CLINICAL STUDY

EVALUATION OF SINGLE AND MULTIPLE ALLERGEN SENSITIVITY IN PATIENTS WITH ALLERGIC RHINITIS: A RETROSPECTIVE SINGLE CENTER CROSS-SECTIONAL STUDY

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SUMMARY

Objective: Allergic rhinitis can affect every stage of an individual's daily life and cause loss of work, so the diagnosis and treatment of allergic rhinitis very important. The present study aims to determine the aeroallergen sensitivity of people living in our region by evaluating the results of the skin prick test (SPT) performed in patients presenting with a picture of allergic rhinitis in our region.

Methods: The SPT results of 1,100 patients were requested to undergo SPT due to the symptoms and signs of allergic rhinitis based on the anamnesis and detailed otorhinolaryngological examination were reviewed retrospectively. Gender, age and SPT results of the patients and the type of allergic sensitization in the SPT were evaluated.

Results: SPT positivity was observed in 472 (42.9%) out of 1,100 patients included in the study. The allergen with the highest frequency of positive test responses were herb mixture (n=303), cereal mixture (n=223) and tree mixture (n=106), in respective order. The majority of the patients had concurrent positivity for multiple allergens, and the most common was double allergen positivity (n=217). The most common double allergen positivity was the combination of grass mixture + cereal mixture (n=119).

Conclusion: Apart from establishing the aeroallergen distribution in a particular region, the authors believe that similar studies should also be carried out to update the aeroallergen distributions of the regions that are subject to alterations especially due to global warming and climatic changes, increase in industrialization, and factors that cause changes in regional humidity.

Keywords: SPT,Aeroallergen map, Allergic rhinitis, Allergic sensitization

ALERJİK RİNİTLİ HASTALARDA TEK VE ÇOKLU ALERJEN HASSASİYETİNİN DEĞERLENDİRİLMESİ: RETROSPEKTİF TEK MERKEZLİ KESİTLİ BİR ÇALIŞMA

ÖZET

Amaç: Alerjik rinit, bireyin günlük yaşamının her aşamasını etkileyerek iş kaybına neden olabilir, bu nedenle alerjik rinitin tanı ve tedavisi çok önemlidir. Bu çalışma, bölgemizde alerjik rinit tablosu ile başvuran hastalarda yapılan deri prik testi (SPT) sonuçlarını değerlendirerek bölgemizde yaşayan kişilerin aeroalerjen duyarlılığını belirlemeyi amaçlamaktadır.

Gereç ve Yöntemler: Anamneze dayalı olarak alerjik rinit belirti ve bulguları nedeniyle 1.100 hastanın SPT sonuçları istenmiş ve ayrıntılı kulak burun boğaz muayenesi retrospektif olarak incelendi. Hastaların cinsiyet, yaş ve SPT sonuçları ile SPT'deki alerjik sensitizasyon tipi değerlendirildi.

Bulgular: Çalışmaya alınan 1.100 hastanın 472'sinde (%42,9) SPT pozitifliği gözlendi. En yüksek pozitif test yanıtı sıklığına sahip alerjen sırasıyla bitki karışımı (n=303), tahıl karışımı (n=223) ve ağaç karışımı (n=106) olmuştur. Hastaların çoğunda aynı anda birden fazla alerjen pozitifliği vardı ve en yaygın olanı çift alerjen pozitifliğiydi (n=217). En yaygın çift alerjen pozitifliği çimen karışımı + tahıl karışımı (n=119) kombinasyonuydu.

Sonuçlar : Özellikle küresel ısınma ve iklim değişiklikleri, sanayileşmenin artışı, bölgesel nemin değişmesine sebep olan etmenler (baraj yapımı, tarım ve ormanlık arazilerin azalması gibi) sebebi ile bölgelerin aeroallerjen dağılımlarını belirlemenin yanında güncellemek adına benzer çalışmaların yapılması gerektiği kanaatine varıldı.

