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Extranasal symptoms of allergic rhinitis are difficult to treat and affect quality of life

Veeravich Jaruvongvanich^a, Pungjai Mongkolpathumrat^b, Hiroshi Chantaphakul^{b, c, d}, Jettanong Klaewsongkram^{b, c, d, *}^a Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand^b King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand^c Division of Allergy and Clinical Immunology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand^d Allergy and Clinical Immunology Research group, Chulalongkorn University, Bangkok, Thailand

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ABSTRACT

Background: Total nasal symptom score is widely used to evaluate the severity of allergic rhinitis, but the clinical significance of extranasal symptoms is largely unknown. We wished to analyze the presenting symptoms in allergic rhinitis, as well as their relationship with quality of life (QoL) and therapeutic outcomes.

Methods: Presenting symptoms and QoL were assessed using the OptumTM SF-12v2[®] Health Survey in 260 patients with allergic rhinitis. Clinical response at 3 months after treatment was measured.

Results: Ten most common symptoms presenting with at least moderate severity in allergic rhinitis were: blocked nose (82.7%), rhinorrhea (75.0%), sneeze (70.9%), itchy nose (68.5%), fatigue (63.6%), mouth breathing (61.1%), daytime somnolence (52.7%), postnasal drip (49.1%), itchy eyes (47.3%), and dry mouth (46.3%). Severity of sneeze was correlated with physical component summary (PCS) whereas postnasal drip and daytime somnolence were correlated with mental component summary (MCS). Severity of dry mouth was correlated with PCS and MCS. The symptoms with the highest severity scores after treatment were blocked nose, postnasal drip, fatigue, and dry mouth, respectively.

Conclusions: Extranasal symptom scores correlated well with physical health and mental health in allergic rhinitis patients. Assessment of extranasal symptoms should be included to evaluate disease severity and assess therapeutic outcomes. Clinical trial NCT02000648, <http://www.clinicaltrials.gov>.

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Introduction

Chronic rhinitis is a common respiratory disease and can be categorized broadly as “allergic” and “non-allergic” in origin. Estimated prevalence of allergic rhinitis and non-allergic rhinitis varies between studies because the etiologies of non-allergic rhinitis are diverse (e.g., vasomotor rhinitis; non-allergic rhinitis with eosinophilia; atrophic rhinitis; drug-induced rhinitis; gustatory rhinitis; occupational rhinitis) but, comparatively, the prevalence of allergic rhinitis is higher.^{1,2} In temperate climates, seasonal variation can be a feature of allergic rhinitis due to fluctuations in pollen exposure.³ In tropical countries, however, symptoms of allergic rhinitis can be

quite persistent because perennial allergens commonly contributing to rhinitis symptoms are abundant throughout the year.

Summation of the individual nasal score (sneeze, itchy nose, rhinorrhea, and blocked nose) or “total nasal symptom score” was introduced as an endpoint for clinical trials for seasonal allergic rhinitis and perennial allergic rhinitis.^{4,5} Most of these data, however, come from studies in temperate areas.^{3,6} Few studies have focused on the presenting symptoms of allergic rhinitis in tropical regions, where the weather is hot and humid all-year-round.^{7,8} Due to persistent exposure to allergens in the tropics, the clinical patterns of allergic rhinitis and non-allergic rhinitis in such a warm climate may not be distinguishable, and the presenting symptoms of allergic rhinitis in the tropics may differ from those reported in temperate climates.

Studies have shown that allergic rhinitis can impair quality of life (QoL).⁹ Most reports, however, have relied on the total nasal symptom score to assess disease severity and treatment. Other extranasal symptoms frequently overlooked in patients with

* Corresponding author. Division of Allergy and Clinical Immunology, Department of Medicine, Faculty of Medicine, Allergy and Clinical Immunology Research Group, Chulalongkorn University, Bangkok, Thailand.

E-mail address: Jettanong.K@chula.ac.th (J. Klaewsongkram).

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chronic rhinitis may also impact on QoL, particularly in some patients who fail to recognize that their complaints (e.g., breathing difficulties, tiredness) are due to chronic nasal obstruction.¹⁰ It has been shown that patients from Thailand with allergic rhinitis have impaired QoL compared with healthy control subjects assessed using the Short Form-36 questionnaire.¹¹ Allergic rhinitis can present with various symptoms and is sometimes overlooked. Hence, identification of the common presenting symptoms of allergic rhinitis and knowing which symptoms impact on general health is important. Treatment methods targeting these symptoms would improve the QoL of these patients.

