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Sensitization to Common Allergens, Especially Pollens, among Children with Respiratory Allergy in the Trakya Region of Turkey

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SUMMARY Asthma and allergic rhinitis are common problems in children and the causative pollen allergens vary according to the geographical area. The aim of this study was to investigate patterns of sensitization to common inhalant allergens, especially pollens, in Turkish children living in the Trakya region and to determine differences between rural and urban areas. Allergen skin testing was prospectively performed on 539 children aged between 4 and 17 years with respiratory allergy. The reaction was considered to be positive if the mean wheal diameter was at least 3 mm greater than that of the negative controls. We detected positive skin reactions in 420 (77.9%) children. Two hundred and eighty-one (52.1%) mite, 277 (51.4%) pollen, 174 (32.3%) mold, 65 (12.1%) animal dander, 12 (2.2%) cockroach and 6 (1.1%) latex skin sensitivities were detected. Among the pollen allergies 173 were cereal pollen (32.1%), 170 grass pollen (31.5%) and 144 tree pollen allergies (26.7%). The most common positive skin test among the pollens was to cultivated wheat (*Titicum vulgare*) (n = 116, 21,5%), followed by rye grass (*Lolium perenne*) and orchard grass (*Dactylis glomerata*). Positive skin reactions to *Alternaria*, to *Candida albicans*, and to all pollens except *Ulmus competris, Pinus sylvetris, Platanus vulgaris* and *Tilia platyphyllos*, were higher in children with allergic rhinitis than in those with asthma. In children from rural areas, allergic skin reactivity was found to be more common against *Candida albicans*, sheep dander and all pollens except *Corylus avellana, Fraxinus excelsior, Populus alba, Pinus sylvetris, Platanus vulgaris* and *Chenopodium album*, than in urban children. Although Trakya is close to Greece and other Mediterranean countries, this study suggests that the pollens, which sensitize children, are not similar.

The prevalence of allergic diseases in various parts of the world has increased steadily.[1,2] The geographical distribution of allergens determines the allergic manifestations. In the Trakya region, situated at $41^0 40'$ north, $26^0 34'$ east in northwestern Turkey, allergic diseases are common.[3] This is not surprising because the climate is humid and hot during summer, cold in winter and there are many pollen-producing plants around. This condition is considered favorable for the availability of aeroallergens such as mites and pollens.

Sensitization to allergens seems to be influenced by different factors, including genetic susceptibility, the age of first exposure, the degree of allergen exposure and the type of allergen.[4-10] Recent improvements in the insulation of houses have lead to a reduced exposure to common indoor allergens, but it is nearly impossible to prevent exposure to common outdoor allergens such as pollens. The aim of this study was to investigate patterns of sensitization to common inhalant allergens, especially pollens, in Turkish children, living in the Trakya region and to determine the

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differences between rural and urban areas.

METHODS

This study was performed prospectively between April 2000 and April 2002 at the Pediatric Allergy and Pulmonology Clinic of the Trakya University Hospital. We analyzed allergy skin prick tests to common airborne indoor and outdoor allergens in 539 patients, who were grouped according to their diagnosis of allergic asthma, allergic rhinitis (AR) or both. Asthma was considered to be present in children with a history of episodic shortness of breath, wheezing, difficulty in expiration and/or a high IgE level and/or positive Alatop allergy screening (multiallergen specific IgE antibody test to 12 different allergens [Diagnostic Product Corporation, Los Angeles, USA]) and/or a positive food panel FP5E for peanut, wheat, egg white, salmon fish, milk, soybean and/or previous positive skin tests. The diagnosis of AR was established by a combination of clinical history, physical examination and/or a high IgE level and/or positive Alatop Allergy screening for inhalant allergens and/or a positive food panel FP5E and/or previous positive skin tests. Subjects who had used antihistamines within the last two weeks were excluded from the study. The study was approved by the Ethics Committee of the Medical Faculty of the Trakya University and informed written consent was obtained from all parents.