Anahtar Sözcükler: SPT, Aeroallerjen haritası, Alerjik rinit, Alerjik duyarlılık

INTRODUCTION

Allergic rhinitis, which occurs as an immunoglobulin E (IgE) dependent, Type I hypersensitivity reaction; It is an inflammatory disease of the nasal mucosa characterized by bouts of sneezing, profuse and watery nasal discharge, nasal congestion and itching.[1]

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The fact that it can affect every stage of an individual's daily life and cause loss of work makes the diagnosis and treatment of allergic rhinitis very important.[2,3] Allergic rhinitis manifests as sneezing, runny nose, nasal itching and nasal congestion after exposure to the allergen to which an individual has previously sensitized. According to the time pattern of symptoms, it is called seasonal allergic rhinitis if the symptoms appear in a certain season, and it is called perennial allergic rhinitis if the symptoms are present throughout the entire year. According to the frequency of the symptoms, patients with a symptom duration of less than four days a week in four consecutive weeks are considered to have

intermittent and those who exhibit symptoms for a longer period are considered to have persistent (continuous) allergic rhinitis.[4] Patients with allergic rhinitis usually have many atopic comorbidities, and 75% of asthma patients also suffer from allergic rhinitis.[1]

The most commonly used diagnostic tests in individuals presenting with a picture of allergic rhinitis are skin prick test (SPT) and specific IgE measurement. In particular, the skin prick test is frequently used in otolaryngology because of the advantage of being fast, easy-to-perform, and of low cost.[5] The detection of specific responsible allergen in the skin prick test is very valuable for avoiding the allergen, which is one of the important steps in the treatment phase, and administering specific allergen immunotherapy.

Because of geographical differences in the distribution of allergens, particularly for aeroallergens, the intensity of allergens vary in a particular region. For this reason, each region has specific aeroallergen distribution according to its geographical and plant cover characteristics, and this distribution varies in aeroallergen maps. The present study aims to determine the aeroallergen sensitivity of people living in our region by evaluating the results of the skin prick tests performed in patients presenting with a picture of allergic rhinitis in our region.

MATERIAL and METHODS

In this study, the symptoms and test results of 1152 cases who applied to the Mardin State Hospital Otorhinolaryngology polyclinic with a preliminary diagnosis of allergic rhinitis between the dates of January 2017 and January 2021 were evaluated retrospectively. Ethics committee approval was obtained from the University of Health Sciences, Diyarbakır Gazi Yaşargil Training and Research Hospital Clinical Research Ethics Committee (848/09.07.2021). Gender, age and skin prick test results of the patients and the type of allergic sensitization in the SPT were evaluated. Pediatric patients were not included in the study because they were tested in the pediatric allergy immunology department. The rate of SPT positivity, the frequency distribution of all allergens, the most common allergens according to gender, and sensitization to single or multiple allergens were examined.

SPT and Reading the Results

In order to prevent false negative interpretation of the test before the SPT, it was confirmed that the subjects did not use oral corticosteroids, antihistamines, LTRAs (leukotriene receptor antagonists), mast cell stabilizers or immunosuppressive drugs in the last two weeks. The equipment and medications were made readily available for emergency use for possible occurrence complications.

The test was performed by the same healthcare worker in the room set up for the test using the standard technique. The medial surface of the forearm was pierced 2 mm with a lancet and allergens were dropped in consecutive order (Allergopharma, Germany). Histamine (1.7 mg/ml histamine hydrochloride) was used for the positive control, and saline (9 mg/ml sodium chloride) was used for the negative control. In the assessment made after 15-20 minutes, the test was considered positive when the induration diameter of the skin was 3 mm or more. The allergen extracts used were tree mixture (Alder, Poplar, Willow, Hazelnut, Elm), herb mixture (rye grass, timothy grass, velvet grass, meadow grass, fruit grass, bluegrass), weed mixture (plantain grass, cleavers, dandelion, nettle, wormwood), cereal mix (barley, oats, wheat, rye), mite 1 (D. farinae), mite 2 (D. pteronyssinus), aspergillus fumigatus (moisture and mold fungus), and cockroach epithelium.

Statistical Analysi

IBM SPSS 21.0 for windows statistical software package was used for the statistical analysis of the research data. The quantitative variables were presented as mean ± standard deviation (SD), and categorical variables were presented as number and percentage (%). The chi-square ($\chi 2$) goodness of fit test was used to evaluate whether the observed frequencies of the variables were consistent with the expected frequencies. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

SPT positivity was observed in 472 (42.9%) out of 1,100 (495 female, 605 male) patients included in the study. Of the 472 patients with a positive SPT, 272 (57.6%) were

female and 200 (42.4%) were male. The patients included in the study were between the ages of 18-69. The mean age was 33.59±14.59 years in females and 30.64±13.15 years in males (Table 1). When the positivity rate was evaluated separately for each allergen, it was observed that the positivity frequencies were significantly different from each other according to the chi-square goodness of fit test ($p<0.05$). The allergen with the highest frequency of positive test responses were herb mixture (n=303), cereal mixture (n=223) and tree mixture (n=106), in respective order (Table 2).

