

Time trends in the prevalence of asthma and allergy among 6–7-year-old children. Results from ISAAC phase I and III studies in Kaunas, Lithuania

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Key words: asthma; rhinitis; eczema; children; International Study of Asthma and Allergy in Childhood.

Summary. *Objective.* To assess the changes in the prevalence of asthma and allergy in 6–7-year-old schoolchildren in Kaunas, Lithuania, using the International Study of Asthma and Allergy in Childhood (ISAAC) core questionnaire.

Material and methods. Two cross-sectional surveys (1994/1995–2001/2002) according to the ISAAC protocol were carried out. Lithuanian version of the ISAAC core questionnaire was completed by parents randomly selected from Kaunas primary schools. A school-based sample of 1879 participants in the 1994/1995 survey and 2772 participants in the 2001/2002 survey was study population.

Results. The response rates in 1994 and 2002 were 93.95% and 92.4%, respectively. There is a tendency towards an increase in the prevalence of current symptoms and diagnoses for all three conditions, but it was more pronounced in boys. Significant increases in the prevalence of asthma (0.9% vs 2.6%), allergic rhinitis (1.4% vs 2.4%), and atopic dermatitis (1.4% vs 3.5%) were observed comparing two surveys. Still a lot of allergic diseases remain undiagnosed.

Conclusions. Our study shows that the prevalence of symptoms of asthma, allergic rhinitis, and atopic dermatitis is increasing, reflecting the changes in morbidity from these conditions in our country.

Introduction

The prevalence of allergic diseases in children has been increasing in the world over the past few decades (1). Atopy (allergy) is described as “a personal or familiar tendency to produce immunoglobulin E antibodies in response to low doses of allergen, usually proteins, and as a consequence, to develop typical symptoms such as asthma, allergic rhinitis, or atopic dermatitis” (2).

Among the broad spectrum of allergic diseases, asthma (A) is the most prevalent, dangerous, and life-threatening disease. According to World Health Organization (WHO) estimates, 300 million people suffer from asthma, and 255 000 people died of asthma in 2005 (3). Asthma is the most common chronic disease among children. The prevalence of asthma is increasing in all age groups but especially among children younger than 18 years. It is estimated that there may be an additional 100 million people with asthma by 2025 (4). The prevalence of asthma in different countries varies from 1.2% to 32.2% and depends on age, sex, race, and place of living (5). One of the defining

features of asthma as a disease is its early age of onset. Majority of cases of all childhood asthma (80% to 90%) is diagnosed by the age of 6 years (6). Prevalence of asthma is increasing, with concomitant increases in morbidity, economic costs, and in some countries, mortality. It has a significant impact on the quality of life. Often restriction of activities, interrupted sleep, disturbed routines, increased stress, and poor school performance are present. Poorly controlled moderate-to-severe persistent asthma can be associated with some degree of growth retardation. Asthma can and has an impact on the child's physical health, social and emotional health and has a significant economic impact on the family's finances and the national health care budget (7, 8). Approximately 15 000 children suffer from asthma in Lithuania, and around 10% of them have disability (9).

Allergic rhinitis (AR) is a very common chronic condition in both the adult and pediatric populations, affecting 10 to 30% of adults and 20 to 40% of children. Studies have shown that children with allergic rhinitis are more likely to exhibit shyness, depression,

anxiety, and fearfulness than their peers, and that the resulting sleep disturbances may have a significant negative effect on both their school performance and self-esteem. Approximately half of the patients with allergic rhinitis experience symptoms for more than 4 months each year, and 20% are symptomatic for at least 9 months of the year. In addition to the symptoms of rhinorrhea, nasal congestion, pruritus, postnasal drip, and sneezing, many allergic rhinitis patients also experience headache and fatigue. Chronic nasal obstruction can cause severe complications in children, with excessive mouth breathing resulting in such facial abnormalities as increased facial length, high arched palate, and dental malocclusions. Allergic rhinitis is also associated with conjunctivitis, loss of olfaction and taste, sleep apnea, and an increased frequency of asthma. Two common medical conditions – otitis media and sinusitis – often result from the obstruction of the eustachian tube and sinus ostia (10). From 2001 to 2003, the incidence of allergic rhinitis among 10–14-year-old children has doubled in Lithuania (9).

