

Seasonal Rhinitis, Clinical Characteristics and Risk Factors for Asthma

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Key Words

Asthma · Risk factors · Rhinoconjunctivitis, seasonal

Abstract

Background: The aim was to determine the clinical characteristics of patients with seasonal rhinitis (SR) and to disclose differences in the treatment of SR between an adult allergy clinic and other clinics over time. **Methods:** A retrospective study was conducted based on clinical records of 774 out of 955 patients diagnosed with SR in an adult allergy clinic between 1 January 1991 and 31 December 2003. **Results:** The mean age of the patients was 29.1 ± 9.29 years and 62.7% were female. The most common major complaints of the patients were nasal symptoms in 82.3%. The mean duration of the disease was 6.76 ± 6.8 years. The patients were symptomatic with a mean of 3.5 ± 1.7 months a year, mostly during the period between April and July. Skin prick tests were positive in 685 patients (90.3%), where the most common sensitivity was against timothy grass (85.1%). The most common accompanying allergic diseases were food hypersensitivity in 14%, bronchial asthma in 13.4%, and drug allergy and/or intolerance in 9.6%. Although the use of specific immunotherapy and short-acting sedative antihistamines decreased over time, the use of nasal steroids and long-acting nonsedative antihistamines tended to increase before admission to our clinic. Older

age (OR: 1.77, 95% CI: 1.06–2.94), presence of familial atopy (OR: 1.72, 95% CI: 1.04–2.85), respiratory symptoms (OR: 2.10, 95% CI: 1.75–2.50), ocular symptoms (OR: 0.77, 95% CI: 0.61–0.98) and metal allergy (OR: 0.25, 95% CI: 0.07–0.89) were associated with the development of asthma in patients with SR. **Conclusion:** SR lasts approximately 3.5 months and the main cause in Ankara, Turkey is grass pollen sensitivity. Patients with any other allergic conditions make up 39.8% of the patients. SR patients are referred to allergy clinics quite late, which might be due to SR not being considered as a serious disease.

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Introduction

Seasonal allergic rhinitis (SR), a chronic disorder of nose and sometimes airways, is one of the most commonly seen allergic diseases, which is totally IgE-mediated. It is a disease of younger age groups which tends to resolve spontaneously in middle age.

Allergic rhinitis is generally characterized by nasal obstruction, rhinorrhea, sneezing, itching of the nose and/or postnasal drainage which is often associated with respiratory and ocular symptoms. The association between rhinitis and conjunctivitis is a typical feature of patients with seasonal pollen allergy. Conjunctival symptoms are often

considered to be of minor importance and possibly not spontaneously reported by patients with rhinitis and/or asthma during medical interviews or in questionnaire-based studies such as the ISAAC and the ECRHS [1, 2]. On the other hand, asthma and rhinitis are common comorbidities suggesting the concept of 'one airway, one disease'. Rhinitis and asthma are linked by epidemiological, pathological and physiological characteristics and by a common therapeutic approach [3].

The capacity of pollen sensitizing the patients is theoretically universal, but the nature and number of pollen vary with geography, temperature and climate. The pollen concentration in the atmosphere depends on the vegetation and climate of a given geographic zone causing important regional differences. The main cause of seasonal rhinitis in Turkey seems to be grass pollen sensitivity according to recent studies [4–8].

It is a highly prevalent condition that exacts a high cost in terms of morbidity, loss of productivity, and use of healthcare resources. Despite the recognition that SR is a global health problem affecting up to 40% of the population worldwide and is increasing in prevalence, there are insufficient epidemiological data with regard to its clinical features and treatment trends in our country [9–12]. Various recent studies in children and university students from different parts of Turkey show an SR prevalence of 9.1–13.6%, which is lower than the prevalence in western countries [4, 5, 13, 14].

Our aim was to determine retrospectively the clinical characteristics of the patients diagnosed with SR in our allergy clinic and disclose the differences in the treatment modalities between the other clinics to which the patients were referred before attending a university adult allergy clinic over a 13-year period.

