (94.1)	<0.001	—	—	—	152 (93.3)	28 (32.6)	<0.001
SCUAD	—	—	—	3 (1.7)	58 (84.1)	<0.001	—	—	—

Data are presented as number (percentage) or means ± SD, unless otherwise specified.

* χ^2 - and Wilcoxon–Mann–Whitney tests were used for qualitative and quantitative variables.

AR = allergic rhinitis; ARIA = Allergic Rhinitis and its Impact on Asthma; ARCT = Allergic Rhinitis Control Test; ENT = ear, nose, and throat; SCUAD = severe chronic upper airway disease.

according to symptom severity impacting daily quality of life. For different types of AR, the ARIA recommends different treatment regimens, which make it easy to apply in clinical practice.³ However, some patients still have very severe symptoms after adequate treatment

according to ARIA guidelines. Bousquet *et al.*⁹ defined this form of the disease as SCUAD and addressed attention to the control of AR patients using simple clinical tools. Our study aim was to investigate the prevalence of SCUAD and uncontrolled AR patients consulting the Allergy

Table 3 Risk factors for SCUAD, uncontrolled AR, and insignificant improvement in symptoms at day 15

Patients' Characteristics	SCUAD			Uncontrolled AR			Insignificant Improvement in Symptoms		
	OR	95% CI	p Value	OR	95% CI	p Value	OR	95% CI	p Value
History of atopic dermatitis	0.257	(0.096–0.688)	0.007	—	—	—	—	—	—
Smell disturbance	2.922	(1.129–7.562)	0.027	—	—	—	—	—	—
Treatment with oral corticosteroid	32.167	(1.847–560.199)	0.017	15.772	(1.594–156.040)	0.018	—	—	—
Treatment with nasal corticosteroid	—	—	—	—	—	—	0.250	(0.104–0.600)	0.002
Treatment with antileukotrienes	0.023	(0.003–0.197)	0.001	0.080	(0.022–0.298)	0.000	0.067	(0.023–0.197)	0.000
Treatment with "others"	6.264	(2.142–18.324)	0.001	6.826	(2.336–19.948)	0.000	4.348	(1.661–11.383)	0.003
Impact of AR on work life	—	—	—	9.409	(1.049–84.427)	0.045	—	—	—

The *p* values of Hosmer and Lemeshow test were 0.508, 0.173, and 0.740.

AR = allergic rhinitis; SCUAD = severe chronic upper airway disease; OR = odds ratio.

Table 4 Correlations between symptoms, impact of AR, VAS, and ARCT

	VAS (total)			ARCT		
	Inclusion	Day 15	Change	Inclusion	Day 15	Change
Nasal symptoms	0.749	0.817	0.634	−0.512	−0.816	0.428
	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001
Ocular symptoms	0.415	0.551	0.279	−0.496	−0.557	0.393
	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001
Impact of sleep	0.504	0.698	0.395	−0.734	−0.708	0.630
	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001
Impact of work	0.559	0.661	0.343	−0.698	−0.668	0.560
	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001
Social activities	0.482	0.597	0.350	−0.642	−0.628	0.522
	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001
Physical activities	0.479	0.667	0.374	−0.669	−0.679	0.509
	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001
Overall discomfort	0.339	0.593	0.202	−0.562	−0.637	0.422
	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001
VAS (total)	—	—	—	−0.482	−0.884	−0.588
	—	—	—	<i>p</i> < 0.0001	<i>p</i> < 0.0001	<i>p</i> < 0.0001

Spearman's rank test.

AR = allergic rhinitis; ARCT = Allergic Rhinitis Control Test; VAS = visual analog scale.

Department of Wuhan University Hospital and determine the characteristics of these patients. In addition to VAS, ARCT are simple tools for assessing AR severity and control. VAS has long allowed the assessment of subjective symptoms such as pain,¹⁹ and it is considered to be a sensitive, robust, and reproducible method of expressing severity and control (although two different concepts) in AR.¹² Bousquet *et al.*¹³ found that a 0- to 10-cm VAS score and the Rhinitis Quality of Life Questionnaire score were significantly correlated. Demoly *et al.*¹¹ showed that the ARCT is a sensitive self-questionnaire to distinguish poor and well-controlled rhinitis and is correlated to VAS for symptoms and symptom impacts. In the present study, we used both VAS and ARCT to investigate the prevalence and characteristics of SCUAD and uncontrolled AR in our Wuhan Hospital consultation cohort.

VAS score of ≥ 5 is an easy way to distinguish mild and moderate/severe AR at inclusion of patients, and our study showed that 82.9% of the patients with moderate/severe AR had allergic conjunctivitis, moderate/severe persistent AR according to ARIA classification and symptoms usually with an impact on sleep, work life social activities, and physical activities. In the telephone survey of Zhang *et al.*² including patients with self-reported AR in 11 major cities in China, 74.4% had intermittent AR, 25.6% had persistent AR, and only 39.3% had presented to a clinic. This reflected that the impairments were correlated more strongly with severity than duration, and severity of

symptoms was an important factor to drive the patients to the hospital allergy clinic.