Atopic dermatitis (AD) is estimated to affect 15–20% of the childhood population, and there is considerable evidence that the prevalence is increasing. The prevalence is believed to be highest in young children: in 60% of affected individuals, onset is in the first year of life and in 85% – within the first 5 years. Children affected with AD experience itch, sleep loss, bleeding from the skin, and interference with nearly all aspects of daily life. This condition is frequently undertreated and dismissed as a nuisance, and it can have a large social/economical and financial effect on the child and family. In general, the clinical signs of AD predate the development of asthma and allergic rhinitis, suggesting that AD is an “entry point” for subsequent allergic disease (11). WHO and ARIA concluded that more and more children and adults are affected by more than one allergic disorder (12).

There is a wide consensus that asthma and allergies are witnessing a rising trend among children and adults worldwide especially in the Western societies. Changes in the prevalence of asthma and allergic diseases were related to environmental factors, as the time period was too short for the occurrence of a genetic change that would influence the prevalence of a disease. Asthma and allergies rank high on the public health agenda in many countries, highlighting the need for continuous monitoring and assessment of the dynamics of these disorders and factors that influence their trends (3, 7, 8). The International Study of Asth-

ma and Allergies in Childhood (ISAAC) is one of the pioneer and most comprehensive efforts aiming at the creation of a reliable map on the international trends in asthma and allergies that will foster better understanding of their patterns as well as hint towards possible etiological factors. In brief, it is a three-phase multi-centre, multi-national project, with phases I and III involving the conduction of identical surveys at least 5 years apart to look at the spread and time trends in childhood asthma and allergies worldwide (13). Our study is the part of the ISAAC study showing the time trends in symptoms of asthma, allergic rhinitis, and atopic dermatitis (eczema) based on data collected from phase I (1994/1995) and phase III (2001/2002) in Kaunas, Lithuania.

Material and methods

The aim of the present study was to provide a detailed analysis of the prevalence and severity of self-reported symptoms and diagnoses of asthma, allergic rhinitis, and atopic eczema in 6–7-year-old children, making comparisons between boys and girls and assessing the extent of underdiagnosis of asthma, and to compare the prevalence of severe and frequent symptoms of asthma with those observed in other countries. The ISAAC standardized written questionnaire was used to identify symptoms of asthma, allergic rhinitis, and atopic eczema. The study design and data quality assurance followed the ISAAC protocol in all aspects, including the double entry of data and translation guidelines. The English version was translated into Lithuanian by one translator, and this was translated back into English by another translator. The original English and back translation versions were reviewed, and any differences between them were eliminated. The questionnaires were completed by parents of the 6–7-year-old children. Data were collected and entered according to the ISAAC protocol and were analyzed using the SPSS package for Windows version 9.0. Prevalence rates were calculated by dividing the number of positive responses to each question by the number of completed questionnaires.

Methods of the worldwide ISAAC project have been described in details elsewhere (14). Repeated cross-sectional epidemiological study was performed in 1994–1995 and 2001–2002 following the ISAAC protocol. Both surveys were conducted in the same population of children, randomly selected from the same primary schools in Kaunas. In the first survey, 1879 6–7-year-old children (965 girls and 914 boys) were examined, and in the second survey – 2772 children (1 376 girls and 1 396 boys). Response rate was more than 90% in both surveys (Table 1). The study

Table 1. Descriptive statistics of the study population

Survey	6–7-year-old children						Response rate (%)
	boys		girls		total		
	n	%	n	%	n	%	
1994–1995	914	48.6	965	51.4	1879	100	93.95
2001–2002	1396	50.3	1376	49.7	2772	100	92.4

was carried out having received the written consent form from the Ethics Committee of Kaunas Region. Identical ISAAC core questionnaire in Lithuanian, which had been previously translated, was used in both studies.

Data analysis

Statistical Package for the Social Sciences (SPSS) for Windows computer package was used for data analysis. Differences between proportions of groups were compared using χ^2 test. For 2×2 tables, where an expected cell was less than 5, Fisher exact test was used. The differences were considered statistically significant when P was <0.05; very significant, when P was <0.01; and extremely significant, when P was <0.001. Missing or inconsistent responses were excluded.

