



Sensitization to Aeroallergens on Skin Prick Tests in Atopic Children Living in the Southwest of Turkey

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Abstract

Objective: This study aimed to identify aeroallergens susceptibility patterns of atopic children living in the city of Antalya, southwest of Turkey.

Methods: One thousand seven hundred five patients (2-18 years) who applied to the pediatric allergy immunology outpatient clinic between April 2018-March 2020 were included in the study. The demographic and clinical characteristics of patients with at least one allergic sensitization in the skin prick test were evaluated.

Results: A total of 761 patients were evaluated, comprising 57.69% males and 42.31% females, with a median age of 9.25 years (range, 6.25-12.9 years). Of the total patients 54.01% had asthma (AS), 89.22% had allergic rhinitis (AR), (45.33%) had both AS and AR and 11.83% had atopic dermatitis. Sensitivity to house dust mites (HDMs) was the most common sensitivity (66.23%), followed by animal dander (39.68%) and cockroach (34.56%). Other allergens were grass pollen (32.33%), mold (31.54%), weed mixture pollen (29.04%), olive tree (27.86%), and tree mixture (14.98%), respectively. More than one allergen sensitization was detected in 537 (70.6%) patients. AR was more common in boys ($p=0028$). Pollen sensitivity was higher in children with AR than in children without AR ($p<0.001$).

Conclusion: In our study in which allergen sensitivity was determined in atopic children in our region, the most common allergens were HDMs, cockroaches and animal dander, which are indoor allergens.

Keywords: Aeroallergens, atopy, allergic diseases, children, sensitization

INTRODUCTION

The prevalence of asthma and other allergic diseases (e.g., rhinitis and eczema) has increased worldwide over the last twenty years (1). The origins of these diseases are complex, but understanding genetic and environmental risk factors can shed light on possible measures which can be taken to prevent the development of the disease (2).

Atopy is an individual predisposition to the development of allergic diseases. IgE-mediated sensitization to food or at least one environmental allergen can be detected with SPT, which is an easy-to-use, fast, and highly sensitive method for diagnosing IgE-mediated allergies (3). Studies have suggested that the type of

allergen sensitization may influence the development, duration, and severity of allergic diseases (4,5). Aeroallergens are an important causal factor in the pathogenesis of these disorders, and sensitivity to allergens varies by country and region. This can be explained by differences in climate and variations in the presence of allergens in different geographical areas (6). Identifying sensitization patterns in specific geographic areas allows specific interventions such as allergen reduction and/or avoidance and encourages the use of specific immunotherapy (7). In two previous studies conducted in our region to determine childhood aeroallergens sensitivity, house dust mites (HDMs), molds and pollens were found to be the most common allergens (8,9). There may be changes in aeroallergens sensitivity over



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time and locally. This study aimed to evaluate the aeroallergens sensitization and its frequency in atopic children living in Antalya, southwest of Turkey by using epidermal skin prick test.

METHODS

Patients

This cross-sectional observational study included 1.705 patients aged 2-18 years who presented with allergic complaints and underwent SPT in the Pediatric Allergy Outpatients Clinic of University of Health Sciences Turkey, Antalya Training and Research Hospital, between April 2018 and March 2020. The demographic and clinical characteristics of 761 (44.63%) patients with at least one allergic sensitization in the SPT were evaluated. This study was conducted in concordance with ethical standards and the World Health Organization Helsinki Declaration. It was approved by the Local Ethics Committee of University of Health Sciences Turkey, Antalya Training and Research Hospital (2020, 10/16). Informed consent was obtained from all the patients.

The Skin Prick Test

Patients were subjected to SPT for a panel of standard allergen solutions for aeroallergens (Allergopharma GmbH & Co. Hamburg/Germany), including 2 types of HDMs [Dermatophagoides pteronyssinus (Dp) and Dermatophagoides farinae (Df)], animal dander (cat epithelia, dog epithelia, horse epithelia), early and mid-term blooming tree pollens (alder, elm, hazel, poplar, willow, birch, beech, oak, plane tree), olive tree pollen, grass and cereal pollens (Kentucky blue grass, Timothy grass, Meadow fescue, Rye grass, Velvet grass, Orchard grass, Barley, Oats, Wheat, Rye) weeds (Mugwort, Dandelion, Nettle, English plantain, Wall pellitory), molds (*Alternaria alternata*, *Aspergillus fumigatus*, *Cladosporium herbarum*), and cockroach (*Blattella germanica*). The selection of aeroallergens was based on their aerial dominance and availability.