We wished to evaluate the common presenting symptoms of allergic rhinitis, their impact on QoL, and therapeutic response.

Methods

The study protocol was approved by the Ethics and Research Committee of the Faculty of Medicine, Chulalongkorn University (Bangkok, Thailand). The study is registered at www.clinicaltrials.gov (NCT02000648).

Patients aged ≥ 18 years visiting allergy clinics within King Chulalongkorn Memorial Hospital and Chulalongkorn University Health Service Center in Bangkok and diagnosed with chronic rhinitis between 2012 and 2014 were recruited. Patients were requested to complete a clinical record form regarding presenting symptoms and clinical patterns. Health-related QoL was self-evaluated using the Optum™ SF-12v2® Health Survey (Thai version) on the first visit before starting treatment. Medications used and symptom severity after treatment was recorded by patients at follow-up visits. Patients were asked to rank the severity of 18 symptoms (sneeze, itchy nose, rhinorrhea, blocked nose, post-nasal drip, itchy eyes, tearing, frequent cough, frequent sore throat, chronic headache, dry mouth, fatigue, snoring, mouth breathing, poor sleep, daytime somnolence, and loss of sense of smell) they might have on a four-point scale (0 = none, 1 = mild, 2 = moderate, 3 = severe).

Anterior rhinoscopy had been undertaken to exclude anatomic abnormalities along with measurement of peak nasal inspiratory flow using In-Check Nasal® (Clement Clarke International, Harlow, UK). Classification of chronic rhinitis was based on Allergic Rhinitis and its Impact on Asthma guidelines (2010).¹² Skin-prick tests with common aeroallergens in Thailand (mixed dust mites, mixed cockroaches, mixed molds, cat dander, dog hair, and southern grass mix; ALK-Abello, Hørsholm, Denmark) were examined. Wheal size ≥ 3 mm was considered to denote a positive test.

A total of 344 patients were recruited for skin-prick test on the first visit. According to the results of aeroallergen skin tests, allergic rhinitis and non-allergic rhinitis were diagnosed in 260 and 84 patients, respectively. Patients with symptoms and signs

suggesting bacterial sinusitis (fever, facial tenderness, or purulent discharge) were excluded from this study. Correlations between the ten most common presenting symptoms before treatment and physical component summary as well as mental component summary were analyzed using the SF-12v2 Health Survey. Medications were prescribed based on the allergist's decision in real-life settings. Therapeutic response was evaluated in 55 selected patients followed-up at 1- and 3-month periods after treatment compared with baseline symptoms. Each symptom was considered to be "controlled" if the symptom score was ≤ 1 .

Statistical analyses

The Student's *t*-test and chi-square test were used for quantitative and qualitative analyses, respectively. Data were represented as means \pm standard errors. Multinomial logistic regression was used for multivariate analysis. $P < 0.05$ was considered significant.

Results

Baseline characteristics of patients with allergic rhinitis

A total of 344 chronic rhinitis patients had undergone skin prick test during the study period. Almost two-thirds were female and 260 patients (75.6%) were confirmed to have an allergy (Table 1). Positive skin prick tests to mixed dust mites, mixed cockroaches, mixed molds, cat dander, dog hair, and southern grass mix were demonstrated in 85.4%, 59.2%, 13.1%, 9.2%, 1.9%, and 7.3% of allergic rhinitis patients, respectively.

Patients diagnosed with allergic rhinitis were significantly younger and had an earlier age of onset than patients with non-allergic rhinitis. Total nasal symptom scores at baseline in patients with allergic rhinitis were higher than those of those with non-allergic rhinitis, but peak nasal inspiratory flow was comparable. Interestingly, the prevalence of familial atopic history was significantly higher in patients with allergic rhinitis compared with those with non-allergic rhinitis, but the prevalence of associated allergic diseases and concurrent medical illnesses between the two groups was not significantly different.

Prevalence and severity of individual symptoms in patients with allergic rhinitis

Percentages of patients with allergic rhinitis presenting with at least moderate severity of each symptom were ranked as follows: blocked nose, 86.8%; rhinorrhea, 80.4%; itchy nose, 76.2%; sneeze, 73.8%; fatigue, 61.2%; postnasal drip, 56.3%; itchy eyes, 54.9%; daytime somnolence, 54.1%; dry mouth, 53.1%; mouth breathing, 51.2%; chronic headache, 49.4%; poor sleep, 44.6%; sore throat, 39.7%;

Table 1
Clinical characteristics of patients with chronic rhinitis who underwent the skin-prick test.

