



Evaluation of Allergen Sensitization in Patients with Allergic Rhinitis and/or Asthma in Tekirdağ

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ABSTRACT

Aim: Allergic rhinitis (AR) and asthma are the most prevalent allergic diseases, and environmental allergens are important factors in the pathogenesis and the exacerbation of these diseases. Although there are many studies investigating aeroallergen sensitivities in different regions of our country, this study aimed to identify the aeroallergen sensitization in the Tekirdağ province in the part of Turkey in Europe, namely Thrace, where it is important to know aeroallergen sensitivities.

Materials and Methods: Four hundred and sixty children with asthma and AR who were followed up and had at least one aeroallergen sensitivity in a skin prick test (SPT) were retrospectively evaluated. All patients had undergone a SPT using the standard extracts, including house dust mites, molds, animal dander, pollens, and latex.

Results: The mean age of the patients was 10.2±3.4 (5-18) years, 57.6% of them were male. The diagnoses of the patients were AR in 57.8%, asthma in 22.6% and both in 19.6%. 42.6% (n=196) of the patients were sensitized to more than one allergen. The most common aeroallergens in SPT were house dust mites (63%), grass-rye mix (26.5%), grass mix (26.1%), molds (19.8%), cat epithelium (11.3%), cockroach (8.5%), weed mix (7%), olive tree (7%), dog (5.7%), cupressus (4.3%), tree pollen mix (3.5%), poplar (1.5%), mugwort (1.3%), and latex (0.4%). Although the cockroach, pet, olive tree and multiple allergen sensitivities were more frequent among male children (p<0.05), there was no association between gender and sensitivity to the other allergens. There was no difference between the aeroallergen distributions of the patients according to diagnoses (p>0.05). House dust mites were the most common allergens throughout all seasons.

Conclusion: The results of this study will be important in guiding elimination measures against the triggering allergens which are important for the treatment and the course of the disease of the those patients with asthma and/or AR in this region.

Keywords: Aeroallergen sensitivity, children, Tekirdağ, allergic rhinitis, asthma

Introduction

Allergic rhinitis (AR) is one of the leading causes of morbidity worldwide, and its prevalence is gradually increasing. AR is also frequently associated with asthma and is a risk factor. AR and asthma affect the quality of life and the school and work performances of the patients and they lead to frequent hospital visits (1).

AR is the most common atopic disease and it affects more than 500 million people worldwide (2). It is characterized by symptoms such as runny and itchy nose, sneezing and nasal obstruction. It has been reported to affect 10-40% of children and adults in the United States and other industrialized countries (3-5).

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Asthma is characterized by bronchial hyper-reactivity and chronic inflammation, causing reversible obstructions of the airways due to an interaction between hereditary and environmental factors (6). Three hundred million people worldwide are diagnosed with asthma (7). Asthma, commonly seen in childhood, is one of the critical reasons for morbidity. A variety of environmental factors such as viral infections, aeroallergens such as house dust mites (HDMs) or pollens, and tobacco exposure can result in asthma exacerbation (8).

Allergen sensitization refers to allergen-specific immunoglobulin E (IgE) production and it is assessed by using a skin prick test (SPT) or by measuring allergen specific IgE levels. Although allergen sensitization does not cause symptoms in some individuals, some may experience allergic symptoms. Atopy is an important risk factor for asthma, AR, and other allergic diseases. The elimination of triggering allergens is important for the optimal management of allergic diseases in order to reduce symptoms and control these diseases, and it constitutes the first-line therapy (9).

The SPT is a quick, affordable, and effective method with high sensitivity and specificity to detect aeroallergen sensitivity in IgE-mediated allergic diseases such as asthma and AR. The most commonly seen aeroallergens are HDMs, grasses, trees, weed pollens, animal dander, and molds (10).

Tekirdağ is a coastal city situated on the northwest coast of the Marmara Sea in the Marmara region of Turkey, consisting of different regions presenting a variety of climate characteristics. It has coasts on both the Marmara and the Black Sea and it has a sub-humid climate.