The prevalence of SCUAD in our cohort was 24.5%, which was higher than that in France: 18.9¹⁰ and 22%.¹⁶ However, our cohort had few mild intermittent/persistent AR patients (5.2%) compared with that of Bousquet *et al.* (20.2%), which implied that the prevalence of SCUAD might be overestimated in our cohort or reflect the reality. Both studies being performed with different methodologies in different countries, it is not possible to draw any conclusion. As we have mentioned before, ARCT proved to be a sensitive tool to judge if AR is controlled or not, and we found that 27.7% of our patients had uncontrolled AR. This study validates the Chinese translation of ARCT. The changes between VAS and NS after 2 weeks can also reflect a clinically relevant improvement of symptoms during treatment.^{11,15,16} In our study, the percentage of patients with insignificant improvement was 34.5%. It was slightly higher than in the study of Zhang *et al.*,² reporting that 27.2% of the patients received treatment in a clinic, and among them, 71.1% were satisfied. To obtain the control of AR, it is probably necessary to better phenotype severe AR patients and patients with no response to current treatment and treat according to phenotype and not according to severity only, as it is the case nowadays.

Compared with non-SCUAD patients, SCUAD patients had less history of atopic dermatitis but more smell disturbance problems,

more history of ENT infection or antibiotics administration in the last 12 months, and more significant impact on quality of life. This may reflect either a higher susceptibility of these patients with upper respiratory infections or some participation of nonallergic components. Thus, bacterial infection may play an important role in SCUAD. The history of asthma and recurrent sinusitis were not significantly more prevalent in SCUAD compared with non-SCUAD patients, and more data are needed to better understand SCUAD pathophysiology. We also found weight, smoking, history of ENT infection or antibiotics administration in the last 12 months, and smell disturbance had impacts on AR control and, especially, on work life (OR = 9.4); however, we do not know through which exact mechanisms; 27.7% of the patients with uncontrolled AR (ARCT of <20) presented higher prevalence of SCUAD, which also suggested that ARCT had a strong correlation with VAS and could be used as a surrogate indicator in future AR surveys.

Based on our results, we propose a simple and effective practical method for the management of AR. First, a careful history, a nasal examination (using a nasal speculum/otoscope), and allergy tests (primarily skin tests and sometimes *in vitro* tests or even nasal allergen challenge) to confirm or exclude an allergic etiology are recommended to confirm the diagnosis of AR.⁸ Second, a VAS is used to evaluate the severity of AR and the threshold of 5 is satisfied to distinguish mild (VAS score of <5) and moderate/severe (VAS score of ≥5) AR. Alternatively, an ARCT can be used. The first-line treatment based on the ARIA guidelines is thereafter followed according to the assessment of severity using VAS score. Third, a reevaluation should be practiced after 15 days of treatment using a VAS or ARCT. A step-up/step-down approach according to VAS or ARCT is not yet fully validated in real life. When dealing with SCUAD or uncontrolled AR, the first question one should ask is about a patient's compliance in correct medication use and adherence to the prescribed therapy. Correct use of the prescribed medication is a key factor for obtaining control by medical treatment.²⁰ For the AR patients with associated anatomic obstruction (including nasal valve dysfunction and/or malformations such as septal deviation), a consensus has to be made by allergist and otolaryngologist and some local surgery carefully envisaged. Li *et al.*²¹ reported 68.9% of patients with AR had skin-prick test positivity to more than one allergen in China. Allergen avoidance, although important for the patients with positive skin-prick testing and/or serum-specific IgE and symptomatic when in contact with relevant allergen sources, is difficult to control and therefore it was not applied for this simple prospective 2-week cohort study. It is likely that allergen immunotherapy can improve severe symptoms that are uncontrolled by medications, but more studies are required. Novel treatment is needed as well.

Some limitations exist in this trial: (1) patients were selected from hospital consultation, but because we included response to treatment, there is no real other way in China to include and follow treated patients, private medicine being very limited; (2) the reevaluate data of rhinitis severity were acquired by telephone interview but not by a rescheduled follow-up visit to assure patients' compliance; however, the scores filled out by patients in a print scale directly under the doctors' guide were considered to be reliable; and (3) similar to other trials, few patients may have had poor compliance, which may have an influence on the final outcome.

In conclusion, our study provided the prevalence and demographic characteristics of uncontrolled AR and SCUAD in the Wuhan Allergy Clinic. We suggest that physicians in charge of AR patients use VAS and/or ARCT as a simple and quantitative method for the global evaluation of AR severity and response to treatment.

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