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Journal of Asthma

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597262>

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Online Publication Date: 01 October 2008

To cite this Article Celikel, Serhat, Isik, Sacide Rana, Demir, Ahmet Ugur, Karakaya, Gul and Kalyoncu, Ali Fuat(2008)'Risk Factors for Asthma and Other Allergic Diseases in Seasonal Rhinitis', Journal of Asthma, 45:8, 710 — 714

To link to this Article: DOI: 10.1080/02770900802249156

URL: <http://dx.doi.org/10.1080/02770900802249156>

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ORIGINAL ARTICLE

Risk Factors for Asthma and Other Allergic Diseases in Seasonal Rhinitis

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Background. Rhinitis and asthma are common comorbidities. The aim of this study was to determine the risk factors for asthma and other allergic diseases in seasonal rhinitis (SR) patients. **Methods.** Records of 922 patients diagnosed as SR between 1991 and 2005 were evaluated retrospectively. Patients were grouped according to the results of our standard skin prick tests as follows: I-No sensitization: no sensitization to any allergen; II-Mono-pollen sensitization: sensitization to only one pollen allergen; III-Poly-pollen sensitization: sensitization to more than one pollen allergen; IV-Mite sensitization: sensitization to mite with or without any other allergen sensitization. **Results.** The mean age of the patients was 29.5 ± 9.6 and 587 patients (63.2%) were females. Age at onset of SR was median 21 years (16–29 years). Of the 922 patients, 99 had no sensitization, 335 had poly-pollen sensitization, 346 had mono-pollen sensitization, and 142 had mite sensitization. The most prevalent allergens were *P. pratense* (85.3%) and *O. europae* (31.5%). No sensitization group as compared to poly-pollen sensitization group had significantly higher prevalence of asthma as a single accompanying disease (14.1%, $p < 0.05$). Mono-pollen sensitization was significantly associated with lower risk of any accompanying allergic disease (OR: 0.7, 95% CI 0.5–0.9) while no sensitization group (OR: 2.8, 95% CI 1.3–5.9) and mite sensitization were associated with asthma (OR: 2.3, 95% CI 1.2–4.4). **Conclusion.** SR is a condition that presents with different phenotypes. The group with no sensitization and mite sensitization has the highest prevalence of asthma while SR patients with mono-pollen sensitization are unlikely to have an accompanying allergic disease, including asthma.

Keywords asthma, allergic diseases, seasonal rhinitis, skin prick tests

INTRODUCTION

Seasonal rhinitis (SR), which is the best example for IgE-mediated disease, is an inflammatory condition of nasal mucosa induced by seasonal aeroallergens, especially pollens. This inflammation is not restricted to nasal mucosa; it also affects other neighboring mucosal surfaces, such as those of the conjunctiva, soft palate, and most importantly, lower airways. This is why patients present with a wide range of symptoms. Intermittent nasal congestion, watery rhinorrhea, sneezing, itching of the nose, palate, and ears are the most common symptoms, which significantly impair quality of life, school, and work performance (1).

Conversely, it is widely accepted that allergic rhinitis and allergic asthma are manifestations of the same disease (2–7). Of the patients with allergic rhinitis, 19% to 38% may have asthma, which is significantly more than the prevalence reported among the general population (i.e., 3% to 5%) (7). It is known that bronchial inflammation and hyperreactivity are present in patients with allergic rhinitis and increase during pollen seasons (8), and asthma exacerbations may occur in pollen allergic patients, especially during thunderstorms (9).

Pollen grains from the plant cover of a region participate in the composition of aeroflora of that region. Pollen content and diversity are strictly related with the climate of a given region and the combination of different sensitizations might have a role in developing certain allergic diseases. It has previously

been shown that skin test reactivity to pollen is more closely correlated with allergic rhinitis than asthma (10,11).

Although patients with rhinitis seem to be more likely to develop asthma, it has not been possible to predict which patients are at greatest risk for manifesting lower airway symptoms (12). We planned this retrospective study to disclose the clinical and demographic characteristics of the patients with SR and determine whether any pattern of skin prick test (SPT) sensitization represents an increased risk for asthma and other accompanying allergic diseases.

