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Allergic sensitization prevalence in a children and adolescent population of northeastern Greece region

Michael Katotomichelakis [a,*], Gerasimos Danielides [a], Theodoros Iliou [b], George Anastassopoulos [b], Christos Nikolaidis [c], Efthimios Kirodymos [a], Evangelos Giotakis [d], Theodoros C. Constantinidis [c]

[a] Department of Otorhinolaryngology, Medical School, Democritus University of Thrace, Alexandroupolis, Evros, Greece
[b] Laboratory of Informatics, Medical School, Democritus University of Thrace, Alexandroupolis, Evros, Greece
[c] Laboratory of Hygiene and Environmental Protection, Medical School, Democritus University of Thrace, Alexandroupolis, Evros, Greece
[d] Department of Otorhinolaryngology, Facial Plastic and Reconstructive Surgery, Städtisches Klinikum Karlsruhe, Karlsruhe, Germany

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ABSTRACT

Objectives: To evaluate the prevalence of allergic sensitization in a childhood and adolescent population, to explore age- and gender-specific variations and finally to discover co-sensitivities among allergens.
Methods: A two-stage cross-sectional survey among school-aged children. The two stages of the study involved enrollment of schools and then skin prick testing (SPT) within schools. A total of 675 school children were included in the study. Of those, 231 were diagnosed with allergic rhinitis (AR), according to the medical history as provided by parental-completed questionnaires and positive SPT results. The antigen panel consisted of common allergens and more specifically *house dust mites-HDM* (*Dermatophagoides farinae and Dermatophagoides pteronyssinus*), *grass mix*, *trees* (*olive*, *cypress and pine*), *weeds* (*Parietaria* spp.), *cat* and *dog* epithelium and *moulds* (*Alternaria* spp., *Cladosporium* spp.). The SPT sensitivity was graded according to SPT-USA Standards.
Results: The overall prevalence rate of AR was 34.22%. In total, 93 school children (40.3%) were mono- and 138 (59.7%) were poly-sensitized. Overall, the most prevalent sensitizations in decreasing order were to *HDM* (59.74%), to *grasses* (48.9%), to *Alternaria* (34.6%) and to *olive* (14.71%). There were no age- and sex-specific differences, except for *Alternaria* mould that showed a significant prevalence among primary school-aged children and predominance in the female gender, by contrast to *grass* pollen allergy that was predominant to males. A 32% of SPT-positive individuals were not aware of their allergy, with no statistically significant differences between ages. Co-sensitivities were detected for *grass* pollens and *pine* and *olive* trees, for *Alternaria* and *Cladosporium* moulds, for *cypress* and *pine* trees, and finally for *dog* and *cat* danders.
Conclusions: Given data among school-aged children should be a baseline from which to monitor disease trends and is considered important for the optimal management of AR patients.

1. Introduction

Allergic rhinitis (AR) represents a common problem in both childhood and adolescence [1], with a negative impact on patients' quality of life (QoL) [2] and furthermore a considerable socioeconomic burden [3,4]. It has been described as one of the three most important public health problems worldwide [5]. Typically, patients can be diagnosed as having AR on the basis of rhinitis symptoms in the presence of sensitization [6]. The allergens mostly involved are *house dust mites (HDM)*, *grass*, *tree* and *weed* pollens, *cat* and *dog* epithelia and finally *moulds* [7]. There is a wide variability described in the literature, concerning the sensitivity rates among populations not just between different regions and countries but also between geographic regions in the same country [5,8]. This can be mainly attributed to environmental factors (economic development, dietary habits, climate, and pollens) that possibly cause these variations [1]. Based on the finding that prevalence in

* Corresponding author. Alexandroupolis University Hospital, Alexandroupolis, 68100, Greece.
E-mail address: katotomihelakism@yahoo.gr (M. Katotomichelakis).

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children is much higher than in adults [9], early diagnosis and screening are clinically significant, especially in sight of future co-morbidity prevention (e.g. asthma, chronic rhinosinusitis, nasal polyps etc.). Epidemiologic studies are, thus, of great importance, since they can help monitor disease trends and optimize patient management.

