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Distribution and Characterization of Aeroallergens in the Etiology of Allergic Rhinitis Patients in İstanbul Kartal Region

İstanbul Kartal Bölgesi Alerjik Rinit Hastalarının Etiyolojisindeki Aeroalerjenlerin Dağılımı ve Karakterizasyonu

Kadriye TERZİOĞLU[1], Meltem AĞCA ÇOBAN[2]

[1]*Kartal Dr. Lütfü Kırdar City Hospital, Clinic of Internal Disease, İstanbul, Turkey*
[2]*İstanbul Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital, Clinic of Intensive Care, İstanbul, Turkey*

ABSTRACT

Aim: Allergic rhinitis (AR) is a common disease and the first step in its treatment is to determine the allergen responsible for its etiology and to take preventive measures. The aim of this study was to determine the distribution of aeroallergens in AR patients in İstanbul Kartal region and to investigate other factors affecting the severity of AR.

Materials and Methods: The study was performed in a tertiary hospital on the Anatolian side of İstanbul among patients who were admitted to the allergy and clinical immunology outpatient clinic and diagnosed with AR. Data of patients were obtained from medical records retrospectively. Age, gender, concomitant atopic disease, family transition history, serum total IgE and serum eosinophil (Eo) levels were evaluated. Skin prick tests were performed with 25 allergens.

Results: One hundred and sixty patients were included in our study. Ninety-six (65.8%) of the patients were female and the median age of the study population was 31 (18-75) years. Distribution of aeroallergens according to skin test results was as follows; D. pteronyssinus (78.1%), D. farinae (75.2%), Tyrophagus putrescentlae (59.6%), Acurus siro (57.5%), Lepidoglyphus destructor (40.4%), cereals mix (37.7%), and cat hair (33.6%). It was found that there was a significant increase in total IgE levels ($p<0.001$) consistent with the increase in serum Eo level.

Conclusion: In our study, mite sensitivity has been found to be the most common allergen sensitivity in accordance with the geographic and climatic characteristics of the İstanbul region. Secondly, cat hair sensitivity and pollen (grasses mix) sensitivity were similarly high due to the increase in the number of domestic animals in the modern age. We think that our study contributes to the literature by examining the distribution of these allergens that cause AR and patients are guided to take preventive measures in this regard.

Keywords: Allergic rhinitis, aeroallergen, sensitization

ÖZ

Amaç: Alerjik rinit (AR) yaygın görülen bir hastalıktır ve tedavisinde ilk basamak, etiyolojisindeki sorumlu alerjeni saptayıp koruyucu önlemleri almaktır. Çalışmamızın amacı, İstanbul Kartal yerleşkesinde yaşayan AR hastalarının etiyolojisinde rol alan aeroalerjenlerin dağılımını tespit etmek ve AR şiddetini etkileyen faktörleri araştırmaktır.

Gereç ve Yöntem: Çalışma, İstanbul Anadolu yakasında bulunan üçüncü basamak bir hastanede gerçekleştirildi. Alerji ve klinik immünoloji polikliniğine rinit şikayeti ile başvurup AR tanısı konulan hastalar çalışmaya dahil edildi ve dosyaları geriye dönük olarak incelendi. Hastaların yaş, cinsiyet, eşlik eden diğer atopik hastalıkları, aile geçiş öyküsü, serum total IgE ve serum eozinofil (Eo) seviyeleri değerlendirildi. Deri prick testleri 25 adet alerjen ile yapıldı.

Bulgular: Çalışmamıza 146 hasta dahil edildi. Hastaların 96'sı (%65,8) kadındı. Medyan yaş 31 (18-75) yıl olarak saptandı. Deri prick test sonuçlarına göre aeroalerjenlerin dağılımı sırasıyla; D. pteronyssinus (%78,1), D. farinae (%75,2), Tyrophagus putrescentlae (%59,6), Acurus siro (%57,5),

Address for Correspondence: Kadriye TERZİOĞLU MD, Kartal Dr. Lütfü Kırdar City Hospital, Clinic of Internal Disease, İstanbul, Turkey
E-mail: dr.kadriyete@gmail.com **ORCID ID:** orcid.org/0000-0002-0674-417X
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Lepidoglyphus destructor (%40,4), cereals mix (%37,7), kedi tüyü (%33,6) şeklindeydi. Hastaların serum Eo seviyesindeki artışa paralel olarak total IgE düzeylerinde de anlamlı artış olduğu (p<0,001) görüldü.