Skin testing

Purified and immunochemically characterized aeroallergens (Stallergenes, Germany) were applied to the forearm by an experienced pediatric allergy nurse, in a standardized order with the aid of an uncoated Phazet® needle. The panel consisted of extracts of mites (*Dermatophagoides farinae, Dermatophagoides pteronyssinus*), molds (*Alternaria, Aspergillus, Candida albicans, Mucor Racemasus*), animal dander (cat, dog, sheep dander), grass pollens (orchard grass [*Dactylis glomerata*], sweet vernal grass [*Anthoxanthum odoratum*], rye grass [*Lolium perenne*], timothy grass [*Phleum pratense*], Kentucky bluegrass [*Poa pratensis*]), tree pollens (*Alnus glutinosa, Quercus robur*), hazelnut (*Corylus avellana), Fraxinus excelsior, Populus alba, Salix caprea,* olive (*Olea europea), Juglans regia, Ulmus compestris, Pinus sylvetris, Platanus vulgaris, Tilia platyphyllos, Acacia dealbata*), cereal pollens (oat [*Avena sativa*], wheat [*Triticum vulgare*], barley [*Hordeum vulgare*], corn [*Zea mays*], rye [*Secale cereale*]), weeds (mugwort [*Artemisia vulgaris*], *Chenopodium album, Rumex acetosa, Parietaria officinalis*, English plantain [*Plantago lanceolata*]), latex, and cockroach. Histamine hydrochloride (10 mg/ml) and sodium chloride (9 g/l) were applied as positive and negative control solutions, respectively. The mean wheal size of 2 orthogonal diameters was determined after 15 minutes.[11] The reaction was considered to be positive if that mean wheal size was at least 3 mm greater than the negative control.

A study questionnaire requesting demographic data and a family history of respiratory allergy was also administered to each patient. Venous blood samples were taken once from each patient and IgE, Alatop Allergy Screening and Allergy Food Panel FP5E were measured by chemiluminescent enzyme-labeled immunoassay (BioDPC, Los Angeles, USA).

Statistical analyses

Statistical analyses were performed using Minitab Release 13, reference number: wcp 133100197 (Trakya University, Faculty of Medicine, Data Processing Center). Age and total IgE that were nonparametric data were compared with the Mann Whitney U test. Results were expressed as mean ± SD for continuous variables. χ^2 tests were used as statistical method for other variables. A $p < 0.05$ was considered as statistically significant.

RESULTS

Positive skin reactions were observed in 77.9% of the subjects, whereas 22.1% of the subjects included in the study did not react to common allergens. Demographic data, total IgE, Alatop and food screening results are shown in Table 1. Two hundred and eighty-one (52.1%) mite, 277 (51.4%) pollen, 174 (32.3%) mold, 65 (12.1%) animal dander, 12 (2.2%) cockroach and 6 (1.1%) latex skin sensitivities were detected (Fig. 1). Among the pollen allergies 173 (32.1%) cereal pollen, 170 (31.5%) grass pollen and 144 (26.7%) tree pollen allergies were detected. The most common positive skin tests among the pollens were to cultivated wheat (n = 116; 21.5%), followed by rye grass (n = 109; 20.2%), orchard grass (n = 106; 19.7%), barley (n = 105; 19.5%), sweet vernal grass (n = 87; 16.1%), oat (n = 85; 15.8%), Kentucky bluegrass (n = 77; 14.3%) and corn (n = 61; 11.3%), respectively. Cultivated wheat was one of the most common

pollen allergens among the asthmatic children as well as children with allergic rhinitis (Table 2).

Fifty-four percent of subjects (n = 289) were diagnosed as asthma (Group 1), 9% (n = 49) had allergic rhinitis (Group 2) and 37% (n = 201) had both (Group 3). The frequency of sensitization to common allergens among the subjects with asthma, AR and both diseases is illustrated in Fig 2. Allergic skin sensitivities to mites, molds except *Altermaria* and *Candida albicans*, animal danders, latex and cockroach were not different between Group 1 and Group 2. Skin sensitivities to all pollen allergies except *Ulmus competris, Pinus sylvetris, Platanus vulgaris* and *Tilia platyphyllos*, were more likely to be observed in children with AR than in those with asthma (Table 2). The frequency of sensitization to pollens in the different patient groups is illustrated in Fig 3.