The most important feature of this research is that Tekirdağ, the province where the study was conducted, is located in the part of Turkey in Europe, namely Thrace. Since this region has different climatic characteristics, the distribution of allergens may be variant. Therefore, studies are required in order to identify allergen sensitivities in those children with asthma and AR in Tekirdağ, a city located in the Marmara region of Turkey.

The purpose of this study was to determine the distribution of aeroallergen sensitivities in those children with AR or/and asthma in Tekirdağ by using a SPT.

Materials and Methods

Patients aged between 5 and 18 years with asthma and AR were followed up between September 2018 and February 2020 in the Pediatric Allergy and Immunology Outpatient Clinic and they were confirmed to have at least one aeroallergen sensitivity. SPTs were included in this

study. Their demographic characteristics, total IgE levels, eosinophil counts and percentages in peripheral blood, and aeroallergen sensitivities in SPTs were investigated retrospectively. Those patients with a chronic disease other than an allergic disease were excluded from this study.

The diagnosis and management of asthma were made in line with the Global Initiative for Asthma guidelines (8). AR was diagnosed based on the AR and Their Impacts on Asthma guidelines (1).

This study was approved by the Tekirdağ Namık Kemal University Faculty of Medicine, Non-Invasive Clinical Research Ethics Committee (date: 25/03/2020, no: 2020.66.03.16).

Skin Prick Test

Medicines which may affect SPT results were discontinued at an appropriate time before the test. The SPTs of all of the patients were performed on the forearms and evaluated 15-20 minutes after the application by measuring the wheal diameter (11). Positive control (histamine 10 mg/mL), negative control (0.9% NaCl), and standardized commercial allergen solutions were used in the SPTs (®ALK-Abelló, Copenhagen, Denmark). The allergens applied in SPTs were: HDMs (*Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*); molds (*Alternaria alternata*, *Aspergillus fumigatus*, *Cladosporium herbertatum*); grass pollen mixture; weed pollen mixture; 9 tree pollen mixture; grass-rye mixture; animal dander (cat, dog); cockroach (*Blattella germanica*); cupressus; Engl. Plantain; mugwort; olive; poplar; nettle; and latex allergen extracts.

A wheal diameter ≥ 3 mm larger than the negative control was considered as allergen sensitivity (11).

Mite sensitivity was defined as a sensitivity to at least one of the HDMs. Animal dander and epithelium sensitivity was defined as a sensitivity to at least one of the cat or dog epitheliums. Mold sensitivity was defined as a positive reaction to at least one of the molds in the SPT. Tree pollen sensitivity was defined as a sensitivity to at least one of the tree pollens.

Statistical Analysis

Statistical analyses were performed using the SPSS Version 22.0 statistical software package (IBM SPSS Statistics Chicago, Ill). Descriptive statistics were expressed as mean, standard deviation, median, minimum and maximum values, frequencies, and percentages. A chi-square test was used in the analysis of the categorical data. Whether the distribution of each variable in the dataset

fitted the normal distribution was tested, and variables that were not normally distributed were evaluated by non-parametric tests (Kruskal-Wallis test and Mann-Whitney U test). $P < 0.05$ was considered statistically significant.

Results

Four hundred and sixty children aged between 5 and 18 years with asthma and/or AR who were followed up and had at least one aeroallergen sensitivity in SPT were retrospectively evaluated. The aeroallergen sensitivities with SPT were 63% for HDMs, 26.5% for grass-rye mix, 26.1% for grass mix, 19.8% for molds, 11.3% for cat epithelium, 8.5% for cockroach, 7% for weed mix, 7% for olive tree, 5.7% for dog, 4.3% for cupressus, 3.5% for tree pollen mix, 1.5% for poplar, 1.3% for mugwort, and 0.4% for latex (Figure 1).

The mean age of the patients was 10.2 ± 3.4 (5-18) years, and 57.6% were male. The diagnoses of the patients were AR in 57.8%, asthma in 22.6%, and both AR and asthma in 19.6%. 16.7% (n=31) of the patients had concomitant atopic dermatitis. 42.6% (n=196) of the patients were sensitive to more than one allergen. The clinical and laboratory findings of the patients are summarized in Table I.

