ORIGINAL ARTICLE

Extent and Burden of Allergic Diseases in Elementary Schoolchildren: A National Multicenter Study

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Abstract

Background: Scarcity of standardized, comparable data on allergic diseases in schoolchildren in Turkey requires further multicenter studies based on the use of objective tools in addition to parent-completed questionnaires to improve the validity and reliability of results.
Methods: Using International Study of Asthma and Allergies in Children (ISAAC) Phase II tools, elementary schoolchildren aged 9 to 11 years were surveyed in 5 city centers in different regions of Turkey.
Results: We surveyed 6963 children from 70 schools and found that 35% had had at least 1 symptom of allergic diseases in the past year. Based on parental reports, the overall prevalence rates for wheezing, rhinoconjunctivitis, and eczema in the past year were 15.8%, 23.5%, and 8.1%, respectively. The overall frequencies of atopy, flexural dermatitis, and bronchial hyperreactivity were 18.9%, 3.6%, and 24.2%, respectively. There were large variations in the prevalence of both symptoms and objective signs between study centers. Absence from school for at least 1 day was reported for 34.2% of children with a diagnosis of asthma or allergic rhinitis.
Conclusions: Approximately one third of elementary schoolchildren reported symptoms compatible with allergic diseases in the past year. The interregional differences in both symptoms and objective test results are possibly due to differences in environmental conditions. Unfortunately, serious problems are still encountered in the timely and proper diagnosis and treatment of allergic diseases.

Key words: Allergy. Asthma. Atopy. Childhood. Epidemiology. ISAAC. Prevalence.

Resumen

Antecedentes: La escasez de datos estandarizados y comparables sobre enfermedades alérgicas en escolares en Turquía requiere estudios multicéntricos adicionales basados en el uso de herramientas objetivas además de cuestionarios rellenados por los padres para mejorar la validez y fiabilidad de los resultados.
Métodos: Se estudió a niños de educación primaria de 9 a 11 años de edad utilizando herramientas de la fase II del estudio ISAAC (*International Study of Asthma and Allergies in Children*) en 5 centros urbanos de diferentes regiones de Turquía.
Resultados: Se encuestó a 6.963 niños de 70 escuelas y se observó que el 35% había presentado al menos 1 síntoma de enfermedad alérgica durante el último año. Según la información proporcionada por los padres, la prevalencia global de sibilancias, rinoconjuntivitis y eccema durante el último año fue del 15,8%, el 23,5% y el 8,1%, respectivamente. Las cifras correspondientes para atopia, dermatitis flexural e hiperreactividad bronquial fueron del 18,9%, el 3,6% y el 24,2%, respectivamente. Se observaron grandes variaciones en la prevalencia de los síntomas y los signos objetivos entre los centros de estudio. Se notificó absentismo escolar durante al menos 1 día en el 34,2% de los niños con diagnóstico de asma o rinitis alérgica.
Conclusiones: Aproximadamente una tercera parte de escolares de educación primaria habían presentado síntomas compatibles con enfermedad alérgica durante el último año. Las diferencias interregionales en los síntomas y los resultados de las pruebas objetivas probablemente se deben a diferencias en las condiciones ambientales. Desafortunadamente, queda mucho por hacer para garantizar un diagnóstico y un tratamiento a tiempo y adecuados de las enfermedades alérgicas.

Palabras clave: Alergia. Asma. Atopia. Infancia. Epidemiología. ISAAC. Prevalencia.

Introduction

Allergic diseases constitute an important public health problem given their current prevalence and socioeconomic burden [1, 2]. Epidemiologic data for allergic diseases are mainly based on questionnaire-based surveys about the prevalence and frequency of symptoms and the existence or not of a physician diagnosis [3]. Even with standardized questions, however, responses can vary greatly depending on the level of social awareness of allergic diseases and the availability and accessibility to both information and medical services.

With the development of the International Study of Asthma and Allergies in Childhood (ISAAC) Phase II modules, it became possible to determine the frequency of symptoms and to test for objective markers of asthma and allergy using pulmonary function tests (PFTs), bronchial hyperreactivity (BHR) measurements, and assessment of atopy and flexural dermatitis. The use of objective tools has improved the validity of results by minimizing detection bias due to variations in language, awareness, perception, and accessibility to health services. Validity and reliability have also been enhanced by supplementing standardized methods with these objective measures. About 30 ISAAC Phase II studies have been performed to date, mostly in developed countries, but few have included multiple centers within a country [4-6]. Multicenter studies within a country can provide novel information on prevalence, public burden, and risk factors for allergic diseases, enabling investigation of various confounding factors and effect modifiers that may vary across centers.