When the patients with a positive skin prick test were grouped according to the number of positive allergens, it was determined that there was a statistically significant difference between the numerical distributions of the groups ($p<0.05$). The majority of the patients had concurrent positivity for multiple allergens, and the most common was double allergen positivity (n=217). (Table 3)

Single allergen positivity was determined in 145 patients. It was determined that the most common allergens with the highest frequency of positive test responses in patients with single allergen positivity were grass mixture (n=67), cockroach (n=19) and tree mixture (n=15), in respective order. (Table 4)

It was determined that 217 patients with double allergen positivity were statistically distributed into double allergen subgroups ($p<0.05$). It was observed that the most common double allergen positivity was the combination of grass mixture + cereal mixture (n=119). It was followed by wood mix+grass mix (n=22) and mite 1 (D.farinea)+Mite 2 (D. Pterinus) combination (n=17), in respective order. (Table 5)

When the first three allergens with the highest frequency of positive test responses were examined according to gender, the same allergens were the most common in both males and females, namely grass mixture, cereal mixture and tree mixture.

Table 1: Age and gender variables of patients

Gender	Number (%)	Age±SD
Female	272 (%57.6)	33.59±14.59
Male	200 (42.4%)	30.64±13.15
Total	472	

S.D.: standard deviation

Table 2: The result of the chi-square goodness of fit test performed to determine whether there is a difference between the frequencies of positive test responses for the studies 8 allergens.

Allergen Type	*ObservedN (%)*	*Expected N*	X^2	*Sd*	*p*
Tree Mixture	106 (10.67%)	124.1	463.234	7	<0,001
Herb Mixture	303 (30.51%)	124.1			
Weed Mixture	72 (7.25%)	124.1			
Grain Mixture	223 (22.45%)	124.1			
Mite I (D.farinea)	83 (8.35%)	124.1			
Mite II (D.pteronyssinus)	94 (9.46%)	124.1			
Cockroach	76 (7.65%)	124.1			
AspergillusFumigatus	36 (3.62%)	124.1			

X^2: Chi-square goodness of fit test, DF: Degrees of freedom, p: Statistical significance. According to the results of the chi-square goodness of fit test performed to determine whether there is a difference between the frequencies of positive test responses for the studied 8 allergens, a significant difference was found between the frequencies of allergens ($X2(7)=463.948$, $p<0.001$).

Table 3: The chi-square goodness of fit test to determine whether there is a difference between the number of patients with single versus multiple allergen positivity

Number of Allergens	***ObservedN***	***Expected N***	***X^2***	***Sd***	***p***
Single	145	59	768.305	7	<0,001
Double	217	59			
Triple	67	59			
Quadruple	19	59			
Quintuple	13	59			
Sextuple	5	59			
Septuple	4	59			
Octuple	2	59			

X^2: Chi-square goodness of fit test value, DF: Degrees of freedom, p: Statistical significance. According to the results of the chi-square goodness of fit test performed to determine whether there is a difference between the number of patients with single and multiple allergen positivity, double allergen positivity was more common in the patients. ($X^2(7)=768,305$ $p<0,001$).

Table 4: Chi-square goodness of fit test for patients with single allergen positivity

Allergen Type	***ObservedN***	***Expected N***	***X^2***	***Sd***	***p***
Tree Mixture	15	18.1	158.172	7	<0,001
Herb Mixture	67	18.1			
Weed Mixture	7	18.1			
Cereal Mixture	12	18.1			
Mite I (D.farinea)	9	18.1			
Mite II (D. pteronyssinus)	11	18.1			
Cockroach	19	18.1			
AspergillusFumigatus	5	18.1			
Total	145	18.1			

X^2: Chi-square goodness of fit test value, DF: Degrees of freedom: Statistical significance. According to the results of the chi-square goodness of fit test performed for patients with single allergen positivity, the allergen with the highest frequency of positive test response was herb mixture in patients with single allergen positivity. ($X^2(7)=158,172$ $p<0,001$).