Methods

Clinical records of patients diagnosed with SR in an adult allergy clinic between January 1991 and December 2005 were evaluated retrospectively and of 1,124 patients, 922 patients with complete data of skin prick testing were enrolled in the study. Patients presenting with seasonal symptoms of sneezing, watery rhinorrhea, nasal congestion, and itching of the nose with or without ocular symptoms were diagnosed as SR whether they had prick test positivity. Patients who presented with seasonal respiratory and dermatological symptoms and who also have SR symptoms were included in the study as well. The data about demographic features, SPTs, initial symptoms, accompanying allergic diseases, and the treatment they had received for SR were collected.

Atopy and allergen spectra were assessed by our standard SPT panel to 16 common aeroallergens, prepared by the firms ALK (Denmark), Stallergens (France), and Greer (USA) (*Dermatophagoides pteronyssinus*, *Phleum pratense*, *Artemisia vulgaris*, *Parietaria officinalis*, *Corylus avellana*, *Betula verrucosa*, *Olea europae*, cat, dog, horse, *Alternaria alternata*, *Cladosporium herbarum*, *Aspergillus fumigatus*,

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TABLE 1.—Association of the allergic sensitization groups with personal characteristics of the patients.

	<i>n</i>	No sensitization (<i>n</i> : 99) %	Poly-pollen sensitization (<i>n</i> : 335) %	Mono-pollen sensitization (<i>n</i> : 346) %	Mite sensitization (<i>n</i> : 142) %	Total (<i>n</i> : 922) %
Female gender	582	73.7	64.8	59.8	59.9	63.1
Age, years, median (interquartile range)*		33 (25–40)*	28 (21–35)	28 (22–34.25)	27 (21–35)	28.0 (22–35)
Age at onset of SAR, years, median (interquartile range)*		24 (19–33)*	20 (16–28)	22 (16–29)	20.5 (15–27)	21.0 (16–29)
Pet holding	164	19.2	15.5	18.2	21.1	17.8
Smoking status						
Nonsmoker	672	70.5	72.3	73.0	79.6	72.9
Ever smoked	242	29.5	27.7	27.0	20.4	27.1
Family atopy*	536	46.5*	59.1	57.5	65.5	58.1
Family rhinitis*	226	13.1*	25.4	26.2	26.8	24.6
Born in coastal region	183	17.2	18.8	19.7	24.6	19.8
Living in coastal region	69	7.1	7.5	6.6	9.9	7.5

**p* < 0.05, in comparisons with the poly-pollen sensitization group.

cockroach, *Apis mellifera*, *Vespula* species). Tests were performed as described by Österballe and Weeke (13) 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 minutes. A positive reaction was defined as wheal with a geometric mean diameter of 3 mm or more greater than saline control. 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.

Association between allergen sensitization and allergic diseases accompanying SR was investigated to assess the risk factors for another allergic disease in the cohort of SR patients. Allergic diseases were grouped exclusively as follows: I- Only SR, II-SR + eczema, III: SR + metal allergy, IV: SR + drug allergy, V: SR + food allergy, VI: SR + asthma, VII: SR + more than one allergic disease (multiple allergies). In this classification, patients with only one accompanying allergic disease were included in the disease groups, and those with more than one allergic disease were in a separate group. The aim was to assess the association specific for an accompanying allergic disease. Another grouping, including multiple allergies in the disease groups, was also used in the analysis.

Asthma was defined as physician diagnosis of asthma. Diagnosis of accompanying allergic diseases was based on patients' reports. Sensitization groups were defined according to the results of SPTs as follows: No sensitization: no sensitization to any allergen; Mono-pollen sensitization: sensitization to only one pollen allergen; Poly-pollen sensitization: sensitization to more than one pollen allergen; Mite sensitization: sensitization to mite with or without any other allergen sensitization. Poly-pollen sensitization group was selected as the reference group as it included a large number of patients and could be a typical feature of SR. Mite sensitization was grouped separately, as it could be a risk factor for asthma. The reference group for allergic diseases was only SR, and for allergen sensitization poly-pollen sensitization group. Associations between the allergen sensitization groups and the accompanying allergic diseases were also adjusted for sensitization to other allergens, including cat, dog, horse, and molds and for pollen allergens separately (results not shown).