Despite this realization however, there is very limited data concerning the epidemiology of allergic disorders in Greece [10–13]. Furthermore, there are no recent epidemiological studies performed at primary and secondary school-aged children. Especially for the large area of Eastern Macedonia and Thrace (NE Greece), this is the first study ever to be presented.

The aims of this study were: i) to evaluate the prevalence of allergic sensitizations to common allergens, based on Skin Prick Test (SPT) results, from a cohort of children living in this area of Greece, ii) to explore variations of prevalence by age and gender, iii) to detect SPT's sensitivity scores to allergens, and finally iv) to discover co-sensitivities among allergens.

2. Materials & methods

2.1. Study area

This work is the first part of a two-stage, cross-sectional study in school-aged children, living in a region of NE Greece. It was carried out by the Rhinology team of the Tertiary University Hospital of Evros. The study area is situated in the Evros region, in the Eastern Macedonia and Thrace Evros regional unit (NE Greece). The climate in the region is typical Mediterranean with an average daily temperature of 17 °C, a relative humidity of 57% and mostly southern winds. Its ecology includes forests and shrubs that dominate most parts of the surrounding environment.

2.2. Study group and sampling technique

In total, 843 children were invited to participate. The response rate was 82.1% (151 refused to participate) and 17 children were excluded from the study. Among the 675 children who participated, 231 (34.2%) were diagnosed with AR. The diagnosis was based on medical history as provided by their parents and confirmed by the positive SPT results. All children lived in the same area for a long time period. Criteria for exclusion were history of anaphylaxis or angioedema and dermographism and recent use of oral or nasal corticosteroids for 4 weeks prior to inclusion and oral antihistamines for 1 week prior to SPT. All patients fulfilled the criteria of AR according to the 2008 ARIA guidelines [6].

The sampling technique that was used is stratified random sampling. Our study of the public schools in the geographic region involved two stages. The first stage of the study included the registration of schools. For this reason, a list of all public schools in the study area was obtained from the General Directorate of Education of Evros region. After registration, all schools were invited to participate with a letter of explanation to the head teachers outlining the aims of the study and the following procedures. Additionally at the same time, the parents of the children received via the school, a letter explaining clearly the significance of the study and the following procedures, a consent form and a questionnaire, which they were invited to complete and return to the class teacher. The parental-completed questionnaires involved questions concerning childhood disease and family history, as well as demographic characteristics of the study group (age, gender, place of residence, concomitant diseases etc.). Permission to perform this study was obtained from the local educational authorities and from the respective school head teachers. The study protocol was also approved by the local Institutional Review Board. All parents were asked to give their signed informed consent, too.

After the enrollment of schools participating in the study, we went further to the second stage that included SPT conducted by doctors within randomly selected schools. SPTs were evaluated as described by the European Academy of Allergy and Clinical Immunology [14]. The antigen panel consisted of common allergens, according to the environmental characteristics of the area [10,11] and more specifically *HDM (Dermatophagoides farinae and D. pteronyssinus)*, *grass mix*, *trees (olive*, *cypress and pine)*, *weeds (Parietaria* spp.*)*, *cat and dog epithelium* and *moulds (Alternaria* and *Cladosporium* spp.*)*. The SPT sensitivity was graded as provided by Demoly et al. [15] according to the SPT-USA Standards (SPT: neg = 0 reaction, 1+ = 1 mm wheal above saline control; 2 + = 1–3 mm wheal above saline control; 3 + (the first point we consider a positive reaction) = 3–5 mm wheal above saline control plus an accompanying flare; and 4 + = > 5 mm wheal above saline control, plus an accompanying flare).

2.3. Statistical analysis

Statistical analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS), version 22.0 (IBM). Descriptive statistics were used to describe the main features of our study group. Co-relations among allergens were detected by bivariate correlation analysis using the Spearman's rank correlation coefficient. Finally, a cross tabulation analysis (contingency table analysis) was used to display the frequency distribution of age and gender for each allergen, discovering interrelations and any interaction between the sensitivities to allergens and age and gender of the study group.

