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Research paper

Aeroallergen sensitisation patterns of children aged 5 years and younger with asthma and/or allergic rhinitis in Istanbul

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ABSTRACT

Aim of the study: The purpose of the study was to determine the aeroallergen sensitisation patterns of children aged 5 years and younger with asthma (AS) and/or allergic rhinitis (AR) in Istanbul, Turkey. **Methods:** This cross-sectional observational study was conducted between January and December 2018 in the outpatient clinic of a hospital department of pediatric allergy. Patients, who had regular outpatient controls, full clinical and laboratory records, positive skin prick test results, and were willing to participate in the study, were included.

Results: In total, 148 children aged 5 years or younger who had positive skin prick test results were included in the study. The male/female ratio and the mean age at onset of symptoms were 87/61 and 2.13 ± 1.33 (0.4–4.5) years, respectively. Of the 148 patients, 63 (42.6%) had AS, 11 (7.4%) AR, and 74 (50.0%) had both AS and AR. The age of the patients, age at symptom onset, male/female ratio, number of allergen sensitivities, total IgE levels, total eosinophil levels, and skin prick test results for aeroallergens did not differ between the patients with AS, AR, and AS + AR. House dust mite (HDM) was the most common aeroallergen in patients, while the cockroach was the least common aeroallergen. The severity of asthma and control levels were not found to be associated with aeroallergen sensitisation in children.

Conclusion: One out of every four atopic children aged 5 years or younger is sensitised to aeroallergens. The most common sensitisation is to house dust mites. Weed aeroallergen may be related to severity of asthma in children aged 5 years or younger in Istanbul. We speculate that HDM and weed allergens could be used in the diagnostic or treatment strategies for the management of asthmatic children aged 5 years or younger.

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1. Introduction

Atopy is described as immunoglobulin E (IgE)-mediated sensitisation to at least one allergen in the environment or food and can be identified by skin prick testing (SPT). The prevalence of atopic diseases now seems to have reached a plateau in many countries, but they are still increasing in the developing world [1]. Exposure to aeroallergens such as house dust mites, pollens, mold, and animal dander are related to sensitisation, a significant risk factor for the development, persistence, and severity of allergic airway disease in children [2,3]. The numbers and types of

aeroallergens an individual is sensitised to differ across geographic regions [4–6]. Allergen sensitisation is associated with early-onset times and more severe symptoms in patients with allergic rhinitis [7]. Sensitisation to aeroallergens acquired in the first few months of life has been reported to be a risk factor for the development of persistent wheeze in childhood [8]. SPT remains the most appropriate in vivo diagnostic test for the evaluation of specific IgE [9]. Determining patterns of sensitisation in certain geographic areas helps to target specific procedures, such as allergen avoidance and/or allergen reduction, and promotes the use of specific immunotherapy against the most common allergens [10,11].

The aim of the study was to determine the aeroallergen sensitisation patterns of children aged 5 years and younger with

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asthma (AS) and/or allergic rhinitis (AR) and to investigate the clinical and laboratory characteristics associated with aeroallergen sensitisation in Istanbul, Turkey.

2. Materials and methods

2.1. Study design

This cross-sectional observational study was conducted between January 2018 and December 2018 in the outpatient clinic of the department of pediatric allergy at Bakırköy Dr. Sadi Konuk Training and Research Hospital in Istanbul, Turkey. The study was conducted on 148 children (aged < 5 years) diagnosed with AS and/or AR in the pediatric allergy outpatient clinic. Children with diagnosed atopic dermatitis and/or food allergies were excluded from the study. The children had regular outpatient controls, full clinical and laboratory records, positive skin prick test results, and were willing to participate in the study. Gender, asthma control levels, total IgE, total eosinophil levels, and SPT results were recorded. AS and AR were defined according to the diagnostic criteria used for the Global Initiative for Asthma (GINA) 2018 guidelines and Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines [12,13].

The study protocol was approved by the ethics committee of the hospital and informed written consent was given by parents for each child prior to the study (ethical approval number: 2019-05-24/04.03.2019).

2.2. Measurements

Chemiluminescent immunometric assay (CLIA) was used to evaluate serum total IgE levels (Immulite; Diagnostic Products Corp., Los Angeles, USA). Total blood count was measured using a blood analyser (Abbott Diagnostics, Santa Clara, USA).