SPSS MS Windows Release 10.0 was used for statistical analysis. Personal characteristics and disease-related factors were compared between groups of allergen sensitization. Age and age at onset of SR were not normally distributed and described with the median and interquartile range values. Chi-square testing and Mann-Whitney U test were used for categorical and continuous variables, respectively. Bonferroni correction was applied for multiple comparisons. Association of the allergen sensitization groups with allergic diseases was adjusted for age, gender, and age at onset of SR, which reported odds ratios (ORs) and 95% confidence interval as the effect measure. Statistical significance was defined for *p* values less than 0.05.

RESULTS

Demographic features presenting symptoms and accompanying atopic diseases of the patients are summarized in Table 1. Of the 922 patients, 99 had no sensitization, 335 had poly-pollen sensitization, 346 had mono-pollen sensitization and 142 had mite sensitization. Median age and interquartile range in parenthesis was 28 years and (22–35 years), respectively. Age at onset of SR was median 21 years (16–29 years). Age and age at onset for SR were significantly different between the no sensitization group and poly-pollen sensitization group (age in years: 33, 25–40 and 28, 21–35, respectively; age at onset of SR in years: 24, 19–33 and 20, 16–28, respectively). Of the patients, 587 (63.2%) were females.

Familial atopy and familial rhinitis were reported significantly less frequent in no sensitization group than poly-pollen sensitization group (familial atopy: 46.5% and 59.1%, respectively; familial rhinitis: 13.1% and 25.4%, respectively). Allergen spectra of the mite sensitization group included 94.4% pollen, 19.7% cat, 7% dog, and 11.3% horse allergens.

The patients had been symptomatic with a mean duration of 3.6 ± 1.8 months a year, most frequently in May (92%) and June (83%). Positive skin prick testing to at least one inhalant allergen was present in the 89.8% of the patients, and the most prevalent allergens were *P. pratense* (85.3%) and *O. europae* (31.5%). SPTs of 99 patients (10.7%) were negative, although they have been clinically diagnosed as SR. The allergen spectra of the patients tested by SPT are shown in Table 2. Onset of the SR symptoms were between March and June in 96.6% of the patients. Seasonality of the symptoms

TABLE 2.—Allergen spectra of the patients tested by SPT.

Allergens	Test performed, <i>n</i>	Positive test, <i>n</i>	Positive test, %
At least one allergen positivity	922	823	89.3
Pollen (total)	922	817	88.6
Pollen only	922	381	41.3
Grass (total)	920	785	85.3
<i>P. pratense</i>	920	785	85.3
<i>P. pratense</i> only	920	361	39.2
Weeds (total)	922	230	24.9
Weeds only	922	11	1.2
<i>A. vulgaris</i>	922	213	23.1
<i>A. vulgaris</i> only	922	9	0.9
<i>P. officinalis</i>	922	55	6.0
<i>P. officinalis</i> only	922	2	0.2
Tree (total)	922	368	39.9
Tree only	922	8	0.9
<i>O. europae</i>	922	290	31.5
<i>O. europae</i> only	922	5	0.5
<i>C. avellana</i>	886	155	17.5
<i>C. avellana</i> only	886	1	0.1
<i>B. verrucosa</i>	922	150	16.3
<i>B. verrucosa</i> only	922	2	0.2
Mite (D. Pteronyssinus)	922	142	15.4
Mite only	922	4	0.4
Pet animals (total)	922	112	12.1
Cat	922	81	8.8
Horse	922	36	3.9
Dog	922	26	2.8
Molds (total)	922	10	1.1
<i>A. fumigatus</i>	259	5	1.9
<i>C. herbarum</i>	768	3	0.4
<i>A. alternata</i>	922	3	0.3

were pertinent with the allergen spectra of the patients, who had SPT positivity. Similarly, 97 % of the patients without any sensitization, reported onset of their symptoms between March and June.

