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An Analysis of Skin Prick Test Reactions in Allergic Rhinitis Patients in Istanbul, Turkey

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SUMMARY This retrospective, population-based study reviewed skin prick test (SPT) results against various allergens of 1,552 patients with allergic rhinitis (AR) in the district of Kartal, Istanbul, Turkey. The skin prick tests yielded a positive result in 946 patients (60.9%). Seven hundred and forty-give (48%) patients had perennial AR, 558 (36%) perennial AR with seasonal exacerbations and 249 (16%) had seasonal AR. The prevalence of AR was highest in the age of 21-40 years with 48.7%. The allergen group with the highest SPT positivity was pollens at 44.3%, followed by molds at 38.4%, mites at 35.1%, and epithelia-insect at 30.8%. The strongest single allergen was *Alternaria alternata* with 33.3%, followed by *Dermatophagoides farinae* with 29.3%, *Dermatophagoides pteronyssinus* with 25.3% and a mix of four cereals (barley, maize, oat, wheat) with 25.2%. This information will help etiological research as well as the development of more efficient treatment plans for patients with allergic rhinitis in our country.

Allergic Rhinitis (AR) is the most common form of rhinitis and is characterized by a symptom complex that consists of any combination of the following: sneezing, nasal congestion, nasal itching, and rhinorrhea. The onset of AR is usually in childhood, adolescence, or during early adult years. The causes of AR vary depending on whether the symptoms are seasonal or perennial. Seasonal AR is commonly caused by seasonal pollens and outdoor molds. Perennial AR is typically caused by allergens within the home but can also be caused by outdoor allergens that are present all year around.[1]

Testing for specific allergens can be helpful to confirm the diagnosis of AR and to determine specific allergic triggers. If such specific triggers are known, appropriate measures can be recom-mended. Allergy testing can be performed in one of three ways; mucosal challenge testing, skin testing and *in vitro* testing. Epicutaneous (prick or puncture) or intracutaneous (intradermal) applications of potential allergens are clinically useful methods of allergy testing. With any of these methods, an allergen-specific response can be qualitatively or quantitatively measured. Skin prick (SP) testing (single or multiple pricks) is widely used, relatively safe, well controlled, and has a long track record. SP testing is commonly used as a screening tool by otolaryngologists and general allergists. It requires few supplies and has become relatively standardized in its application, although there is some variation in the interpretation.[2]

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The prevalence of AR is roughly 20% and seems to vary among different populations and cultures which may be due to genetic, environmental or geographic differences in the types and potency of the different allergens and the overall aeroallergen burden. In surveys carried out in other parts of the world the prevalence of different aeroallergens has been defined.[3-9]

This study was conceived to detect the prevalence of skin positivity to different aeroallergens in patients with AR in Istanbul in order to improve the management strategies.

MATERIALS AND METHODS

Study design

The study was performed retrospectively, between February 2002 and September 2006, in the Outpatient Clinic of the ENT Department of Kartal Teaching and Research Hospital. One thousand five hundred and fifty-two patients clinically diagnosed with AR were included in this study. On admission, patients were evaluated by the means of a questionnaire regarding their AR symptoms in detail such as sneezing, pruritus, rhinorrhea, and/or nasal congestion. Patients were evaluated on physical findings such as a pale, swollen mucosa with mucoid secretions, swollen inferior turbinates, edematous appearance of the posterior end of the inferior turbinate and “cobblestone” appearance of the posterior pharyngeal wall. The diagnosis was based on AR symptomatology and clinical examination. After an anterior and posterior nasal endoscopic examination, patients underwent skin tests to inhalant allergens. Inhabitants of both inner cities and neighborhoods were included. Subjects who had used antihistamines within the last two weeks were excluded from the study. The study was approved by the Ethics Committee of the hospital and a written informed consent was obtained from all participants.

The allergens

The respiratory allergen panel comprising extracts of 15 different allergens was obtained from Stallergenes Laboratories (Fresnes, France). These extracts included grass (mixture of five grasses), tree (*Betulaceae, Fagaceae)* and weed (*Compositae,* a mixture of four cereals [barley, maize, oat, and wheat]) pollens, mold spores (*Alternaria alternata, Aspergillus* mix, *Cladosporium, Penicillium* mix), house dust (HD) mites (*Dermatophagoides pteronyssinus* [*der.p.*] and *Dermatophagoides farinae* [*der.f.*]), epithelia and insect allergens (feather mix, cat hair, dog hair, cockroach).