	All cases with known skin test result (N = 344)	Allergic (N = 260)	Non-allergic (N = 84)	P values
Male: female (% female)	124:220 (63.95%)	91:169 (64.75%)	33:51 (60.71%)	0.28
Age (years)	33.19 \pm 0.76	30.60 \pm 0.78	40.31 \pm 1.71	<0.01**
Age of onset (years)	24.89 \pm 1.12	22.47 \pm 1.17	33.63 \pm 2.58	<0.01**
Persistent rhinitis	272/344 (79.07%)	198/260 (76.15%)	74/84 (88.10%)	0.02*
Total nasal symptom scores	8.13 \pm 0.15	8.50 \pm 0.16	6.96 \pm 0.32	<0.01**
Nasal peak inspiratory flow rate (L/min)	134.59 \pm 4.70	134.47 \pm 5.49	135.00 \pm 9.18	0.96
Associated allergic diseases	57/344 (16.57%)	47/260 (18.08%)	10/84 (11.91%)	0.12
Concurrent medical illnesses	42/344 (12.21%)	28/260 (10.77%)	14/84 (16.67%)	0.11
Family history of atopy	126/344 (36.63%)	105/260 (40.38%)	21/84 (25.00%)	<0.01**

Patients diagnosed with allergic rhinitis were significantly younger, had more severe nasal symptoms than patients with non-allergic rhinitis, and had higher prevalence of familial atopic history; * represents $P < 0.05$ and ** represents $P < 0.01$ comparing the differences between both groups.

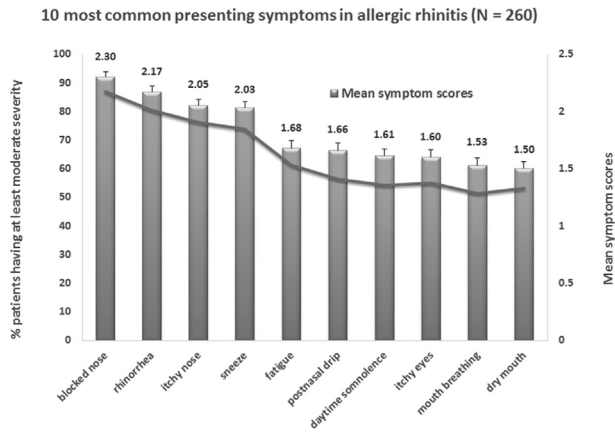


Fig. 1. Presenting symptoms ranked by percentages of patients whose symptom scores denoted at least moderate severity (N = 260). Four typical nasal symptoms were the most severe presenting symptoms in allergic rhinitis, followed by fatigue, postnasal drip, daytime somnolence, itchy eyes, mouth breathing, and dry mouth, respectively.

frequent clearing of throat, 37.1%; snoring, 36.9%; loss of sense of smell, 36.0%; tearing, 33.1%; and chronic cough, 25.5%. Only the first top-ten most common presenting symptoms are shown in [Figure 1](#).

Quality of life in patients with allergic rhinitis and correlation with symptom severity

Physical health and mental health was evaluated using the SF-12v2 Health Survey (physical health domains comprised physical functioning, role physical, bodily pain, and general health; mental-health domains comprised vitality, social functioning, role emotional, and mental health; [Fig. 2](#)). Norm-based scores were summarized and reported as physical component summary (PCS) and mental component summary (MCS).

PCS and MCS in patients with allergic rhinitis were 45.7 ± 0.9 and 43.4 ± 1.0 , respectively. Based on mean scores, health domains impaired most in patients with allergic rhinitis were general health and role emotional. Most symptoms of rhinitis in patients with poor QoL (PCS or MCS <50) were significantly more severe than those in patients with good QoL (PCS and MCS ≥ 50) ([Fig. 3](#)).