Results

The results of time trends in the prevalence of asthma, allergic rhinitis, and atopic dermatitis in 6–7-year-old children are shown in Table 2. The prevalence of current asthma symptoms such as wheeze (4.6% vs 6.6%), night cough (3.2% vs 8.8%), and exercise-induced wheezing (1.8% vs 3.2%) increased significantly. The prevalence of severe asthma symptoms (sleep disturbance caused by wheezing and speech-limiting wheezing) did not differ significantly comparing the surveys. The prevalence of lifetime asthma diagnosis (0.9% vs 2.6%) increased significantly in 2001–2002. In both surveys, a significantly higher proportion of boys, comparing to girls, answered positively to the questions about “wheeze ever” and “wheeze in past year” ($P<0.05$). Boys had lifetime asthma diagnosis more frequently, but significant differences ($P<0.01$) were found only in the second survey. Seven years apart, the prevalence of night cough significantly increased in both boys and girls, the prevalence of exercise-induced wheezing – only in boys, and the prevalence of wheezing in the past 12 months – only in girls. The prevalence of asthma significantly increased for both boys and girls.

In 6–7-year-old children, the prevalence of “nose problems at any time in the past” has significantly increased. However, no significant changes in the prevalence of allergic rhinitis symptoms in the past 12 months were found. About 10% of the children who had allergic rhinitis symptoms in the past 12 months reported having a negative interference with daily activities, whereas the prevalence of diagnosed allergic rhinitis increased significantly.

In the second survey, the prevalence of allergic rhinitis symptoms (nose problems at any time in the past, interference with daily activities in the past 12 months) was significantly higher in boys than girls. The prevalence of diagnosed allergic rhinitis was significantly higher in boys than girls in both surveys. In the second survey, the prevalence of “nose problems at any time in the past” increased significantly only in boys, whereas the prevalence of “nose problems interference with daily activities” decreased significantly in girls. The changes in the prevalence of diagnosed allergic rhinitis increased, when compared the two surveys, between years in both boys and girls, but the differences were not significant.

Comparing the surveys, the prevalence of atopic dermatitis symptoms (itchy rash for at least 6 months, itchy rash in the past 12 months, itchy rash affecting typical places) slightly increased, but only prevalence of itchy rash in the past 12 months increased significantly. In the second survey, more children had itchy rash cleared in the past 12 months, and the difference was significant. The prevalence of atopic dermatitis increased significantly as well (from 1.4% to 3.5%). Comparing the surveys, the prevalence of atopic dermatitis symptoms in the past 12 months increased in both boys and girls, but significant changes were found only in boys. The prevalence of diagnosed atopic dermatitis significantly increased in both boys and girls. In both surveys, no significant differences in the prevalence of symptoms and diagnosed atopic dermatitis between boys and girls were found.

Indices related to lifetime diagnosis (ever asthma, ever allergic rhinitis, ever atopic dermatitis) increased

Table 2. Time trends in the prevalence (%) of asthma, allergic rhinitis, atopic dermatitis, and their symptoms in 6–7-year-old children, 1994–1995 and 2001–2002