Skin-prick test

The skin-prick tests were performed on the ventral side of the forearm. After cleaning the forearm with alcohol, 0.01 ml to 0.02 ml of standardized antigens (1:50 dilution) were placed in a parallel array to the axis of each sterile forearm two centimeters apart. The Stallerpoints device was used to perform the prick test. Histamine hydrochloride 10 mg/ml and 50% glycerol-saline solutions were used as positive and negative controls, respectively. The results were recorded after 20 minutes and allergic reactions were graded as "+", "++", "+++", "++++" and "-" on the basis of intensity of reaction, erythema or wheal formation.[10] Medications inhibiting wheal and flare reactions to histamine were withdrawn at least 7 days prior to the testing procedures.

Statistical analysis

Data were analyzed by computer using the Statistical Package for Social Sciences (SPSS) for Windows, version 11.5. The results of the allergic reactions were analyzed with the chi-square and Spearman’s rho tests. A *p*-value less than 0.05 was considered statistically significant.

RESULTS

Among the 1,552 patients, 1,136 (73.2%) were females, 416 (26.8%) were males with a ratio of females to males of 2.73:1. Their age ranged from 11 years to 80 years (mean ± SD, 38.12 ± 14.4 years). In our study, AR was observed mostly in the age between 21-40 years with a prevalence in this group of 48.64% (36.98% females and 11.66 % for males) (Table 1).

The SPT was positive in 946 (60.9%) and negative in 606 (39.1%) of the 1,552 patients. In 745 (48%) patients AR was perennial, in 558 (36%) the

Table 1 Age distribution according to gender

	Female N (%)	**Male** N (%)	**Total** N (%)
11-20 years	146 (9.4%)	86 (5.54%)	232 (14.94%)
21-40 years	574 (36.98%)	181 (11.66%)	755 (48.64%)
41-60 years	362 (23.32%)	114 (7.34%)	476 (30.67%)
61-80 years	54 (3.47%)	35 (2.25%)	89 (5.73%)
Total	1,136 (73.19%)	416 (26.80%)	1,552 (100%)

Table 2 The distribution of allergen positivity according to gender

	Female N (%)	**Male** N (%)	**Total** N (%)
Pollens	499 (43.9%)	188 (45.6%)	687 (44.3%)
Molds	446 (39.3%)	150 (36.1%)	596 (38.4%)
Mites	387 (34.1%)	158 (38%)	545 (35.1%)
Epithelia-Insect	382 (33.6%)	97 (23.4%)	479 (30.8%)

* The total in this table exceeds 100% as positivity to multiple allergens was sometimes observed in the same patient.

Table 3 The distribution of allergen positivity according to age

Allergen	**11-20 years** (%)	**21-40 years** (%)	**41-60 years** (%)	**61-80 years** (%)	**Total** (%)
Pollens	52.2%	53.1%	47.1%	49.3%	44.3%
Molds	44.7%	44.4%	44.6%	45.9%	38.4%
Mites	58.5%	44.4%	32.6%	24.7%	35.1%
Epithelia-insect	35.6%	34.6%	30.4%	29.2%	30.8%

*The total in this table exceeds 100% as positivity to multiple allergens was sometimes observed in the same patient.

symptoms were perennial with seasonal exacerbations, while 249 (16%) suffered from seasonal AR.

The patients with a positive SPT were classified according to the allergen groups (mites; pollens; molds and epithelia-insect). Looking at the frequency distribution of these specific allergen groups, we found that the most common SPT positivity was with pollens (44.3%), followed by molds (38.4%), mites (35.1%), and the epithelia-insect (30.8%) group (Table 2). The latter group was statistically significantly higher in women in comparison to men (33.6% *versus* 23.4%) ($p < 0.05$).

Looking at the age distribution of the allergen groups, mite allergy was seen more frequently in patients between 11-20 years of age with an incidence of 58.5%. This difference from the other age groups was statistically significant ($p < 0.001$). There was no correlation between pollens, molds and epithelia-insect groups and any specific age range (Table 3). *Compositae* allergy was seen 2.45 times more frequently in women than in men which was statistically significant ($p < 0.05$).

