

Short communication

Survey of the allergic status of patients with bronchial asthma in Turkey: a multicenter study

Kalyoncu AF, Çöplü L, Selçuk ZT, Emri AS, Kolaçan B, Kocabaş A, Akkoçlu A, Erkan L, Şahin AA, Barış Y. Survey of the allergic status of patients with bronchial asthma in Turkey: a multicenter study. *Allergy* 1995; 50: 451-455. © Munksgaard 1995.

Patients diagnosed with bronchial asthma (BA) were prospectively enrolled to assess their allergen spectra and atopic status. The patients came from five major cities (Ankara, İzmir, Samsun, Elazığ, and Adana) in different regions of Turkey. Atopic status, total IgE levels, and allergen spectra were determined in 1149 patients and 210 controls who were spouses of the patients sharing the same environment but not consanguinity with the patients. Total IgE levels were significantly higher in the asthmatic patients. For both groups, total IgE levels were higher in both atopic and male subjects. Atopy rates were 42% in asthmatics and 26.1% in controls, declining notably by age in both groups. The most common allergen in both groups was house-dust mite (HDM), which was more frequently detected in coastal regions (Samsun, İzmir, and Adana). Allergen spectra of the patients included HDM, pollens, cockroach, pet animals, and molds in decreasing order of frequency. *Phleum pratense* and *Artemisia vulgaris* were the most common pollens in all regions, whereas *Olea europaea* was the most common in İzmir. Pollen sensitivity was least frequent in Elazığ. For all of the regions, pet sensitivity was less common than, and mold sensitivity was comparable to, that of Western countries. In conclusion, BA patients in Turkey displayed significant differences in their allergen spectra and total IgE levels from control subjects and BA patients in Western countries.

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Key words: allergen spectrum; atopy; bronchial asthma; geographic differences in allergy; total IgE; Turkey.

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Accepted for publication 20 January 1995

Atopy is defined as sensitivity to common aeroallergens which can be demonstrated by skin tests and specific IgE in the serum. Its association with both bronchial asthma (BA) and other allergic diseases is well established as the major identified risk factor for these disorders. The prevalence of atopy among adult patients with BA has been reported to range from 30% to 50% in different countries (2, 10). Allergen spectra of atopic patients exhibited differences not only among countries, but also between regions of the same country (13). Variations in geography, climate, and social and possibly ethnic factors may account for these differences. Like a bridge, Turkey is located between Europe and Asia, and all four seasons can take place in different regions of the country at the same time of the year. Coastal regions of Turkey in the north, west, and south have a warm

and humid climate, whereas central and eastern parts have dry weather with hot temperatures in summer and a long, snowy winter. It is supposed that all these factors concurrently result in differences in both the indoor and outdoor fauna of the country, differences which influence the allergen spectra of its population. Since these data should play an important role in both evaluation and treatment, we conducted this study to assess the atopic status and allergen spectra of BA patients in Turkey.

Materials and methods

Patients previously diagnosed with BA by chest specialists were prospectively surveyed in five major cities (Ankara, Samsun, İzmir, Elazığ, and Adana) in different regions of Turkey from October 1991 to

October 1992. A total of 1149 asthmatic patients and 210 controls who were spouses of the patients, sharing the same environment but not exhibiting consanguinity, were evaluated. Although we planned to form a separate control group for each region, 322 patients were single, and exclusion of 85 spouses who were working abroad, 412 who refused to participate in the study, and 120 who were consanguineous resulted in a sample of 210 controls for the whole country.

The five major cities were selected on the basis of each being representative of a population of at least 200 000 settled in different regions with different climates. Geographic and meteorologic data of these five cities are presented in Table 1.

A questionnaire was filled in by investigators via interview, comprising questions on age, sex, smoking status, medical history of asthma, pets at home, and atopic heredity.