Symptoms	1994–1995				2001–2002			
	total	boys (%)	girls (%)	P	total	boys (%)	girls (%)	P
12-month prevalence of asthma symptoms								
Wheeze	4.6*	5.6	3.6°	<0.05	6.6*	7.6	5.6°	<0.05
Night cough	3.2*	3.8•	2.7°	NS	8.8*	9.8•	7.8°	NS
Exercise-induced wheeze	1.8*	2.1•	1.6	NS	3.2*	3.9•	2.6	NS
Number of wheeze attacks								
None	1.0	1.2	2.5	NS	1.6	1.9	1.3	NS
1–3	3.1	3.7	0.4	NS	3.7	4.1	3.3	NS
4–12	0.6	0.8	0.1	NS	0.9	1.1	0.6	NS
More than 12	0.2	0.2	0.2	NS	0.4	0.4	0.4	NS
Speech-limiting wheeze	0.7	0.8	0.7	NS	0.6	0.8	0.4	NS
Sleep disturbance due to wheeze								
None	2.6	3.1•	2.2°	NS	4.6	5.2•	4.0°	NS
Less than 1 night per week	1.3	1.8	0.8	NS	1.6	1.8	1.4	NS
1 or more nights per week	0.6	0.7	0.6	NS	0.4	0.6	0.2	NS
Lifetime diagnosis								
Asthma ever	0.9*	1.1•	0.7°	NS	2.6*	3.5•	1.7°	<0.01
12-month prevalence of rhinitis symptoms								
Rhinitis	20.1	19.9	20.3	NS	21.9	22.9	20.9	NS
Rhino-conjunctivitis	3.2	3.2	3.3	NS	3.8	3.7	3.8	NS
Interference with daily activities								
Yes	10.3	10.0	10.6	NS	8.9	10.2	7.6	<0.05
No	9.3	9.2•	9.5	NS	11.8	11.9•	11.7	NS
Lifetime diagnosis								
Allergic rhinitis ever	1.4*	2.0	0.8	<0.05	2.4*	3.0	1.8	<0.05
12-month prevalence of eczema symptoms								
Itchy rash	2.6*	2.1•	3.1	NS	3.9*	4.2•	3.6	NS
Average nights of sleeplessness								
Yes	0.0	0.0	0.0	NS	0.8	1.1	0.5	NS
No	0.2	0.0	0.4°	NS	2.8	2.7	3.0°	NS
Lifetime diagnosis								
Eczema ever	1.4*	1.4•	1.5°	NS	3.5*	3.7•	3.4°	NS

*P<0.05 difference between total samples in 1994/1995 and 2001/2002.

•Significant difference comparing boys of different surveys.

°Significant difference comparing girls of different surveys.

to a lower extent than indices related to current symptoms.

The prevalence of allergic disease combinations (AR+AD, A+AR+AD, A+AD, A+AR) was increased in 6–7-year-old children comparing the surveys (Fig. 1). Changes in the prevalence of two allergic

disease combinations (AR+AD, A+AR) were significant. The prevalence of two combinations of allergic diseases (A+AR+AD and A+AR) was higher in boys than in girls, but significant difference was found only in the prevalence of A+AR combination in 2001–2002 (0.7% vs 0.1%, $P<0.05$).

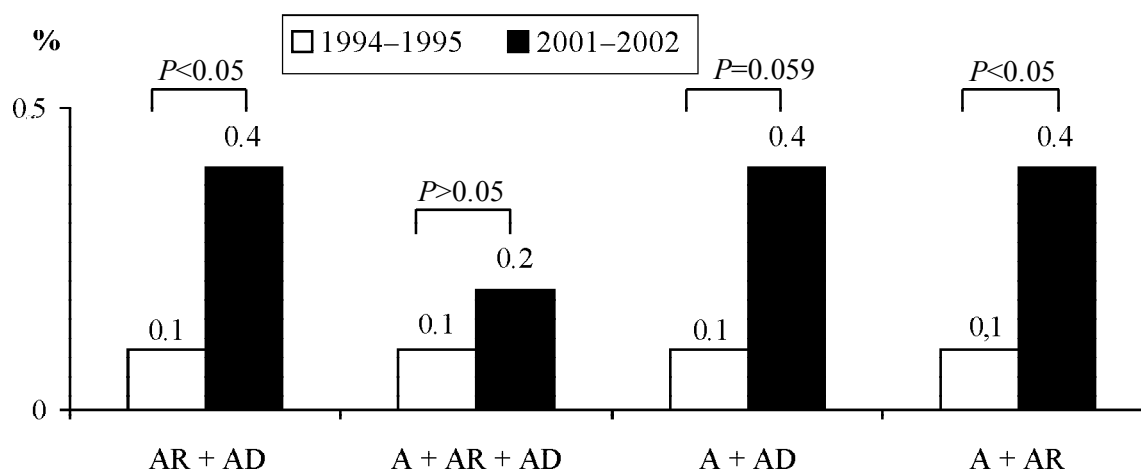


Fig 1. Changes in the prevalence of allergic disease combinations in 6-7-year-old children comparing both surveys

AR – allergic rhinitis, AD – atopic dermatitis, A – asthma.

Discussion

Using identical study methods with high and similar response rates in both surveys, examining a large sample representative of children within the general population, we think that we have arrived at credible estimates of time trends in the prevalence of symptoms of asthma, allergic rhinitis, and eczema within the studied population. Our data show that there is a general tendency towards an increase in the prevalence of symptoms of these disorders as well as in diagnoses of all three allergic conditions among 6-7-year-old children in Kaunas, remarkably more expressed among boys than girls.