Using the ISAAC phase II methodology, this study aimed to investigate the frequency of symptoms of allergic diseases and potential risk factors and to evaluate possible associations between these in randomly selected elementary schoolchildren from 5 geographical areas of Turkey. This article also presents the extent and public burden of allergic diseases with an explanation of the survey methodology used.

Materials and Methods

This cross-sectional study was conducted using the ISAAC Phase II tools on a group of randomly selected schoolchildren from 5 city centers in different parts of Turkey (Van, Manisa, Ankara, Antalya, and Trabzon) (Figure 1) between September 15, 2005 and May 30, 2006. The study was not registered with the ISAAC study group as it was conducted after completion of the phase II studies.

Target Population

Turkey, with approximately 70 million citizens, is the second most populated country in Europe, with 40% of its population aged under 18 years. The geography and climate vary widely since Turkey is partially located in the Balkans, has a significant coastline with the Mediterranean and the Black Sea, and is also a Middle Eastern country. The mean annual income per person is about US $5000 and the mean duration of education is 6 years; internal migration is quite high [7].

The target population of our study comprised children from 5 cities located in 5 different geographical regions that are representative of the significant variations that characterize Turkey in terms of geographic, economic, climatic, educational, and lifestyle parameters and availability of health care facilities (Table 1). While Antalya is on the coastline of the Mediterranean, for example, Van sits on the banks of a lake at an altitude of 1727 meters. Prevalence of college graduates varies from 3.2% (Van) to 11% (Ankara). The study evaluated fifth-grade students attending public elementary schools in the center of 5 cities in different provinces.

Sample Size Calculation and Sample Selection

In accordance with the ISAAC II methodology (option B), the study aimed to enroll at least 1000 students from each city, to be recruited from at least 10 schools, with the aim of recruiting at least 100 children with reported wheezing over the last 12 months [8]. City-specific minimum sample sizes were calculated for α=.05, 1–ß=0.80, δ=6.9% (percentage of physician-diagnosed asthma cases recorded in the previous ISAAC study conducted in Turkey) [9], and σ=1.2 (Table 2). The number of students attending school did not always match the official numbers provided by the Ministry of National Education at the start of the academic year. In Ankara and Antalya, for example, the total number of fifth-grade students in the selected schools was slightly lower than the calculated sample size, but given the high completion rates, this did not significantly affect our data analyses.

Figure 1. Map of Turkey and study centers.