There was no difference between the diagnoses according to age, presence of atopic dermatitis, laboratory findings, or multiple allergen sensitivity (Table II).

When aeroallergen sensitivities were assessed according to diagnoses, there was no difference between the aeroallergen distributions of the patients ($p > 0.05$). The percentages of aeroallergen sensitivities according to diagnoses are shown in Figure 2.

There was no difference between the genders according to age, the presence of the accompanying atopic dermatitis, total IgE levels, eosinophil count and the percentages ($p > 0.05$, data not shown). The cockroach sensitivity ($p = 0.004$), the pet sensitivity ($p = 0.006$), and the olive tree sensitivity ($p = 0.01$) were more frequent among male children. However, there was no relationship between the genders in terms of the sensitivity to the other allergens (data not shown). In this study, 52.4% (n=243) of the patients had more than 4% of eosinophils, and there was no difference between the genders ($p = 0.07$). 51.7% (n=238) of the patients had a total IgE level higher than the age-appropriate reference range.

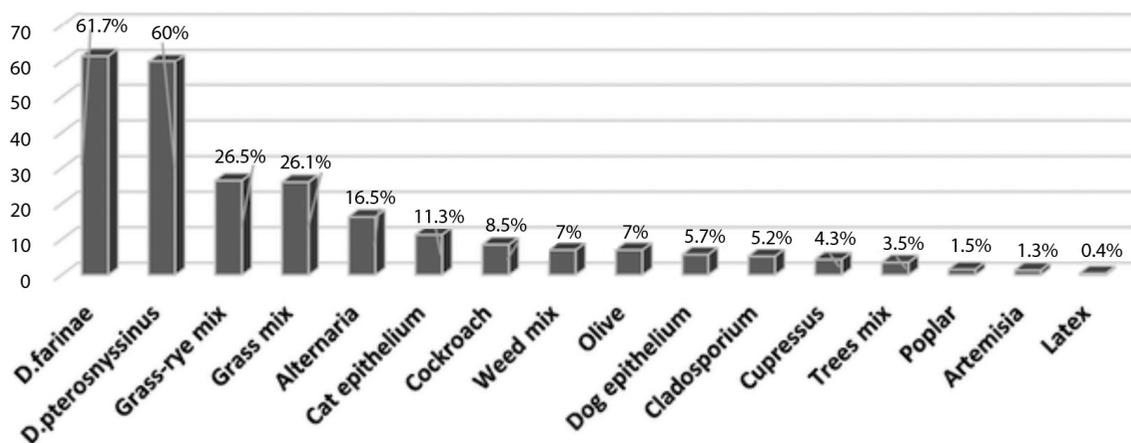


Figure 1. Allergens sensitization in skin prick test

Age	10.2±3.4 (5-18) years
Gender, n (%)	n=195 (42.4) female, n=265 (57.6) male
Distribution of diagnoses, n (%)	n=266 (57.8) allergic rhinitis, n=104 (22.6) asthma, n=90 (19.6) allergic rhinitis and asthma
Multiple allergen sensitivity, n (%)	n=196 (42.6)
Total IgE (median) kU/L	166 (4-2,582)
Eosinophil count (/mm ³)	368±270 (77-1,450)
Eosinophil percentage (%)	4.5±3.5 (0.5-28)

The presence of the accompanying atopic dermatitis was not related to gender, aeroallergen sensitivities, or laboratory parameters ($p>0.05$, data not shown).

Aeroallergen sensitivities in the SPT were evaluated according to the seasons. There was no seasonal difference between the distribution of the aeroallergen sensitivities, and HDMs were the most common allergens throughout all of the seasons (Figure 3).

Multiple allergen sensitivity was more frequent among males (65.3%, $n=128$) than females (34.7%, $n=63$) ($p=0.004$). The distribution of the diagnoses and the presence of the multiple allergen sensitivity were not associated ($p=0.54$).