Table 4 The distribution of positive SPT reactions to specific allergens (values are stated as %)

Specific allergens	"+"(%)	"++"(%)	"+++"(%)	"++++"(%)	Total (%)
Alternaria alternata	13.9	12.8	3.3	-	30
D. farinae	7.9	9.9	8.6	2.9	29.3
D. pteronyssinus	5.7	8.4	9.5	1.7	25.3
Mix of 4 cereals	9	9.4	5.5	1.3	25.2
A. betulacees	11.4	9.7	2.4	-	23.5
Mix of 5 grasses	9	7.7	5.5	0.7	22.9
Feather mix	9.2	10.1	1.7	0.2	21.2
***Aspergillus* mix**	10.8	7.5	1.7	0.2	20.2
A. fagacees	9.5	7.5	2.4	-	19.4
Cladosporium	9	6.2	1.3	0.4	16.9
Cat hair	9.7	5.7	1.1	-	16.5
Compositae	7.2	3.5	1.3	-	12
***Penicillium* mix**	5	4.6	1.3	-	10.9
Dog hair	6.1	2.0	0.9	-	9
Cockroach	0.9	2.2	0.2	-	3.3

The frequency of positive SPT reactions with specific allergen extracts are given in Table 4. *Alternaria, der.f., der.p.,* and a mixture of four cereals (barley, maize, oat, and wheat) were the most important allergens causing skin test positivity (33.3%, 29.3%, 25.3% and 25.2%, respectively). SPT results of "+++" and "++++' were found in 795 patients (51.2%) and the percentages of *der.f.* and *der.p.* allergy were remarkable with 11.5% and 11.2%, respectively.

DISCUSSION

Epidemiological studies have shown considerable variations in allergen source and allergen potency concerning the etiology of AR in different populations. In addition to genetic factors, environmental factors, such as geographic and meteorological conditions, are important for allergic sensitization and the development of symptoms.

A study performed by mail survey in London on 7702 individuals with an age range from 16 to 65 years demonstrated a prevalence of 3% for seasonal symptoms, 13% for perennial symptoms and 8% for perennial symptoms with seasonal exacerbations.[11] Another study conducted by mail survey in Northern Italy on 7000 subjects with an age range from 20 to 44 years showed a prevalence of 11.2%, 29.6%, and 51.5% for perennial rhinitis, seasonal rhinitis and perennial rhinitis with seasonal exacerbations, respectively.[3] Both of these studies with high participant numbers revealed a significantly high prevalence of perennial symptoms, which was reflected in our study where only 16% of the patients had seasonal symptoms whereas 84% exhibited a perennial pattern.

Previous studies have found that the prevalence of nasal symptoms and AR peaked in the 16-24 years age group and that there was a decline in prevalence in the 65-70 age group.[3-5,12] Our study showed a similar, although not the same trend; the highest prevalence of symptoms was in the age group between 21 and 40 (48.7%). The SPT positivity rate was previously reported to be approximately between 50 – 70 % in patients with clinically overt AR. In this study, 60.9% of patients tested positive to at least one allergen which is in agreement with previous reports in the literature.[4, 9, 13-15]

In this study, a female/male ratio was 2.73 to 1. The first Italian mail survey study on the 20-44 years age group showed no statistically significant difference between genders in AR.[3] In the first Austrian allergy report, the cumulative prevalence of al-

lergies in the Viennese population was 32.2% in women and 27.6% in men.[4] Although the results suggest a higher prevalence in women, our study lacks the power to make an accurate comment due to the limited number of study subjects and the non multi-center nature of our study. Several reports in the literature found no gender difference in the prevalence of AR in the adult population.[1,4,5,16,17.]

Air-borne pollen and spore allergens have been implicated as some of the main causes of allergic respiratory disorders in countries with temperate climates.[18] The major allergenic pollens (grasses, weeds and trees) are derived from wind-pollinated rather than from insect-pollinated plants, and the clinically important pollens vary depending on the geography.[19] Sensitivity to pollens was the leading cause of positive test results in our retrospective evaluation of SP tests. This high frequency of pollen sensitivity may be related to the wide variety of plants inherent to our region. We evaluated the allergen sensitization in the Turkish population living in Istanbul and its suburbs and found that the highest rate of SP test positivity was with the pollen group (44.3%). Similar studies have been conducted in other regions of Turkey, but no concrete data from a high number of study participants have been available for our region.[8,9,12,13,20] Our study provides these data to close the information gap regarding allergen prevalence in our region.