Table 1. Descriptive Characteristics of Study Centers

	Van	Manisa	Ankara	Antalya	Trabzon
Demographics (2007)					
Total population, No.	413 907	332 346	3 901 201	913 568	292 513
Male, %	50.6	51.6	49.8	50.2	49.7
Resident in city center, %	80.2	84.8	96.5	84.8	78.2
0-19 y, % of total population	50.3	31.1	30.2	31.8	31.3
Males aged 0-19 y, % of total population	51.5	51.6	51.3	51.4	51.3
10-14 y, % of total population	12.9	7.8	7.7	8.4	8.2
Males aged 10-14 y, % of total population	51.5	51.3	51.4	51.4	51.1
Females and children (2000)					
Total fertility rate, No. of births per woman	6	2.14	1.9	1.93	2.1
Infant death rate, No. of deaths per 1000 live births	61	41	36	32	31
Death rate below the age of 5 y (per 1000)	74	47	41	36	35
Status of housing (2000)					
Individuals per room, No.	2.5	1.2	0.9	1	1.3
Mean family size, No.	7.53	3.85	3.82	3.98	5.23
Health facilities per 100 000 individuals (2004)					
Specialist physicians, No.	30	61	172	82	45
Hospital beds, No.	147	239	379	156	274
General practitioners, No.	40	72	150	72	72
Dentists, No.	5	18	64	26	17
Pharmacists, No.	9	35	65	42	25
Allied health personnel (midwife-nurse-health technician), No.	133	248	397	262	298
Educational status (2000)					
College graduates in population, %	3.2	5.4	11.7	9.2	9.0
College graduates among males, %	4.4	6.4	13.3	10.6	10.8
College graduates among females, %	1.9	4.3	10.1	7.7	7.1
Air pollution, climate, and geography (2005)					
Mean particulate matter (smoke), $\mu g/m^3$ (min-max)	No data	36 (2-407)	50(10-367)	54 (18-171)	51 (27-218)
Mean SO_2, $\mu g/m^3$ (min-max)	No data	64 (8-482)	30 (8-170)	40 (17-1139)	44 (22-202)
Altitude, m	1727	78	850	0	20
Average relative humidity in year, %	64	62.8	61.7	59.6	71.5
Average temperature, ºC	9.9	17.2	12.4	18.7	15.2
Rainy days, mean No. per month	7	7	9	6	13
Sunny days, mean No. per month	7	8	7	12	7
Mean air pressure, Mb	832.1	1006.1	913.6	1005.4	1012.2
Economic indices					
Proportion of gross national income, % (2001)[a]	0.5	2.1	7.6	2.6	1.0
Gross income per individual by current prices, US dollar (2001)	859	2459	2752	2193	1506
Gross income per individual by purchase potential, US dollar (2001)	2455	7024	7861	6266	4302
Personal cars, No. per 1000 individuals (2006)	19	76	179	113	40
Electric consumption per individual, KWh (2006)	330	1770	1669	1873	711

[a] Proportion of Gross National Income (GNI) contributed by city.

Table 2. Sample Size and Completion Rates by Study Center

	Van	Manisa	Ankara	Antalya	Trabzon	Total
Fifth-grade students, No.	9444	4178	58 438	14287	3955	90 302
Target minimum sample size, No.						
Questionnaires	1450	1215	1665	1530	1196	6801
Distributed, No.	1450	1488	1557	1504	1624	7623
Collected, No. (% of total distributed)	1447 (99.8)	1462 (98.3)	1371 (88.1)	1437 (95.6)	1584 (97.5)	7301 (95.8)
Fully completed, No. (% of total distributed)	1354 (93.3)	1405 (94.4)	1354 (87.0)	1403 (93.3)	1447 (89.1)	6963 (91.3)
Physical examinations, No. (%)[a]	1198 (82.6)	1239 (83.3)	1167 (75.0)	1203 (80.0)	1216 (74.9)	6023 (79.0)
Skin prick tests, No. (%)[a]	1196 (82.5)	1275 (85.7)	1178 (75.7)	1264 (84.0)	1221 (75.2)	6134 (80.5)
Current wheezing, No. of positive results	296	203	199	225	198	1121
Bronchial provocation tests (No. of positive vs negative current wheezing results)	92 vs 102	94 vs 97	98 vs 93	99 vs 98	100 vs 100	483 vs 490

[a] Percentage of total No. of students approached for the study.

The school lists were obtained from the Head of National Education in each city and a representative sample of fifth-grade students in these cities was selected using a cluster sampling method from the Turkish Institute of Statistics, where clusters were individual schools.

Questionnaire

All the questions from the ISAAC Phase II questionnaire modules were included in the questionnaire [8]. The previously used translation of the questionnaire was used, with visual improvements and minor changes in question order [9]. The questionnaire was pilot tested on a convenience sample of school-aged children in Ankara preceding the full survey.

The questionnaires were distributed to all fifth-grade students in the selected schools. For students absent on the day of distribution, it was ensured that these students also received their questionnaires. All the questionnaires were sent to the parents and completed at home preferably by the mother or father.

Asthma symptoms were investigated based on a positive answer to the question: "Has your child had wheezing or whistling in the chest in the past 12 months?" Current rhinoconjunctivitis symptoms were evaluated as positive if both of the following questions were answered as 'yes': "In the past 12 months, has your child had a problem with sneezing or a runny or blocked nose when you (he/she) did not have a cold or the flu?", "In the past 12 months, has this nose problem been accompanied by itchy watery eyes?". Similarly, symptoms for current eczema were studied on the basis of positive answers to 2 questions: "Has your child had this itchy rash at any time in the past 12 months?" and, "Has this itchy rash at any time affected any of the following places: folds of the elbows; behind the knees; in front of the ankles; under the buttocks; or around the neck, ears, or eyes."