Discussion

Identifying the triggering allergens and taking elimination measures as early as possible is important in asthma and AR courses. Several studies have shown that the aeroallergen distributions vary significantly from

country to country and region to region according to factors such as climate, humidity, and temperature (11-13). Therefore, it is necessary to know the aeroallergen sensitivities of each region. Although there are many studies investigating aeroallergen sensitivities in different regions and provinces of our country, this study's difference and importance is that it was conducted in Tekirdağ province in the Thrace region where aeroallergen sensitivities were in need of investigation.

This study evaluated the aeroallergen sensitivities via SPTs of those children with AR and/or asthma in Tekirdağ, Turkey. The most common aeroallergens were seen to be HDMs, grass-rye mix, grass mix, and molds.

The prevalence of AR has gradually increased, especially in early childhood (14,15). It was reported that 38% of patients with AR have asthma (16). In this study, 76.4% ($n=356$) of the patients had AR, and 25.2% ($n=90$) of patients had asthma.

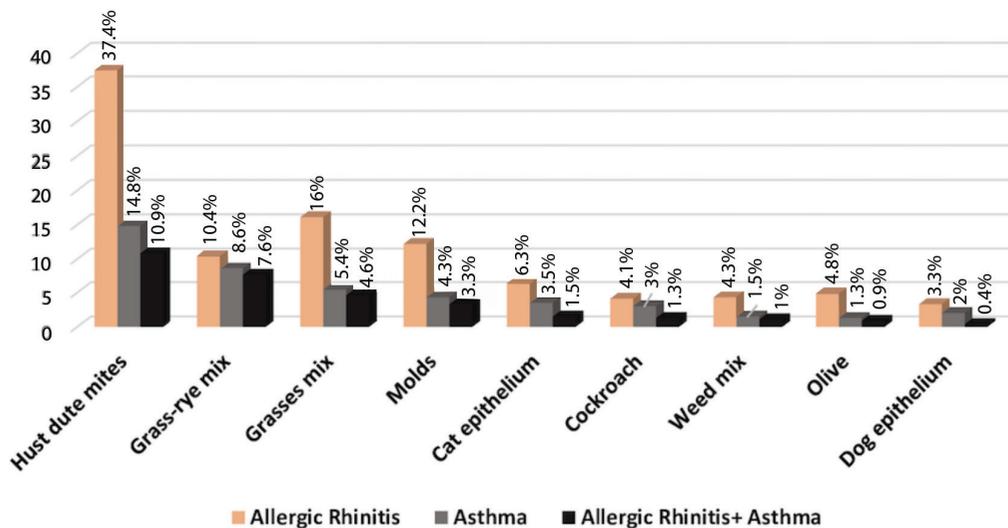


Figure 2. Distribution of allergens sensitization according to diagnoses

	Allergic rhinitis $n=266$	Asthma $n=104$	Allergic rhinitis and asthma $n=90$	p-value
Age (years)	10.3±3.3 (5-18)	9.9±3.6 (5-17)	10.5±3.5 (5-17)	0.8
Gender (male)	57.5%	65.5%	53.3%	0.66
Total IgE (median) (kU/L)	176 (4-2,980)	201 (5-2,500)	148 (10-2,500)	0.4
Eosinophil count (/mm ³)	382±281 (77-1470)	373±273 (60-1800)	300 250 (30-1,450)	0.52
Eosinophil percentage (%)	5.2± 3.8 (0.5-28)	5±3.1 (0.5-17.3)	4.9±3 (0.6-14.2)	0.6
Presence of atopic dermatitis	5.5%	1.1%	0.7%	0.6
Multiple allergen sensitivity	45.1% ($n=120$) yes	42.3% ($n=44$) yes	35.6% ($n=32$) yes	0.12