Istanbul is the largest city in Turkey and is located at the junction of southeast Europe and west Asia. The weather is somewhat a cooler version of the Mediterranean climate. The average annual temperature is 13.7°C. The humidity is constantly high which creates ideal conditions for the growth of a variety of plants that constitute the natural vegetation. Therefore, the climate is ideal for the generation of a wide array of pollens. The climate enables twice-yearly cultivation. Similar to several other regions in the world, barley, maize, oat and wheat are cultivated in Turkey as well. For this reason, the 25.2% SPT positivity directed to these crops is not an unexpected finding in our study. A high sensitivity to pollens was already demonstrated in other studies conducted in other regions of Turkey.[8,9,12,13,20] The second leading allergic offender in our study was the *Betulaceae* group with a rate of 23.5%, followed by the mixture of five grasses which was responsible for 22.9% of the cases. Tezcan *et al*.[9] studied 5,055 cases in the Aegean Region; grass pollen sensitivity rate was 54%, cereal pollen sensitivity 45% and wild grass pollen sensitivity 20%. Sener *et al.*[12] studied skin tests to aeroallergens in Ankara and reported grass pollens to be the major allergens (74.3%). In a study carried out by Sin *et al.*[13] sensitivity to pollens was described in 34.5% of 277 cases in the Aegean Region.

Like pollens, mold spores are important air-borne allergens. Mold spores favor damp homes with high humidity and cold surfaces onto which moisture can condense. Therefore, damp basements or humid bathrooms within an otherwise dry house can serve as the source of generation and spread of mold spores throughout the house.[21] The prevalence of respiratory allergy to fungi is estimated to be 20% to 30% among atopic individuals and up to 6% in the general population.[22,23] We studied *Alternaria*, *Aspergillus*, *Cladosporium* and *Penicillium* species which are known to have a high allergenic potency. *Alternaria* is the best-studied mold spore, and its extracts can produce highly positive skin tests.[7] In our study it caused the highest rate of allergic sensitivity with 33.3%. This was followed by *Aspergillus* species, *Cladosporium*, and *Penicillium* species with a rate of 20.2%, 16.9% and 10.9%, respectively. Previous studies in Turkey showed the sensitivity to fungi ranging from 2% to 26%.[8,13,20,24] The wide variation in the reported sensitivity can be explained by the differences in temperature and humidity between different regions in Turkey. European and U.S. originated studies reported sensitization rates to fungi between 3% to 20%.[3,6,7,14] Extremely high rates of sensitization to molds are found in tropical countries like Singapore and Malaysia, perhaps underscoring the role of a climatic factor.[25,26]

Probably the most common and best studied indoor allergen is dust mite. *Der. p.*, once considered the European mite, and *Der. f.*, considered the North American mite, are the most common HD mites worldwide. Mites' waste product particles are the main substances embedded in HD to which allergic subjects react.[3] In previous studies, 27.5-95% of patients with respiratory symptoms demonstrated an allergic reaction to HD mites.[14,15,25-27] HD mites have been reported to cause the highest rate of sensitization in patients with AR in Far East countries where

the humidity is high.[12,15,26,27] On the other hand, local prevalence studies in various regions of Turkey found sensitivity rates to HD mites from 33% to 81%.[9,12,13,16,20] In our study, 29.3% of patients were sensitive to *der.f.* and 25.3% were sensitive to *der.p*. The high sensitization rate to both species of HD mites is consistent with the ubiquitous nature of the allergen. Climate characteristics, including the high humidity in our region, and socio-economic factors like residing in old houses due to low income, may play a role in the rate of sensitization to HD mites.

In summary, we retrospectively evaluated epidermal SP tests in patients with clinically evident AR residing in Istanbul and its suburbs. Our study had by far the largest patient population compared to previous studies conducted in our region. Our data indicate that the most prevalent sensitizing allergens are pollens (especially a mixture of four cereals) followed, in order of prevalence, by molds (especially *Alternaria*), mites (*der.f.* and *der.p.*), and epithelia (especially a feather mix). We believe that our data bring valuable information that will guide allergists to develop cost effective allergen testing panels in our region. We should mention, however, that larger-scale multi-center studies with a higher number of patients are needed for a more detailed characterization of allergic pathogens in Istanbul.

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