Skin Prick Tests

All participants underwent skin prick testing (SPT) for *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Alternaria alternata*, cat dander, grass mix (*Phleum pratense*, *Poa pratensis*, *Dactylis glomerata*, *Lolium perenne*, *Festuca pratensis*, and *Avena eliator*), tree mix (*Betula verrucosa*, *Alnus glutinosa*, and *Corylus avellena*), *Olea europea*, horse, *Blatella germanica*, histamine, and negative controls [8]. These tests were performed using a multi-prick test device (Quantitest, Panatrex Inc, Placentia, California, USA) on the volar surface of both forearms, with results recorded after 15 minutes. Results were considered positive when the mean wheal diameter was at least 3 mm larger than that produced by the control. Atopy was defined as the presence of at least 1 positive skin test response.

Flexural Dermatitis

Examination for flexural dermatitis was performed according to an illustrated manual, and the presence of dermatitis signs were recorded for the following areas: around the eyes, sides/front of the neck, ankles and elbows, and antecubital and popliteal regions [8].

Laboratory Tests

According to the protocol, laboratory tests were performed for 2 independent groups in each city, ie, 100 cases and 100 controls (children with and without wheezing in the last 12 months, respectively). Cases and controls were randomly

selected from among the study participants and identified through the standard questionnaires. Laboratory tests included PFTs, BHR measurement with hypertonic saline (4.5% NaCl), complete blood count, and serum total immunoglobulin E (IgE). The bronchial provocation test was conducted with hypertonic saline using a De Vilbiss ultrasonic nebulizer (De Vilbiss, Langen, Germany) and the ZAN100 Spirometry System (nSpire Health, Longmont, Colorado, USA) in accordance with the recommended method [8].

Complete blood counts were performed using an automatic complete blood counter (LH 500 Hematology Analyzer, Beckman Coulter, California, USA) in the central laboratories of the 5 participating university hospitals in the respective cities.

Sera obtained at each center were frozen at –80ºC and subsequently studied using the Pharmacia ImmunoCAP assay (Phadia AB, Uppsala, Sweden) in the central laboratory in Ankara.

Ethical Issues

Permissions were obtained from the ethics committees of the Hacettepe University Medical School, the Turkish Ministry of Health, and the central and provincial directors of the Ministry of Education and city governors. Written parental and student consent was obtained separately for each participant.

The Study Team

The core study team consisted of a pediatric allergy specialist, a pediatric allergy fellow, and 2 PFT technicians. This core team was actively involved in all the activities in the 5 centers. In addition, 3 nurses, 1 pediatrician, 2 senior medical students, 1 allied health professional, and 1 driver participated in each of the provincial study teams. In order to improve SPT repeatability and consistency, all the participating nurses were trained in advance on the objectives and content of the survey and the SPT method to be used. All SPTs and PFTs were evaluated by a pediatric allergy fellow and two PFT technicians, respectively.

Statistical Analysis

All analyses were conducted separately for each city, and totals were presented as appropriate. Prevalence was presented as percentages per city. The prevalence values for specific allergic diseases in the results section are given as overall figures, with minimum and maximum values observed in individual cities shown in parentheses. A *P* value was provided to indicate the statistical significance of geographic variations. Analyses were performed using the SPSS statistical software package (version 15) (SPSS Inc. Chicago, Illinois, USA). The complex samples module was used to obtain weighted estimates and to correct for the cluster sampling design used. Weights were calculated as inverses of the sampling fractions.

Results

A total of 70 schools and 244 classes were visited; 7623 questionnaires were distributed, 7301 collected, and 6963 included in the analyses. The main reasons for excluding questionnaires (n=338) were because they were missing data on allergic disease symptoms or because the parents had completed the questionnaires for children with allergic symptoms other than the student to whom the questionnaire had been sent. The overall rate of participation was 91.3% (range, 87.0%-94.4%). Flexural dermatitis examination and SPT were successfully performed in 79.0% (74.9%-83.3%) and 80.5% (75.2%-85.7%) of participants, respectively. PFTs and BHR measurements were completed in 97.3% of participants (Table 2).

