



Sensitization Prevalence of Children with Allergic Rhinitis for Inhalant and Food Allergens in the Province of Sakarya, Turkey

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ABSTRACT

Objective: Sensitization prevalence studies have been rarely reported in children with allergic rhinitis from different regions of Turkey, and the exact rates of some sensitizations in humid regions such as Sakarya are still unknown. The aim of this study was to explore what kind of allergens play a role in sensitizations of allergic rhinitis patients during childhood in the Sakarya province of Turkey.

Methods: This cross-sectional study involves 623 patients, 1–18 years of age, who have allergic rhinitis symptoms and were referred to the only pediatric allergy outpatient clinic in Sakarya between May 2013 and June 2015. Firstly, a questionnaire containing demographic data and patient history was completed. The multiple skin prick test system was used to detect sensitization. With 0 x 0 mm negative control, any positive test result with an allergen was defined as a wheal ≥ 3 mm diameter.

Results: Overall, 289/623 (46%) children showed a positive response. 37% of them were found to have multiple sensitizations. Among the 289 patients, there were sensitizations to pollens (252/289: 87%), mites (51%), grasses (66%), trees (21%), molds (8%), animals (6%), and foods (6%). Sensitizations above 5 years of age were as follows: grasses, 72% (168/233); mites, 49.4%; trees, 24.5%; molds, 6.9%; and animals, 6%. Under 5 years were as follows: mites, 59% (33/56); grasses, 42.9%; foods, 25%; molds, 10.7%; trees, 5.4%; and animals, 3.6%.

Conclusion: There were significant sensitizations detected for pollens and mites. Overall, a lower sensitization (8%) to molds is found in our patients who were referred to us from the humid Sakarya province.

Keywords: Sensitization, allergic rhinitis, allergen, prevalence.

INTRODUCTION

Allergic rhinitis (AR) is a disorder that is comprised of triggered symptoms from exposure to specific inhalant and food allergens. The signs and symptoms of AR include nasal congestion, rhinorrhea, paroxysmal sneezing, and nasal itching caused by the IgE-mediated reaction (1). AR is the most frequently seen chronic respiratory disease in children, and the prevalence changes according to country and age. The global average prevalence of pediatric AR is 8.5% (0.8–45.1%), and the prevalence usually increases with age (1, 2). It has been reported that in Turkey, the prevalence of pediatric AR in the 6–7 and 13–14 years of age groups is 3–44% and 3–23%, respectively, in different studies. The prevalence is higher in western parts of the country and western cities (3–7).

The diagnosis of AR is based on the typical clinical history of the patient, risk factors (history of atopy in the patient and/or in the family), physical examination findings, measurement of serum specific IgE and/or the skin prick test (SPT) (1, 2). The most important step in the therapy of AR is the determination of the symptom-causing allergen and environmental distribution of the allergens. Determination of the responsible environmental allergens is also crucial for

individual protection as well as for approaches in pharmacotherapy as well as immunotherapy. Thus, SPT is very important in the diagnosis and treatment of AR (1, 2). The skin prick test is accepted as the gold standard in allergy diagnosis and is a widely used diagnostic method for detecting IgE-mediated allergic diseases, including AR. The test is also a low-cost, practical, and reliable method used in determining specific allergens responsible for AR symptoms (8, 9).

In Turkey, various studies were done on the prevalence of sensitivity to allergens in AR patients, but there has not been any reported study on the children of Sakarya, a developed province of the Marmara region in Western Turkey (3–7). The purpose of this study was to find out the sensitization rates to prominent inhalant and food allergens causing AR symptoms for which pediatric patients were referred to the first and only allergy outpatient clinic of Sakarya.

METHODS

In this descriptive cross-sectional study, the SPT results of 623 patients, 1–18 years, with symptoms suggesting AR and referred to our outpatient clinic between the dates of May 2013 and May 2015 were retrospectively evaluated. This study was approved by the Eth-

This study was presented in the 10th National Congress of Child Allergy and Asthma, 16-19 April 2015, Sakarya, Turkey.

This study was presented in the 11th Uludağ Pediatrics Winter Congress, 15-18 March 2015, Bursa, Turkey.

This study was presented in the Annals of Allergy Asthma Immunology 115 (5); Supplement: S Pages: A50-A50 Meeting Abstract: P39; Published: November 2015.