In our study, 32.4% of subjects (n = 175) were living in rural areas, while 67.6% in urban areas (n = 364). Subjects living in rural areas generally had more skin reactions to common allergens than those living in urban areas. Allergic skin reactions against all pollens except *Corylus avellana, Fraxinus excelsior, Populus alba, Pinus sylvetris, Platanus vulgaris and Chenopodium album* were found to be more common in subjects from rural areas than in those from urban areas (Table 3). Allergies to mites, molds (except *Candida albicans*), animal danders (except sheep dander), cochroach and latex were not different between the subjects from rural and urban areas.

DISCUSSION

Trakya region is in the north-

Table 1 Demographic characteristics of subjects

Age (years)*	7.8 ± 2.87 (4-17)
Gender (girls/boys)**	239/300 (44.3%/55.7%)
Family history of respiratory allergy**	260 (48.2%)
Maternal respiratory allergy**	110 (20.4%)
Paternal respiratory allergy**	73 (13.5%)
Sibling of respiratory allergy**	33 (6.1%)
Other respiratory allergy in relatives**	122 (22.6%)
IgE* antibodies	263.3 ± 347.7 (5-2260)
ALATOP screening positivity**	301 (55.8%)
Food screening positivity**	130 (24.1%)

*Values are expressed as mean ± SD (range)
**Values are expressed as number of subjects (% in number of subjects)

Fig. 1 Frequency of sensitization to common allergens among the subjects.

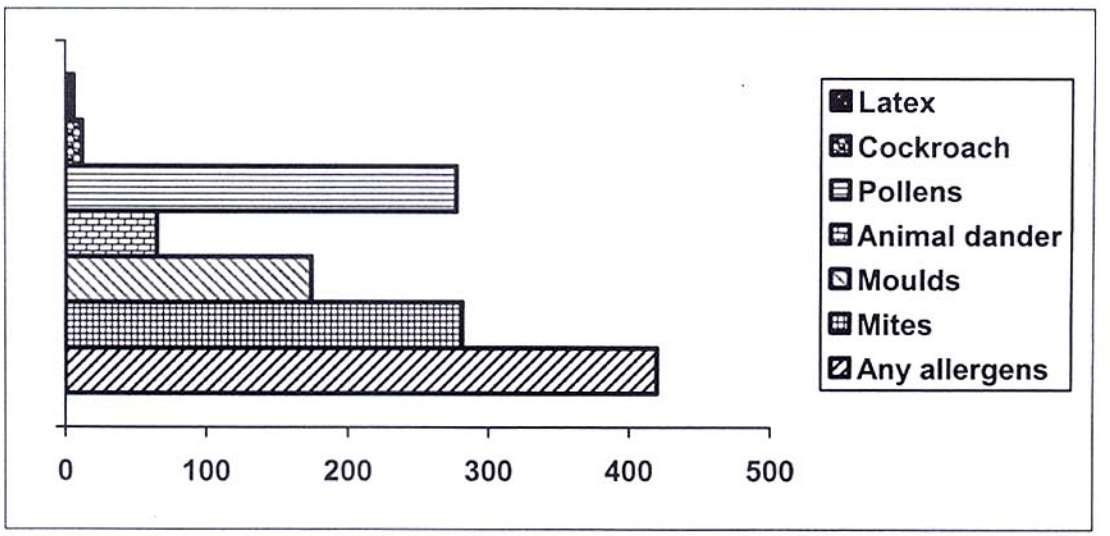


Table 2 Frequency of sensitization to pollen allergens in children with respiratory allergy