The SPT was performed according to the international guidelines (3) as a single test on two forearms with lancets (Mizollen; H. Herenz GmbH, Hamburg/Germany) and standardized allergens. Histamine (10 mg/mL of histamine phosphate) and 0.9% sterile saline were used as positive and negative controls, respectively. The SPTs were evaluated 15 min after application and considered positive if the mean wheal diameter was ≥ 3 mm compared with the negative control. Patients who were sensitive to two or more classes of allergens were defined as polysensitized. House dust mite sensitivity was defined as a positive reaction to at least one of the Dermatofagoides allergens. Tree pollen sensitivity was defined as a positive reaction to at least one of the early

or middle flowering trees. Fungal sensitivity was defined as a positive response to at least one of *Alternaria alternata*, *Aspergillus Fumigatus*, or *Cladosporium herbarum*. Animal dander was defined as a positive response to at least one of the cat epitheliums, dog epithelium, or horse epithelium.

Statistical Analysis

The SAS version 9.4 software was used for statistical analysis. Descriptive statistics were stated as mean, standard deviation, median, minimum and maximum values, or number (n) and percentage (%). The Kolmogorov-Smirnov test was conducted to check the normality distribution of independent data. Since the data were normally distributed, the Independent t-test and analysis of variance (ANOVA) were used for the comparative analysis. The chi-square test was used for the analysis of qualitative independent data. The Pearson correlation coefficient (rs) was used for correlations between parametric data. A value of $p < 0.05$ was set as statistically significant.

RESULTS

Study Population

The evaluation was made of 761 children aged 2-18 years who had a positive skin prick test against at least one aeroallergens. The male/female ratio was 439 (57.69%)/322 (42.31%) and the median age was 9.25 years [6.25-12.9 interquartile range (IQR)]. Of the 761 patients, 411 (54.01%) had AS, 679 (89.22%) had AR, 340 (45.33%) had both AS and AR, 71 (9.47%) had only asthma, 339 (45.2%) had only AR, 90 (11.83%) had AD, 54 (11.61%) had only AD, and 36 (7.74%) had AD+AS.

The serum total IgE level was found to be median 209 IU/mL (78-538 IQR) in 337 patients. The eosinophil count in 352 patients was found to be mean 5.01% and median 4.3%.

More than one allergen sensitization was detected in 537 (70.6%) patients. Total IgE and eosinophil mean levels were higher in polysensitized patients (524/337, $p=0.23$, 5.25%/4.35% $p=0.036$ respectively). *Alternaria alternata* was the most common sensitivity in monosensitized patients (2.3%), followed by Df (1.97%), and Dp (0.53%).

Prevalence of Aeroallergens Sensitization

Sensitivity to HDMs was the most common sensitivity (504, 66.23%, Df 60.3%, Dp 59%), followed by an animal dander (302, 39.68%, cat epithelium 33.5%, dog epithelium 29.2%, horse epithelium 11.3%), cockroach (263, 34.56%), grass and cereal pollen (246, 32.33%), molds (240, 31.54%, *Alternaria alternata* 24.8%, *Aspergillus fumigatus* 11.8%, *Cladosporium herbarum*

13.4%), weed mixture (221, 29.04%), olive tree (212, 27.86%), and tree mixture (114, 14.98%). The frequency of sensitization to aeroallergens is shown in Figure 1.

When the allergen sensitivities were examined according to allergic diseases, HDMs were the most common in all patient groups, followed by animal dander, and cockroach. A significant difference was determined between patients with and without allergic rhinitis, the sensitivity to grass cereal mixture, olea tree and weed mixture was found to be higher in the AR group ($p < 0.001$, $p = 0.031$, $p = 0.016$ respectively). There were no significant differences between these two groups in terms of other allergens.