The frequency of children with ever wheezing per city ranged from 31% to 37.9% (*P*=.028); the corresponding ranges were 14.1% to 22.6% for current wheezing (*P*=.009) and 1.8% to 6.3% for physician-diagnosed asthma (*P*=.001). There was also a significant variation in the proportion of patients with a physician diagnosis of at least 1 of the 3 conditions (asthma, asthmatic bronchitis, and/or allergic bronchitis) (9.1%-15.0%, *P*=.001) (Table 3).

The frequency of ever rhinitis varied between 47.6% and 65.3% (*P*=.001). The figures for current rhinoconjunctivitis ranged from 19.9% to 35% (*P*=.001) and for physician-diagnosed allergic rhinitis from 11.8% to 36.4% (*P*=.001) (Table 3).

The frequency of ever eczema was reported by 14.7% to 27.2% (*P*=.001) and current eczema by 6.5% to 13.7% (*P*=.001). Eczema diagnosed by physician was reported by only 2.1% to 4.5% of participants (*P*=.022). Flexural dermatitis was observed in 1.0% to 9.9%, with rates varying significantly between centers (*P*=.001) (Table 3).

Atopy was observed in 16.3% to 33.3% of participants (*P*=.002) and significant differences between centers were noted for sensitivity to all allergens except grass. Serum total IgE levels (94.5-282.0 kU/L, *P*>.05) and eosinophil percentages (2.2%-3.7%, *P*>.05) also varied significantly between centers.

BHR ranged between 15.5% and 32.4% across cities (*P*=.025) (Table 3). The prevalence of BHR among students without current wheezing, with current wheezing, and with frequent wheezing was 22.5%, 33.1% and 34.6%, respectively.

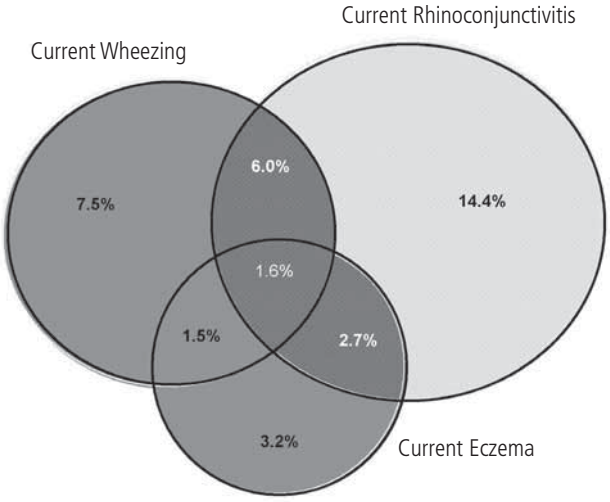
Overall, 60% of the children had experienced at least 1 symptom of wheezing, rhinitis, or eczema in their lifetime and 35% had had at least 1 symptom of wheezing, rhinoconjunctivitis, and/or eczema in the last year. Atopy was present in 20.5%, 19.8%, and 20.4% of those that reported symptoms of current wheezing, current rhinoconjunctivitis, and current eczema, respectively.

The association between reported symptoms (Figure 2) and atopy was evaluated in 81.3% of participants for whom full questionnaire data and SPT results were available. Of these participants, 35.4% had current symptoms corresponding to at least 1 allergic disease. A single disease accounted for these symptoms in 70.3% of cases; the corresponding figures for 2 and 3 diseases were 25.3% and 4.4%, respectively. Interestingly, atopy was observed in 22.3% and 18.3% of children with and without symptoms.

Table 3. Demographic Characteristics, Parent-Reported Symptoms, and Physical Examination and Laboratory Findings by Study Center