The aim of the core ISAAC questionnaire was the ability to catch the clinical spectrum of the problem of interest and to gather all the right information in spite of changing diagnostic labeling.

In our study, we found an increasing number of mild asthma symptoms and diagnosed asthma during 7-year study period, but not severe asthma symptoms. This could be due to increased public attention to asthma in recent years, but on the other hand, improvement in treatment can affect the severity profile of asthma symptoms leading to an increase in the reporting less severe symptoms (15, 16). Similar data were reported by British authors who reported a rising prevalence of asthmatic symptoms among British primary school children between 1991-2002, but on the other hand, a decline in asthma mortality, hospital admission rates for asthma, exercise-induced bronchoconstriction probably due to better control of the disease as more children now are using inhaled corticosteroids as preventive treatment (17, 18). Apart from time trends, a comparison of the frequency of asthma symptoms with asthma diagnosis at each point

of time (1994/1995 and 2001/2002 surveys) shows the discrepancy between reporting of symptoms and diagnosis most likely reflecting underdiagnosis of asthma. Our findings support results of previous studies: among children with asthma-like symptoms, 13% to 85% have a physician diagnosis with many estimates being approximately 66%. Health consequences of asthma-like symptoms in children with no diagnosis are substantial: 20% miss school, 25% have limited activities because of wheeze, 32% – sleep disturbances, 7% visit emergency department, and this means that children are essentially untreated (19). This situation most often occurs when family doctors or pediatricians avoid diagnosing asthma in younger children, still making the diagnosis of obstructive bronchitis or even pneumonia. According to the Central European Study of Air Pollution and Respiratory Health (CESAR) study, in Central and Eastern Europe countries, the prevalence of bronchitis is higher and prevalence of asthma appears to be lower than in Western Europe. If asthma is defined as a diagnosis of either asthma or asthmatic, spastic, or obstructive bronchitis, then its prevalence is comparable to that of Western Europe or higher. Between-country comparisons in doctors' diagnoses appear to be dependent on the choice of definition of asthma. Some of the East-West difference in asthma prevalence may be attributable to differences in diagnostic practice (20). Still we are happy to say that the situation is improving, doctors are getting more aware as asthma diagnostic criteria for children have been revealed, and the percentage of diagnosed asthma increased statistically significantly by years.

However, we believe that the overall increase in three conditions, we report here, reflects for the most