When the patients with asthma and allergic rhinitis were compared to those with only asthma and only AR, sensitization to HDM and aspergillus was found to be higher ($p < 0.001$, $p = 0.033$ respectively).

When evaluated according to season, HDMs were the most common allergen in all seasons. In winter, animal dander ($p = 0.03$) and pollen sensitivity frequencies were lower ($p < 0.001$). The frequency of aeroallergens sensitization by season is shown in Figure 2.

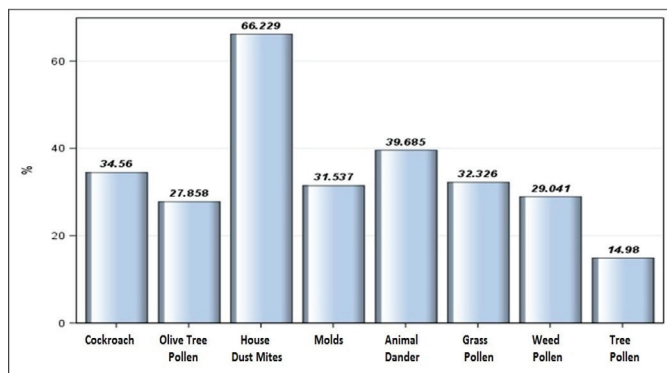


Figure 1. Frequency of sensitization to aeroallergens among atopic children

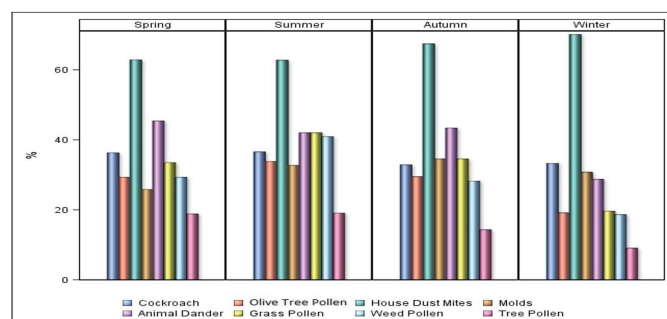


Figure 2. Aeroallergen distribution by seasons

Sex and Allergen Sensitization

AR was more common in boys ($p = 0.028$). Females showed higher test positivity rates for cats compared to males ($p = 0.008$). No significant difference was observed between the sexes with respect to the remaining allergens.

Age and Allergen Sensitization

Patients were categorized into three age groups: 2-5 years (mean age 4.07 ± 0.7 , median 4.25 years), 5-10 years (mean age 7.38 ± 1.43 , median 7.37 years), and more than 10 years (mean age 13.61 ± 2.28 , median 13.4 years). Significant differences were determined between the age groups in AR and AS ($p < 0.001$) AR was lower in the 2-5 year group ($p < 0.001^{***}$) and AS was lower in the > 10 year group (Table 1).

Sensitization to animal dander ($p < 0.001$), cockroach ($p = 0.016$), aspergillus ($p = 0.013$), claudosporium ($p < 0.001$), grass-cereal mix ($p < 0.001$), weed mix ($p < 0.001$), tree mix ($p = 0.002$), and olea tree ($p < 0.001$) showed an increasing trend with age. The sensitization rates were higher in the group aged more than 10 years compared to the 2-5 years and 5-10 year groups. The distribution of aeroallergens by the age group is shown in Figure 3.

Aeroallergens Sensitivities According to Atopic Diseases

In patients with only AR, grass mix (40.4%), grass-cereal mix (40.4%), weed mix (31.27%), and olea tree (30.97%) sensitization rates were higher than in the AS and AS+AR groups ($p < 0.001$, $p = 0.003$, $p = 0.031$, respectively).

In the AS+AR group HDMs (*D. pteronyssinus* 67.82%, *D. pharinaea* 68.82%) and aspergillus (15.29%) sensitization rates were higher than in the AS and AR only groups ($p < 0.001$, $p = 0.03$, respectively).