Sonuç: Çalışmamızda, İstanbul bölgesinin coğrafik yapısı ve iklimi ile uyumlu olarak en fazla akar duyarlılığı saptandı. İkinci olarak modern çağda ev içi hayvan besleme sayısında artmaya bağlı olarak kedi tüyü duyarlılığı ve polen (grasses mix) duyarlılığı benzer şekilde yüksek oranlarda saptandı. Çalışmamızın AR'ye sebep olan aeroalerjenlerin dağılımını inceleyerek literatüre katkı sağladığını ve hastaların bu yönde koruyucu önlemlerini almaları için yol gösterici olacağını düşünmekteyiz.

Anahtar Kelimeler: Alerjik rinit, aeroalerjen, duyarlılık

INTRODUCTION

Allergic rhinitis (AR) is a type 1 IgE-mediated disease of the nasal mucosa and is characterized by recurrent sneezing, runny nose, and nasal congestion[1]. Although its prevalence varies according to countries and age, it affects 10-20% of the population[2]. Detection of aeroallergens that cause allergic sensitization in AR and minimizing exposure are important components of the treatment plan.

Distribution of aeroallergens varies depending on geographical structure, seasons, socioeconomic and cultural structures[3]. In recent years, with the increase in AR prevalence, differences in the distribution of aeroallergens have begun to be detected. Various factors have been identified that lead to this situation, some of which are the hygiene hypothesis, the increase in the time spent indoors in parallel with the technological development, the increase in the release of various allergens such as ragweed pollen and aspergillus fumigatus into the atmosphere due to global climate change and gases released in the air[4-6].

Our aim in the study is to investigate the distribution of aeroallergens that play a role in the etiology of AR patients living in İstanbul Kartal region and the factors affecting AR severity.

MATERIALS AND METHODS

The study was carried out in a tertiary healthcare institution located on the Anatolian side of İstanbul. Patients who applied to the allergy and clinical immunology outpatient clinic with rhinitis symptoms and were diagnosed with AR were included in the study. The study were approved by the Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee (protocol number: 2020/514/180/17, date: 26.06.2020).

Patient Selection

The files of patients admitted with AR between January and March 2020 were retrospectively reviewed. AR diagnosis of all patients was confirmed according to Allergic Rhinitis and its Impacts on Asthma (ARIA) guidelines, and patients with positive skin prick test were included in the study. Patients' age, gender, severity of rhinitis, year of AR, blood eosinophil (Eo) and total IgE values, accompanying atopic diseases (asthma, urticaria, eczema), comorbidity, and family history were investigated. Values of 0.2 µgr (normal range 0-0.2 µgr) for Eo elevation and 100 UI/mL (normal range 0-100 UI mL) for IgE elevation were accepted. The AR classification and severity of the patients were made according to ARIA (mild intermittent, moderate-severe intermittent, mild persistent, moderate-severe persistent). Intermittent AR; symptoms less than four days a week and lasting less than four consecutive weeks. Persistent AR; symptoms more than four days a week, lasting for four consecutive weeks. Symptoms were classified as mild if they did not affect sleep, daily activities, work-school activities, and as moderate-severe if they affected[7] them.

Skin Prick Test

Skin prick test was conducted with 25 allergens (grasses mix, cereals mix, tree mix, Dermatophagoides (D.) pteronyssinus, Dermatophagoides farinae, Acarussiro, cockroach, cat hair, dog hair, Aspergillus fumigatus, Alternaria, Clodosporium, Lepidoglypus destructr, Tyrophagus putrescentlae, wormwood, stickygrass, plantain, grapegrass, hazel, alder, ash, olive, birch, oak, and poplar) and standard commercial allergens were used (Alk-Abello, Lincoln Diagnostics, Dallas, TX, USA). The skin prick test was performed on the anterior surface of both arms in accordance with international guidelines. Histamine (10 mg/mL) was used as the positive control and 0.09% sterile saline was used as the negative control. The test was considered positive if the edema diameter at the test site after 20 minutes was found to be more than 3 mm compared to the negative control[8].