2.3. SPT procedures

SPT was performed according to the international guidelines as a single test on two forearms with lancets and standardised allergens [14]. Common aeroallergens were used for the skin prick test (Allegropharma, Reinbek, Germany): House dust mites (HDMs) (*Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*), *Aspergillus fumigatus*, cat epithelium, cockroach, tree mixture-1 (alder, hazel, poplar, elm, willow tree, ash, and elder), tree mixture-2 (birch, beech, oak, plane tree, and Japanese cedar), grass mixture (velvet, orchard, rye, timothy, Kentucky, meadow, nettle, and Bermuda), weeds (ragweed, mugwort, dandelion), and 10-mg/mL histamine phosphate as a positive control and 0.9% saline as a negative control. A positive SPT was defined as a mean wheal diameter at least 3 mm larger than the negative control. Patients who were sensitive to only one class of allergens were defined as monosensitised, whereas subjects sensitive to two or more classes of allergens were defined as polysensitised [15,16].

2.4. Statistical analysis

Statistical analyses were performed using the Number Cruncher Statistical System (NCSS), 2007, statistical program (Utah, USA). In the assessment of the data, in addition to the descriptive statistical methods (mean and standard deviation), an independent *t*-test was used for the comparison of the binary groups with normal distribution variables. Multiple comparison analysis was calculated using ANOVA test. Correlation analysis was performed using the Pearson correlation coefficient. Statistical significance was defined as $P < 0.05$.

3. Results

A total of 148 children were enrolled in the study. The male/female ratio and the mean age at onset of symptoms were 87/61 and 2.13 ± 1.33 (0.4–4.5) years, respectively. Of the 148 patients, 63 (42.6%) had AS, 11 (7.4%) AR, and 74 (50.0%) had both AS and AR. Among asthmatic patients, 38 (27.7%) had mild, 87 (63.5%) had moderate, and 12 (8.8%) had severe persistent asthma. Of the participants, 67 (48.9%) had well controlled, 48 (32.4%) partly, and 22 (14.9%) uncontrolled AS. The total IgE levels, total eosinophil levels, and SPT results for aeroallergens did not differ between the patients with AS, AR, and AS + AR. Only for *D. pteronyssinus* was a significant difference found between AR patients and AS + AR patients ($P = 0.01$; Table 1). HDM was the most common aeroallergen in patients (Fig. 1). The HDM sensitisation ratio was 42.4% in AS patients, 3.8% in AR patients, and 46.8% in all children. The cockroach was the least common aeroallergen (AS 4% and AR 2%).

Total IgE levels, total eosinophil levels, and SPT results for aeroallergens did not differ between the patients with well, partly, and uncontrolled AS. Weed aeroallergen sensitivity was found to be associated with severity of asthma in children younger than 5 years in Istanbul (r^2 : 0.51, P : 0.04). There was a significant positive correlation between *D. farinae* and *D. pteronyssinus* (r^2 : 0.76, $P = 0.001$).

Polysensitisation was seen in 53.9% of AS patients and 54.5% of AR patients younger than 5 years. The common aeroallergens according to sensitisation types are shown in Table 2. Eosinophil levels and *D. farinae* were higher in polysensitised patients compared to monosensitised patients.

4. Discussion

Aeroallergen sensitisation studies in various countries around the world have reported different rates. A number of studies conducted on aeroallergen sensitisation in different cities in Turkey also reported differing rates. In a study conducted in Adana, Turkey, the sensitivity rate between 0–5 years was reported to be 20.7% [17]. Sahiner et al. conducted a study in Ankara with children aged 2–6 years, where the sensitivity was reported to be 16.1% [18]. Akcakaya et al. [19] found aeroallergen sensitisation in 61% of asthmatic children aged 1–18 years in Istanbul. In the present study, an aeroallergen sensitisation rate of 26.9% was obtained in children younger than 5 years. Due to the differences between age groups, working methods, inclusion criteria, disease diagnoses, test procedures, and allergen selection, it is impossible to make

Table 1
Comparison of patient parameters according to diagnosis.

Parameters	Diagnosis	Mean difference	P	95% Confidence interval	
				Lower	Upper
IgE (IU/mL)	AS				
	AR	72.29	0.90	-335.2	479.8
	AS + AR	45.31	0.87	-168.4	259.1
Eosinophils, mm ³	AS	-72.29	0.90	-479.8	335.2
	AR	-26.98	0.98	-430.0	376.0
	AS + AR	284.97	0.05	-2.5	572.5
SPT, mm	AS	81.95	0.40	-68.8	232.8
	AR	-284.97	0.05	-572.5	2.5
	AS + AR	-203.02	0.21	-487.3	81.3
<i>D. pteronyssinus</i>	AS				
	AR	0.85	0.22	-0.3	2.0
	AS + AR	-0.541	0.14	-1.2	0.1
	AR	-0.85	0.22	-2.0	0.3
	AS + AR	-1.40	0.01	-2.6	-0.1

IgE: immunoglobulin E; AS: asthma; AR: allergic rhinitis, SPT: skin prick test.