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ics Committee of Sakarya University, Medical Faculty (approval number: 71522473/050.01.04/4). The symptoms in the patients were nasal congestion, rhinorrhea, paroxysmal sneezing, and nasal itching considered to be IgE-mediated rhinitis. In the beginning, an interview administered questionnaire containing demographic information, patient history, and symptoms was completed. After taking a detailed clinical history of the patient, a physical examination was performed in all of the patients. The diagnosis of the patients was made by an allergist using the 2008 WHO/ARIA guidelines (2). The prevalence of sensitivity was first determined in the whole, and then was divided in to two groups, namely, under 5 and above 5 years of age.

After withholding the patients' medications for the appropriate length of time, the SPT was performed on the right and/or left forearms of each patient. Patients with inappropriate skin conditions (dermatographism, eczema, ichthyosis, etc.) were excluded from the study. Written informed consent was obtained from the patients and/or their guardians before the SPT application. Allergen extracts in standard activity and concentration (Stallergenes SA, France) and multiple test applicators (10 tests/panel, Medikaperk Express, İstanbul, Turkey) were used for the SPT. The test included positive (histamine hydrochloride) and negative (glycerin saline) controls. Twenty minutes after the application of the allergen, the test result was evaluated. By means of a millimetric ruler, the largest and smallest diameters of each complete reaction were measured; the result was summed and then divided by 2 (mean diameter). The criteria for an SPT evaluation done according to international guidelines (9-11) are as follows: With a 0x0 mm negative control, any positive test result with an allergen was defined as a wheal ≥ 3 mm diameter. A wheal diameter at least 3 millimeters greater than the negative control was considered a positive result.

The evaluation results of the SPTs depended on the distance in between the applied allergens, the appropriate body part used for allergen application, types of instruments used (lancet or multi-test applicator), test season, and quality of the allergen extracts. The skin prick test is quite reliable in determining the specific allergy when the technique is correctly applied and evaluated by an experienced person (8, 9). The multi-test was preferred since it allows simultaneous administration of 10 allergenic extracts, assuring a lower discrepancy between the amounts applied. The multi-test results have been reported to be compatible with the results of the SPT performed with lancets (9-11).

The allergen selection was based on the patients' symptoms, environmental exposures (geography), age, and clinical history. In fact, the SPT is utilized to verify or rule out individual sensitization to allergens. The extracts of allergens used were the following: house dust mite group: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*; animal group: cat, dog; mold group: *Alternaria*, *Cladosporium*; wild grass pollen group: weed mix, mugwort, lambs quarter, nettle, English plantain; grass pollen group: meadow grass, grass mix (Stallergenes 689-coded mixture of 12 grass pollens), cereal mix (oat, wheat, barley, corn); tree pollens: cypress, olive, ash, pine; and foods: milk, egg, wheat, peanut, hazelnut, and fish.

Statistical Analysis

For statistical analyses, the IBM Statistical Package for the Social Sciences (IBM SPSS Statistics; Armonk, NY, USA) version 21.0 software package program (New York, USA) was used. Descrip-

tive statistics were used to examine and compare the relationship between the characteristics of the sample.

RESULTS

Demographics and Sensitization in Overall, Under and Above 5 years of Age Groups

A total of 623 patients with AR symptoms were evaluated (Table 1). The general rate of sensitivity was firstly determined in all the patients aged 1–18 followed by determination in the under and above 5 years of age groups. In the 1–18 years of age group, the SPT showed sensitivity to at least one allergen in 289/623 (46.4%) patients. Of the patients, 54.3% (157/289) were females and 45.6% (132/289) were males. The mean age of the patients was 6.15 ± 3.26 years. Among these 289 SPT-positive patients, 107 (37%) were found to be sensitive to more than one allergen (multiple sensitization). Among the 187 patients under 5 years and among 436 patients above 5 years, 56/187 (30%) and 233/436 (53.4%) were detected as sensitive to at least one allergen, respectively.