Table 5: Frequency distribution of double allergen groups

Double allergen groups	*ObservedN*	*Expected N*	X^2	*Sd*	*p*
herb mix-cereal mix	119	10.9	1201.450		<0,001
tree mix-herb mix	22	10.9			
mite1-mite2	17	10.9			
mite2-aspergillus	3	10.9			
mite2-cockroach	7	10.9			
mite1-cockroach	4	10.9			
herb mix-cockroach	5	10.9			
cockroach-tree mix	2	10.9			
cereal-cockroach	1	10.9			
weed mix-mite1	6	10.9			
tree mix - weed mix	6	10.9		19	
herb mix-weed mix	3	10.9			
weed mix-cereal mix	4	10.9			
tree mix-cereal mix	9	10.9			
tree mix - mite 2	3	10.9			
Aspergillus fumigatus - herb mix	1	10.9			
Aspergillus fumigatus-cereal mix	1	10.9			
Ceral mix -mite1	2	10.9			
herb mix -mite2	1	10.9			
Ceral mix -mite2	1	10.9			
Total	217				

X^2: Chi-square goodness of fit test value, DF: Degrees of freedom, p: Statistical significance. According to the results of the chi-square goodness of fit test performed for the patients with double allergen positivity, the allergens with the highest frequency of positive test response in patients with double allergen positivity were herb mixture and cereal mixture. ($X^2(19)=1201,450$ $p<0,001$).

DISCUSSION

Diagnosis of allergic rhinitis is made by careful anamnesis, symptoms, physical examination and laboratory tests. Nasal examination findings are often not specific and are mostly similar to those seen in other rhinitis. The reliability of skin tests in the diagnosis of allergic rhinitis is controversial[2]. A negative skin test does not exclude the diagnosis of allergic rhinitis. However, positive skin test against any allergen is extremely important in terms of diagnosis and determination of the treatment scheme. The skin test, if performed correctly, is useful in confirming the diagnosis of a specific allergy. Prick test positivity has been reported to be between 56.7% and 85.5% in cases with allergic rhinitis.

In our study, the sensitivity of SPT for allergic rhinitis was found to be 42.9%. In the last study of Cingi et al using questionnaire (SFAR), it was stated that the overall prevalence of allergic rhinitis in Turkey was 36.7%. In the same study, it was emphasized that the prevalence of allergic rhinitis was 36.9% in the southeastern region of Anatolia, including the province of Mardin, where our study was also conducted.[6] The high rate in our study can be attributed to the fact that SPT was performed and the patients were selected from a narrower pool.

The literature search reveals that the rate of SPT positivity ranges between 39.7% and 75% in studies conducted in different geographic regions of Turkey (Table 6).

Table 6. SPT positivity rates by province

Provinces	SPT positivity %
Diyarbakir[7]	40.3
Kayseri[8]	68.1
Karaman[9]	42.3
Tekirdag[10]	39.7
Giresun[11]	48.2
Manisa[12]	67.1
Mediterraneanregion[13]	43.2
Sanliurfa[14]	75
Duzce[15]	56.7
Mardin	**42.9**

In Diyarbakir, which has geographical and climatic features similar to our region, Demir et al. reported a SPT positivity rate of 40.3% among patients presenting to the chest diseases and otorhinolaryngology departments with allergic respiratory tract complaints.[7] In similar studies conducted in different regions, SPT positivity rate was reported to be 68.1% by Kökoğlu et al. in Kayseri province, 42.3% by Canbal et al. in Karaman province, 39.7% by Nalbantoğlu et al. in Tekirdağ province, 48.2% by Oğuz et al. in Giresun province and 67.1% by Birgir et al in Manisa province.[8-12] In a study involving atopic children living in the Mediterranean region, Basaran et al. reported at least one aeroallergen a positivity 43.2% of the patients.[13] The extent of difference in SPT positivity rates in studies conducted in different regions indicates that the tendency towards atopy also vary across geographic regions. Although the SPT positivity rate in our study is parallel to the literature, very high SPT positivity rates encountered in some regions can be attributed to the fact that these studies consisted of patients with atopic diseases on a wider scale, unlike our study.