In patients with only AD, HDMs, cockroach, animal dander and grass pollen sensitization were observed. The distribution of aeroallergens by allergic diseases is shown in Figure 4.

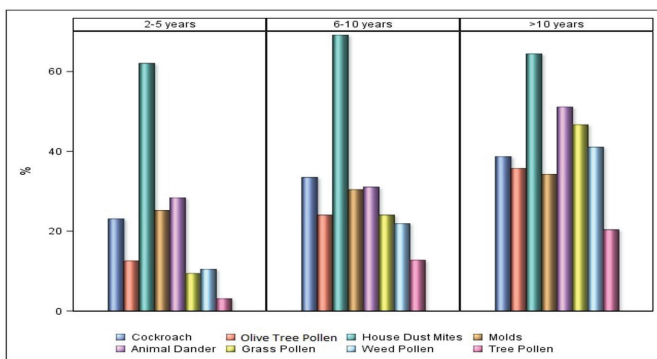
DISCUSSION

Aeroallergens sensitization is increasing world-wide. The variability in aeroallergens sensitivity of children may differ not only between countries but also between cities in the same country with different climatic conditions (6). Climate change, pollution, altitude, and diverse human activities affect aeroallergens sensitivity. Identifying allergens is an important step in diagnosing allergic respiratory disease. Epidemiological studies show that the global distribution of aeroallergens, such as HDMs and pollen, varies geographically and seasonally. Pollen

Table 1. Age group categorisation of patients

	2-5 years		6-10 years		>10 years		p value
	n	%	n	%	n	%	
Total	95	12.48	328	43.10	338	44.42	
Boys	61	64.21	190	57.93	188	55.62	0.32
Girls	34	35.79	138	42.07	150	44.38	
AD	16	16.84	41	12.5	33	9.76	0.15
AR	73	76.84	286	87.2	320	94.67	<0.001***
AS	64	67.37	207	63.11	140	41.42	<0.001***
Polysensitisation	45	8.38	215	40.04	277	51.58	<0.001***
Monosensitisation	50	22.32	113	50.45	61	27.33	

AD: Atopic dermatitis, AR: Allergic rhinitis, AS: Asthma

**Figure 3. Aeroallergen distribution by age groups**

allergens are usually found in subtropical or temperate climates rather than tropical, and their surrounding concentrations vary throughout the year depending on the ecological season (10,11).

In our study, sensitivity to HDMs was the most common, followed by animal dander and cockroach. Other aeroallergens sensitivities were to molds and pollens. The sensitization rates to pollen were determined to be higher in the AR only group than in the AS and AS+AR groups.

In the AS+AR group, HDMs and aspergillus sensitization rates were higher than in the AS only and AR only groups.

In a study by Hazar Sayar (8), conducted in Alanya region in an other region of southwestern Turkey between 2017 and 2018, of children aged 2-18 years, the most common sensitivities were determined to be HDMs (76.1%), followed by fungal spores (51.8% *Alternaria alternata*, 41.7% *Cladosporium herbarum*), and grass and cereal pollen (39.8%). In another study by Basaran et al. (9) in the Mediterranean region covering the years 2014-2015, the most common sensitivity was to HDMs at 69% followed by tree pollen mixture at 54.9% and grass and cereal pollen mixture at 52.5%. Previous studies conducted in Turkey have determined HDMs to be a significant allergen. Harmançi et al. (12) reported house dust mite sensitivity of 46.3% in pre-school-age children in

Ankara, Yazicioglu et al. (13) reported this rate as 52.1% in children aged 4-17 years in the Thrace region, and Şaşıhüseyinoğlu et al. (14) determined the most common allergen sensitivities to be Dp (73.8%) vs. Df (71.6%). Ozkaya et al. (15) compared two regions at different altitudes and reported that house dust mite sensitivity was greater in İstanbul at sea level than in Erzurum at high altitude (72.3% vs. 22.6%), and pollen sensitivity was higher in Erzurum. Thus, it was stated that the mite allergy is associated with high humidity and low altitude (15).

A previous study that included various regions of Turkey showed that the presence of mites was related to an increase in both mean temperature (>15 °C) and humidity (40%), as well as low altitude (<300 m) (16).