Pollen allergen	All children	Children with Asthma (Group 1)	Children with AR (Group 2)	Children with both diseases (Group 3)	Significances of groups and *p* values
Titicum vulgare (cultivated wheat)	116 (21.5%)	25 (8.7%)	28 (57.1%)	63 (31.3%)	1-3: $p < 0.01$ 1-2: $p < 0.01$ 2-3: $p < 0.01$
Lolium perenne (rye grass)	109 (20.2%)	23 (8.0%)	18 (36.7%)	68 (33.8%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Dactylis glomerata (orchard grass)	106 (19.7%)	17 (5.9%)	17 (34.7%)	72 (35.8%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Hordeum vulgare (cultivated barley)	105 (19.5%)	18 (6.2%)	19 (38.8%)	68 (33.8%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Anthoxanthum odoratum (sweet vernal grass)	87 (16.1%)	16 (5.5%)	11 (22.4%)	60 (29.9%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Secale cereale (cultivated oat)	85 (15.8%)	14 (4.8%)	16 (32.7%)	55 (27.4%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Poa pratensis (Kentucky bluegrass)	77 (14.3%)	9 (3.1%)	14 (28.6%)	54 (26.9%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Zea mays (cultivated corn)	61 (11.3%)	11 (3.8%)	11 (22.4%)	39 (19.4%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Avena sativa (cultivated rye)	57 (10.6%)	10 (3.5%)	11 (22.4%)	36 (17.9%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Phleum pratense (timothy grass)	49 (9.1%)	8 (2.8%)	8 (16.3%)	33 (16.4%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Artemisia vulgaris	49 (9.1%)	9 (3.1%)	12 (24.5%)	28 (13.9%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Olea europea (olive)	48 (8.9%)	13 (4.5%)	7 (14.3%)	28 (13.9%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Corylus avellana (hazelnut)	45 (8.3%)	7 (2.4%)	7 (14.3%)	31 (15.4%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Fraxinus excelsior	45 (8.3%)	8 (2.8%)	5 (10.2%)	32 (15.9%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Salix caprea	39 (7.2%)	4 (1.4%)	13 (26.5%)	22 (10.9%)	1-3: $p < 0.01$ 1-2: $p < 0.01$ 2-3: $p < 0.01$
Alnus glutinosa	32 (5.9%)	5 (1.7%)	5 (10.2%)	22 (10.9%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Rumex acetosa	31 (5.8%)	6 (2.1%)	5 (10.2%)	20 (10.0%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Populus alba	31 (5.8%)	4 (1.4%)	6 (12.2%)	21 (10.4%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Quercus robur	21 (3.8%)	2 (0.7%)	4 (8.2%)	15 (7.5%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Juglans regia	27 (5.0%)	1 (0.3%)	4 (8.2%)	22 (10.9%)	1-2: $p < 0.01$ 1-3: $p < 0.01$
Ulmus competris	19 (3.5%)	3 (1.0%)	1 (2.0%)	15 (7.5%)	1-3: $p < 0.01$
Pinus sylvetris	11 (2.0%)	1 (0.3%)	-	10 (5.0%)	1-3: $p < 0.01$
Platanus vulgaris	21 (3.8%)	4 (1.4%)	2 (4.0%)	15 (7.5%)	1-3: $p < 0.01$
Tilia platyphyllos	15 (2.8%)	3 (1.0%)	1 (2.0%)	11 (5.5%)	1-3: $p < 0.01$

All values are expressed as number of subjects (% in number of subjects)

Fig. 2 Frequency of sensitization to common allergens among the subjects with asthma, AR and both diseases.