Table 3 shows the prevalence of allergic diseases in the allergic sensitization groups. SR without any accompanying allergic disease (only SR) was reported significantly more common in the mono-pollen sensitization group (63.3%) and less common in the no sensitization group (40.4) than the poly-pollen sensitization group (54.3%). No sensitization group as compared to the poly-pollen sensitization group had significantly higher prevalence of drug allergy as a single

disease (13.1% and 6.9%, respectively), asthma as a single disease (14.1% and 6.3%, respectively), and multiple allergies (13.1% and 10.7%, respectively).

The mono-pollen sensitization group as compared to the poly-pollen sensitization group had significantly lower prevalence of drug allergy as single disease (4.3% and 6.9%, respectively), food allergy as single disease (7.2% and 11.6%, respectively), and multiple allergies (5.8% and 10.7%, respectively). The mite sensitization group had higher prevalence of asthma than the poly-pollen sensitization group (13.4% and 6.3%, respectively), but the difference did not reach statistical significance. Comparisons were repeated for the disease groups including any combination of accompanying allergic diseases. No sensitization group as compared to the poly-pollen sensitization group had significantly higher prevalence of metal allergy (19.2% and 11.6%, respectively), drug allergy (20.2% and 12.5%, respectively), asthma (19.2% and 9.6%, respectively), and multiple allergies (13.1% and 10.7%, respectively). The mono-pollen sensitization group as compared to the poly-pollen sensitization group had significantly lower prevalence of drug allergy (7.2% and 12.5%, respectively), food allergy (10.4% and 20.0%, respectively), and multiple allergies (5.8% and 10.7%, respectively). The mite sensitization group had higher prevalence of asthma than the poly-pollen sensitization group (15.5% and 9.6%, respectively), but the difference did not reach statistical significance.

Association between allergic diseases and allergen sensitization groups after the adjustment for age, gender, and age at onset of SR is shown in Table 4. Disease groups were defined as exclusive groups including single accompanying allergic disease, excluding combination of allergic diseases. No sensitization was significantly associated with any allergy (OR: 1.6, 95%CI 1.0–2.6), drug allergy (OR: 2.3, 95%CI 1.1–5.1), and asthma (OR: 2.8, 95%CI 1.3–5.9). Mono-pollen sensitization was significantly associated with any allergy (OR: 0.7, 95%CI 0.5–0.9), and food allergy (OR: 0.5, 95%CI 0.3–0.9). The mite sensitization group was associated with asthma (OR: 2.3, 95%CI 1.2–2.4). Associations were not changed after the adjustment for sensitization to other allergens, including cat, dog, and horse.

TABLE 3.—Prevalence of allergic diseases† in the allergic sensitization groups.

	<i>n</i>	No sensitization (<i>n</i> : 99) %	Poly-pollen sensitization (<i>n</i> : 335) %	Mono-pollen sensitization (<i>n</i> : 346) %	Mite sensitization (<i>n</i> : 142) %	Total (<i>n</i> : 922) %
Only SAR	515	40.4*	54.3	63.3*	52.1	55.9
SAR + allergic disease‡						
SAR + eczema	26	1.0	4.2	2.3	2.1	2.8
SAR + metal allergy	65	9.1	6.0	8.4	4.9	7.0
SAR + drug allergy†*	62	13.1*	6.9	4.3*	7.7	6.7
SAR + food allergy†*	91	9.1	11.6	7.2*	12.7	9.9
SAR + asthma†*	84	14.1*	6.3	8.7	13.4	9.1
SAR + multiple allergies*	79	13.1*	10.7	5.8*	7.0	8.6
SAR + allergic disease‡						
SAR + eczema	37	3.0	5.4	3.2	3.5	4.0
SAR + metal allergy	109	19.2*	11.6	11.3	8.5	11.8
SAR + drug allergy*	103	20.2*	12.5	7.2*	11.3	11.2
SAR + food allergy*	146	18.2	20.0	10.4*	17.6	15.8
SAR + asthma*	112	19.2*	9.6	11.3	15.5	12.1

† Disease groups included only those with one of the accompanying disease (e.g., for SAR + eczema only patients who reported eczema as a single accompanying disease constituted the disease group).