SPT Positivity to Allergen Groups and Types in the Overall (1–18 years) Age Group

Among 289 AR patients, the distribution rates of SPT positivity to major allergen groups were determined as follows (Figure 1): grasses, 66.4% (192/289); mites, 51.2% (148/289); trees, 20.8% (60/289); molds, 7.6% (22/289); and animals, 5.5% (16/289). The distribution rates of SPT positivity to specific allergens were found as follows: grass pollen group: 34.6% (100/289) [cereal, 10% (29/289), meadow 13.8% (30/289); grass mix, 10.7% (31/289)]; wild grass pollen group: 31.8% (92/289) [weed, 4.8% (14/289); lambs quarter, 3.1% (9/289); nettle, 9.3% (27/289); mugwort, 4.2% (12/289); English plantain, 10.4% (30/289)]; mites: 21.5% (62/289) *Dermatophagoides pteronyssinus* and 29.8% (86/289) *Dermatophagoides farinae*; tree pollen group: 7.6% (22/289) olive, 6.2% (18/289) pine, 3.8% (11/289) cypress, 3.1% (9/289) ash; molds: 5.2% (15/289) *Alternaria* and 2.4% (7/289) *Cladosporium*; animals: 4.2% (12/289) cat and 1.4% (4/289) dog. Results of the SPT positivity to food allergens are not given since the evaluation was only done in the under 5 years of age group.

SPT Positivity to Allergen Groups and Types in the Under 5 Years of Age Group

Among 56 AR patients, the rates of SPT positivity to allergen groups were detected as follows (Figure 2): mites, 59% (33/56); grasses, 42.9% (24/56); foods, 25% (14/56); molds, 10.7% (6/56); trees, 5.4% (3/56); and animals, 3.6% (2/56). The SPT positivity rates to allergen types were estimated as follows: mites: 12.5% (7/56) *Dermatophagoides pteronyssinus* and 46.4% (26/56) *Dermatophagoides farinae*; grasses: 25% (14/56) grass and 17.9% (10/56) wild grass; foods: 10.7% (6/56) hazelnut, 8.9% (5/56) fish, 1.8% (1/56) peanut, 1.8% (1/56) whole egg, 1.8% (1/56) cow's milk; molds: 7.1% (4/56) *Alternaria* and 3.6% (2/56) *Cladosporium*; trees: 5.4% (3/56) cypress; animals: 1.8% (1/56) cat and 1.8% (1/56) dog.

SPT Positivity to Allergen Groups and Types in the Above 5 Years of Age Group

Among 233 AR patients, the SPT positivity rates in the allergen groups were determined as follows (Figure 3): grasses, 72% (168/233); mites, 49.4% (115/233); trees, 24.5% (57/233); molds,

Table 1. Sensitization prevalence of children with allergic rhinitis for inhalant and food allergens in different age groups

	< 5 years		> 5 years		1–18 years	
Sensitized Subjects (n:)	56/187		233/436		289/623	
Age (Year)	3.42±0.74		8.50±3.36		6.15±3.26	
Genders (M/F)	30/26		102/131		132/157	
Allergen Types	n	%	n	%	n	%
Grasses	24	42.9	168	72	192	66.4
Mites	33	59	115	49.4	148	51.2
Trees	3	5.4	57	27.4	60	20.8
Molds	6	10.7	16	6.9	22	7.6
Animals	2	3.6	14	6	16	5.5
Foods	14	25	ND	ND	ND	ND

ND: not done; n: subject number; M: male; F: female

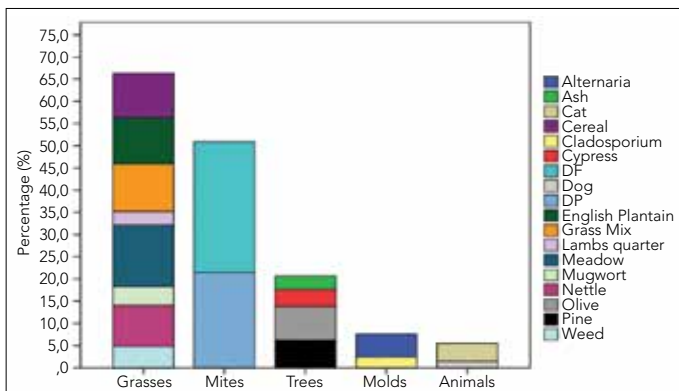


Figure 1. General sensitivity rates for allergen types between 1 to 18 years of age