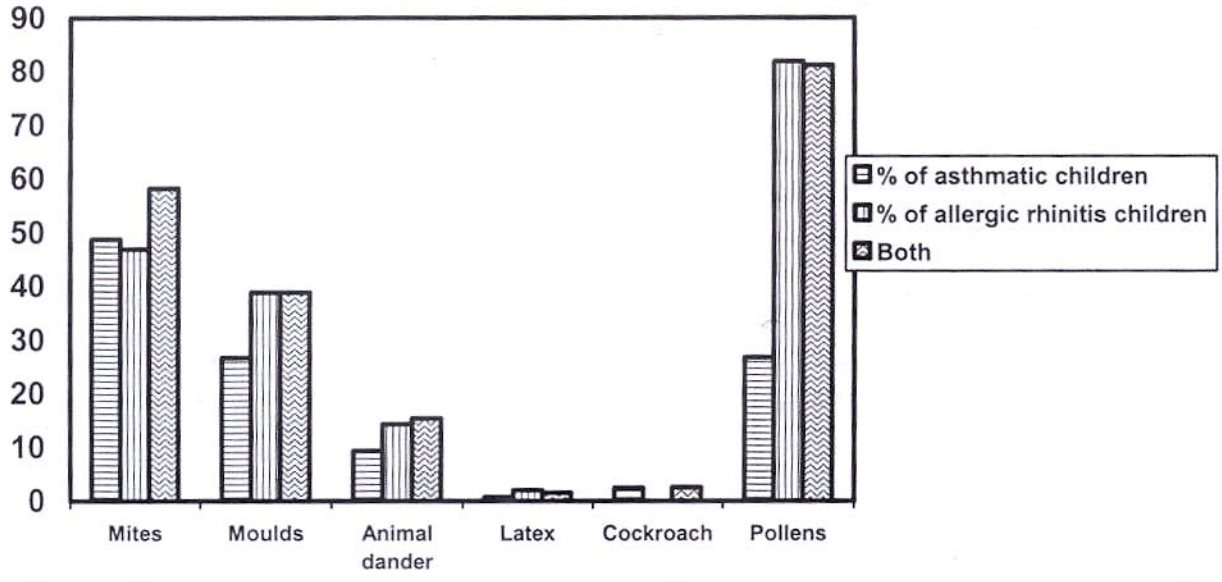
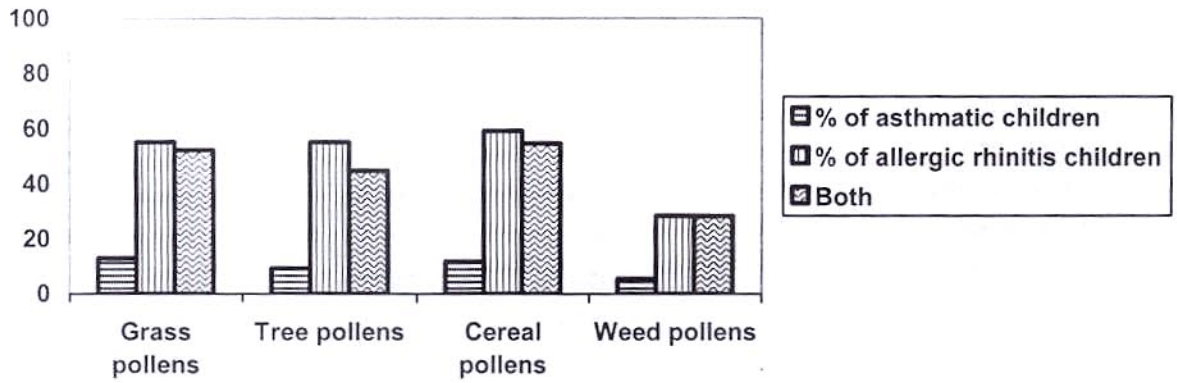


Fig. 3 Frequency of sensitization pollens among the subjects with asthma, AR and both diseases.



west of Turkey with mild climate. The average temperature is 12.2°C in spring, 26.8°C in summer, 13.8°C in autumn and 3.6°C in winter. This region neighbors on Bulgaria and Greece, and also has access to the Black Sea, Aegean Sea and Marmara Sea. Agriculture is vital in Trakya's economy as 73% of the area is cultivated with wheat, sunflower, rice, sugar beet, tomato, bean, melon, watermelon, barley, rye, oats and dane. The atmospheric pollen concentration and skin sensitivities to pollens are considered to be different from other neighboring regions.