Statistical Analysis

Data statistics were performed using Statistical Package for the Social Sciences (SPSS) 22.0 (SPSS for Windows, version 19.0). The normality of the data distribution was checked with the Kolmogorov-Smirnov test. Quantitative variables were expressed as mean±standard deviation or median (25^{th}-75^{th} percentile), categorical variables were expressed as percentages. Student's t-test or Mann-Whitney U test was used to compare the differences of continuous variables. The x^2 test was used to compare categorical variables. Relationships between continuous variables were calculated with the Spearman correlation coefficient. P value of <0.05 was considered statistically significant.

RESULTS

Of the 146 AR diagnosed patients included in the study, 96 (65.8%) were female. The median age in the study group was 31 (18-75) years. When the severity of rhinitis was classified, mild persistent 35.6%, moderate-severe persistent 22.6%, mild intermittent 21.2%, moderate-severe intermittent 20.5% were found in order of frequency. In 45.9% of the patients, the rhinitis duration was longer than 5 years. As comorbid diseases, asthma was the first with 26.7%, eczema was 18.5% and urticaria was 6.8%. Elevated blood Eo was detected in 60 patients (41.1%), and total IgE elevation was found in 78 patients (53.4%) (Table 1). In Spearman correlation analysis, a positive and significant correlation was found between blood Eo value and total IgE (r=0.335; p<0.001) (Figure 1). When the family history of the patients was questioned; most of the patients (79.5%, n=116) had a family history. While the majority of patients with a family history were female (69.8%, n=81), the difference was significant compared to male gender (p=0.041).

Table 1. General data of patients with allergic rhinitis

	n	%
Gender		
Female	96	65.8
Male	50	34.2
Allergic rhinitis severity classification		
Mild intermittent	31	21.2
Moderate to severe intermittent	30	20.5
Mild persistent	52	35.6
Moderate to severe persistent	33	22.6
Duration of allergic rhinitis		
0-1 year	25	17.1
1-5 years	54	37
Over 5 years	67	45.9
Serum eosinophilia		
<0.2 µgr	86	58.9
>0.2 µgr	60	41.1
Total Ig E		
0-100 UI/mL	68	46.6
100-500 UI/mL	55	37.7
>500 UI/mL	23	15.8
Asthma		
Yes	39	26.7
None	107	73.3
Urticaria		
Yes	10	6.8
None	136	93.2
Eczema		
Yes	27	18.5
None	119	81.5
Comorbid		
Yes	17	11.6
None	129	88.4

Distribution of Sensitization to Aeroallergens

The allergens that were found to be positive in the skin prick test results of the patients, in order of frequency were: D. pteronyssinus (78.1%), D. farinae (75.2%), Tyrophagus putrescentlae (59.6%), Acurus siro (57.5%), Lepidoglyypus destructor (40.4%), cereals mix (37.7%), cat hair (33.6%), grasses mix (31.5%), dog hair (29.5%), cocroaches (21.2%), plantain (14.4%) and wormwood (13.7%) (Figure 2).

In total, any house dust mite and/or warehouse mite positivity was 89% (n=130), sensitivity to any pollen group (grass, grain, tree, weeds) was 52.7% (n=77) and sensitivity to any mold fungus was 13.7% (n=20) and no significant difference was found between the female and male genders in terms of sensitivity distributions (p=0.569, p=0.789, p=0.939). Among the aeroallergens, while cat hair sensitivity was found to be significantly higher in those who were sensitive to mold fungus and pollen (p=0.007, p<0.000, respectively), a similar relationship was not found in mite sensitivity (p=0.742).