After adjustment for duration of symptoms, associated allergic diseases, and underlying medical illnesses, it was demonstrated that the symptom severity of sneeze was correlated significantly

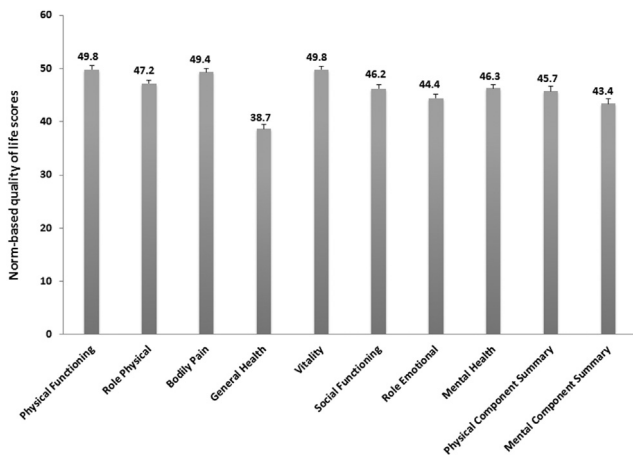


Fig. 2. Quality of life in patients with allergic rhinitis assessed using the SF-12v2[®] Health Survey (N = 260). Quality of life scores in patients with allergic rhinitis were lower than those in normal populations, particularly in terms of general health.

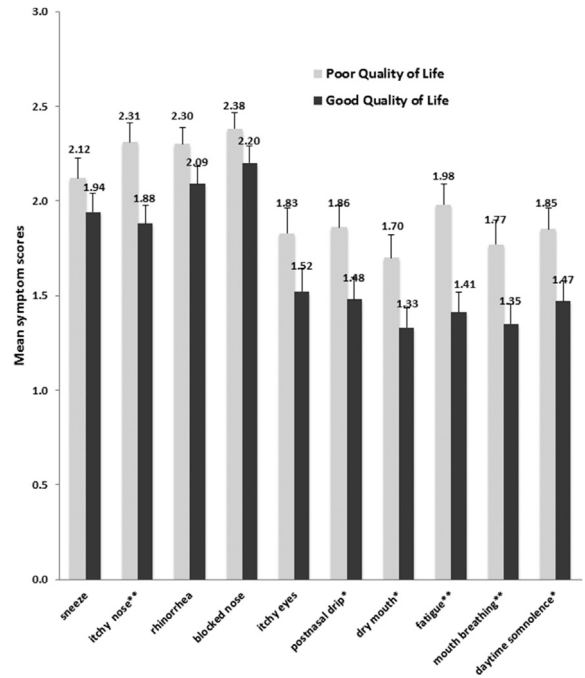


Fig. 3. Severity of rhinitis symptoms in patients with good quality of life compared with patients with poor quality of life (N = 260). Data demonstrate that patients with poor quality of life had more severe symptoms of rhinitis than patients with good quality of life; * represents $P < 0.05$ and ** represents $P < 0.01$ comparing the differences between both groups.

with PCS alone, whereas severity of postnasal drip and daytime somnolence were correlated significantly with MCS alone. Severity of dry mouth was correlated significantly with both PCS and MCS ([Table 2](#)). Nasal symptom scores (sneeze, itchy nose, rhinorrhea, and blocked nose) did not significantly correlate with the physical or mental components whereas extranasal symptom scores (postnasal drip, itchy eyes, dry mouth, fatigue, mouth breathing, and daytime somnolence) correlated with the physical and mental components of QoL.

Therapeutic response of various symptoms in patients with allergic rhinitis

Fifty-five patients with allergic rhinitis followed up at 1- and 3-month periods after the first visit were assessed for symptom severity and controlled symptoms. Baseline symptom scores at the first visit revealed that blocked nose, rhinorrhea, sneeze, and itchy nose were the most severe presenting symptoms in patients with allergic rhinitis. Daily intranasal corticosteroid alone and combination therapy with both intranasal corticosteroid and oral antihistamine were prescribed in 37.5% and 52.5% of patients, respectively (data not shown). Symptoms with high scores after 3 months were blocked nose, postnasal drip, fatigue, and dry mouth ([Fig. 4](#)).

Baseline symptoms with the highest uncontrolled symptom score (≥ 2) in patients with allergic rhinitis were blocked nose, rhinorrhea, sneeze, itchy nose, and fatigue. At 3 months, however, the proportion of patients with uncontrolled symptoms was 43.9% for blocked nose, 37.2% for postnasal drip, 33.3% for itchy nose, 31.7% for dry mouth, and 28.6% for fatigue.

Discussion

In our cohort, the prevalence of persistent rhinitis in non-allergic subjects was higher than that in the allergic group. In

Table 2
Correlations between symptom severity and the quality of life in patients with allergic rhinitis.