3. Results

3.1. Study group characteristics

The total study group included 675 children. Among them a total of 231 showed sensitization (34.2%). Of those, 117 (50.6%) were males and 114 (49.4%) were females. According to age, 166 (71.9%) were primary school children (6–11 years old), whereas 65 (28.1%) were secondary school children (12–17 years old). A 37.7% of SPT-positive individuals reported a family history of allergies. In total, 32% of SPT-positive individuals were not aware of their allergy, with no statistically significant differences between ages (32.5% in primary school children vs 30.8% in secondary school children). The characteristics of the study group are presented in Table 1.

3.2. Sensitizations

According to SPT results, 93 children (40.3%) were mono-

Table 1
Demographic characteristics of AR children group.

	AR Patients (n = 231)
Sex, [(%)]	
Male	117 (50.6%)
Female	114 (49.4%)
Age	
6–11 years old	166 (71.9%)
12–17 years old	65 (28.1%)
Sensitizations	
Monosensitization	93 (40.3%)
Polysensitization	138 (59.7%)
Family history	87 (37.7%)
Aware of allergic disease	74 (32%)
Asthma presence [(%)]	37 (16%)

sensitized and 138 children (59.7%) were poly-sensitized to the study allergens. Overall, the most prevalent sensitizations in decreasing order were found to *HDM* (59.74%), to *grasses* (48.9%), to *Alternaria* (34.6%), and *olive* (14.71%). Prevalence characteristics for all the allergens tested are presented in detail in Table 2. Grass pollen allergy was more profound in males ($p = 0.017$), whereas females were significantly more sensitized to *Alternaria* moulds ($p = 0.021$). There was also a strong significant prevalence of *Alternaria* sensitization among primary school-aged children. Age and sex specific incidence rates are depicted in detail in Table 2.

3.3. Sensitivity scores

The sensitivity scores of each patient are presented in Table 3. In total 69.5% of allergic children sensitized to *HDM* and 81.4% sensitized to *grasses* were found to be extremely sensitive (SPT grade score = 4+), followed by a 77.5% of those allergic to the mould *Alternaria* (Table 3). All co-sensitivities among allergens were explored and are presented in detail in Table 4. Significant correlations were recorded between *grass* and *olive* ($p < 0.001$), and between *grass* and *pine* ($p = 0.003$), between *Alternaria* and *Cladosporium* ($p < 0.001$), between *cypress* and *pine* ($p = 0.006$), and finally between *cat* and *dog* epithelia ($p < 0.001$).

Table 3
Sensitivity grade scores to the most prevalent allergens.

Allergens	3+ grade score	4+ grade score
Dermatophagoides (Pteronnyssinus & farinae)	30 (21.7%)	96 (69.5%)
Grasses	17 (15%)	92 (81.41%)
Alternaria	13 (16.25%)	62 (77.5%)
Olive	8 (23.52%)	24 (70.58%)

4. Discussion

4.1. Epidemiology of allergic rhinitis worldwide

It is widely accepted that AR represents a common disease with considerable increase in prevalence worldwide over the last decades [16–20], so much that allergic disorders are now amongst the most common chronic disorders of childhood and adolescence [17,19]. Based on major international epidemiological studies such as the International Study of Asthma and Allergy in Childhood (ISAAC) [1,21], the differences in prevalences from place to place and even among countries have been revealed [8,22,23]. However, in Greece there is a lack of epidemiological studies [10–13], especially in childhood and adolescence, despite the higher incidence rates and health importance compared to adults [22]. Here we have provided epidemiological evidence of allergic rhinitis and sensitization patterns for the first time in this target group for a large uncharted region of NE Greece.