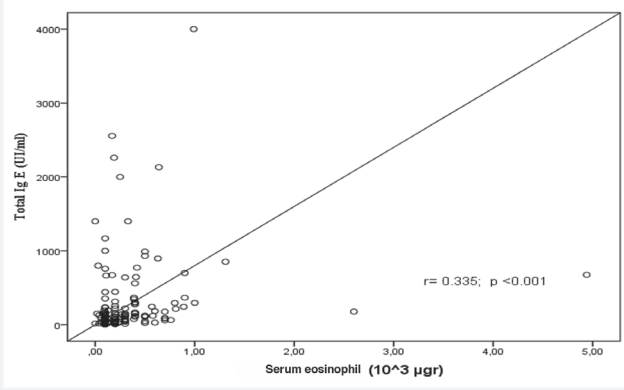

Figure 1. Correlation between serum eosinophil and total IgE

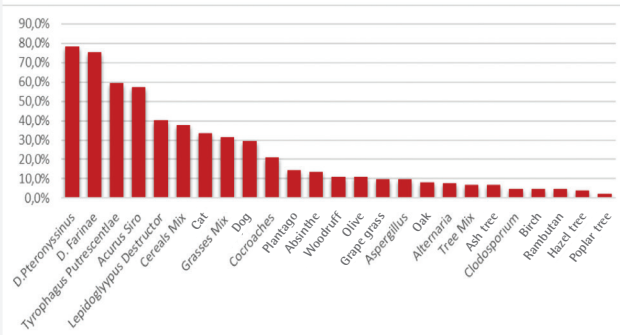

Figure 2. Distribution of sensitization to aeroallergens

When the characteristics and laboratory findings of the patients were evaluated according to the severity of AR, no significant difference was found (Table 2). AR severity and aeroallergen distributions are given in Figure 3 and Figure 4.

DISCUSSION

Allergens play an important role in the etiology of AR. The distribution of allergens and their effects on individuals may vary depending on geographical regions, socioeconomic level, living conditions and genetic structure. In our study, when the aeroallergen distribution of AR patients in the İstanbul Kartal region was examined, it was determined that D. pteronyssinus 78.1%, D. farinae 75.2%, Tyrophagus putrescentlae 59.6%, Acurus siro 57.5% and Lepidoglypus destructor 40.4% were in the top five with mite sensitivity and then pollen and cat hair sensitivity were determined to be effective. The ideal humidity for the reproduction and accumulation of house dust mites is 65-80% and they die at humidity levels below 50%[9]. In studies from various geographical regions around the world, it was shown that the level of dust mite was clinically insignificant at high altitudes such as New Mexico Alamos region (2,195 m), Italy Misurina region (1,756 m), and in cold climate regions such as Sweden Norbotten, where the average temperature is -10 to 15 °C and humidity is 0%[10-12]. However, İstanbul has an

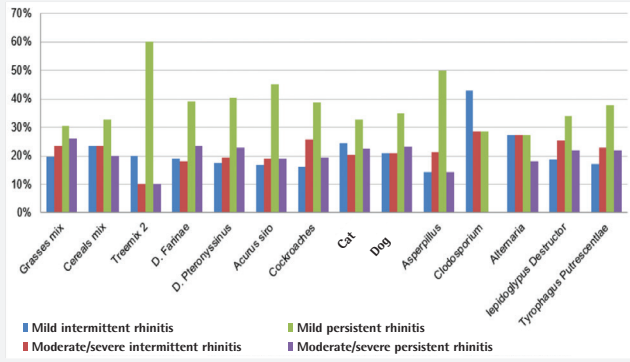

Figure 3. Distribution of aeroallergens by severity classification of allergic rhinitis