The first three allergens with the highest frequency of positive test response in the present study were grass mix (30.51%, n=303), cereal mix (22.45%, n=223), and tree mix (10.67%, n=106). In a previous study in the province of Şanlıurfa, which is very close to our province, grass pollens (66.7%), tree pollens (20%) and grain pollens (31.1%) were reported as having the highest frequency of positive test response.[14] In a study by Demir et al. conducted in Diyarbakir province, the allergens with the highest frequency of positive test response were meadow pollen (70%), wheat pollen (46%), and tree pollen (46%).7 Ozturk et al. reported the highest frequency of positive test response for house dust mites in patients with allergic rhinitis in Duzce province.[15] Similarly, the highest frequency of positive test response was reported for house dust mites in Tekirdağ (58%), Giresun (66.7%) and Mediterranean region (69%).[10,11,13] Our province has high altitude (1083 m), low humidity, high agricultural land (mostly cereal) and pasture density.[16] In many previous studies conducted in Turkey, house dust mites have been reported as the most common antigen responsible for allergy in regions with high humidity, while the rate of sensitivity to house dust mites was lower in terrestrial areas with low humidity.[17,18] In our study, the total positivity rate for house dust mites was 17.82% (n=177), and it was not among the first three allergens with the highest frequency of positive test response. When evaluated together with other studies from different regions, the absence of house dust mites in the top three most common allergens was attributed to the fact that our city is not suitable for the living environment of house dust mites due to dry and warm climatic conditions with low humidity. The studies conducted in the Mediterranean region with high humidity and temperate climate and in the Black

Sea region report the highest frequency of positive test response for house mite, while lower rates have been reported in Kayseri, Diyarbakir and Elazığ provinces, the areas with low humidity and continental climate.[7,8,13,19] In our study, the allergen with the highest frequency was herb mixture with a rate of 30.51% (n=303). Similarly, the highest frequency of allergic sensitivity was found against weed in atopic children living in Ankara (43%) and Şanlıurfa (67%), while the most common allergen was found to grass mixture-meadow pollen in Diyarbakır(70%).[7,11,20]

The majority of our patients had multiple allergen positivity, and double allergen positivity was the most common. The most common was double positivity to herb mixture and cereal mixture. Since the type of allergen being sensitized is closely related to the plant cover in a particular geographic area, these findings are expected in our province, which intensively cultivates cereals and has a high pasture rate.

While allergic rhinitis is more common in men during childhood and early adulthood, it is more common in women in adulthood. In their study, Kokoglu et al. reported high sensitivity rates in women in the second decade of life, which constituted the largest group in their study.[8] The study by Birgir et al. found no relationship between gender and SPT positivity in their study, while Başaran et al. found higher SPT positivity rate in males in their study reporting on a population aged 18 and under.[12,13] The rate of SPT positivity was higher in women in the present study, which evaluated the results of a population over the age of 18 and which was relatively homogeneous in terms of gender. The higher rate of SPT positivity in women with a rate of 57.6% in our study is parallel to those reported in the literature. Although previous studies have reported differences in the type of sensitized allergens in different genders, in our study, the three allergens with the highest frequency of positive test response for both genders were similar (herb mix, cereal mix, tree mix).[7]

Limitations

Since the study was designed to evaluate the aeroallergen sensitivity frequencies in our region and patient data were retrospectively analyzed; patients' laboratory test results, clinical findings, type of allergic rhinitis and severity of allergic rhinitis were not included in the study. There is a need for multicenter studies with broad participation to be carried out on a regional basis in which all age groups are represented, in which the parameters not mentioned in our study are also taken into consideration.

CONCLUSION

Conclusion In conclusion, the responsible allergen in individuals with atopy is closely related to the climatic and geographical characteristics of the region where they live. For this reason, it is very important to determine the aeroallergen distributions of the regions, as it is important in allergen avoidance and treatment stages. Since the present study is the first to make such evaluation for Mardin province, the authors consider that current findings will be beneficial to the literature. Apart from establishing the aeroallergen distribution in a particular region, the authors believe that similar studies should also be carried out to update the aeroallergen distributions of the regions that are subject to alterations especially due to global warming and climatic changes, increase in industrialization, and factors that cause changes in regional humidity (such as water reservoir construction, decrease in agricultural and forestry lands).

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