4.2. Sensitizations prevalences

To the best of our knowledge, this is the first study to provide recent epidemiological data of AR among school-aged children who lived for a long period in the same area in typical Mediterranean climate conditions of northeastern Greece. The high incidence showed by our study is between the spread limits (1.8%–40%) as described in the literature among childhood populations worldwide [17–23]. Moreover, there were no differences in allergen sensitizations among children with different age (primary vs secondary school children). Literature shows [6,22] that the peak sensitization prevalences are estimated in the third and fourth decades of life. The most prevalent sensitizations among allergens in decreasing order were found to *HDM* (59.7%), *grasses* (48.9%) and *Alternaria* (34.6%), followed by *olive*, animal danders and *parietaria* at lower rates. *HDM* and *grass* pollen have been described as the most frequent sensitizing allergens in previous studies from countries with similar climatic conditions [24–26]. There was no significant incidence rates according to gender, with the exception of *grass* pollen allergy that was more common in males than females and *Alternaria* that was more often in females. This comes in agreement with a previous study of Blomme et al. [22] who found a male predominance of *grass* pollen allergy in a Belgian population. A clinically relevant finding, was the significantly higher prevalence of *Alternaria* mould allergy among primary school children (6–11 years old) compared to secondary school ones (12–17 years old). This is an important finding since *Alternaria* has been described as a risk factor for asthma [27]. Additionally, we found that most of AR children were sensitive to more than one allergens, in agreement to what has been published before [5,7,22,28]. This means that management of allergic diseases in children should be more complicated and strengthens the importance of early screening during childhood. This is further supported by the finding that a high percentage of 32% of sensitized individuals ignored their morbidity status (allergic disease). This finding underlies the problem of possible under-diagnosis of allergic rhinitis, and possibly asthma, which leads to clinical and epidemiological under-estimates of the true health burden in populations. No statistical significant difference concerning sensitization was found among the two different age groups (32.53% among primary school children and 30.76%

Table 2
Patients' sensitizations to pollens presented as percentages of patients examined and sex and gender distribution.

Pollens	Sensitization N (%)	Gender distribution			Age		
		Men	Women	p	6–11 y	12–17 y	p
		N (%)	N (%)		N (%)	N (%)	
D. pteronnyssinus & D. farinae	138 (59.74)	76 (55.07)	62 (44.93)	0.377	94 (68.1)	44 (31.9)	0.413
Grasses	113 (48.9)	68 (60.17)	45 (39.83)	0.017*	83 (73.4)	30 (26.6)	0.945
Alternaria	80 (34.6)	32 (40)	48 (60)	0.021*	66 (82.5)	14 (17.5)	0.035*
Cladosporium	18 (4.7)	10 (55.5)	8 (44.5)	0.447	14 (77.7)	4 (22.3)	0.896
Olive	34 (14.7)	20 (58.8)	14 (41.2)	0.759	22 (64.7)	12 (35.3)	0.637
Dog epithelia	30 (13.0)	19 (63.3)	11 (36.7)	0.525	21 (70.0)	9 (30.0)	0.419
Cat epithelia	27 (11.7)	14 (51.9)	13 (48.1)	0.596	22 (81.5)	5 (18.5)	0.245
Parietaria	24 (10.4)	17 (70.8)	7 (29.2)	0.154	16 (66.7)	8 (33.3)	0.795
Pine	16 (6.9)	9 (56.2)	7 (43.8)	0.657	13 (81.3)	3 (18.7)	0.237
Cypress	11 (4.8)	6 (54.5)	5 (45.5)	0.693	7 (63.6)	4 (36.4)	0.455

*Statistically significant at the $p < 0.05$ level.
**Very statistically significant at the $p < 0.01$ level.
***Extremely statistically significant at the $p < 0.001$ level.

Table 4
Co-sensitivities among allergens.

