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Allergen Sensitivity in Patients with Allergic Respiratory Tract Symptoms in Izmir and its Environs, Aegean Region of Turkey

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ABSTRACT

Objective: Respiratory tract allergies are common chronic diseases worldwide. Allergens have regional differences and vary from time to time. In this study, the aeroallergen sensitivity in our region was intended to be updated.

Materials and Methods: This was a retrospective, regional study evaluating the skin prick test (SPT) results and information forms of 13410 patients who presented atour institution between January 2014 and March 2020. The relationship of allergen positivity with age and gender was analyzed.

Results: The mean age of the study population was 38 years. In terms of gender, 71.1% of them were female, and 28.9% were male. The SPT positivity was 41.1%. Of the 13.7% of the patients had sensitivity toa single allergen, and 27.4% had sensitivity to multiple allergens. The most common allergens were weeds (54%), grass-ryepollens (45%), olive pollen (44%), and dust mites (38%). It was observed that allergen positivity was associated with age and gender. Most of our patients were women, but allergen positivity was higher in men. It was observed that allergen positivity decreased with increasing age.

Conclusion: Recognition of regional allergens contributes to protective measures and leverages immunotherapy. This study has enabled us to learn about aeroallergen sensitivity in our region.

Keywords: Allergic sensitization, skin prick test, age, gender

Abbreviations

AR: Allergic rhinitis, **CI:** Confidence interval, **DF:** Dermatophagoidesfarinae, **DP:** Dermatophagoidespteronyssinus, **Ig E:** Immunoglobulin E, **OR:** Odds ratio, **SD:** Standard deviation, **SPSS:** Statistics Package for the Social Sciences, **SPT:** Skin Prick Test

INTRODUCTION

Allergic rhinitis (AR) and allergic asthma are common chronic respiratory diseases with increasing prevalence all over the globe (1,2). Ig E-mediated chronic inflammatory response of the respiratory mucosa is responsible for the pathogenesis of the disease. An exaggerated response to normally harmless aeroallergens leads to disease. Atopy is a genetic predisposition that causes an exaggerated IgE response to the allergen. It is the most important risk factor for the emergence of allergic diseases (3,4). Age and gender are other risk factors. While allergic sensitization is higher at younger ages, it decreases with age (5,6). It is known that sex hormones are effective in allergic sensitization (7,8). Allergic sensitization is observed more frequently in men in childhood and women in later ages (8).

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Allergic diseases occurdue to the interaction between genetic and environmental factors (9,10). It is shown in many studies that air pollution exacerbates pollen release and antigenicity. The climate, altitude, humidity, vegetation, and habits of the regions, and lifestyles affect allergen sensitivities. Global climate change as a warmer environment also affects concentration, allergic potential, and structure of pollens. The remote pollen migration influences the pollen distribution in the area, the pollen season, and the course of allergic respiratory diseases (11-14).

The primarily responsible allergen should be detected in order to initiate immunotherapy and further achieve protection measures. The evolution of aeroallergens and their allergens requires the update of the allergen panel at certain intervals.

No research elaborating on the allergen sensitivity of our region has been published in recent years. In this study, we aimed to contribute to treatment streamlining and protective measures by determining the current allergen sensitivity.

MATERIALS and METHOD

The data of 13410 patients who presented to the Izmir Atatürk Training &Research Hospital's Immunology and Allergic Diseases Department between January 2014 and March 2020 due to allergic complaints, AR, and/or asthma has been analyzed retrospectively.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all participants. The ethics committee approval was granted on 22 October 2020 with protocol number 1025.

The relevant patient information has been obtained fromthe hospital medical records database. The age, occupation, duration, and severity of complaints, treatment regimen, and comorbid diseases, physical examination findings, laboratory and imaging findings were analyzed.

SPT was used in our patients because of its advantages in detecting allergen sensitivity and providing a wide allergen panel. SPT has a high sensitivity to the allergen-specific IgE antibody with low cost, ease of use, and safe testing methodology. It is accepted as the most valuable diagnostic method used to determine atopy (15,16). IgE was measured in the blood of our patients with dermographism. The study did not include these patients who could not undergo SPT due to the limited number of allergens in our SpIgE panel.

The SPT panel comprised 22 allergens selected according to our region and vegetation. *Dermatophagoides farinae, Dermatophagoides pteronyssinus, Alternaria, Cladosporium, Aspergillus, Penicillium, Cat, Dog, Blatella, Grass-rye mix, Secale, Phleum, Lolium, Chenopodium, Wheat, Zea, Olive tree, Trees mix (Betula, Corylus, Populus), Plantago, Artemisia, Parietaria, Latex* containing allergen extracts and the Prick Test Lancet *(Allergopharma, Germany)* were utilized. Histamine *(10 mg/ml)* was used as the positive control, and physiological saline as the negative control specimen. The test solutions were rated according to the skin response as the erythema and edema diameter 20 minutes after being applied to the forearm. Cases with an induration diameter of ≥ 3mm from negative control have been interpreted as positive skin reactions. Cases presenting dermatography were not evaluated.