	Van	Manisa	Ankara	Antalya	Trabzon	*P*[a]	Total
Boys[b]	54.2±2.8	50.4±1.1	50.3±1.1	51.5±1.3	50.3±1.3	.300	50.9±1.0
Age, y[c]	10.8±0.1	10.7±0.1	10.7±0.0	10.9±0.0	10.9±0.0	>.05	10.8±0.0
Respiratory system							
Lifetime wheezing[b]	31.0±1.7	36.1±0.9	34.1±1.3	37.9±0.9	35.4±0.7	.028	34.5±0.9
Current wheezing[b]	22.6±1.4	15.0±2.0	14.7±1.3	16.4±1.4	14.1±0.6	.009	15.8±1.0
≥4 wheezing episodes in last 12 mo[b]	7.3±0.9	4.2±1.1	3.1±0.5	2.6±0.6	3.7±0.3	.001	3.6±0.4
Awakening due to wheeze ≥1 night per week in last 12 mo[b]	16.8±1.0	13.5±1.5	10.1±1.1	11.3±2.2	6.3±0.8	<.001	11.3±0.9
Wheeze-limiting speech in last 12 mo[b]	30.6±1.7	27.3±2.2	28.1±1.5	26.5±2.1	26.2±2.3	.524	28.1±0.9
Current wheezing with exercise[b]	21.1±1.6	13.8±2.4	11.5±1.6	11.6±2.0	8.7±0.6	.011	12.5±1.1
Lifetime asthma diagnosed by physician[b]	5.0±0.62	3.9±0.6	1.8±0.2	3.3±0.5	6.3±0.9	<.001	2.7±0.2
Lifetime asthma, asthma bronchitis, or allergic bronchitis diagnosed by physician[b]	13.0±1.0	13.0±1.7	9.1±0.8	15.0±0.8	11.8±1.0	<.001	10.7±0.5
Use of medication for asthma in last 12 mo[b]	13.3±1.3	11.2±1.7	6.9±1.1	8.9±1.0	8.4±0.7	.016	8.1±0.8
Rhinitis							
Lifetime rhinitis[b]	65.3±2.4	54.7±3.5	50.3±1.9	48.2±2.4	47.6±2.0	.001	51.6±1.3
Current rhinitis[b]	55.7±2.4	46.0±3.6	42.2±1.6	41.4±2.2	39.3±1.7	.001	43.5±1.2
Current rhinoconjunctivitis[b]	35.0±1.6	25.3±3.1	22.0±1.7	22.6±1.5	19.9±1.5	<.001	23.5±1.1
Considerable activity disturbance due to nose symptoms in last 12 mo[b]	33.4±1.6	31.6±2.5	30.9±1.3	26.0±1.7	30.2±1.5	.041	30.1±0.9
Lifetime allergic rhinitis diagnosed by a physician[b]	36.4±2.3	18.4±2.2	14.8±1.1	14.3±1.7	11.8±0.8	<.001	16.9±1.0
Use of treatments for allergic rhinitis in last 12 mo[b]	13.5±1.2	15.7±0.9	16.4±1.5	21.6±1.9	22.7±0.9	.011	17.2±1.1
Eczema							
Lifetime eczema[b]	27.2±1.8	18.1±1.8	16.1±1.1	14.7±1.3	15.0±1.1	<.001	17.1±0.7
Current eczema[b]	13.7±1.2	9.6±1.1	7.6±0.7	6.5±0.6	7.1±0.5	<.001	8.1±0.5
Lifetime eczema diagnosed by a physician[b]	4.5±0.8	2.6±0.6	2.1±0.4	3.3±0.5	3.7±0.6	.022	2.61±0.3
Loss of sleep due to eczema ≥1 night a week in last 12 mo[b]	14.5±2.1	11.2±2.1	5.1±0.9	4.8±1.3	4.3±0.9	<.001	7.1±0.6
Use of medication for eczema in last 12 mo[b]	12.3±1.1	9.2±1.3	7.3±0.8	9.4±0.9	9.5±0.6	<.001	8.3±0.6
Physical examination							
Flexural dermatitis[b]	9.9±1.2	1.0±0.4	3.0±0.6	1.8±0.5	7.8±2.4	<.001	3.6±0.5
Pulmonary Function Test-Laboratory Findings							
Bronchial hyperreactivity[b]	32.4±4.9	18.1±2.8	15.5±3.1	27.3±3.6	27.7±4.4	.025	24.2±1.9
Serum total IgE (kU/L)[c,d]	282.0±31.1	196.5±37.1	94.5±16.2	132.4±23.2	118.5±20.8	<.05	165.7±10.9
Eosinophil count, %[c,d]	3.7±0.2	3.7±0.3	2.2±0.2	3.3±0.2	3.1±0.6	<.05	3.1±0.1
Atopy							
≥1 positive reaction[b]	19.8±2.5	18.1±1.9	16.3±1.7	25.0±2.1	33.3±2.4	.002	18.9±1.2
Pollens[b]	5.4±1.0	8.5±1.4	6.4±1.0	7.9±1.1	10.2±1.5	.259	6.8±0.7
Gramineae family[b]	4.7±0.9	5.2±1.1	5.1±0.9	5.1±0.8	7.6±1.0	.588	5.2±0.6
House dust mites[b]	7.3±1.3	4.6±0.4	4.6±0.7	13.8±2.4	19.5±1.6	<.001	7.0±0.7
Horse[b]	4.4±0.5	3.2±0.6	1.8±0.4	3.1±0.6	3.5±0.9	.010	2.4±0.3
Cat[b]	2.1±0.5	4.1±1.2	2.4±0.4	5.8±0.8	2.8±0.5	<001	3.0±0.3
Alternaria[b]	0.5±0.2	0.6±0.2	0.6±0.2	0.9±0.3	0.7±0.3	.622	0.6±0.1