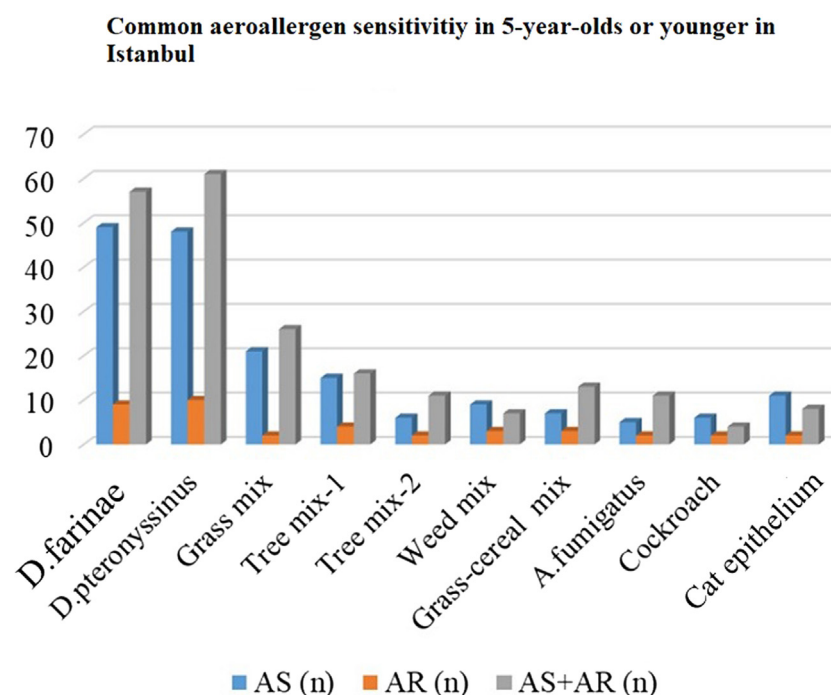


Fig. 1. Aeroallergen sensitisation in 5-year-olds or younger in Istanbul. AS: asthma; AR: allergic rhinitis.

Table 2

Comparison of patient parameters according to sensitisation types.

Parameters	Type of sensitisation	n	Mean	SD	P
IgE (IU/mL)	MS	64	3.44	462.59	0.04
	PS	84	5.17	556.95	
	PS	84	5.53	4.03	
Eosinophils, mm ³	MS	64	5.19	396.66	0.53
	PS	84	4.80	361.98	
SPT, mm <i>D. farinae</i>	MS	45	4.91	1.16	0.03
	PS	70	5.47	1.46	
<i>D. pteronyssinus</i>	MS	50	5.36	1.35	0.06
	PS	69	5.88	1.62	
Grass mix	MS	1	3.00	.	0.30
	PS	48	4.31	1.24	
Tree mix-1	MS	0	.	.	NC
	PS	35	4.05	0.72	
Tree mix-2	MS	3	4.00	1.00	0.91
	PS	16	4.06	0.85	
Weed	MS	3	4.00	1.00	0.81
	PS	16	3.87	0.80	
Grass/cereal	MS	1	3.00	.	0.30
	PS	22	5.09	1.94	
<i>A. fumigatus</i>	MS	1	3.00	.	0.52
	PS	17	3.58	0.87	
Cockroach	MS	0	.	.	NC
	PS	12	3.58	0.90	
Cat epithelium	MS	1	3.00	.	0.26
	PS	20	4.55	1.31	

IgE: immunoglobulin E; MS: monosensitised; PS: polysensitised; NC: not calculated; SD: standard deviation.

firm comparisons between the studies. Low aeroallergen sensitisation compared to previous studies can be explained by changes in environmental factors and the protective behaviour of families against aeroallergens over the years.

D. pteronyssinus and *D. farinae* are the two pyroglyphid HDM species most detected in allergic diseases [20]. HDM survival relies on ambient humidity and it has been among the top sensitising allergens in different geographical regions with humid climates [21]. In previous studies, the HDM sensitisation rate was reported

to be between 50% and 72.2% in Istanbul [19,22]. In the present study, the HDM sensitisation rate was 46.8%. In recent years, high buildings have increased in Istanbul due to rapid urbanisation, resulting in humidity change. As the temperature increases, domestic environments get warmer and more humid, creating the perfect microclimate for the proliferation of HDM. Istanbul city's average range of humidity is 62–77% according to 2018 hygrometric results (Fig. 2) [23]. This result could explain the development of HDM sensitisation in children due to the high range of humidity in Istanbul.