According to our study, allergic skin sensitivity to most pollen, *Alternaria* and *Candida albicans* were more prevalent in children with AR than in those with asthma. However, other indoor and outdoor allergies were not different between the two groups. The type of allergen may influence the type of allergic manifestation, which may be related to its size or other properties. Pollen particles (20 to 60 μm in diameter) are generally larger than mite (1-10 μm) and mold spores (3-30 μm) and can be more easily trapped in

Table 3 Comparison of the sensitization to pollen allergens in children with respiratory allergy according to living area

Pollen allergen	Rural areas (n = 175)	Urban areas (n = 364)	*p*
Titicum vulgare (cultivated wheat)	56 (32.0%)	60 (16.5%)	<0.01
Lolium perenne (rye grass)	50 (28.6%)	59 (16.2%)	<0.01
Dactylis glomerata (orchard grass)	51 (29.1%)	55 (15.1%)	<0.01
Hordeum vulgare (cultivated barley)	60 (34.3%)	45 (12.4%)	<0.01
Anthoxanthum odoratum (sweet vernal grass)	41 (23.4%)	59 (16.2%)	<0.01
Secale cereale (cultivated oat)	44 (25.1%)	21 (11.3%)	<0.01
Poa Pratensis (Kentucky bluegrass)	40 (22.9%)	37 (10.2%)	<0.01
Zea mays (cultivated corn)	32 (18.3%)	29 (8.5%)	<0.01
Avena sativa (cultivated rye)	28 (16.0%)	29 (8.0%)	<0.05
Phleum pratense (timothy grass)	26 (14.9%)	23 (6.3%)	<0.01
Artemisia vulgaris (mugwort)	29 (16.6%)	20 (5.5%)	<0.01
Olea europea (olive)	25 (14.3%)	20 (5.5%)	<0.01
Corylus avellana (hazelnut)	20 (11.4%)	25 (6.9%)	NS
Fraxinus excelsior	20 (11.4%)	25 (6.9%)	NS
Salix caprea	23 (13.1%)	16 (4.4%)	<0.01
Alnus glutinosa	20 (11.4%)	12 (3.3%)	<0.01
Rumexa Acetosa	16 (9.1%)	15 (4.1%)	<0.01
Populus alba	15 (8.6%)	16 (4.4%)	NS
Juglans regia	18 (10.3%)	9 (2.5%)	<0.01
Ulmus competris	12 (6.9%)	7 (1.9%)	<0.01
Pinus sylvetris	7 (4.0%)	4 (1.1%)	NS
Platanus vulgaris	10 (5.7%)	11 (3.0%)	NS
Tilia platyphyllos	9 (5.1%)	6 (1.6%)	<0.05
Chenopodium album	10 (5.7%)	16 (4.4%)	NS
Parietaria officinalis	19 (10.9%)	7 (1.9%)	<0.01

All values are expressed as number of subjects (% in number of subjects); NS: Non-significant.

the nasal mucosa, inducing a local allergic response.[8,10] In our study, sensitization to indoor allergens seemed to contribute to both AR and asthma, while exclusive sensitization to pollens and molds was found to be more common in subjects with allergic rhinitis. Elsewhere latex and cockroach were reported to be important allergens in children with respiratory allergy,[12-14] however, we found only few children with sensitization to cockroach (2.2%) and latex (1.1%). Alp *et al.*[13] from Eskisehir, Turkey, reported similar results, but Saraclar *et al.*[12] from Ankara reported a higher incidence of latex allergy (10%) in atopic children.

In our study, the most common pollen allergens were cultivated wheat, closely followed by grasses and other cereal pollens. Cultivated wheat provides the staple food for about one third of the world's population. This widely cultivated cereal is grown in temperate and subtropical regions all

over the world. Similar to our study, another Turkish study from the agricultural area of Adana reported cultivated wheat, rye, and corn as important pollens among children with respiratory allergy.[9] In the Trakya region, wheat is cultivated in two seasons. Winter wheat flowers in midsummer and spring wheat flowers in late summer. Therefore, summer is hazardous for children with respiratory allergy.

Rye is also widely cultivated for its grain and rye flowers in early summer giving a well-known odor. It was found to be a very important allergen in a Middle-European study.[15] It produces about 8 to 35 times more pollen per anther than wheat. Von der Hardt *et al.*[16] from Netherlands found 55.2% rye and 50.7% wheat sensitivity in asthmatic children. Similarly Horak *et al.*[15] found that rye was the most important allergen in AR in Austria. Cultivated barley, oat and corn were also very important allergens in our subjects. In a French study, Lelong *et al.*[17] reported that pollen allergy to barley and rye were common in children with summer respiratory problems.