Several studies have shown that mite sensitivity is associated with an increased risk of rhinitis and asthma in both children and adults (17,18) and that exposure to HDMs, pollens, molds, and animal dander is a significant risk factor in the development of allergic diseases in children (19). Mite allergy is the most important and most common indoor allergen associated with airway sensitivity.

Turkey acts as a bridge between Asia and Europe, and is surrounded by sea on three sides. Geographical and climatic changes cause aeroallergens diversity and various aeroallergens sensitivities are observed.

Antalya is located in western Anatolia. According to the Köppen-Trewarta climate classification, Antalya is Cshk; scalding summers, cool winters, subtropical dry summer climate, Mediterranean climate (20). The average annual humidity is 65% and the average monthly relative humidity ranges from 58% in July to 70% in December. The temperature typically varies from 5 °C to 34 °C and is rarely below 1 °C or above 39 °C. The warm and humid climate provides an ideal environment for mites and cockroaches.

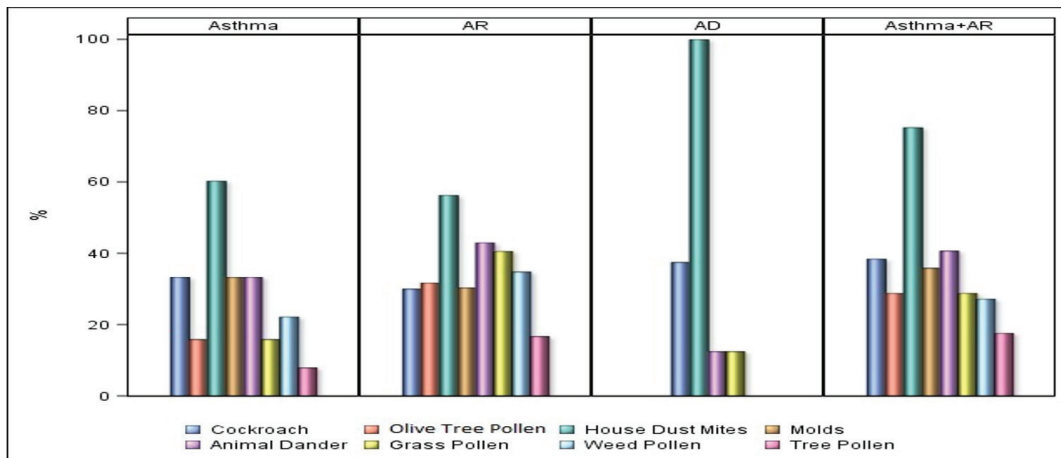


Figure 4. Aeroallergen distribution by allergic diseases

AR: Allergic rhinitis, AD: Atopic dermatitis

In this study, sensitization to HDMs is expected to be high due to regional geography with 60-70% humidity and the location at an altitude of 100 m above sea level.

Sensitization to pet allergens from domestic exposure is gradually increasing. As the rate of pet ownership increases, direct or indirect exposure to pets may also increase the rate of sensitization to pet allergens. Animal dander can also cause allergies in those without an animal at home, as animal danders sticky and airborne. As pet owners carry animal dander to public places on their clothes, it can be found in the air, even in public places where there are no animals present (21,22). Animals are the third leading cause of allergic asthma, after mites and pollen (23). In this study, animal dander was the second most common sensitivity. Cats and dogs can be found in almost every area of Antalya. Females showed higher test positivity rates for cats. It was thought that cat sensitivity was more common in females as females are more likely to own cats than males.

It is common for many patients to be sensitized to both cats and dogs (23) and 75% of pet-sensitized patients are 14 times more likely to be sensitized to other animals (24). In a study conducted in Korea, sensitization to cats was found to be a risk factor for sensitization to dogs, and vice versa (22). In the current study, 81.5% of patients with cat sensitivity also had dog sensitivity, and 71% of those with dog sensitivity also had cat sensitivity. Of the patients with horse sensitivity, 89.5% also had dog sensitivity and 90.7% had cat sensitivity. Structural similarities and/or homology between various dogs and cat allergens (such as albumin and lipocalin) explain the cross-reactivity between them and with other mammals (23,25).