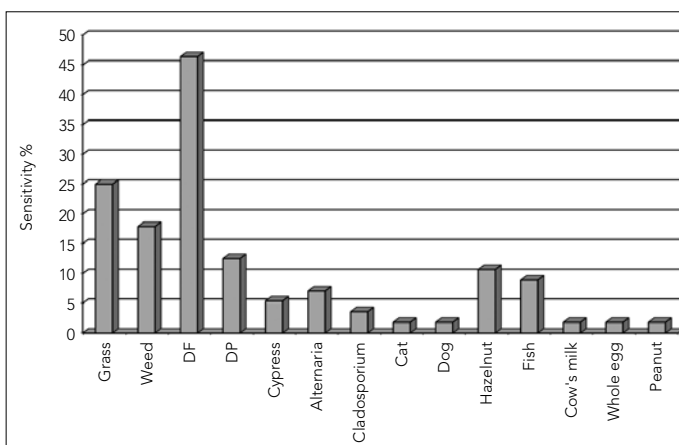


Figure 2. Sensitivity rates for allergen types under 5 years of age

6.9% (16/233); and animals, 6% (14/233). The SPT positivity rates to allergen types were found as follows: grasses: 37% (86/233) grass and 35% (82/233) wild grass; mites: 25.8% (60/233) *Der-*

matophagoides farinae and 23.6% (55/233) *Dermatophagoides pteronyssinus*; trees: 9.5% (22/233) olive, 7.7 (18/233) pine, 3.9% (9/233) ash, 3.4% (8/233) cypress; molds: 4.7% (11/233) *Alternaria* and 2.2% (5/233) *Cladosporium*; and animals: 4.7% (11/233) cat and 1.3% (3/233) dog. Food allergens were not looked at in this age (>5 years) group.

Comparison of SPT Positivity to Allergen Groups in the Under and Above 5 Years of Age Groups

The comparison of the allergen test (sensitization) results in both age groups (under and above 5 years of age) is shown in Figure 4. This figure obviously shows the sensitization difference for pollens and dust mites between the age groups. In the above 5 years of age group, although mite sensitivity partly decreased, the pollen sensitivity increased, probably due to more outdoor activity in this age group. In the under 5 years of age group, mite sensitivity seemed to be higher than pollen sensitivity owing to more indoor activity in the age group.

DISCUSSION

In this study, SPT was positive in 46.4% of the patients in the 1–18 years age group presenting with AR. The reported sensitivity rates ranged from 19% to 81.6%, which render our results comparable with the literature (12-15). Relevant studies done in various regions of Turkey have reported different rates of sensitivity in various allergic disorders. In Karaman, Turkey, the SPT positivity rate in children with asthma/rhinitis was reported as 42.3% (12). Akaya et al. (16) demonstrated SPT positivity in 57% of patients suspected of having asthma and/or AR in Isparta. Topal et al. (17) showed a SPT positivity rate of 64% in children having AR and/or asthma in Malatya. İğde et al. (18) reported 46% SPT positivity in children with AR, asthma, and/or eczema in the Middle Black Sea Region. Ayvaz et al. (19) found SPT positivity in 55.6% of the children with AR, allergic conjunctivitis, eczema, and/or asthma in the East Black Sea Region of Turkey. Different rates of SPT positivity have been reported in various countries as well. In Texas, USA, SPT was found positive in 82% of the patients showing allergic symptoms in 1137 patients aged 4–79 years old (15). A study done in New Zealand reported SPT positivity at 46% in 714 atopic children (20). A Swiss study reported the SPT positivity rate at 43% in children with asthma and/or rhino-conjunctivitis (21).

Kuyucu et al. (22) determined the highest rates of sensitivity for grass pollen (43%) and mites (31%) in atopic children of Ankara. Erel et al. (23) reported the rates of pollen and dust mite sensitivity at 60% and 21%, respectively, in Ankara. Ayvaz et al. (19) in the East Black Sea Region demonstrated 70% and 61% sensitivity rates to grass pollens and mites, respectively. Tezcan et al. (24) showed that grass pollen was the most frequent cause of sensitivity in İzmir. Ceylan et al. (25) determined that the most frequent cause of sensitivity (67%) among AR patients in Şanlıurfa was grass pollen. Kucukosmanoglu et al. (26) found SPT positivity to meadow pollens to be 19% in Istanbul. In Malatya, SPT positivity to grass/cereal and mixtures of wild grass pollens was found to be 49% and 49%, respectively, in children with asthma/rhinitis. As example rates of sensitivity types from other countries, Sears et al. (20) found SPT positivity rates of 33% and 30% to meadow grass and mites, respectively, in atopic children of New Zealand. In this study, the grass pollen and mite sensitivity rates in 289 AR