Table 2. Evaluation of factors affecting the severity of allergic rhinitis

	Mild intermittent n (%)	Moderate-severe intermittent n (%)	Mild persistent n (%)	Moderate-severe persistent n (%)	p*
Age (years)					
18-29	10 (6.8)	15 (10.3)	22 (15.1)	18 (12.3)	0.532
30-49	15 (10.3)	13 (8.9)	24 (16.4)	12 (8.2)	
>50	6 (4.1)	2 (1.4)	6 (4.1)	3 (2.1)	
Gender					
Female	25 (17.1)	20 (13.7)	35 (24)	16 (11)	0.058
Male	6 (4.1)	10 (6.8)	17 (11.6)	17 (11.6)	
Rhinitis duration (years)					
0-1	6 (4.1)	8 (5.5)	6 (4.1)	5 (3.4)	0.502
1-5	14 (9.6)	8 (5.5)	19 (13)	13 (8.9)	
>5	11 (7.5)	14 (9.6)	27 (18.5)	15 (10.3)	
Concomitant atopy					
Asthma+	8 (5.5)	7 (4.8)	17 (11.6)	7 (4.8)	0.649
Asthma-	23 (15.8)	23 (15.8)	35 (24)	26 (17.8)	
Urticaria+	2 (1,4)	2 (1.4)	5 (3.4)	1 (0.7)	0.709
Urticaria-	29 (19.9)	28 (19.2)	47 (32.2)	32 (21.9)	
Eczema+	4 (2.7)	6 (4.1)	13 (8.9)	4 (2.7)	0.386
Eczema-	27 (18.5)	24 (16.4)	39 (26.7)	29 (19.9)	
Serum eosinophilia (10^3 µgr)					
≤0.2	18 (12.3)	19 (13.0)	33 (22.6)	16 (11)	0.536
>0.2	13 (8.9)	11 (7.5)	19 (13)	17 (11.6)	
Serum total IgE (UI/mL)					
0-100 U	17 (11.6)	14 (9.6)	19 (13)	18 (12.3)	0.675
100-500	10 (6.8)	11 (7.5)	24 (16.4)	10 (6.8)	
>500	4 (2.7)	5 (3.4)	9 (6.2)	5 (3.4)	

+ / yes, - / none, *p<0.005

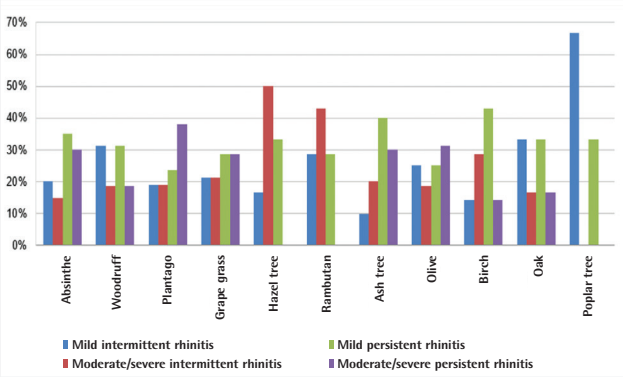

Figure 4. Distribution of aeroallergens by severity classification of allergic rhinitis

altitude at sea level, the lowest temperature is -11, the highest temperature is +40 degrees, the average relative humidity is 75%, and this rate goes up to 80-85% in certain months.

As a result, İstanbul has a climate with high humidity most of the year due to its geographical structure. For this reason, a high mite sensitivity rate is an expected result. In studies from different regions of Turkey, sensitivity rates for house mites D. pteronyssinus and D. farinae were 72.5% and 63.7% in Düzce, 62.2% and 51.3% in Eskişehir, 50% and 44% in Bursa, and 84% and 78.2% in the Eastern Black Sea region, which is similar to the data obtained in our study[13-16]. The high sensitivity to house dust mites in our study is thought to be due to the high humidity and mild climate of the İstanbul Kartal region, which is located at sea level. In a recent study by Ediger et al.[15], the most frequently observed aeroallergens in Bursa region after D. pteronyssinus and D. farine were grasses mix (38.6%), olive (33.2%), cereals pollen (32.3%), Acarus siro (26.3%) and cat hair (12%)[14].

In our study, the sensitivity rate of Acarus siro was found to be approximately 2 times higher with 57.5%, and the sensitivity rate of cereals mix (37.7%) and grasses mix (31.5%) was similar. It is an expected result that olive pollen causes high sensitivity similar to grasses mix due to olive cultivation in Bursa region. In our study, sensitivity to olive tree pollen was found to be lower (11%). This result shows that geographical vegetation closely affects the allergen etiology in AR patients. According to the results, it is important for allergy specialists to create an allergen panel according to the characteristics of the geography they are in.