Cockroach allergy has been identified as an important cause of respiratory allergic diseases and exposure to

cockroach may lead to exacerbations of asthma and/or allergic rhinitis in sensitized patients.

More than 20 different cockroach species have been identified in Turkey, of which *Blattella germanica* has been reported to be the most common (26). Cockroach allergen levels are correlated with the severity and increase in morbidity of asthma. Previous studies have reported that the cockroach allergy prevalence rate varies from 17- 58% of atopic allergies in the USA and 4-26% in Europe and 2.2-51.4% in Turkey in various studies of both children and adults (13,26-28). In a study of respiratory-allergic adults in İzmir, cockroach allergy was seen in 36.2% and sensitivity to cockroach allergens was determined to be more frequently associated with other indoor allergen sensitivities, especially dog, cat dander and mite sensitivity. This co-existence was attributed to the fact that patients might be simultaneously exposed and thus become sensitized to these allergens, and this co-sensitization with other indoor allergens might also contribute to the early development of asthma and a more severe course of the disease (29). Similarly, in the current study, indoor allergen sensitivities to mite, animal dander and cockroach were the three most common allergens. Cockroach-sensitive patients were also sensitized to mites at a rate of 89% and to animal dander at 48.3%. Cockroach sensitivity in the current study was 34.56% and 89% of cockroach-sensitive patients were also sensitive to HDMs. Previous studies have demonstrated that 70% of patients with a cockroach allergy were also sensitive to HDMs, suggesting cross-reactivity between the two allergens in both adults and children (26,30). The co-existence of cockroach and house dust mite allergen sensitivity is well known. Tropomyosin causes a cross-reaction between house dust mite allergen, cockroach allergen, parasites and shrimp allergens (31).

A previous study has shown that in addition to homes, kindergartens and schools are highly exposed to mite and

cockroach allergens, which may contribute to sensitization (32).

As cockroaches prefer to live in high temperatures and humid environments, there is increased exposure in seaside regions, which explains the higher frequencies of cockroach sensitivities among patients living in Antalya. Cockroach infestations are considerably higher in patients with a low socioeconomic level and poor housing conditions. Unfortunately, the socioeconomic status of the patients in this study could not be assessed. The eradication of cockroaches depends on meticulous attention to hygiene and regular use of insecticides.

Atopy is more common in the male sex (33). In this study 57.69% of the patients were male and 42.31% were female, and AR was more common in boys, which was consistent with the literature.

Aspergillus sensitization has been reported in previous adult and pediatric studies to be associated with poorly controlled and severe asthma (34,35). In this study, aspergillus sensitivity was found to be high in patients with asthma only, but since asthma control was not evaluated in this study, the relationship with poorly controlled or severe asthma could not be evaluated.

When we examined the aeroallergens sensitivities according to age, it was observed that the house dust mite allergy was observed most frequently and polysensitization increased with age.

CONCLUSION

The results of this study detected environmental aeroallergens sensitivity and common allergens in our region. Indoor allergen sensitivity was common in this study, which was attributed to rising temperatures and humidity recently in Antalya. Global climate change, seasonal changes, and aeroallergens concentrations are expected to influence the future prevalence, severity, and manifestation of allergic diseases. Regional studies can provide important clinical information about the nature and course of allergic diseases and future treatment options.

Ethics

Ethics Committee Approval: It was approved by the Local Ethics Committee of University of Health Sciences Turkey, Antalya Training and Research Hospital (2020, 10/16).

Informed Consent: Informed consent was obtained from all the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Ş.K., S.F., Design: Ş.K., S.F., Data Collection or Processing: Ş.K., Analysis or Interpretation: Ş.K., S.F., Literature Search: Ş.K., S.F., Writing: Ş.K., S.F.