Atopy was assessed by skin prick test (SPT) reactions to 14 allergens commercially available in liquid form. SPT was not performed in pregnant subjects or those with dermatographism, and total IgE levels were measured in those who accepted blood drawing. SPT was performed as described by Østerballe et al. (12). Drops of allergen extracts were placed on the volar aspect of the forearm and were penetrated with a lancet having a 1-mm point. Extracts of timothy, mugwort, *Parietaria officinalis*, *Olea europaea*, hazelnut, birch, *Dermatophagoides pteronyssinus* (Dpt), *D. farinea* (Df), cockroach, cat, dog, horse, *Alternaria alternata*, *Aspergillus fumigatus*, and *Cladosporium herbarum*, purchased from Greer (USA) and ALK (Denmark), were employed. Histamine 1 mg/ml and saline were used as positive and negative controls, respectively. Resulting wheals were measured after 15 min. The largest horizontal and perpendicular diameters were recorded, and the geometric mean was calculated. A mean diameter of at least 3 mm was considered positive. Subjects were considered atopic if they had at least one positive SPT reaction to common allergens.

Total serum IgE (Phadebas PRIST) was mea-

sured using the method recommended by the manufacturer (Pharmacia AB, Sweden). Measurements were randomly performed in 64% of asthmatics and 73% of controls due to financial limitations.

Comparisons were made via Student's *t*-test, the chi-square test, and unpaired *t*-test as required. *P* values less than 0.05 were considered significant. Logarithmic values were utilized for comparison of total IgE levels, and 95% confidence limits were calculated for differences where appropriate.

Results

A total of 1149 asthmatic patients and 210 controls were enrolled in the study. There were 801 women (69.7%) and 348 men (30.3%) in the patient group, and 38 women (18.1%) and 172 men (81.9%) in the control group. The cause of female predominance among asthmatics is unclear. Distribution of patients and controls regarding age, sex, smoking status, and place of residence are shown in Table 2.

Of the BA group, 147 patients (12.8%) then had pets, and 89 (7.8%) had had them in the past. Those pets at home were either cats (66%), birds (19.7%), or dogs (10.9%). There was no significant difference between sexes or regions in relation to having pets ($P > 0.05$).

Table 2. Demographic data of patient and control groups

	Patient group		Control group	
	Male	Female	Male	Female
Total (%)	348 (30.3)	801 (69.7)	172 (81.9)	38 (18.1)
Mean age $\pm$ SD (minimum-maximum)	40.4 $\pm$ 14.4 (15-91)	39.7 $\pm$ 12.9 (15-84)	42.7 $\pm$ 10.8 (24-73)	42.8 $\pm$ 12.2 (18-68)
Smoking status (%)				
Smoker	47 (13.5)	86 (10.7)	85 (49.4)	2 (5.3)
Ex-smoker	130 (37.4)	80 (10)	33 (19.2)	0
Nonsmoker	171 (49.1)	635 (79.3)	54 (31.4)	36 (94.7)
Location				
Ankara	124	335	73	10
Adana	60	128	16	2
Elaizig	78	153	32	14
Izmir	51	93	19	9
Samsun	35	92	32	3

Table 1. Geographic and meteorologic data of five cities in Turkey

City	Altitude (meters)	Relative humidity (%)		Temperature $^{\circ}$ C (daily mean)		Mean rainfall (mm)*
		07 am	14 pm	minimum	maximum	
Ankara	845	65	35	3.8	36.4	6.8
Adana	23	77	45	9.2	42.8	5.8
Elaizig	1100	45	25	4.0	37.8	2.7
Izmir	2	64	43	9.5	41.3	2.8
Samsun	2	74	75	9.0	32.6	12.5

* Mean rainfall was based on means for last 65 years in June. Mean relative humidity and daily temperature are given for June 1992 (11).

Table 3. Allergen spectra of atopic individuals in patient and control groups

	Patient group				Control group			
	Male (n=347)	%	Female (n=791)	%	Male (n=171)	%	Female (n=36)	%
Mites	100	28.8	250	31.6	34	19.9	7	19.4
Pollen	63	18.2	141	17.8	11	6.4	4	11.1
Cockroach	43	12.4	96	12.1	19	11.1	4	11.1
Dander	27	7.8	67	8.5	4	2.3	2	5.6
Mold	16	4.6	43	5.4	3	1.8	2	5.6