Abbreviations: BHR, bronchial hyperreactivity; HDM, house dust mites; Ig, immunoglobulin.
[a] Statistical significance was set at <.05 based on comparisons of the 95% confidence intervals.
[b] Center-specific prevalence presented as mean±SEM.
[c] Center-specific mean±SEM.
[d] Exact *P* value not calculated.



No symptoms 64.6%
At least 1 symptom 35.4%
Atopy in patients with no symptoms 18.3%
Atopy in patients with at least 1 symptom 20.3%

Figure 2. The relationship between the frequencies of symptoms of asthma, rhinoconjunctivitis, and eczema (Calculations were performed on 5664 individuals with a complete set of data [81.3% of total sample]).

The Burden of Allergic Disease

Physician-diagnosed asthma was reported for 13.2% of participants with 4 or more wheezing episodes, for 7.2% of those with at least 1 nocturnal awakening due to wheeze per week, and for 7.8% of those with exercise-induced wheezing upon exercise. Of the children with physician-diagnosed asthma, 58% reported current wheezing, 14.4% at least 1 nocturnal awakening due to wheeze per week, 56.9% speech limitation due to wheezing, and 37.3% exercise-induced wheezing. Furthermore, school absenteeism and/or current hospitalization were reported in 31.6% of these children.

Of the children that were reported to have current rhinoconjunctivitis symptoms, 39.7% had a diagnosis of rhinitis, approximately one third needed to be seen by a physician, 28.2% needed treatment, and 42.2% and 23.9%, respectively, were reported to have moderate to severe activity disturbance and school absenteeism for at least 1 day due to rhinitis.

Only 36.3% of those with current eczema had been admitted to a health institution over the last year, and of these, 11.4% had been diagnosed with atopic eczema. About 71% of those with symptoms were not using drugs or moisturizers and 13.6% had reported loss of sleep due to nighttime eczema at least once a week.

Discussion

Standardized Methodology and Generalizability of Study Results

For international comparison purposes, the study adhered to the ISAAC Phase II method, which has internationally proven validity, safety, and reproducibility [10]. The length of the questionnaire and the need for invasive exams (PFTs, SPTs, blood sampling, and BHR measurements) are the major limitations precluding high participation rates in such studies. In previous ISAAC Phase II studies, the average rates for response to questionnaires, SPTs, and physical examination were reported as 83%, 67%, and 62%, respectively [11,12]. In the present study, they were 93.3%, 84%, and 80%. These completion rates imply high generalizability of the study results for fifth-grade students.

Frequency of Allergic Diseases and Regional Variations

Allergic diseases, particularly asthma, are the most commonly observed chronic diseases in childhood. It has been reported that between 40% and 60% of 13- to 14-year-old children in English-speaking countries have allergic diseases and that one third of children in Europe are atopic [2,13].

In this multicenter cross-sectional study of students aged 10 and 11 years in 5 Turkish cities, 35% of the children were reported to have had at least 1 symptom of allergic disease in the past year. Based on parental reports, the overall (weighted) prevalence of lifetime wheezing, rhinitis, and eczema symptoms was 34.5%, 51.6% and 17.1%, respectively. The corresponding rates for wheezing, rhinoconjunctivitis, and eczema in the past year were 15.8%, 23.5%, and 8.1%, respectively, and the overall frequency of atopy, flexural dermatitis, and BHR were 18.9%, 3.6%, and 24.2%, respectively. Although a national surveillance figure for chronic childhood diseases is lacking in Turkey, our results suggest that allergic diseases are also likely to be among the most common chronic diseases of childhood in our setting.