Statistical Analysis

The SPSS 22 (Statistics Package for the Social Sciences) program was utilized to analyze data. Number (n), percentage (%), and numerical variables in the categorical variables in descriptive statistics were given arithmetic mean and standard deviation (SD) values. The assumption of normality has been calculated via univariate analysis Kolmogorov-Smirnov, and Shapiro-Wilk tests, and a histogram was applied. In comparisons between groups, the chi-square test and t-test were used. According to the allergen type, the single logistic regression model formed by the gender variable was performed for the risk of exposure (OR). A p value<0.05 was considered statistically significant.

RESULTS

The mean age of the patients (n=13410) was 38.40±12.83 (min:18, max:86). The age segmentation of the study group was elaborated as 26.5% between 18-28 years old, 25.5% between 29-38 years old, 24.9% between 39-48 years old, 15.7% between 49-58 years old, 6.3% between 59-68 years old and % 1.1 over 68 years old (Table I). The gender distribution was 9539 (71.1%) females and 3871 (28.9%) males.

SPT was positive in 41.1% (n=5512) of the patients. While 1833 patients (13.7%) were sensitive to a single allergen, 3679 patients (27.4%) were sensitive to multiple allergens; polysensitization was therefore two times higher. SPT positivity was higher in the younger age group (Tables I and II).

Table I: Sociodemographic characteristics and allergen distributions of the patients.

Characteristics			n=13410	(%)
Age		18-28 years	3560	26.5
		29-38 years	3415	25.5
		39-48 years	3341	24.9
		49 -58 years	2108	15.7
		59-68 years	842	6.3
		≥69 years	144	1.1
Mean±Standard Deviation:38.40±12.83 (Min:18 - Max:86)				
Gender		Female	9539	71.1
		Male	3871	28.9
Allergen Specifics				
Dust Mites		Positive	2121	15.8
Sub-Group	D.farinea	Positive	256	1.9
	D. pterynisus	Positive	395	2.9
	D.F & D.P	Positive	1470	11.0
Molds		Positive	323	2.4
Sub-Group	Alternaria	Positive	147	1.1
	Cladosporium	Positive	81	0.6
	Aspergillus	Positive	118	0.9
	Penicilium	Positive	42	0.3
Grass-rye mix		Positive	2467	18.4
Olivetree		Positive	2424	18.1
Three mix		Positive	332	2.5
Weeds		Positive	2982	22.2
Sub-Group	Artemisia	Positive	598	4.5
	Plantain	Positive	1435	10.7
	Parietaria	Positive	1421	10.6
Animal Epithelium				
Sub-Group	Cat	Positive	106	0.8
	Dog	Positive	14	0.1
	Cat & Dog	Positive	45	0.3
	Other	Positive	36	0.3
Latex		Positive	134	1.0
Allergen Presence		None	7898	58.9
		Single	1833	13.7
		Multiple	3679	27.4

The frequency of allergen sensitivity was determined according to the main groups of allergens. Pollens have been grouped as grasses, weeds, and trees. Our patients with pollen positivity had 54% weeds, 45% grass-ryepollens, 44% olive pollen, and 6% tree mix positivity. Dust mites were positive in 38%, molds in 6%, animal epithelium in 4%, and latexin 2% of the patients (Figure 1).The distribution of allergens in the entire research group has been denoted in Figure 2.

The relationship between sociodemographic characteristics and allergen positivity was analyzed in Table II. There was 29.6% allergen positivity in the 18 to 28 years oldage group, 28.4% in the 29 to 38 years old age group, 25% in the 39 to 48 years old age group,12.5% in the 49 to 58 years old age group, 3.9% in the 59 to 68 years old age group, and 0.6% in subjects over 68 years of age. The age with the highest allergen positivity was between 18 to 28 years old. It was observed that allergen positivity decreased with increasing age. The relationship between age, gender, and allergen positivity was statistically significant (p<0.001).

The relationship between age and allergen type was examined in Table III. The relationship between dust mites, molds, animal epithelium, grass-rye pollens, weeds, olive pollen and latex positivity with age was statistically significant. There was no significant relationship between tree mix and age.

Table II: Distribution of the relationship between sociodemographic characteristics and allergen positivity (n=13410).