Methods

A retrospective study was conducted based on the clinical records of 955 patients diagnosed with SR at our clinic between 1 January 1991 and 31 December 2003. Out of 955 patients, 774 were enrolled since complete data were available only for these. The collected data included demographic features, allergen spectra, initial symptoms, monthly attack rates, accompanying allergic and nonallergic diseases and the treatment the patients had received for SR before being referred to our clinic. Risk factor analysis was performed for patients with asthma which had been diagnosed according to the GINA guidelines [15].

Atopy and allergen spectra were assessed by skin prick test (SPT) reactions to 17 common aeroallergens, prepared by the firms ALK (Denmark), Stallergens (France) and Greer (USA) (*Dermatophagoides pteronyssinus*, *Phleum pratense*, *Olea europea*, *Artemisia vulgaris*, *Parietaria officinalis*, *Corylus avellana*, *Betula ver-*

rucosa, *Populus alba*, cat, dog, horse, *Alternaria alternata*, *Cladosporium herbarum*, *Aspergillus fumigatus*, cockroach, *Apis mellifera*, *Vespa* species). Tests were carried out as described by Österballe and Weeke [16] by pricking the skin on the volar face of the forearm with a special lancet. Histamine and saline were used as positive and negative controls, respectively. Resulting wheals were measured after 15 min. A positive reaction was defined as a wheal with a geometric mean diameter of at least 3 mm. Prick test positivity was defined as a positive response to at least one of the allergens used. Prick tests were not performed in cases of pregnancy, dermatographism and use of antihistamines.

SPSS MS Windows Release 10.0 (SPSS Inc.) was used for statistical analysis. Personal characteristics and disease-related factors were compared between asthma and allergic rhinitis. χ^2 testing with continuity correction and Student's t test were used for categorical and continuous variables, respectively. Association of the factors with asthma was adjusted for age and gender. Age was categorized into two groups according to the median age. Odds ratios were used to assess the strength of the association between asthma and characteristics of the patients. A final logistic regression model was developed to assess the independent association between asthma and the factors which were significantly associated with asthma in the adjusted analysis. Model selection criteria were 0.05 and 0.10 for entry and removal of the factors, respectively. Statistical significance was defined for p values less than 0.05.

Results

Demographic features, initial symptoms and accompanying disorders of the patients are given in table 1. The mean age of the patients was 29.1 ± 9.29 years and 485 of them were female. The distribution of the patients regarding age, sex, smoking status, place of birth and residence is shown in table 1. The major initial complaints of the patients were nasal symptoms in 82.3%, respiratory symptoms in 9.7%, cutaneous symptoms in 6.2%, and ocular symptoms in 1.8% (table 1). The mean age of onset of the disease was 22.33 ± 9.17 years and the mean duration was 6.76 ± 6.8 years (median 5 years). The patients had been symptomatic with a mean of 3.5 ± 1.7 months a year during March (17.8%), April (53.2%), May (91.3%), June (81.3%), July (49.2%), August (30%) and September (15.1%) (fig. 1). The history of previous referrals to other clinics before admission to our clinic because of SR symptoms was positive in 35% of the patients, with 30.7% having been referred to ear nose throat, 21.8% to adult allergy, 13% to pediatric allergy, 11.7% to chest disease and 10.1% to dermatology clinics. SPT were positive in 685 out of 759 patients in whom tests were performed (90.3%); the number of patients sensitized to a single allergen was 267. The allergen spectrum is shown in table 2. Two hundred and fourteen patients (27.6%) were stu-

Table 1. Demographic features, initial symptoms and accompanying disorders of the patients with SR (n = 774)

	n	%
Mean age $\pm$ SD, years	29.10 $\pm$ 9.29 (18–69)	
Mean age $\pm$ SD at onset, years	22.33 $\pm$ 9.17 (1–61)	
Sex		
Female	485	62.7
History of atopic diseases		
Familial	440	56.8
Personal	308	39.8
Smoking rate		
Never smoked	571	73.8
Smoker	166	21.4
Ex-smoker	37	4.8
Place of birth		
Central and eastern regions	610	78.8
Coastal regions	164	21.2
Place of residence		
Central and eastern regions	713	92.1
Coastal regions	61	7.9
Pet ownership	143	18.5
Initial symptom of the patients		
Nasal	637	82.3
Ocular	75	9.7
Respiratory	48	6.2
Dermatological	14	1.8
Accompanying disorders (n = 381)		
Food hypersensitivity	108	14
Bronchial asthma	100	13.4
Drug allergy and/or intolerance	74	9.6
Goiter	29	3.7
Hypertension	22	2.8
Migraine-like headaches	19	2.4
Gastritis	15	1.9

Unless otherwise indicated the figures represent the number and percentage of patients. Figures in parentheses represent range.