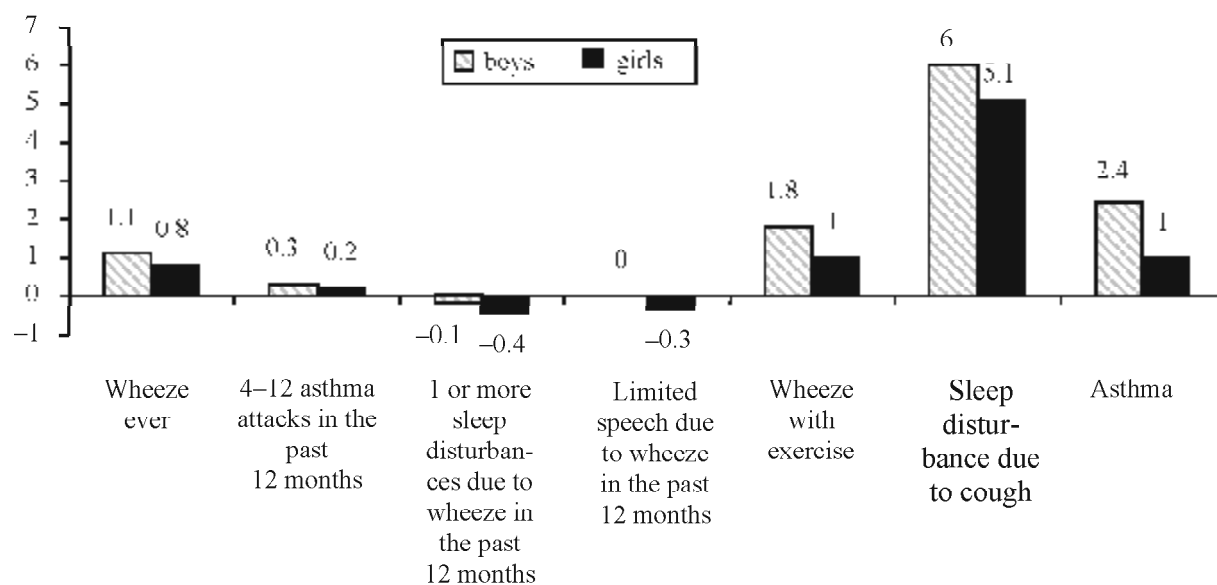


Fig. 2. Absolute percentage change in 1994/1995–2001/2002 prevalence of symptoms and diagnoses of asthma for boys and girls

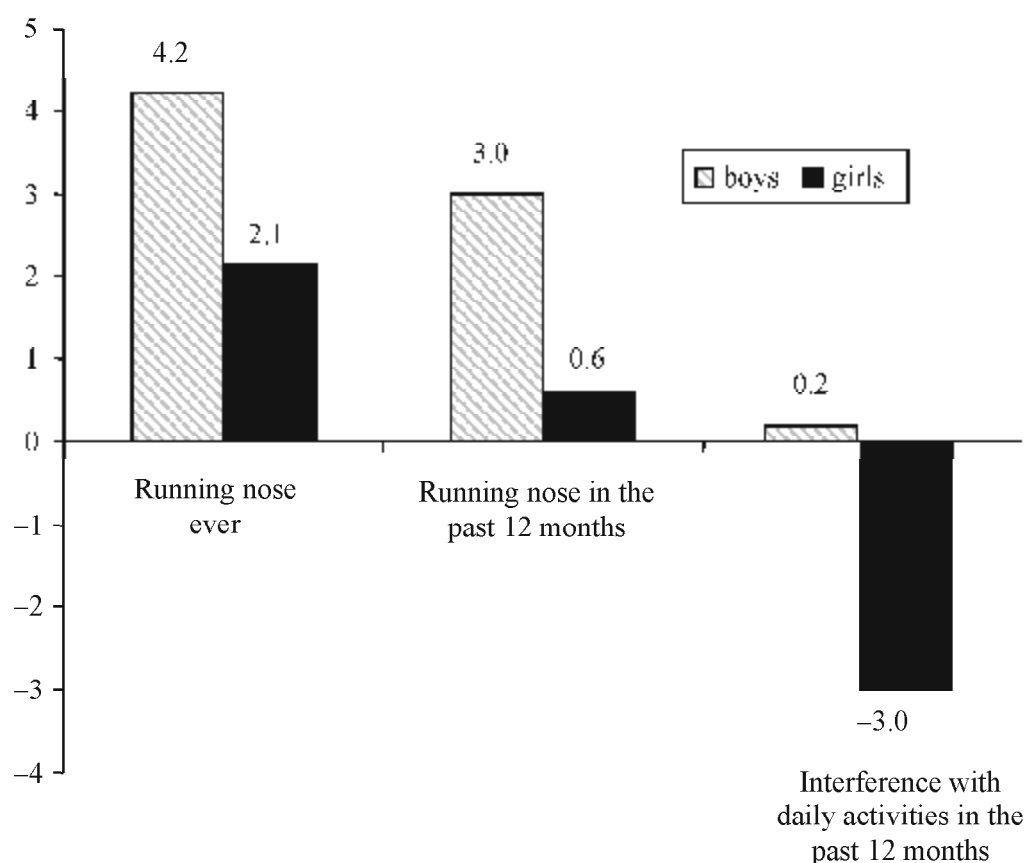


Fig. 3. Absolute percentage change in 1994/1995–2001/2002 prevalence of symptoms of allergic rhinitis for boys and girls