Rhinitis symptoms		Sneeze	Itchy nose	Rhinorrhea	Blocked nose	Postnasal drip	Itchy eyes	Dry mouth	Fatigue	Mouth breathing	Daytime somnolence	Nasal symptom scores	Extranasal symptom scores	Total symptom scores
Physical component summary	Correlation	-0.17	-0.02	-0.14	-0.08	-0.11	-0.03	-0.158	-0.142	-0.097	-0.060	-0.139	-0.152	-0.187
	P values	0.05*	0.85	0.10	0.35	0.20	0.69	0.07*	0.10	0.26	0.49	0.11	0.08*	0.03*
Mental component summary	Correlation	-0.08	0.027	-0.046	-0.020	-0.186	-0.053	-0.251	-0.114	-0.055	-0.151	-0.042	-0.205	-0.183
	P values	0.32	0.75	0.60	0.82	0.03*	0.54	0.00**	0.19	0.52	0.08*	0.63	0.02*	0.03*

Correlations between symptom severity and the physical and mental components of quality of life in patients with allergic rhinitis after adjustment of duration of symptoms, associated allergic diseases, and underlying medical illnesses (N = 260).

*Correlation is significant at the 0.05 level (two tailed), **correlation is significant at the 0.01 level (two tailed).

general, patients with allergic rhinitis were younger, developed symptoms earlier, and had more severe nasal symptoms compared with non-allergic subjects. A family history of atopy in patients diagnosed with allergic rhinitis was also more common. These clinical characteristics were similar to those from other reports in temperate countries.^{6,13}

Our study confirmed that the four typical nasal symptoms (blocked nose, rhinorrhea, sneeze, and running nose) were the major symptoms in allergic rhinitis for >70% of patients having at least moderate severity before treatment. Postnasal drip, fatigue, daytime somnolence, dry mouth, itchy eyes, and mouth breathing also contributed to the top-ten presenting symptoms in patients with allergic rhinitis in terms of symptom severity.

Confounding factors such as underlying medical illnesses, associated allergic diseases, and symptom duration had been excluded, so allergic rhinitis could affect the general health and wellbeing of patients. Impairment of physical health and mental

health in these patients was correlated significantly with severity of extranasal symptoms, whereas correlation between severity of sneeze, one of the four main nasal symptoms of rhinitis, and QoL was observed only in physical-health components. Most symptoms were improved dramatically within 1 month. Follow-up data showed that, although typical nasal symptoms of chronic rhinitis were prominent at baseline, most symptoms could be controlled readily after treatment except for blocked nose. In contrast, extranasal symptoms such as postnasal drip and dry mouth were less severe at the beginning but the recalcitrant nature of these symptoms would probably lead to impaired QoL in the long term.

At present, the total nasal symptom score is used frequently to assess the severity of allergic rhinitis and, to lesser extent, non-allergic rhinitis.^{14–17} In certain circumstances, calculation of the total nasal symptom score alone may not be adequate to assess rhinitis severity. In tropical regions where symptoms of allergic rhinitis persist throughout the year, extranasal symptoms can be