Table 2. Allergen spectra of the patients detected by SPT (n = 759)

Allergens	Tests performed	Positive tests	%
At least one allergen positivity	759	685	90.3
Pollen	758	673	89.1
<i>P. pratense</i>	752	646	85.9
<i>P. pratense</i> alone	752	249	33.1
<i>A. vulgaris</i>	754	171	22.7
<i>A. vulgaris</i> alone	754	7	0.93
<i>P. officinalis</i>	755	52	6.9
<i>P. officinalis</i> alone	755	2	0.26
<i>O. europea</i>	755	237	31.5
<i>O. europea</i> alone	755	2	0.3
<i>C. avellana</i>	719	128	17.8
<i>C. avellana</i> alone	719	1	0.14
<i>B. verrucosa</i>	754	132	17.5
<i>B. verrucosa</i> alone	754	1	0.13
<i>P. alba</i>	154	10	6.5
<i>D. pteronyssinus</i>	753	114	15.1
<i>D. pteronyssinus</i> alone	753	4	0.5
Cockroach	124	20	16.2
Cockroach alone	124	1	0.81
Pet animals	754	98	13.1
Cat	754	71	9.4
Horse	754	27	3.6
Dog	754	25	3.3
Molds	754	9	1.3
<i>A. fumigatus</i>	258	5	1.9
<i>C. herbarum</i>	600	3	0.5
<i>A. alternata</i>	754	2	0.3

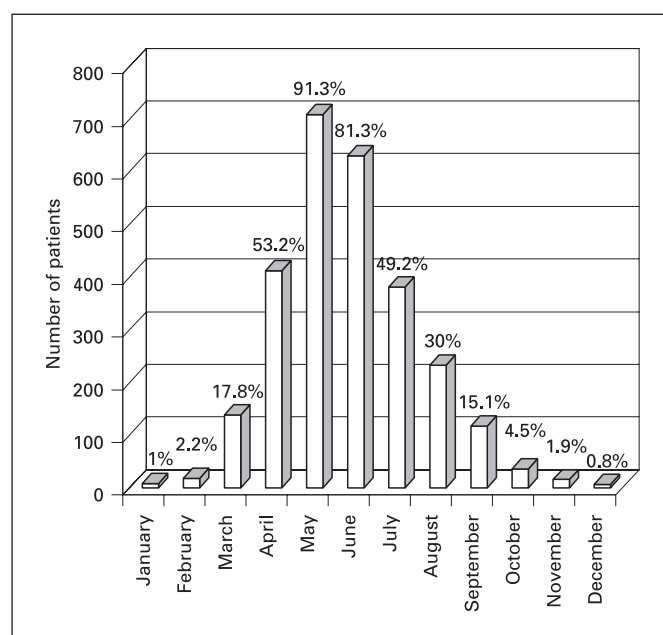
Fig. 1. SR symptoms of the patients according to the time of the year (n = 774).

Table 3. Comparison of the treatment modalities suggested for seasonal rhinoconjunctivitis by an adult allergy clinic and other clinics (n = 774)

Medications	Other clinics		Adult allergy clinic	
	n	%	n	%
Long-acting antihistamines	258	33.3	613	79.2
Short-acting antihistamines	74	9.5	29	3.7
Nasal steroids	102	13.1	718	92.8
Inhaled β -mimetics	49	6.3	106	13.7
Nasal decongestants	41	5.3	–	–
Pseudoephedrine	35	4.5	7	1
Ocular chromones	30	3.9	551	71.2
Inhaled steroids	27	3.5	156	20.1
Oral chromones	19	2.5	1	0.1
Cough suppressants	18	2.4	–	–
Antibiotics	13	1.7	–	–
Nasal chromones	8	1	24	3.1
Intravenous steroids	6	0.8	–	–
Oral steroids	4	0.5	94	12.1
Inhaled chromones	4	0.5	1	0.1
Theophyllines	3	0.4	–	–

p < 0.05 for all medications.