Characteristics		Allergen Negative		Allergen Positive		P*
		n	%	n	%	
Age (Categorical)	18-28 years	1926	24.4	1634	29.6	**<0.001**
	29-38 years	1851	23.4	1564	28.4	
	39-48 years	1963	24.9	1378	25.0	
	49 -58 years	1419	18.0	689	12.5	
	59-68 years	629	8.0	213	3.9	
	≥ 69 years	110	1.4	34	0.6	
Gender	Female	5883	74.5	3656	66.3	**<0.001**
	Male	2015	25.5	1856	33.7	

*Chi - square test

The relationship between gender and allergen type was examined in Table IV. The relationship between dust mites, animal epithelium, grass-rye pollens, weeds, olive pollen, and gender was statistically significant. Men were more likelyto be positive for these allergens than women. There was no significant relationship between tree mix, molds, latex, and gender. The risks of getting the allergen type according to the gender variable were evaluated in Table V.

DISCUSSION

Respiratory allergic diseases cause serious socioeconomic losses and deterioration in the quality of life (17). Reducing these losses is possible with early disease diagnosis, taking necessary precautions, and effective treatment. The first step in managing the disease is to identify the allergen responsible for the disease.

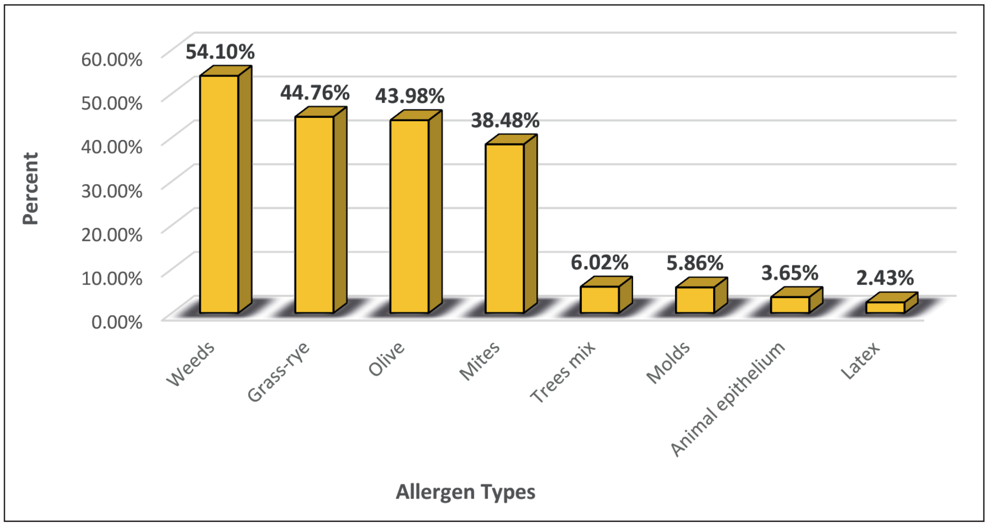
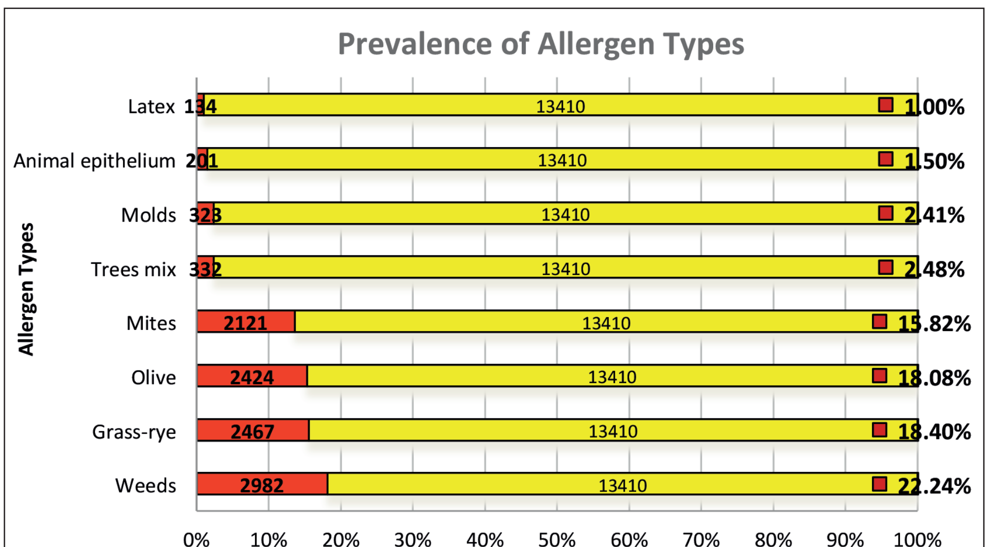


Figure 1. Distribution of allergen types by frequency of occurrence in allergic patients (n=5512).