Another remarkable point obtained in our study is that the rate of cat sensitivity (33.6%) in AR patients is higher than the grasses mix (31.5%), which is one of the main allergens, and it ranks third after the mite and cereals (grain) mix. The cat sensitivity rate in Europe is estimated at around 27%[17]. It is thought that this high sensitivity causes an increase in the amount of cat allergens in places where there are no cats (school, work, nursery) as a result of the increase in domestic cat feeding rates in industrialized countries, and this contributes to sensitization[18,19]. This result was supported by the study of Gulbahar et al.[20] in 387 patients. Although the cat sensitivity rate was found to be 44.7% in this study, it was reported that only 1.6% of the patients kept cats at home.

Another interesting point obtained in our study was that cat hair sensitivity was found to be significantly higher in individuals with mold and pollen sensitivity. Albumin-dependent cross-reactivity is known to be among cat hair and dog hair allergens, but no known cross-reactivity has been detected between molds and pollen groups. Further studies with larger series are needed for the significance of this data.

It is known that genetic transmission is an important factor in the formation of AR. If there is no history of allergy in the parents, the probability of AR is 0-10%, if one of the parents has a history of allergy, this rate is 30-40%, if both parents have a history of allergy, this rate can reach 60-70%[21]. In our study, the presence of allergy history in the mother and/or maternal relatives was 58.2%, and the family history positivity was found to be significantly higher in females than males. This result indicates that the female gender carries the diseased gene at a higher rate.

Recently, AR and asthma have been defined as the single airway diseases, and there are many studies showing elevated serum Eo and total IgE in parallel with airway inflammation in these diseases[22,23]. Similarly, in our study, the total IgE level of patients with AR was found to be significantly higher than the normal population. In the correlation analysis, it was observed that there was a positive correlation between serum total IgE and serum Eo count. These results show the importance of evaluating the total IgE and Eo levels together in patients with AR. However, no significant correlation was found between total IgE elevation and AR severity in our cohort. Similarly, no significant relationship was found between the severity of AR and age, gender, type of aeroallergen, and other concomitant atopic diseases.

Study Limitations

Compared to the population of İstanbul, the small number of patients in our study and the inability to measure serum specific IgE in correlation with the skin prick test are the limitations of our study.

CONCLUSION

AR is a disease whose prevalence increases every year and multifactorial factors play a role in its etiology. Along with genetic predisposition, allergens play an important role in the etiology. In this study, mites, pollen and cat hair were in the top three ranks in the distribution of aeroallergens. Considering the differences in the distribution of allergens according to climatic conditions, geographical structure and socioeconomic

levels, knowing the distribution of allergens in the population admitted to the hospital with AR will guide the patients to take preventive measures in this direction.