Three hundred and eight (39.8%) patients had at least one accompanying allergic disease which was food hypersensitivity (14%), asthma (intermittent or persistent) (13.4%), and drug allergy and/or intolerance (9.6%) (table 1). About half of the patients were prescribed antihistamines (42.8%). In addition, 57 out of 774 patients (7.4%) had previously received specific immunotherapy with a mean duration of 2.9 years (1–7 years). Nasal steroids (92.8%), long-acting antihistamines (79.4%) and ocular chromones (71.2%) were the most commonly suggested drugs for this group of patients in our clinic (table 3). The association between asthma combined with allergic rhinitis and patient characteristics and disease-related factors adjusted for age, gender and potential risk factors was examined in the final model (table 4). In this final model, features including older age (age >40 years, OR: 1.77, 95% CI: 1.06–2.94), presence of familial atopy (OR: 1.72, 95% CI: 1.04–2.85), respiratory symptoms (OR: 2.10, 95% CI: 1.75–2.50), ocular symptoms (OR: 0.77, 95% CI: 0.61–0.98) and metal allergy (OR: 0.25, 95% CI: 0.07–0.89) were associated with the development of asthma in patients with SR. Nasal symptoms and skin test reactivity to cat allergen were associated with asthma after the adjustment for age and gender, but not included in the final model as they did not fulfill the mod-

el inclusion and exclusion criteria. Immunotherapy was not selected in the final model, as it was not considered as an explanatory factor.

Discussion

Even though not a life-threatening disease, SR has a remarkable social impact and cannot be left to its natural course. Pollens appear seasonally and are reflected in the symptoms of patients with SR living in temperate climates. Recent studies have shown that grass pollen in Turkey [4–8], birch and grass pollens in northern Europe [17–21], ragweed pollen in America [22], and mugwort and olive pollens in the Mediterranean area [23–27] are the most common and important allergens of these regions. Since Turkey is located between Europe and Asia like a bridge, all four seasons can be present in different regions of the country at the same time of the year. This is the first large study on clinical characteristics and treatment modalities of SR in Ankara with an adequate number of patients which might represent not only Turkey but also other neighboring countries around Turkey.

This survey shows that the atopy rate detected by SPT was 90.3% and the most common sensitizing allergen was grass pollen in patients with SR in Ankara, the most frequently involved allergen being *P. pratense*. In addition, when the results were evaluated for sensitivity of each single allergen it appeared that the prototype of the grass pollens *P. pratense* was the most common sensitizing allergen. However, 4 patients had monosensitivity against *D. pteronyssinus* and 1 against cockroach, which should be kept in mind for the differential diagnosis of SR. There was a similar study among children in Ankara, which showed 7 mite-allergic children among patients with seasonal rhinitis [5]. Interestingly, 9.7% of the group showed no sensitivity to any of the aeroallergens tested for, which might be due to a possible localized allergic reaction or sensitization with other allergens which were not included in this routine panel. Serum specific IgE level measurements or direct conjunctival and/or nasal provocation tests could be performed to clarify this situation.

Although SR is known to be a disease of younger age groups, the onset was quite late with a mean age at onset of 22.3 compared to western countries where the onset of SR is before the age of 15 years [9–12]. This might be explained by regional variations in the pollen type and concentrations in Turkey. In addition to a higher age at onset, patients with SR had been referred to allergy clinics quite late (about 7 years after the beginning of the symptoms)

Table 4. Association between asthma combined with allergic rhinitis and patient characteristics and disease-related factors adjusted for age, gender and potential risk factors in the final model