It should be emphasized that the 5 cities selected represent different geographical regions known to have different climates and levels of personal and health care facility-related characteristics. As expected a priori, differences in both subjectively reported symptoms and objectively measured variables were statistically significant across study centers, with an overall underdiagnosis of allergic diseases. The large variation in the prevalence of both symptoms and objective signs of allergic disease is one of the most important findings of the ISAAC studies [4,14] and indicates that environmental factors are critical for the occurrence of allergic disease. Several environmental factors such as climate, geographic conditions, economic status, vaccination, diet, and environmental allergens have been shown to be associated with frequencies of allergic diseases, yet none explain the substantial proportion of variation in these diseases [15-17]. In other words, no risk factors have been identified that could be generalized worldwide. Future analyses should examine associations with environmental variables such as physical and social environmental factors and availability and accessibility to health care services.

Economic Burden

Allergic diseases place a huge economic burden on health care systems in Europe and North America [18,19]. A detailed estimation of the direct costs of such diseases was beyond the scope of our study. However, on the basis of reported frequencies and cost-related data [7,20,21], it can be estimated that asthma and allergic rhinitis represent an annual cost of US $1030 million and $80 million, respectively, for children aged 10 to 14 years.

Underdiagnosis and Undertreatment

We noted that about 13% of patients who had had at least 4 episodes of asthma in the past year had been diagnosed with asthma and about 55% of those had persistent symptoms (≥4 episodes of wheezing/year and at least 1 nighttime awakening/week due to wheezing or exercise-induced dyspnea). Moreover, 34.2% of children diagnosed with asthma or rhinoconjunctivitis were reportedly absent from school for at least 1 day. Similar conditions were observed for allergic rhinitis and current eczema. These results indicate serious shortcomings with regards to the diagnosis and control of allergic disease in children [22-24].

Although more than 95% of the population in Turkey and Europe have access to the main medications used in asthma and allergic rhinitis, the very low rates of diagnosis and disease control suggest the presence of other contributory factors. A lack of awareness of symptoms by both patients and parents and inappropriate diagnostic and treatment habits among physicians, even if occasional, might hinder the management of allergic diseases [22,25,26]. Although poorly controlled asthma is associated with a high risk of morbidity and mortality, asthma-related deaths are potentially preventable [27,28]. Awareness campaigns aimed at both physicians and patients should, thus, be implemented to improve the diagnosis and treatment of allergic diseases. Furthermore, health institutions should be properly structured to provide appropriate treatment given the frequency and burden of these diseases.

Strengths and Limitations of This Study

One of the main strengths of this study was its ability to maximize the reliability of results by using the same core team of health professionals for the survey and tests in all the centers. A disadvantage of this design was that it prevented the study from being performed simultaneously in all the centers, possibly resulting in, at least partially, variations in the frequency of allergic rhinoconjunctivitis due to the seasonal influence on answers to questions on allergic rhinitis and BHR [29]. However, if different people had performed the studies, problems related to interpersonal standardization of PFTs and SPTs might have arisen. Another advantage was the remarkably high completion rates.

The nonrandom selection of the study centers limits the generalizability of the study results to all Turkish schoolchildren aged 10 to 11 years. Nevertheless, such a purposeful selection of cities with different geographic, climatic, sociodemographic, economic, and lifestyle characteristics enabled researchers to evaluate a heterogeneous group of children and obtain information on many potential confounders to help to improve the internal validity of results and allow the advanced modeling of allergic diseases in the future, whilst increasing study feasibility.

Conclusions

Allergic diseases are observed quite commonly, and approximately 35% of children have been influenced by allergic disease over the past year. There are inter-regional differences in the frequencies of both symptoms and objective results, possibly resulting from differences (physical, biological, social, medical) in environmental conditions. Serious problems are still encountered in the timely and proper diagnosis and treatment of allergic diseases, which pose quite a public burden. Health policy makers and practitioners should tailor health care services to fit needs in this area and take an active role in devising educational and informational campaigns for both the public and physicians, with an ultimate goal of improving awareness of allergic diseases, their timely and proper diagnosis, and appropriate control.

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