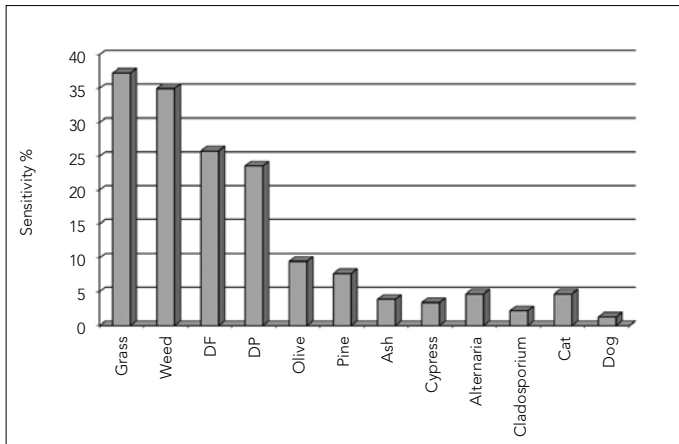


Figure 3. Sensitivity rates for allergen types above 5 years of ages

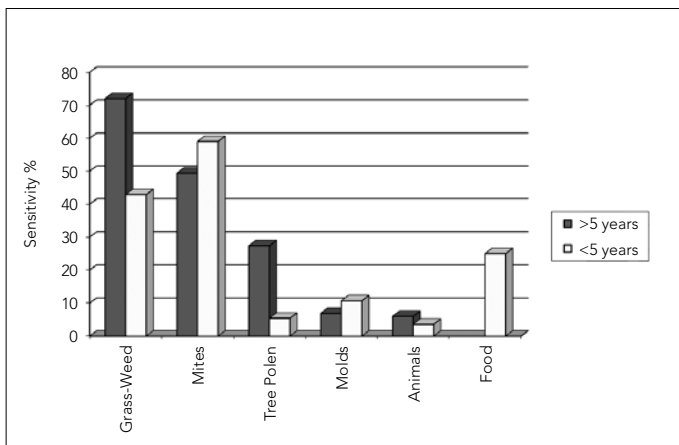


Figure 4. Sensitivity rate comparison of allergens in age groups (Food allergens were not looked at in this age (>5 years) group)

patients in the 1–18 years of age group were detected as 66.4% and 51.2%, respectively. The sensitivity rates found in our study were also comparable with the rates of other studies from Turkey as well as from abroad (14, 15, 20, 21, 27-29). The high prevalence of pollen and mite sensitivity in Sakarya might be due to the damp weather and plant flora of the province, which has particular climatic features and is surrounded by the sea.

In our AR patients with grass pollen group sensitivity (66.4%), the rates of grass sensitivity (34.6%) and wild grass (weed) sensitivity (31.8%) were close to each other. Tree pollen sensitivity was lower than grass pollen sensitivity at 20.8% of AR patients, and this supports the findings of the relevant studies in the literature. Different sensitivity rates reported from different regions of Turkey might be due to regional differences in the climate and plant flora. Likewise, a study carried out in the East Black Sea Region reported the sensitivity rates to tree pollens as 33.2% compared to grass pollens at 70% (19).

In Sakarya, grasses and weeds almost exist in every season because of the regional climate and geography, and there is exposure to pollen from the end of the spring to the end of autumn. Consequently, the rate of sensitivity to grass and wild grass pollens is expected to be higher than tree pollens due to a more limited exposure. Also, it has been long known that although the

concentration of tree pollens in the atmosphere is higher, their allergenicity is lower than that of grass pollens (30, 31).