Table 4. Allergen spectra of atopic asthmatics in relation to place of residence

Allergen n		Ankara		Elazığ		Adana		Samsun		İzmir	
		M (123)	F (331)	M (78)	F (150)	M (60)	F (127)	M (35)	F (90)	M (51)	F (93)
Mites	%	17.1	23.3	18	22	43.3	44.1	42.9	60	47.6	32.3
Pollen	%	19.5	18.1	5.1	5.3	26.7	16.5	17.1	30	25.5	26.9
Cockroach	%	8.1	10.9	18	13.3	8.3	11.8	17.1	13.3	15.7	14
Dander	%	7.3	9.4	3.9	3.3	15	17.1	2.9	15.6	9.8	8.6
Mold	%	3.3	6.3	1.3	2.7	6.7	3.9	5.7	10	7.8	4.3
Dpt	%	17.1	21.8	18	20	41.7	42.5	42.9	58.9	41.2	29
Df	%	14.6	20.5	15.4	19.3	40	38.6	42.9	48.9	43.1	28
<i>Phleum pratense</i>	%	13	12.1	3.9	4	15	13.4	8.6	18.9	13.7	10.8
<i>Artemisia vulgaris</i>	%	11.4	10.6	3.9	3.3	13.3	3.9	2.9	18.9	9.8	12.9
<i>Parietaria officinalis</i>	%	7.3	8.8	1.3	2.7	6.7	1.6	2.9	18.9	7.8	7.5
<i>Betula verrucosa</i>	%	7.3	5.1	2.6	2.7	5	5.5	11.4	10	5.9	6.5
<i>Olea europaea</i>	%	6.5	5.1	—	1.3	11.7	7.9	2.9	11.1	21.6	7.5
Hazelnut	%	6.5	3.9	1.3	0.7	10	5.5	5.7	12.2	5.9	4.3
Cat	%	5.7	5.4	2.6	1.3	8.3	3.9	—	11.1	7.8	5.4
Dog	%	4.9	5.4	2.6	2.7	8.3	0.8	2.9	10	—	2.2
Horse	%	2.4	3.6	3.9	2	10	3.9	—	6.7	3.9	5.4
<i>Alternaria alternata</i>	%	2.4	3.9	—	1.3	1.7	2.4	5.7	5.6	5.9	2.2
<i>Aspergillus fumigatus</i>	%	2.4	3.3	1.3	2	3.3	1.6	2.9	6.7	5.9	2.2
<i>Cladosporium herbarum</i>	%	1.6	2.7	3.9	2	3.3	2.4	—	4.4	3.9	3.2

M: male; F: female.

SPT could not be performed in one male and 11 female patients, and one male and two female controls. The atopy rate, which was 42% in patients and 26.1% in controls, declined notably by age in both groups. Smoking did not affect the atopic status in either group. Allergen spectra of both BA and control groups, and allergen spectra of atopic patients in relation to different cities are shown in Tables 3 and 4, respectively. The most common allergen in all regions was house-dust mite (HDM). HDM

sensitivity was significantly more common at sea level (Samsun, İzmir, and Adana) than at high altitudes and in internal regions (Ankara and Elazığ) ($P < 0.05$). Pollen sensitivity in the BA group was significantly less frequent in Elazığ than in the other four cities ($P < 0.001$ for İzmir, Ankara, and Adana; $P < 0.01$ for Samsun). Timothy and mugwort were the pollens most frequently responsible for hypersensitivity in all cities but İzmir, which had *O. europaea* as the most frequent pollen. Because the con-

Table 5. Correlation of IgE with age, atopy, and smoking status*

	Patient group				Control group			
	Male		Female		Male		Female	
	n=218	CI	n=520	CI	n=125	CI	n=28	CI
Total	122.5 (150.9)	99.4	91.6 (104.4)	80.4	62.4 (81.2)	47.9	25.6 (47.7)	13.8
Age								
≤ 29	140.9 (219.2)	90.6	141 (186.1)	106.7	33.3 (99)	11.1	—	—
30–44	171.4 (239)	122.8	108.4 (131.7)	89.2	58.7 (86.1)	40	52 (138.9)	19.5
45–59	82.4 (115.5)	585.8	60 (77.4)	46.5	88.3 (137.4)	56.8	—	—
≥ 60	69.3 (139)	34.6	41.5 (61.3)	28	47.1 (119.9)	18.5	—	—
Smoking status								
Smoker	150 (297.7)	75.5	95.7 (149.3)	61.4	58.2 (83.7)	40.5	—	—
Ex-smoker	100.9 (142.7)	71.4	101.4 (150.9)	68.1	51.6 (94.3)	28.3	—	—
Nonsmoker	140.3 (183.8)	107	89.9 (103.9)	77.8	79 (133.1)	47	24 (45.2)	12.8
Atopy status								
Atopic	211.3 (160.5)	278.2	180.3 (214.2)	151.7	138.3 (240.4)	79.5	40.5 (102.2)	16
Nonatopic	86.5 (114.8)	65.2	53.7 (63.5)	45.4	47.9 (63.9)	35.9	15.5 (34)	7

* Numbers indicate geometric means with 95% confidence intervals (CI). Groups of less than 10 persons are not included in statistical analysis.

trol group was not large enough for comparison in each city separately, statistical analysis of control and patient groups was performed for the whole study group at once.