Evidence on the association between sensitisation and asthma severity is conflicting [24]. In this study, it was found that sensitivity to weed was significantly associated with severity of asthma in children younger than 5 years in Istanbul. Weeds typically pollinate from August through the first frost and peak around noon time [25]. This can be explained by the fact that frost in Istanbul is very rare and weeds stay in the environment for longer periods.

Based on population studies, it is generally believed that the majority of infants and young children with early atopic eczema will develop asthma in childhood. Current evidence suggests a complex relationship between early eczema and asthma. Food allergy is a triggering cause of atopic dermatitis, and the prevalence of IgE-mediated food allergy among children with AD is around one third of affected children. It is unclear whether children with IgE-mediated food allergy are at risk of developing asthma and allergic rhinitis. In a recent study, it was found that children with a history of IgE-positive cow's milk allergy exhibit greater bronchial susceptibility to increased airway inflammation and histamine. It is unclear whether progression from food allergy to asthma is related to causal or environmental and genetic factors [26].

Polysensitised patients are at higher risk for more serious and persistent allergic respiratory disease [11,16,20]. In a study by Silvestri et al. in children aged between 5 months and 4 years with respiratory symptoms, the polysensitisation rate was 37% [27]. In a study conducted by Harmanlı et al. in < 5-year-old patients with respiratory symptoms, this rate was 41.9% [28]. In our study, polysensitisation was seen in 53.9% of AS patients and 54.5% of AR

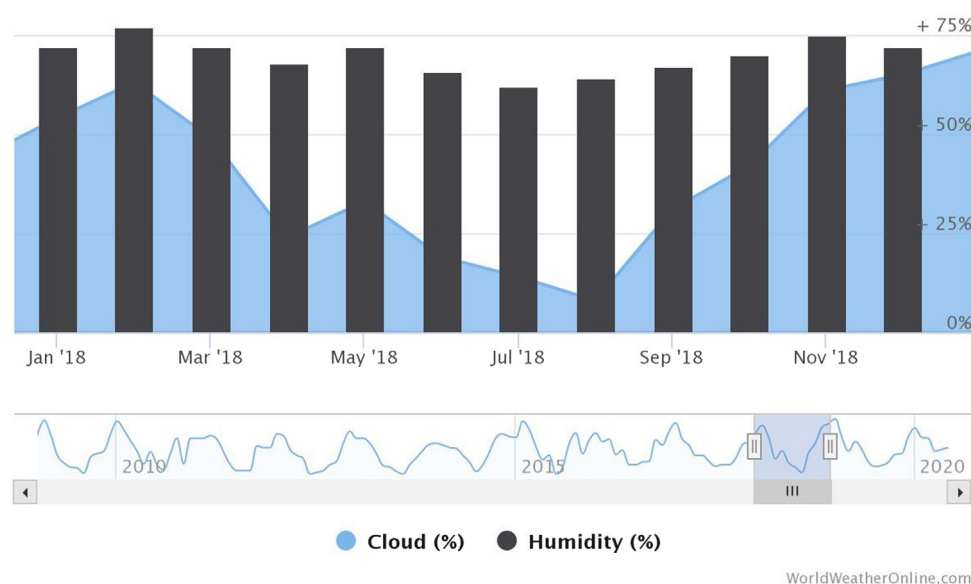


Fig. 2. Cloud and humidity in Istanbul in 2018.

patients younger than 5 years. This difference in polysensitisation rates may be due to the environmental factors prevailing in Istanbul.

4.1. Limitations of the study

The present study has a number of limitations. Firstly, the study does not compare outdoor and indoor allergens, and AR was not classified into seasonal and perennial AR groups. Secondly, the sample size was small due to the specific age group in a single centre. Polysensitisation and its progression with age is very difficult to analyse due to the fact that, during the first 5 years of life, the main atopies switch from mostly digestive to mostly respiratory. We did not include the status of patients with regard to trophallergen sensitisation in this study. This could potentially have an effect on hypereosinophilia in polysensitised children.

5. Conclusion

This study shows that one out of every four atopic children aged 5 years or younger is sensitised to aeroallergens. The most common sensitisation is HDM. Weed aeroallergens may be related to asthma severity in children aged 5 years or younger in Istanbul. We speculate that HDM and weed allergens could be used in the diagnostic or treatment strategies for the management of asthmatic children aged 5 years or younger.

Disclosure of interest

The authors declare that they have no competing interest.

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