In indoor environments, there is heavy exposure to mites, which are aero-allergens with strong immunogenic properties (32). Mites can live in house objects such as carpets and various furniture at 25–30°C and 75–80% relative humidity. *Dermatophagoides pteronyssinus* generally cannot survive below 65% relative humidity. However, *Dermatophagoides farinae* can survive even at a relative humidity <45% and temperatures <15°C (32). A comprehensive Turkish study reported high rates of sensitivity (46%) to house dust mites in warm regions near the sea and with high relative humidity, e.g., the Black Sea Region (33). Mite sensitivity in İzmir has been reported as 42% and 37% for *Dermatophagoides pteronyssinus* and *farinae*, respectively (7, 24). A study carried out in İstanbul reported mite sensitivity as 96.7% and 89.3% for *Dermatophagoides pteronyssinus* and *farinae*, respectively (26). A multi-center study from abroad reported sensitivity to *Dermatophagoides pteronyssinus* and *farinae* as 15.6% and 12.8% in China and as 35.7% and 27% in Hong Kong, respectively (34). In Germany, the respective sensitivity rates to *Dermatophagoides pteronyssinus* and *farinae* were reported as 6.5% and 4.4% (35).

In our study, among the 1–18 age group, patients with mite sensitivity (51.2%) and sensitivity rates to *Dermatophagoides pteronyssinus* and *farinae* were found to be 21.5% and 29.8%, respectively. Our overall mite sensitivity rate was higher and the *Dermatophagoides pteronyssinus* sensitivity rate was lower than those determined in İzmir (7, 24). This difference could be due to the fact that İzmir is warmer and damper than the Sakarya province and is located by the sea. Our mite sensitivity rates were higher than those found in China and Germany (34, 35), but lower than that found in Hong Kong (34). These findings support the fact that specific dust mite sensitivity rates vary according to different climatic zones.

Molds are important aeroallergen sources. Some molds require hosts for multiplication, whereas most molds can readily multiply on dead organic materials in the environment. For growth, they require oxygen, humidity, carbohydrates, and sometimes additional growth factors. Many molds start growing at 20°C and continue multiplication at temperatures under or above 20°C. The most frequent mold allergens are *Alternaria*, *Cladosporium*, *Aspergillus*, and *Penicillium* species (36). Tezcan et al. (24) demonstrated mold sensitivity in İzmir at the rate of 9%. A study carried out in Ankara reported *Alternaria* sensitivity in 30% of children with respiratory complaints (37). The mold sensitivity rate (*Alternaria*, *Cladosporium*) in the East Black Sea Region of Turkey was found to be 13% (19). The general mold sensitivity in England has been reported to be 6% (*Alternaria*, 4.8%; *Cladosporium*, 2.2%) (38). Reijula et al. (39) in Finland detected sensitivity rates to *Alternaria* and *Cladosporium* as 2.8% and 2.7%, respectively. We found the general rate of mold sensitivity in a humid Turkish province of Sakarya to be 7.6% (*Alternaria*, 5.2%; *Cladosporium*, 2.4%). Although mold sensitivity determination is difficult, our results are comparable with those detected in other regions of Turkey and abroad (24, 38).

Animal allergens in houses and work places have clinical importance. Particularly, allergy to indoor cats and dogs is important.

The animal allergens could be animals' feather, fur, epithelium, urine or saliva. Parallel to the degree of economic development, in the western world and in European cities the rates of allergies to animals are higher (24). Tezcan et al. (24) in their study from İzmir reported animal allergies at a rate of 16%. In a study done in the East Black Sea Region, the sensitivity rate to animal fur was 28.7% (19). In contrast, İğde et al. (18) found the sensitivity rate to animal fur in the Middle Black Sea Region was 4.6%. In New Zealand, the SPT positivity to cat fur in atopic children was reported to be 13.3% (20). Chu et al. (40) reported that among school children in Canada the highest rate of sensitivity to cat fur was 8.6%. A study done in England reported a sensitivity rate of 5.8% to cat fur and no difference between children with and without cat as pets (41). Kuehr et al. (35) in their study from Germany reported the rate of cat fur sensitivity as 4.6%. In this study, we found the rate of sensitivity to animals as 5.5% (cat, 4.1%; dog, 1.4%). Our results were quite compatible with the results of the study by İğde et al. in the Middle Black Sea Region, a region socio-economically similar to the Sakarya province (18). Our rates were lower than the rates found in İstanbul and İzmir, provinces with higher socio-cultural and economic level. The presence of more indoor cats in comparison to dogs leads to higher rates of sensitivity to cat fur. Similarly, we found a high rate of sensitivity to cat, a finding comparable with the literature.