Total IgE levels were assessed in 891 persons (Table 5). Total IgE levels were significantly higher in men in both groups ($P < 0.05$ for both groups). IgE levels were significantly higher for both sexes in the patient group ($P < 0.001$). IgE levels of both atopic and nonatopic female patients were significantly higher than those of women in the control group ($P < 0.001$).

Discussion

Thorough clinical and laboratory evaluation forms the basis for successful treatment of BA. Anti-inflammatory therapy is the cornerstone of treatment; however, if the patient is sensitive to an allergen, avoidance should be given priority. Allergens to which asthmatic patients are sensitive vary greatly among countries and even different regions of the same country. Detection of atopy and allergen spectra by SPT has an important role in epidemiologic studies of BA. In Turkey, sensitivity to HDM was the most significant risk factor for patients with BA in all five cities. Temperature and humidity, as well as abundance of carpeted surfaces and textile clothing, and absence of a standard ventilation system, collectively favor infestation of mites indoors. When all these factors are combined, it is not surprising that atopic persons show a high percentage of mite sensitivity. Sensitivity to cockroach, which is one of the important indoor allergens attracting attention in the field of allergy nowadays, was detected in similar ranges in all regions.

Sensitivity to other allergens was variable among cities. The ratio of BA patients with sensitivity to pollens was significantly lower in Elazığ in eastern Turkey, which is 1100 meters above sea level and has a harsh climate and relatively scant herbal flora. In addition, its population is characterized by lower socioeconomic status and negligible immigration. Since *O. europaea* is cultivated in the Aegean region, it is the most common pollen allergen in İzmir, whereas timothy and mugwort are the most common in others. *O. europaea* is not planted in Elazığ and sensitivity to the olive tree is almost nonexistent there. Birch is rarely encountered in the eastern regions in the vicinity of the Caucasus (6). Hazelnut is plentiful on the northern coast of Turkey, which is one of the major growers of the world. Birch sensitivity is in the range of 2.6–11.4%, and hazelnut sensitivity 0.7–12.2% in all regions. There is cross-reactivity for sensitivity between hazelnut and birch, and this cross-reactivity might be responsible for the high ratio of sensitivity to birch (8). The fact that

similar ratios of sensitivity to birch were obtained in all regions except Elazığ, in which hazelnut is not planted, supports this explanation. Sensitivity to pet animals in the BA group was much lower than that reported in Western countries because keeping pets and contact in daily life with horses are rare in Turkey (4, 7).

Previous studies have shown a close relationship between asthma and level of total serum IgE (3). Total IgE levels of healthy adults have not previously been investigated in Turkey. For both patient and control groups, total IgE levels of men were significantly higher than those of women ($P < 0.05$ for both). There is an ongoing debate regarding the influence of sex on IgE levels (1, 9). A possible explanation derives from the fact that IgE levels are influenced by smoking; thus, men, who have higher smoking rates and possibly more frequent exposure to both occupational and nonoccupational allergens outdoors, may have higher IgE levels (14, 15). However, our study does not support the hypothesis that smoking affects total IgE levels. Total IgE levels of nonatopic control subjects were higher than those of a comparable population from Western countries (1, 9), but similar to those of neighboring countries (5).

In conclusion, the first epidemiologic study on allergic characteristics of BA in Turkey has revealed atopy as an important risk factor, and HDM is the major allergen of sensitivity in both patient and control groups. Presumably, detailed studies of allergic status in BA patients, together with ectoparasitologic and pollen investigations, will help to establish more realistic management guidelines.

Acknowledgments

This study was supported by grants from the Scientific and Technical Research Council of Turkey, Medical Sciences Research Grant Committee (grant no. TAG-0759). The authors thank Dr Reha Alpar for his assistance in statistical computations.

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