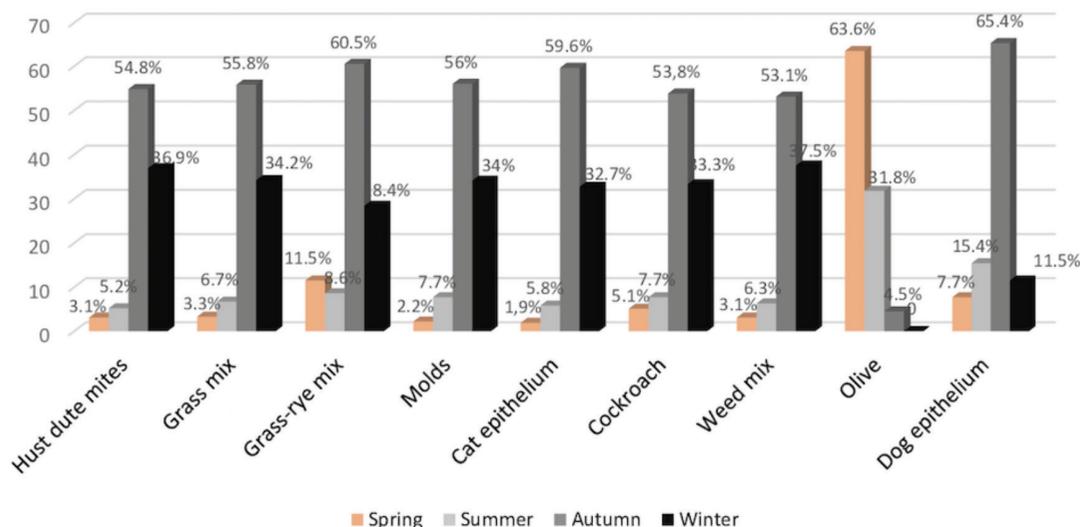


Figure 3. Distribution of allergens sensitization according to seasons

It has been reported that atopy is more common in males (17). In our study, in according with the literature, 57.6% of the patients with a sensitivity via SPT were male, and 42.4% were female.

Inhaled allergens can originate from indoors or outdoors. While HDMs, animal allergens, cockroach allergens, and many molds are indoor allergens, pollens, some other molds, and animal allergens are outdoor allergens, which are affected by the weather and season (18). HDMs are strongly associated with the pathogenesis of AR and asthma, and delays in diagnosis can result in a decrease in the effectiveness of the treatment (19). HDMs are the most common allergens in patients with asthma in central Anatolia, with a prevalence of 63.3%, according to the study by Cengizlier and Misirlioglu (20).

Mites are mostly found in hot and humid environments and optimally live between 25-30 degrees and at 75-80% humidity. In our country, HDMs were founded to be the most common allergens in those studies conducted in warm and humid cities such as Istanbul (96.7% Der. Pteronyssinus, 89.3% Der. Farinae) and Samsun (97%) (21,22). Similar to other studies, the most common allergen sensitivity was HDM (63%) in this study. Leung et al. (23) reported that D. Pteronyssinus and D. Farinae were closely associated with sensitivity. In our study, 89% of those patients sensitive to D. Farinae were also sensitive to D. Pteronyssinus. Regarding the multiple aeroallergen sensitivity of those patients sensitive to house mites, 22.7% (n=66) had pollen mix sensitivity, and 14.4% (n=42) had mold sensitivity.

Tekirdağ is a coastal city situated on the northwest coast of the Marmara Sea in the Marmara region of Turkey, which consists of different regions presenting a variety of climate characteristics. It has coasts on both the Marmara Sea and the Black Sea and has a sub-humid climate. In the only study to date conducted in Tekirdağ by Nalbantoğlu et al. (24) reported that the most common allergen was the HDM (59%) in children with AR.

Pollens are one of the most common causes of airway allergies. Sensitivity to grass, grass-mix, tree, and weed pollens are frequently detected, and pollens with clinical significance vary from region to region. Grass pollens are the most important allergen group in our country and many other European countries. In our cities with hot and dry climates, such as Malatya (48.9%) and Ankara (23.6%), grass pollen was reported to be the most frequent cause of allergen sensitivity (25,26). Tekirdağ has a Mediterranean climate characterized by the hot summers and warm winters. In our study, grass-rye mix (26.5%) and grass mix (26.1%) were found to be the most common pollens, and grass pollen was the second most common allergen causing sensitivity in SPT after the HDMs.

Ay et al. (26) reported that 73 out of 236 children with asthma aged between the 6 and 18 years had coexisting AR and these children had more pollen and grass mix sensitivity than those children with asthma only (total pollen 16.5%, 39.7%; grass pollen 3.7%, 8.7%). There was no difference in aeroallergen sensitivities in our study according to diagnoses.