‡ Disease groups included those with accompanying disease in any combination (e.g., for SAR + eczema patients, who reported eczema as a single accompanying disease and patients who reported eczema with metal allergy and/or drug allergy and/or food allergy and/or asthma a single accompanying disease constituted the disease group).

**p* < 0.05, in comparisons with the poly-pollen sensitization group.

TABLE 4.—Adjusted association between the allergic sensitization groups and allergic diseases.

	Poly-pollen Reference	No OR (95%CI)	Mono-pollen OR (95%CI)	Mite OR (95%CI)
Exclusive†				
Any allergy	1	1.6 (1.0–2.6)	0.7 (0.5–0.9)	1.1 (0.7–1.6)
SAR + eczema	1	0.3 (0.04–2.6)	0.5 (0.2–1.2)	0.5 (0.1–1.8)
SAR + metal allergy	1	1.9 (0.8–4.7)	1.4 (0.7–2.5)	1.0 (0.4–2.6)
SAR + drug allergy	1	2.3 (1.1–5.1)	0.6 (0.3–1.1)	1.2 (0.5–2.5)
SAR + food allergy	1	1.2 (0.5–2.6)	0.5 (0.3–0.9)	1.1 (0.6–2.1)
SAR + asthma	1	2.8 (1.3–5.9)	1.2 (0.7–2.2)	2.2 (1.2–4.4)

†Disease groups included those with only one accompanying disease (e.g., for SAR + eczema, only patients who reported eczema as a single accompanying disease constituted the disease group).

Each allergic disease was compared with the group of only SAR. In the logistic regression models adjustments were made for age, gender, and age at onset of SAR.

Reference group for the allergen sensitization was the group with poly-pollen sensitization.

Significant associations are shown in bold type.

DISCUSSION

In our previous study (14), we evaluated clinical characteristics and treatment modalities of 774 patients who have been diagnosed as SR between 1991 and 2003 in a university adult allergy clinic. In this study, we added 148 more patients with SR in the following 2 years to our previous data and investigated whether there was an association between SPT sensitizations and coexistence of asthma and other allergic diseases in SR patients in an adult allergy clinic which admits patients from all regions of Turkey.

In this study, our main finding was that prevalence of SR with any single accompanying allergic disease (13.1%) and SR with asthma (14.1%) was significantly higher in the no sensitization group than the poly-pollen sensitization group. OR's were 2.8 and 1.6, respectively, which suggested increased risk of another allergic disease, and asthma in SR patients with no allergen sensitization. Mite sensitization in SR patients was also associated with asthma (OR: 2.3), which suggested increased risk of asthma in SR patients with mite sensitization.

There are considerable amounts of data in literature about associations between rhinitis and asthma. In a cross-sectional study conducted in 1995–1996 in Leipzig, a city of former East Germany in which tremendous changes towards western lifestyle have occurred after unification, the prevalence of seasonal allergic rhinitis and atopic sensitization increased significantly compared to a previous study conducted with same methods shortly after the unification in 1991–1992 (15). However, there was no significant change in the prevalence of asthma or bronchial hyperresponsiveness.

In another study, data of the patients between 20 to 44 years of age from ECRHS study were used to assess the associations between asthma and rhinitis (16). Asthma was present in 0.8 % of subjects without rhinitis, in 6% of subjects with seasonal rhinitis only, and in 18% of subjects with both seasonal and perennial rhinitis. Asthma was associated with rhinitis in both atopic subjects (OR: 8.1) and nonatopic subjects (OR: 11.6) (16). Similar associations have also been reported in another ECRHS study (17). In this study, the risk of asthma was higher in the subjects sensitized only to pollen allergens than in nonsensitized subjects (17). However, among subjects without rhinitis, when rhinitis was taken into account, the risk of asthma was similar in subjects sensitized to pollen and