	Rhinitis ¹ (n = 674)	Asthma (n = 100)	Adjusted OR ² (95% CI)	Final model OR ² (95% CI)
Age >40 years	139 (20.6)	33 (33)**		1.77 (1.06–2.94)
Female sex	426 (63.2)	59 (59)		
Current smoker	144 (21.4)	22 (22)	1.02 (0.40–2.60)	
Ex-smoker	31 (4.6)	6 (6)	1.02 (0.601–1.70)	
Nasal symptoms	638 (94.7)	82 (82)****	0.25 (0.13–0.46)	
Dermatological symptoms	91 (13.5)	7 (7)	0.84 (0.70–1.03)	
Ocular symptoms	509 (79.5)	60 (60)***	0.72 (0.57–0.90)	0.77 (0.61–0.98)
Respiratory symptoms	195 (28.9)	80 (80)****	2.14 (1.80–2.54)	2.10 (1.75–2.50)
Metal allergy	67 (9.9)	3 (3)*	0.28 (0.09–0.93)	0.25 (0.07–0.89)
Familial atopy	368 (54.6)	72 (72)***	2.22 (1.39–3.54)	1.72 (1.04–2.85)
Familial rhinitis	149 (22.1)	22 (22)	0.97 (0.58–1.62)	
Bee allergy	11 (1.6)	0 (0)	0	
Having a pet	126 (18.7)	17 (17)	0.94 (0.53–1.64)	
Having a cat	28 (4.2)	6 (6)	1.53 (0.61–3.83)	
Having a dog	21 (3.2)	4 (4)	1.34 (0.44–4.03)	
Having a horse	25 (13.8)	2 (2)	0.50 (0.12–2.17)	
Born in the coastal region	144 (21.4)	20 (20)	0.84 (0.49–1.42)	
Residing in the coastal region	49 (7.3)	12 (12)	1.60 (0.82–3.16)	
SPT positivity to cat	57 (8.6)	14 (14)	1.91 (1.01–3.62)	
SPT positivity to pollen	595 (88.9)	82 (82)	0.61 (0.34–1.08)	
SPT positivity to mite	197 (14.6)	20 (20)	1.50 (0.87–2.57)	
SPT positivity to trees	267 (40)	36 (36)	NA	
SPT positivity to cockroach	17/81 (21)	3/6 (50)	NA	
SPT positivity to fungus	7 (1.1)	2 (2)	NA	
SPT positivity to latex	1/431 (0.2)	1/73 (1.4)	NA	
Received immunotherapy	39 (5.8)	18 (18)****	3.27 (1.77–6.03)	

* p < 0.05; ** p < 0.01; *** p < 0.005; **** p < 0.0001. NA = Not available.

¹ Figures in parentheses represent percentage.

² Figures in parentheses represent range.

possibly due to the Turkish lifestyle (both patients and physicians not considering SR as a serious disease), genetic, sociocultural and geographic differences or a moving population with people included in general social security system of the government or students constituting 71.4% of the SR patients. Although no significant difference in gender was reported in patients with SR in previous epidemiological studies worldwide, 62.7% of our patients were female. There has been no clear data on this up to date [9–12].

Generally, after a 10- to 15-year course of the disease, remission (spontaneous disappearance) and improvement can be reported in about 50% of patients with SR [12, 28]. In fact, this trend can also be observed in some of our patients.

In this study, SR symptoms had a duration of approximately 3.5 months. According to previous data about

pollen concentrations in Ankara between 1990 and 1993, grass pollen appeared throughout the year with a maximum flowering period from the end of March to the end of September with an overall maximum value at the beginning of June [29]. However, regular daily reports on pollen concentrations are not available for the country yet.

Although the patients with SR have mainly rhinitis symptoms (major complaints being nasal in 82.3%), they also have some other accompanying allergic conditions like food hypersensitivity, asthma (intermittent or persistent), and drug allergy and/or intolerance. Furthermore, 308 patients (39.8%) had at least one accompanying allergic disease (food hypersensitivity and/or asthma and/or drug allergy and/or intolerance). This is a retrospective clinical study. If we could conduct a prospective survey and perform more sophisticated tests (such as some prov-