Under 5 years of age group of Sakarya, we found that the highest rate of sensitivity as shown by SPT was to mites (59%) followed by grass pollens (43%), foods (25%), molds (11%), tree pollens (5%), and animal allergens (4%). An SPT study carried out in Ankara reported sensitivity to mites (47.5%) and grass pollens (45.1%) as the most frequent allergies in children with AR/asthma coming from 5 different regions of Turkey (42). Talay et al. (43) in Düzce determined that house dust mites caused the highest rate of sensitivity (71%) in children with AR/asthma/AR-asthma co-morbidity. A study on atopic children in Samsun (18) also found house dust mites as the cause of the highest rate of SPT sensitivity (97%). Harmançi et al. (37) also detected that house dust mites were responsible for the highest rate of SPT sensitivity (46.3%) in pre-school children of Ankara with respiratory problems. Ayvaz et al. (19) demonstrated house dust mites as the highest rate of SPT sensitivity (61%) in the East Black Sea Region. Among foreign studies, Arshad et al. (41) showed that the most frequent allergen in children aged <4 years old with AR was house dust mites (40%). In the US, particularly in regions with dense apartment buildings, children stay indoors for long periods and thus experience more exposure to indoor allergens, leading to increased sensitivity to house dust mites and other indoor allergens (44).

High sensitivity to house dust mites is strongly related to a high concentration of house dust mites and exposure to mites. In the province of Sakarya, which has a humid climate, high concentrations of indoor mites are to be expected. Children under 5 years of age spend a longer time in mite-rich environments like home and day-care centers than children above 5 years of age and are more exposed to mites. This fact explains why the high rate of mite sensitivity was found in our study in this age group. An interesting result was the 25% sensitivity rate for food allergies in children under 5 years of age. Although the prevalence of

food sensitization in the population has not been fully clarified, a SPT study carried out in İzmir has reported sensitivity to food allergens in 6% of atopic children (24). Ayvaz et al. (19) have determined the rate of food allergy was 13.1% in the East Black Sea Region. In England, the rate of food sensitivity in children under 4 years of age has been found as 3% (41). However, this is just a sensitization ratio and was not proven with food challenges in this study, which is out of this article's scope.

In the above 5 years of age group, we found the highest rate of sensitivity to grass pollens (72%) followed by mites (49.4%), tree pollens (24.5%), molds (6.9%), and animal allergens (6%). When these findings are compared with those of the under 5 years of age group, it showed increased sensitivity to grass pollens, tree pollens, and animal allergens but decreased sensitivity to mites and molds. The increased sensitivity to grass and tree pollens can be explained by spending more time outdoors and being more exposed to pollens (1). In this age group, the increase in sensitivity to animal allergens is probably due to increased exposure to animals indoors/outdoors as well. Decreased sensitivity to mites in the above 5 years of age group can be explained by spending less time indoors and being less exposed to mites. Sensitivity to mites, which comes after sensitivity to grass pollens, can be due to the climatic conditions of the region as well as spending time indoors, like in school. Likewise, a decrease in sensitivity to molds can be due to spending less time in closed and humid environments. It is remarkable to us that in the humid climate of Sakarya, the sensitivity to molds is lower than the rates of sensitivity to mites and grass pollens.

There are also some limitations in our study. For instance, this study reflects the sensitization rates from just one province of the western geographical region in Turkey. It was performed in certain patients with AR and certain age groups, 1–18 years of age, with selected allergen types. Therefore, the readers should be careful in the generalization of the results from this study.

CONCLUSION

Children in all age (1–18 years) groups with AR showed high rates of mite and grass pollen sensitivity as expected, but both groups under and above 5 years of age showed mold sensitivity rates lower than expected. This low rate of sensitization to molds is unexpected in the regions of heavy rain and high humidity like the Sakarya province.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Sakarya University.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – Ö.Ö.; Design – B.E.; Supervision – Ö.Ö.; Resources – B.E.; Materials – B.E.; Data Collection and/or Processing – B.E.; Analysis and/or Interpretation – Ö.Ö.; Literature Search – B.E.; Writing Manuscript – Ö.Ö., B.E.; Critical Review – Ö.Ö.; Other – B.E.

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