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REFERENCES

- Barreto ML, Cunha SS, Alcântara-Neves N, Carvalho LP, Cruz AA, Stein RT, et al. Risk factors and immunological pathways for asthma and other allergic diseases in children: background and methodology of a longitudinal study in a large urban center in Northeastern Brazil (Salvador-SCAALA study). *BMC Pulm Med* 2006;6:15.
- Hossenbaccus L, Linton S, Ramchandani R, Gallant MJ, Ellis AK. Insights into allergic risk factors from birth cohort studies. *Ann Allergy Asthma Immunol* 2021;127:312-7.
- Bousquet J, Heinzerling L, Bachert C, Papadopoulos NG, Bousquet PJ, Burney PG, et al. Practical guide to skin prick tests in allergy to aeroallergens. *Allergy* 2012;67:18-24.
- Manise M, Bakayoko B, Schleich F, Corhay JL, Louis R. IgE mediated sensitisation to aeroallergens in an asthmatic cohort: relationship with inflammatory phenotypes and disease severity. *Int J Clin Pract* 2016;70:596-605.
- Marogna M, Massolo A, Berra D, Zanon P, Chiodini E, Canonica GW, et al. The type of sensitizing allergen can affect the evolution of respiratory allergy. *Allergy* 2006;61:1209-15.
- Bousquet PJ, Chinn S, Janson C, Kogevinas M, Burney P, Jarvis D, et al. Geographical variation in the prevalence of positive skin tests to environmental aeroallergens in the European Community Respiratory Health Survey I. *Allergy* 2007;62:301-9.
- Ciprandi G, Alesina R, Ariano R, Aurnia P, Borrelli P, Cadario G, et al. Characteristics of patients with allergic polysensitization: the POLISMAIL study. *Eur Ann Allergy Clin Immunol* 2008;40:77-83.
- Hazar Sayar E. Aeroallergen sensitivity of atopic children in Alanya region. *Selcuk Med J* 2020;3:226-31.
- Basaran AE, Torun NK, Uygun DFK, Bingöl A. Akdeniz bölgesinde yaşayan atopik çocukların deri prick testlerindeki aeroallerjen dağılımları. *Astım Allerji İmmünoloji* 2018;16:132-7.
- Sheffield PE, Weinberger KR, Kinney PL. Climate change, aeroallergens, and pediatric allergic disease. *Mt Sinai J Med* 2011;78:78-84.
- Davies J. Grass pollen allergens globally: the contribution of subtropical grasses to burden of allergic respiratory diseases. *Clin Exp Allergy* 2014;44:790-801.
- Harmancı K, Bakırtaş A, Türkteş İ. Sensitization to aeroallergens in preschool children with respiratory problems in Ankara, Turkey. *Turkish Respiratory Journal* 2006;7:10-4.
- Yazıcıoğlu M, Oner N, Celtik C, Okutan O, Pala O. Region of Turkey. *Asian Pacific Journal of Allergy and Immunology* 2004;22:183-90.
- Şaşıhüseyinoğlu AŞ, Kont Özhan A, Serbes M, Duyuler GA, Bingöl G, Yılmaz M, et al. Distribution of allergen sensitization in childhood with the skin test. *Asthma Allergy Immunol* 2017;15:43-8.
- Ozkaya E, Sogut A, Küçükkoç M, Eres M, Acemoglu H, Yuksel H, et al. Sensitization pattern of inhalant allergens in children with asthma who are living different altitudes in Turkey. *Int J Biometeorol* 2015;59:1685-90.