Fungus spores are also one of the important indoor allergens. In studies conducted in the cities of Turkey, mold sensitivity rates were high, being 51.2% in Sakarya, 43.4% in Antalya, and 30% in Ankara (27-29). In our study, mold (19.6%) was the third most frequent allergen, and its frequency was similar to that of Mersin (19.4%) (30). In places where pets are frequently found, associated pet allergies through sensitization gain importance. The frequency of pet allergies is higher in European countries, in parallel with their economic development. In our country, animal dander allergy is 28.7% in the Eastern Black Sea region, 16% in Izmir, and 6% in Sakarya (27,31,32). In our study, the pet sensitivity ratio was 13.9%, cat sensitivity was 11.3%, and dog sensitivity was 5.7%.

Cockroaches are important environmental allergens, and cockroach exposure occurs most commonly in the urban regions where there is a higher cockroach density, gloomy rooms, kitchens, and bathrooms, especially in the temperatures between 20-25 °C and relative humidity of 60-75%. Cockroaches are found more in places where the living conditions and socio-economic status are poor. In the study by Celmeli et al. (33), cockroach sensitivity was found to be 25.4% and was associated with AR and asthma in Turkish children. In different studies, cockroach allergy was as high as 30% in Malatya and as low as 16.9% and 2.5% in Antalya and Ankara (25,26,28). The cockroach allergy was relatively low, at 8.5% in our study, and this was thought to be due to the socio-economic and cultural development of the Tekirdağ region.

Multiple allergen sensitivity was detected in our study in 42.6% of the patients. This result was similar to a study conducted in Mersin that found the rate of poly-sensitization to be 39.5% (30). Although the aeroallergen sensitivities, total IgE levels, eosinophil counts, and percentages were not associated with the presence of poly-sensitization in our study; poly-sensitized patients had higher total IgE levels in the study of Arıkoğlu et al. (30), but the presence of poly-sensitization was not related to age, gender, total IgE level or eosinophil count in the study by Topal et al. (25).

In a study conducted in the USA to determine the eosinophil counts and serum IgE levels of children with asthma, eosinophil percentages were more than 4% in 48.3% of the male children and 35.1% of the female children (34). In our study, 52.4% (n=243) of the patients had an eosinophil percentage of more than 4%, but there was no difference according to gender.

High IgE levels can be seen in patients with atopic diseases (35). However, the level of total IgE alone is

insufficient to confirm allergic diseases (36). In our study, age-appropriate Total IgE elevation was found in only 52.7% of the patients, according to the reference values defined in the literature (37).

When the SPT results were evaluated according to the seasons, in our study, similar to a study in the Antalya region (28), HDMs were the most common allergen in all seasons. This result shows the necessity of being careful about HDMs throughout the year. However, in a study in Malatya province, it was reported that sensitivity to HDMs was most common in winter and sensitivity to grass-cereals pollen mixture most frequently in summer (25).

Conclusion

In conclusion, aeroallergen sensitivities play an important role in childhood AR and asthma. Our study identified the environmental allergen sensitivities and common allergens in the SPTs of those children with AR and/or asthma in Tekirdağ. According to SPT results, the most common sensitivity was to HDMs. Cockroach, pet, and olive sensitivities were more common among male children. Aeroallergen sensitivity in SPT were not associated with the diagnoses. We think that this study will be a guide to help in taking appropriate elimination measures which are important in managing airway allergies.

Ethics

Ethics Committee Approval: This retrospective analysis was approved by the Local Ethics Committee of Tekirdağ Namık Kemal University (date: 25.03.2020, approval no: 2020.66.03.16).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: N.C.G., C.T., N.S., Design: N.C.G., C.T., E.T., A.N., B.N., Supervision: N.C.G., B.N., N.S., Materials: N.C.G., C.T., E.T., A.N., Data Collection and/or Processing: N.C.G., C.T., E.T., Ş.G.K., A.N., Analysis and/or Interpretation: N.C.G., C.T., B.N., Ş.G.K., N.S.

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