	Weeds	Grass-rye	Olive	Mites	Trees mix	Molds	Animal epithelium	Latex
Number	2982	2467	2424	2121	332	323	201	134
Total Group	13410	13410	13410	13410	13410	13410	13410	13410
Percent	22.24%	18.40%	18.08%	15.82%	2.48%	2.41%	1.50%	1.00%

Figure 2. Distribution of allergen types by frequency in the research group (n=13410).

Table III: Relationship distributions between age variable and allergen type (n=13410).

Characteristics		Age (Mean ±Standard Deviation)	P*
Allergen Types			
Dust mites	Positive	36.29±11.99	**<0.001**
	Negative	38.79±12.94	
Molds	Positive	40.51±12.35	**0.003**
	Negative	38.34±12.84	
Grass-rye mix	Positive	35.44±11.53	**<0.001**
	Negative	39.06±13.01	
Olive tree	Positive	36.28±11.26	**<0.001**
	Negative	38.86±13.10	
Three mix	Positive	37.76±12.32	0.344
	Negative	38.41±12.84	
Weeds	Positive	36.60±11.98	**<0.001**
	Negative	38.91±13.02	
Animal Epithelium	Positive	33.63±11.11	**<0.001**
	Negative	38.47±12.84	
Latex	Positive	36.75±9.61	**0.049**
	Negative	38.41±12.86	
Allergen Presence	Positive	36.53±11.84	**<0.001**
	Negative	39.70±13.33	

*t-Test in Independent Groups

Table IV: Relationship distributions between gender variable and allergen type (n=13410).

Characteristics		Gender				P*
		Female		Male		
Allergen Type		**n**	**%**	**n**	**%**	
Dust Mites	Negative	8115	85.1	3174	82.0	<0.001
	Positive	1424	14.9	697	18.0	
Molds	Negative	9308	97.6	3779	97.6	0.878
	Positive	231	2.4	92	2.4	
Grass-rye mix	Negative	8066	84.6	2877	74.3	<0.001
	Positive	1473	15.4	994	25.7	
Olive tree	Negative	7962	83.5	3024	78.1	<0.001
	Positive	1577	16.5	847	21.9	
Three mix	Negative	9316	97.7	3762	97.2	0.106
	Positive	223	2.3	109	2.8	
Weeds	Negative	7594	79.6	2834	73.2	<0.001
	Positive	1945	20.4	1037	26.8	
Animal Epithelium	Negative	9412	98.7	3797	98.1	0.012
	Positive	127	1.3	74	1.9	
Latex	Negative	9438	98.9	3838	99.1	0.276
	Positive	101	1.1	33	0.9	

*Chi Square Test

Allergen sensitivity in patients living in Izmir and its environs was investigated 20 years ago in a study in which most children with respiratory allergies were present (18). To date, a few studies have investigated allergen sensitivity in other provinces in the Aegean region (19,20). In our study, we analyzed the results of rhinitis and/or asthma patients living in Izmir and its environs. SPT positivity and polysensitization frequency were similar compared to previous studies in our region (18-20).

Studies investigating the factors in respiratory tract allergic diseases have revealed the relationship between age and gender. As age progresses, susceptibility to chronic infections and autoimmunity increases due toevolving immune systems, while allergic responses to external factors decrease (21,22).

Allergic sensitization is higher at younger ages but decreases with age (5-7). When we examined the relationship of allergens with age and gender, it was seen that allergen positivity was higher at younger ages and decreased

Table V: Evaluation of the risk of catching the allergen type according to the gender variable of the participants.

Allergen Type				
Dust Mites				
Gender	Female	Reference 1		
	Male	1.25	1.13	1.38
Grass-rye mix				
Gender	Female	Reference 1		
	Male	1.89	1.72	2.07
Olive tree				
Gender	Female	Reference 1		
	Male	1.41	1.29	1.55
Weeds				
Gender	Female	Reference 1		
	Male	1.43	1.31	1.56
Animal Epithelium				
Gender	Female	Reference 1		
	Male	1.44	1.08	1.93

as age progressed, and was quite low after 50 years of age. Most of our patients were in the young-middle age group (Tables I and II).