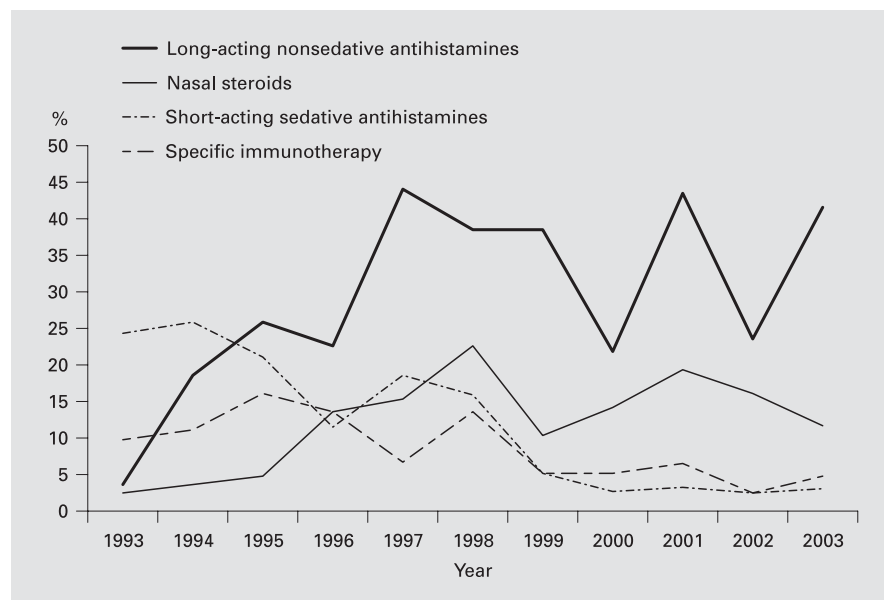


Fig. 2. Changing treatment modalities over time.

ocation tests or detailed specific IgE analysis), the frequency of the patients with any other allergic conditions might have increased. Allergy does not necessarily limit itself to the nose. The nose and/or conjunctiva are probably the most commonly involved organs in SR which can be accepted as a systemic disease. In addition, the high frequency of accompanying allergic conditions in contrast to the low frequency of systemic disorders (goiter, hypertension, migraine-like headaches, gastritis shown in table 1) in these patients, which may be due to their young age, points to the need that at least the initial evaluation of SR patients should be done at adult allergy clinics.

There is no available data for the treatment modalities for SR in our country. When the medications prescribed for SR patients in other clinics before admission to our clinic and those suggested by our clinic are compared, statistically significant differences and important therapeutic defects were noted. For example, the rate of nasal steroid usage, which is the drug of choice for SR [30], was only 13.1% before admission. In addition, these patients were mostly prescribed antihistamines as a monotherapy. It was observed that nasal steroids were administered to most of the patients only irregularly on an as-needed basis. This condition could possibly be explained by the educational deficiency of the patients and their physicians in our country and/or corticophobia, which is still widely spread all over the world. In addition, 57 patients (7.4%) had received specific immunotherapy in a former

allergy center with a mean duration of 2.91 years, which was discontinued due to no response or side effects. Treatment for SR consists of allergen avoidance, education and medication in our clinical practice.

Asthma and SR frequently appear as comorbid conditions. In some instances, they may appear one after the other as a part of nasobronchial allergy. Although there are various studies on asthma risk factors among children and adults, the factors which are involved in the development of seasonal rhinitis into asthma are still not clear. Analysis of our data suggested respiratory symptoms and familial atopy as risk factors for the development of asthma in patients with SR. Ocular symptoms and the presence of metal allergy were less frequent in asthma patients. SR is a disease of a younger age group, which could progress to asthma. As this was a cross-sectional study it is not possible to assess the temporal association and causality of the associations. History and the allergen spectrum of patients should carefully be evaluated in order to determine the risk factors of SR patients for asthma. Metal allergy could be a related to a genetic factor which could prevent the SR patients from developing asthma. Positive association of familial atopy could also be related to a genetic background of asthmatic SR patients, which could make them more susceptible to develop multiple allergies. A prospective study of patients with SR would help to elucidate our findings.

In summary, SR lasts approximately 3.5 months and the main cause in Ankara, Turkey is grass pollen sensitiv-

ity. SR patients are referred to allergy clinics quite late, approximately 6.7 years after the onset of the symptoms, which might be due to not considering SR as a serious disease. Other allergic conditions accompany SR in 39.8% of the patients. The change over time in the treatment

modalities was appropriate but not sufficient for global trends and drug consumption profiles (fig. 2). It seems that this group of patients is generally not treated appropriately, which points out the need for continuous education of both the public and the physicians in Turkey.

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