nonsensitized subjects (1.9% vs 1%). In parallel with these studies (15–17), we did not find an increased prevalence of asthma in SR patients by a pattern of pollen sensitization. On the contrary, the prevalence of asthma (14.1%) was significantly higher in the no sensitization group. Overall, these data might show that although asthma and rhinitis generally present together, this comorbidity cannot be explained only by a similar atopic predisposition to these diseases, and it seems that rhinitis itself might be a risk factor for asthma in SR patients as proposed before (10,16,17). In this study, SR without any accompanying allergic disease (only SR 63.3%) was significantly more prevalent in the mono-pollen sensitization group, and mono-pollen sensitization was significantly associated with lower risk of any accompanying allergic disease (OR: 0.7). It has been shown that increasing number of sensitizations are associated with high prevalence of asthma and allergic rhinitis in adults and children (18–22). In one of these studies performed in adults, the prevalence of allergic rhinitis was 41.8% among those sensitized to at least one inhalant allergen, whereas it was 66.7% for three allergens and 80.3% for four and more allergens (20). Contrary to this in our study, SR was significantly higher in mono-pollen sensitization group (63.3%) compared to poly-pollen sensitization (54.3%). Drug allergy and food allergy were significantly lower in the mono-pollen sensitization group. Our findings suggest that, mono-pollen sensitization does not increase the risk of an accompanying allergic diseases in a patient with seasonal rhinoconjunctivitis.

The prevalence of different pollen sensitizations in SR may vary greatly in the individuals according to the region and the climate in which they live. The majority of temperate zones in the world are dominated by grass pollens (23). Studies have shown that grass pollen in Turkey (24–26), birch and grass pollens in northern Europe, ragweed pollen in America, and mugwort and olive pollens in Mediterranean area are the most common and important allergens of these regions (27,28).

According to the panel we used, at least one inhalant allergen positivity was present in 89.8% of the SR patients, and pollen sensitization was 88.6%. The most common sensitizing allergen was a grass pollen, *P. pratense* (85.3%), followed by a tree pollen, *O. europae* (31.5%), which is a well-known tree of coastal Mediterranean region. Although the study was conducted in the capital city of Turkey, Ankara, which is in the inner part of Turkey and far from the coastal regions of Turkey, high sensitization of *O. europae* was attributed to the cross-reactions with other grass and tree pollens that are also prevalent in the inner regions, such as birch, pine, cypress, and ryegrass, and the migration of population from the coastal regions to the capital city for various reasons such as education and employment. Although these patients had clear-cut histories of seasonal symptoms, 10.7% of the patients showed no sensitivity to any of the aeroallergens tested. This might be owing to a possible localized allergic reaction or sensitization with other allergens, which were not included in this routine panel, although it is very similar to the panel suggested in GA²LEN Pan-European core SPT panel (29).

In our study, we also found that presence of mite sensitization in SR patients was associated with asthma (OR: 2.3). This finding was not surprising as association between sensitization to mite and other indoor allergens and asthma was shown in several studies (18,19,30).

These findings might have some clinical implications. First, because SR patients with mono-pollen sensitization have lower risk of an accompanying allergic disease, patient groups can be selected more reasonably in studies about the impact of some treatment modalities to natural course of allergic rhinitis. Second, SR patients with no sensitization or mite sensitization should be followed carefully with the consideration of increased risk of asthma. Third, mite sensitization among SR patients could indicate increased risk of asthma. These associations could be due to factors other than the allergen sensitization patterns. Analysis of specific allergen sensitizations including cat, dog, and horse did not change these findings. The tentative association found between the group with no allergen sensitization and asthma could be tested in studies with the assessment of bronchial hyperresponsiveness.

In conclusion, compared to the poly-pollen sensitization group, the groups with no sensitization and mite sensitization had a higher risk of asthma while SR patients with mono-pollen sensitization group were unlikely to have any other allergic disease including asthma. These findings suggest that SR is a condition that probably presents with different phenotypes, including different patterns of allergen sensitization and accompanying allergic diseases. The role of factors other than atopic sensitization in the development of accompanying allergic diseases and the predictive role of atopic sensitization should be investigated in prospective studies of SR patients.

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