It is known that sex hormones are effective in allergic sensitization (7,8). While respiratory tract allergies are more common in males in childhood, they are more common in females in adolescents and adults (8). Most of our patients were women, but the risk of allergen positivity was higher in men (Tables I and II). The fact that allergen positivity was lower in our female patients than in males may be due to other factors causing respiratory tract complaints. The location, climate, vegetation, humidity, and lifestyle of the territories affect the distribution of aeroallergens (11,12,14). The Aegean region is located in western Turkey and part of the Mediterranean phytogeographic region. The Aegean region is under the influence of the Mediterranean climate and maquis-dominated vegetation, woody and herbaceous plants, and especially the olive tree, are dense .Recently, pollen studies in our country have shown that woody and herbaceous plants, especially olive trees, are dense in our region (23).

Pollens are common aeroallergens as they are spread over long distances by the wind and are the main allergens responsible for respiratory allergies in warm climates. Pollen positivity was the first in our patients, but the frequency order of pollen had changed. Weeds were our patients' most common allergen (54%), followed by Plantago, Parietaria, and Artemisia. In some European countries and Iran studies, a dramatic increase in weed pollen sensitivity was reported (24-27). Since our region is located between these two geographies, it was affected by similar climate changes. The increase in weed susceptibility observed in our study was consistent with these results. Recent studies have emphasized that climate change and global warming increase the atmospheric density and spread areas of Artemisia, Parietaria, and Plantago pollens, which are highly resistant to drought (25,26). In a study conducted in Italy, changes were observed in the pollen season and pollen sensitivity in 27 years, and it was stated that there was an increase in the amount of Parietaria pollen and the duration of the season (24). At this stage, one can conclude that the increase in weed sensitivity observed in our patients may be due to climate change.

In our study, grass-ryepollen positivity was in second place (45%), and olive pollen positivity was in third place (44%). A previous study investigating allergen positivity in İzmir and its environs reported that olive pollen was the most common after grass-rye pollens (18). Studies conducted in previous years in different cities in the Aegean region stated that grass-rye pollens were the most common allergens (19-20). In recent years, studies examining the pollen density in the atmosphere have reported that the concentrations of woody plant pollen have increased in Turkey (23). Olive pollen, which is very dense in the Mediterranean and Aegean regions, is very allergenic due to its molecular structure. It is easily released and spreads far, and the season lasts long (28). Tree mix positivity, including Betula, Corylus, and Populus trees, was 6% in our patients.

In our research, dust mites positivity were 38%. Dermatophagoides pteronyssinus (DP) positivity was higher than dermatophagoides farinae (DF) positivity. A previous study conducted in Izmir reported that DP sensitivity was higher than DF (18). Dust mites susceptibility is high in humid areas. The average annual humidity of the Aegean region is 50-70%, providing suitable conditions for dust mites. In recent years, it has been reported that house dust mite susceptibility is in the first place in studies conducted in the pediatric age group and in a study conducted with a small number of adults (29-31). Alternaria, Cladosporium, Aspergillus, and Penicillium are molds that cause mostrespiratory allergies (32). In our study, mold sensitivity was 6%; the most common was Alternaria, followed by Aspergillus sensitivity. The frequency of animal epithelium was 4% in our patients. Cat epithelial positivity was the most common. Higher susceptibility rates are reported in European countries, as owning a pet is more common. Latex positivity was found as 2%.

When the relationship of allergens with age and gender was examined, it was seen that house dust, animal epithelium, grass-rye pollens, weeds, and olive pollen positivity were associated with both age and gender, and mold and latex positivity were only associated with age. When risk analyses were made, it was seen that the risk of pollen positivity in dust mites, animal epithelium, grass-rye pollens, weeds, and olive pollen was higher in the male gender. There is a need for further studies on this subject in order to make more comments on the relationship of allergens with age and gender.

CONCLUSION

Our study investigated allergen sensitivity in our region and observed that weed sensitivity increased. Grass-rye and olive pollen sensitivity rates were very close to each other. In our study, a change was observed in the aeroallergen trend in our region. Our results will be beneficial in managing respiratory tract allergic diseases.

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Competing Interests

The authors declare that they have no competing interests.

Informed Consent

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all participants.

Institutional Review Board Approval

The study has been approved by the ethics committee on 22 October 2020 with protocol number 1025.

Authorship Contributions

Concept: **Ferda Bilgir, Yusuf Üzüm,** Design: **Ferda Bilgir, Orhan Balıkçı,** Data collection or processing: **Yusuf Üzüm, Uğur Bayram Korkmaz,** Analysis or Interpretation: **Uğur Bayram Korkmaz, Bahadır Dede,** Literature search: **Yusuf Üzüm, Orhan Balıkçı,** Writing: **Ferda Bilgir, Uğur Bayram Korkmaz,** Approval: **Ferda Bilgir, Bahadır Dede.**

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