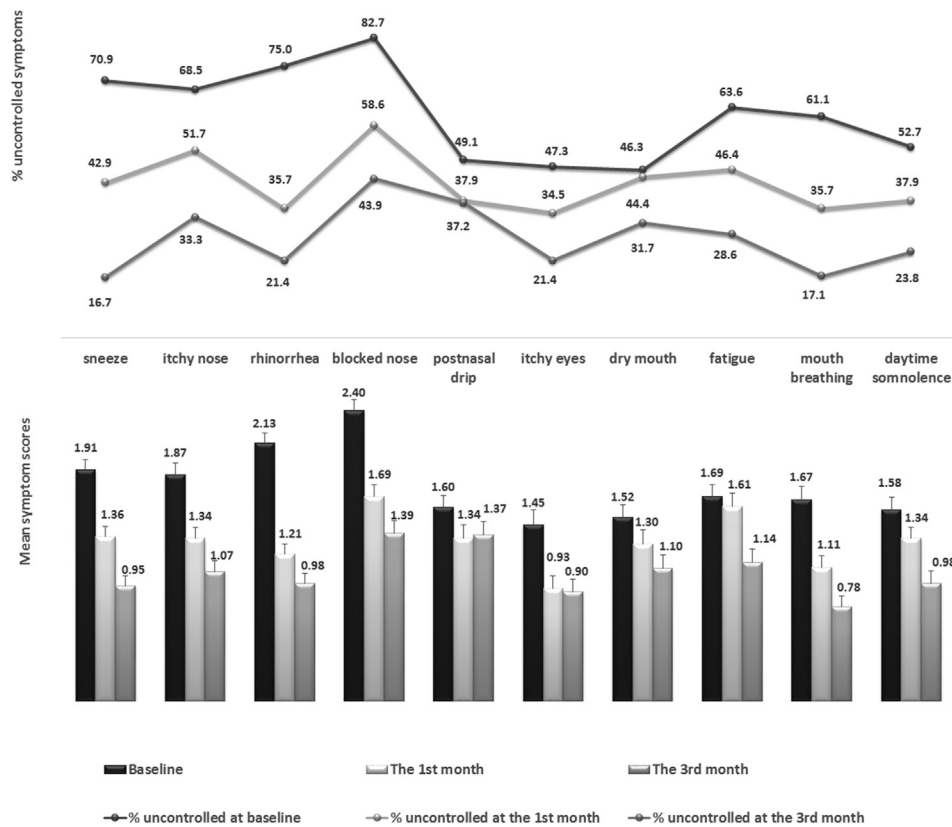


Fig. 4. Symptom severity and clinical improvement in patients with allergic rhinitis (N = 55). Blocked nose, rhinorrhea, sneeze, and itchy nose were the most severe presenting symptoms at baseline while blocked nose, postnasal drip, fatigue, and dry mouth were the most recalcitrant symptoms at 3 months after treatment.

refractory to treatment and affect QoL. According to our study, use of the total nasal symptom score is not an ideal tool to assess the severity of allergic rhinitis because these symptoms barely impact on physical health alone whereas the extranasal or “atypical” symptoms of chronic rhinitis are closely associated with the physical and mental components of QoL. Improvement in extranasal symptoms should also be considered when evaluating disease severity, monitoring therapeutic response in a clinical trial, or developing new drugs targeting chronic allergic rhinitis.

According to our study, symptoms that were difficult to control in patients with allergic rhinitis were blocked nose, postnasal drip, fatigue, and dry mouth. It is well known that chronic rhinitis has a detrimental effect on sleep.¹⁸ Blocked nose is one of the most bothersome symptoms in persistent rhinitis. In fact, chronic nasal obstruction has a significant impact on sleep quality, daytime somnolence, fatigue, and QoL.^{19–21} It is likely that extranasal symptoms such as dry mouth and mouth breathing were due to chronic nasal obstruction, especially at nighttime, and thereby contributed to daytime somnolence and fatigue. Other than blocked nose, it is worth noting that severity of postnasal drip was also difficult to control. It is possible that the accessibility of intranasal steroid spray to the posterior part of the nasal cavity and pharyngeal wall may be limited, particularly in patients with severe nasal obstruction and excessive mucus secretion in these areas could be responsible for persistent postnasal drip symptoms in these patients. New therapeutic methods targeting chronic nasal obstruction and its consequences should be considered.

The present study had limitations. Allergic status was diagnosed based on the skin-prick test alone, and patients with mixed rhinitis or local allergic rhinitis were not assessed separately. Our study reflected the real-world situation, so the therapeutic response may be not as good as that observed in clinical trials due to the compliance issues. Some extranasal symptoms, such as fatigue or daytime somnolence, may have been secondary to depression. Whether these symptoms were the consequence of chronic rhinitis or depressed mood is not known because depression is reported in about one-quarter of patients with chronic rhinosinusitis, and chronic psychologic stress can modify the severity of chronic rhinosinusitis.^{22,23} Use of diagnostic psychologic tests in patients with allergic rhinitis may help to resolve this problem.

In summary, extranasal symptoms of allergic rhinitis, which are more difficult to treat than nasal symptoms of allergic rhinitis, can affect QoL in aspects of physical health and mental health. Better scoring systems comprising nasal symptoms and extranasal symptoms should be used to evaluate disease severity, monitor therapeutic response in clinical trials, or assess the efficacy of drugs targeting allergic rhinitis.

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Conflict of interest

The authors have no conflict of interest to declare.

Authors' contributions

VJ assisted with data analysis and wrote the manuscript. PM collected the data and HC provided helpful feedback on the manuscript. JK designed the study, performed the statistical analysis and interpretation of the results, and wrote the manuscript. All authors read and approved the final manuscript.

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