Allergens	CC Sig	*HDM*	*Grasses*	*Alternaria*	*Cladosporium*	*Olive*	*Parietaria*	*Cypress*	*Pine*	*Dog*	*Cat*
HDM		1.000.	−0.021	−0.175**	−0.007	−0.004	0.093	−0.052	0.127	0.057	−0.002
			0.749	0.008	0.918	0.948	0.159	0.431	0.053	0.391	0.976
Grasses		−0.021	1.000	−0.069	0.048	**0.249*****	0.089	0.115	**0.197****	0.035	−0.038
		0.749	.	0.295	0.464	**0.000**	0.179	0.081	**0.003**	0.594	0.569
Alternaria		−0.175**	−0.069	1000	**0.288*****	−0.078	−0.213**	−0.160*	−0.156*	−0.013	0.029
		0.008	0.295	.	**0.000**	0.240	0.001	0.015	0.018	0.839	0.665
Cladosporium		−0.007	0.048	**0.288*****	1.000	−0.072	0.010	0.010	−0.079	−0.017	0.131
		0.918	0.464	**0.000**	.	0.276	0.883	0.874	0.231	0.802	0.047
Olive		−0.004	**0.249*****	−0.078	−0.072	1.000	0.099	0.029	−0.022	0.011	−0.007
		0.948	**0.000**	0.240	0.276	.	0.135	0.663	0.740	0.867	0.917
Parietaria		0.093	0.089	−0.213**	0.010	0.099	1.000	0.125	0.121	0.046	0.012
		0.159	0.179	0.001	0.883	0.135	.	0.058	0.067	0.488	0.862
Cypress		−0.052	0.115	−0.160*	0.010	0.029	0.125	1.000	**0.179****	−0.086	−0.081
		0.431	0.081	0.015	0.874	0.663	0.058	.	**0.006**	0.192	0.219
Pine		0.127	**0.197****	−0.156*	−0.079	−0.022	0.121	**0.179****	1.000	−0.057	−0.051
		0.053	**0.003**	0.018	0.231	0.740	0.067	**0.006**	.	0.392	0.441
Dog		0.057	0.035	−0.013	−0.017	0.011	0.046	−0.086	−0.057	1.000	**0.434*****
		0.391	0.594	0.839	0.802	0.867	0.488	0.192	0.392	.	**0.000**
Cat		−0.002	−0.038	0.029	0.131*	−0.007	0.012	−0.081	−0.051	**0.434*****	1.000
		0.976	0.569	0.665	**0.047**	0.917	0.862	0.219	0.441	**0.000**	.

*Statistically significant at the $p < 0.05$ level.
**Very statistically significant at the $p < 0.01$ level.
***Extremely statistically significant at the $p < 0.001$ level.

among secondary school children, respectively). This can be mainly attributed to the fact that symptoms of AR are frequently mistaken as common cold or just as something non important. Also children often fail to share these problems at home or at school. Therefore this problem does not receive the attention it should be from the patients, their families, as well as the health care professionals, espesially in developing countries. Moreover, only patients with severe symptoms seek medical help with a significant proportion of sufferers not receiving treatment [17]. This finding points out the need for policies that encourage SPT-screening in early childhood and pollen calendars construction of each area for early diagnosis and appropriate treatment of AR [10,11,29].

An interesting hypothesis that could be further pursued is if sensitivity to a specific allergen is associated with sensitivity to another allergen (i.e. prevalence of co-sensitivities). This can help guide targeted interventions e.g. in the form of immunotherapy. Accordingly, in this study co-sensitivities were detected between *grass* pollens and *pine*, between *grass* and *olive*, between *Alternaria* and *Cladosporium*, between *cypress* and *pine*, and finally between *dog* and *cat* danders. This finding is of great importance as it can be used as a finding with a predictive value in everyday clinical practice. Finally we measured the sensitivity scores for each allergen, based on SPT results. According to these data, high sensitivity scores (SPT grade score = 4+) were detected to all allergens tested. This indicates that once sensitization is recorded, there is a high probability that the allergic reaction and/or response to an allergen is going to be severe.

4.3. Study strengths and weaknesses

The main strengths of this study include the very high response rate among subjects, which is likely to be due to the combination of achieving good support from the participating schools and the fact that we were undertaking work in a population that has not previously been investigated, therefore research fatigue was not an issue. On the other hand the major limitation of this work is the relatively small sample size and that it was conducted in only one specific geographical region; these findings may therefore not be generalisable to other populations or region of Greece or Europe. However this is the most up-to-date epidemiological study of this type and further work has to be done, in order to monitor allergic disease trends all over Greece.

5. Conclusions

In this population-based cross-sectional study, we demonstrated a 34% prevalence of a positive SPT to one or more common aeroallergens among primary and secondary school-aged children in a norh-eastern Greece area. However among them, a high percentage of 32% were not aware of their allergic disease. That makes screening for AR an important preventive measure. The most prevalent sensitizations in decreasing order were found to *HDM*, to *grasses* with a male predominance, and to *alternaria alternate* mould with a female predominance and a significant correlation to primary school-aged children. Co-sensitivities were detected for *grass* pollens and *pine* and *olive* trees, for *alternaria* and *cladosporium* moulds, for *cypress* and *pine* trees, and finally for *dog* and *cat* danders. This work should be a baseline from which to further assess the prevalence of allergic problems in other parts of Greece, monitoring disease trends and is required for optimal management of allergic disease in early childhood.

Conflict of interest

None.

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