Ethics

Ethics Committee Approval: The study were approved by the Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee (protocol number: 2020/514/180/17, date: 26.06.2020).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: K.T., Design: K.T., M.A.Ç., Data Collection or Processing: K.T., M.A.Ç., Analysis or Interpretation: M.A.Ç., Literature Search: K.T., Writing: K.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Dykewicz MS, Hamilos DL. Rhinitis and sinusitis. J Allergy Clin Immunol. 2010;125(2 Suppl 2):S103-15.
2. Stewart M, Ferguson B, Fromer L. Epidemiology and burden of nasal congestion. Int J Gen Med. 2010;3:37-45.
3. Seidman MD, Gurgel RK, Lin SY, Schwartz SR, Baroody FM, Bonner JR, et al. Clinical practice guideline: allergic rhinitis executive summary. Otolaryngol Head Neck Surg. 2015;152:197-206.
4. Platts-Mills TAE, Schuyler AJ, Erwin EA, Commins SP, Woodfolk JA. IgE in the diagnosis and treatment of allergic disease. J Allergy Clin Immunol. 2016;137:1662-70.
5. D'Amato G, Vitale C, Lanza M, Molino A, D'Amato M. Climate change, air pollution, and allergic respiratory diseases: an update. Curr Opin Allergy Clin Immunol. 2016;16:434-40.
6. Cecchi L, D'Amato G, Annesi-Maesano I. External exposome and allergic respiratory and skin diseases. J Allergy Clin Immunol. 2018;141:846-57.
7. Brozek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines-2016 revision. J Allergy Clin Immunol. 2017;140:950-8.
8. Nelson HS. Variables in allergy skin testing. In: Dolen W, ed. Skin Testing. Philadelphia, PA: WB Saunders, 2001;21:281-90.
9. Calderón MA, Linneberg A, Kleine-Tebbe J, De Blay F, Hernandez Fernandez de Rojas D, Virchow JC, et al. Respiratory allergy caused by house dust mites: What do we really know? J Allergy Clin Immunol. 2015;136:38-48.
10. Ingram JM, Sporik R, Rose G, Honsinger R, Chapman MD, Platts-Mills TA. Quantitative assessment of exposure to dog (Can f 1) and cat (Fel d 1) allergens: relation to sensitization and asthma among children living in Los Alamos, New Mexico. J Allergy Clin Immunol. 1995;96:449-56.
11. Boner AL, Niero E, Antolini I, Valletta EA, Gaburro D. Pulmonary function and bronchial hyperreactivity in asthmatic children with house dust mite allergy during prolonged stay in the Italian Alps (Misurina, 1756 m). Ann Allergy. 1985;54:42-5.
12. Arlian LG, Neal JS, Morgan MS, Vyszenski-Moher DL, Rapp CM, Alexander AK. Reducing relative humidity is a practical way to control dust mites and their allergens in homes in temperate climates. J Allergy Clin Immunol. 2001;107:99-104.
13. Öztürk Ö, Tokmak A, Güçlü E, Yıldızbaş Ş, Gültekin E. Düzce'de allerjik rinitli hastalarda prick testi sonuçları. Düzce Tıp Fakültesi Dergisi. 2005;7:11-4.
14. Harmanci E, Us T, Ozdemir N, Akgun Y, Aydinli A, Mutlu S. The relationship between skin prick tests and serum specific IgE which is determined by chemiluminescence method in the diagnosis of respiratory system allergies. Solunum. 2000;2:31-5.
15. Ediger D, Günaydin FE, Erbay M, Şeker Ü. Trends of sensitization to aeroallergens in patients with allergic rhinitis and asthma in the city of Bursa, South Marmara Sea Region of Turkey. Turk J Med Sci. 2020;50:330-6.
16. Coskun ZO, Erdivanlı OC, Kazıkdas KÇ, Terzi S, Sahin U, Ozgur A, et al. High sensitization to house-dust mites in patients with allergic rhinitis in the eastern Black Sea region of Turkey: A retrospective study. Am J Rhinol Allergy. 2016;30:351-5.
17. Heinzerling LM, Burbach GJ, Edenharter G, Bachert C, Bindslev-Jensen C, Bonini S, et al. GA(2)LEN skin test study I: GA(2)LEN harmonization of skin prick testing: novel sensitization patterns for inhalant allergens in Europe. Allergy. 2009;64:1498-506.
18. Salo PM, Arbes SJ Jr, Jaramillo R, Calatroni A, Weir CH, Sever ML, et al. Prevalence of allergic sensitization in the United States: results from the National Health and Nutrition Examination Survey (NHANES) 2005-2006. J Allergy Clin Immunol. 2014;134:350-9.
19. Simpson A, Custovic A. Pets and the development of allergic sensitization. Curr Allergy Asthma Rep. 2005;5:212-20.
20. Gulbahar O, Sin A, Mete N, Kokuludag A, Kirmaz C, Sebik F. Sensitization to cat allergens in non-cat owner patients with respiratory allergy. Ann Allergy Asthma Immunol. 2003;90:635-9.
21. Kjellman NI. Atopic disease in seven-year-old children. Incidence in relation to family history. Acta Paediatr Scand. 1977;66:465-71.
22. Khadadah M, Onadeko BO, Ezeamuzie CI, Mustafa HT, Marouf R, Sugathan TN. The association of skin test reactivity, total serum IgE levels, and peripheral blood eosinophilia with asthma in Kuwait. J Asthma. 2000;37:481-8.
23. Howell WM. HLA immunogenetics and specific IgE responses to allergens. Clin Exp Allergy. 1994;24:401-4.