16. Kalpaklıoğlu AF, Emekçi M, Ferizli A, Misirligil Z. A survey of acarofauna in Turkey: comparison of seven different geographic regions. *Allergy Asthma Proc* 2004;25:185-90.
17. Oncham S, Udomsubpayakul U, Laisuan W. Skin prick test reactivity to aeroallergens in adult allergy clinic in Thailand: a 12-year retrospective study. *Asia Pac Allergy* 2018;8:e17.
18. Guilbert A, Cox B, Bruffaerts N, Hoebeke L, Packeu A, Hendrickx M, et al. Relationships between aeroallergen levels and hospital admissions for asthma in the Brussels-Capital Region: a daily time series analysis. *Environ Health* 2018;17:35.
19. Tham EH, Lee AJ, Bever H. Aeroallergen sensitization and allergic disease phenotypes in Asia. *Asian Pac J Allergy Immunol* 2016;34:181-9.
20. Bölük E, Kömüçü A. Köppen-Trewartha iklim sınıflandırmasına göre Türkiye iklimi. *Klimatoloji Şube Müdürlüğü*, 2018.
21. Plaschke P, Janson C, Norrman E, Björnsson E, Ellbjär S, Järholm B. Association between atopic sensitization and asthma and bronchial hyperresponsiveness in Swedish adults: pets, and not mites, are the most important allergens. *J Allergy Clin Immunol* 1999;104:58-65.
22. Park BW, Park JY, Cho EB, Park EJ, Kim KH, Kim KJ. Increasing prevalence of the sensitization to cat/dog allergens in Korea. *Ann Dermatol* 2018;30:662-7.
23. Dávila I, Domínguez-Ortega J, Navarro-Pulido A, Alonso A, Antolin-Amerigo D, González-Mancebo E, et al. Consensus document on dog and cat allergy. *Allergy* 2018;73:1206-22.
24. Liccardi G, Passacqua G, Salzillo A, Piccolo A, Falagiani P, Russo M, et al. Is Sensitization to Furry Animals an Independent Allergic Phenotype in Nonoccupationally Exposed Individuals? *J Investig Allergol Clin Immunol* 2011;21:137-41.
25. Cabañas R, López-Serrano MC, Carreira J, Ventas P, Polo F, Caballero MT, et al. Importance of albumin in cross-reactivity among cat, dog and horse allergens. *J Investig Allergol Clin Immunol* 2000;10:71-7.
26. Yılmaz A, Tuncer A, Sekerel BE, Adalıoğlu G, Saraçlar Y. Cockroach allergy in a group of Turkish children with respiratory allergies. *Turk J Pediatr* 2004;46:344-9.
27. Sarpong SB, Hamilton RG, Eggleston PA, Adkinson Jr NF. Socioeconomic status and race as risk factors for cockroach allergen exposure and sensitization in children with asthma. *J Investig Allergol Clin Immunol* 1996;97:1393-401.
28. Özdemir Ö, Bingöl Aydın D. Cockroach allergy and its immunotherapy. *Asthma Allergy Immunol* 2016;14:1-10.
29. Gulbahar O, Mete N, Ardeniz O, Kokuludag A, Sin A, Sebik F. Characteristics of sensitization to cockroaches in patients with respiratory allergy in Izmir, Turkey. *Revue française d'allergologie et d'immunologie clinique* 2004;44:620-4.
30. Mungan D, Celik G, Sin B, Bavbek S, Demirel Y, Misirligil Z. Characteristic features of cockroach hypersensitivity in Turkish asthmatic patients. *Allergy* 1998;53:870-3.
31. Asturias JA, Gómez-Bayón N, Arilla MC, Martínez A, Palacios R, Sánchez-Gascón F, et al. Molecular characterization of American cockroach tropomyosin (Periplaneta americana allergen 7), a cross-reactive allergen. *J Immunol* 1999;162:4342-8.
32. Rullo VE, Rizzo MC, Arruda LK, Solé D, Naspiç CK. Daycare centers and schools as sources of exposure to mites, cockroach, and endotoxin in the city of Sao Paulo, Brazil. *J Allergy Clin Immunol* 2002;110:582-8.
33. Pausjenssen ES, Cockcroft DW. Sex differences in asthma, atopy, and airway hyperresponsiveness in a university population. *Ann Allergy Asthma Immunol* 2003;91:34-7.
34. Kumari J, Jat KR, Lodha R, Jana M, Xess I, Kabra SK. Prevalence and risk factors of allergic bronchopulmonary aspergillosis and aspergillus sensitization in children with poorly controlled asthma. *J Trop Pediatr* 2020;66:275-83.
35. Rajagopal T, Kant S, Verma S, Kushwaha R, Kumar S, Garg R, et al. Aspergillus sensitization in bronchial asthma: A separate phenotype. *Allergy Asthma Proc* 2020;41:e26-32.