Ten percent of the land in Trakya is forest and shrubbery, 13% meadows and pastures, 17% planted fields and 60% are unsuitable for agriculture. In the meadows and pastures timothy grass, orchard grass and rye grass are the most common plants. The pollination period of grasses starts at the end of March, continues until the end of June and then decreases in July. The pollen grains of these plants can reach high atmospheric concentrations if the weather conditions are favorable, causing severe clinical symptoms beginning in April. Grass allergy is found to be the most important allergy in Leiden, the Netherlands,[18] in Montpellier, France[19] and Greece.[7] In our region, it is the second etiologic factor of pollinosis, like in Southern Italy.[6] In Northern Greece, neighboring to the Trakya region, grasses are by far the most common pollen allergens.[7] Among the grasses rye grass, orchard grass, sweet vernal grass, timothy grass and Kentucky bluegrass were the most allergic grasses in our subjects. Grass allergy induces mostly nasal and conjunctival symptoms, and is less related with exacerbation of asthma.[5] Although grass pollen allergens were found to be very important allergens in our asthmatic children, these allergens were even more common in children with AR.

Regarding trees, the most potent allergenic tree pollen are produced by *Corylus avellana* (hazelnut), *Fraxinus excelsior* and *Olea europea* (olive). The hazelnut trees grow in the Black sea coast of Trakya and are primarily wind-pollinated which causes particles to travel for miles. Olive is an extensively planted crop tree in the Mediterranean basin, and the density of olive trees is also very high in the southwest of Trakya. Olive tree pollen is a highly sensitizing allergen that causes rhino-conjunctivitis or asthma in children; the latter may be quite severe.[7] D'Amato *et al.*[6] and Papageorgiou *et al.*[7] reported that olive was the most common causative agent of respiratory allergy in their region. Like in our study, *Fraxinus* were also very important allergenic tree pollens in Greek and Dutch studies.[7,18] *Populus* and *Salix* trees were moderate pollen producers, however, due to their high intensity in our region, skin test sensitivities were found to be high especially in children with AR. Pollination of these trees usually occurs in mid-spring, followed for a month by large amounts of airborne seed-carrying tufts of cotton flies during the peak grass pollination.

Concerning the weeds, *Rumex acetosa* and mugwort are the main allergenic plants of this region. The pollination of mugwort occurs from May to September, and like in our study it was found to be an important allergen among children in Central and Southern Greece.[7] In contrast to our results, *Parietaria* was reported to be the commonest allergenic weed in the Mediterranean area.[6] Other pollens in Trakya region were of minor allergenic importance.

Some studies have demonstrated that lower rate of allergic sensitization and allergies in children living in rural areas as compared to those living in urban areas. This has been attributed to the lower levels of air pollution in rural areas.[20-25] D'Amato *et al.*[20] reported that people who live in urban Napoli, Italy, tend to be more affected by pollen induced respiratory allergy (primarily *Parietaria* spp.) than those from rural areas of Napoli. In this study, we found that children living in rural areas with a respiratory allergy were more likely to have skin sensitivities to common allergens, especially to many pollens than those living in urban areas. These pollen sensitivities may be explained by the high atmospheric pollen concentration in the rural areas. On the other hand, air pollution is still not a very important problem in the urban areas

of Trakya, and therefore severe air pollution-induced pollen allergies may not be seen. Children, from rural areas, were also more likely to suffer from sheep dander allergies than those from urban areas, which was not surprising, because sheep and cattle-dealing are very common in villages. Knowledge of the correlation between the concentration of indoor and outdoor allergens and the symptoms of respiratory allergy is important for better management of these diseases.

The main limitation of this study was that it was a hospital-based study. However, our hospital is the main tertiary center of the northwest of Turkey and nearly all children with respiratory allergy in this region are treated by our center. This study showed that pollen allergies in children of the Trakya region are quite different from our neighbors such as Greece and from other parts of Europe, such as Italy. More aerobiological and allergen identification studies at a local level are needed to evaluate the type and specific characteristics of pollen allergens in Turkey and routine panel of aeroallergens should be formulated on the basis of these findings.

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