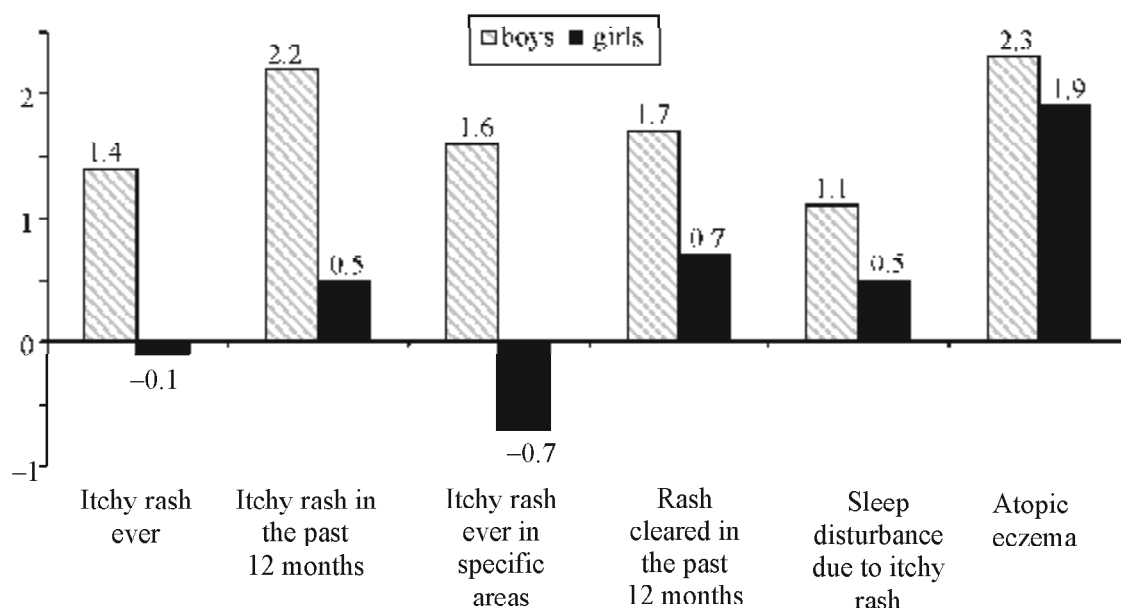


Fig. 4. Absolute percentage change in 1994/1995–2001/2002 prevalence of symptoms and diagnoses of atopic eczema for boys and girls

part a genuine increase in their morbidity within the community.

Generally, the natural history of asthma and allergic rhinitis points towards male predominance in childhood but a female predominance from adolescence onward. This natural history corresponds with our results, which show gender-related male predominance of symptoms and even diagnosis especially in 2001–2002 survey in all three allergic conditions. The same pattern was also seen for asthma, although on a smaller scale, but not for allergic rhinitis and atopic eczema in the 1994–1995 survey. Similar data were reported by Norwegian study on primary school children: though asthma tended to increase in boys, the prevalence decreased in girls from 1995 to 2000 (21). Munich study on 10-year-old asthmatic children indicated male predominance in young children, expressing an early atopy-associated type of asthma with a good prognosis with twice likely late asthma cases in girls (22). Even more, asthma onset during adulthood tends to be more severe, and if it starts around the menopause – quite severe. Therefore, incidence, severity, and prognosis of asthma can be affected by many factors, including the patient age, sex, and sex hormones (23).

WHO concluded that more and more children are affected by more than one allergic disorder (12). Our data were supported by northeast England study reporting the combination of asthma, rhinitis, and atopic eczema in 5.1% of screened children, 51.2% of them having A, AR, and AD, 57% – A and AR, 34% –

A and AD (24). This trend could be seen in our study population with significantly higher combinations of A+AR and AR+AD, predominantly in boys.

We ought to say that the ISAAC design gives no direct information about the incidence of asthma or allergy. Prevalence can be influenced by a variety of factors, such as remission, exacerbation, and treatment. However, given the chronic nature of three studied conditions and the length of the inquiry period (12 months), the calculated estimates reflect to a good extent the morbidity of these conditions within the society at each point of time.

According to our data, boys can be more vulnerable to lifestyle factors that will interfere with their ability to develop normal resistance to allergy.

Thus, although the data of our study do not give specific mechanisms to the noticed gender-related time trends, it can provide a useful framework for future research, looking in depth into factors influencing different trends of asthma and allergies within the population.

Recent evidence from studies on children in Italy and adults in Great Britain suggests that the increase in asthma observed in the 1970s and 1980s may be coming to an end (25, 26). Similarly, a significant reduction in prevalence of reported asthma in Melbourne schoolchildren was observed, whereas the prevalence of eczema and allergic rhinitis continued to increase (27). In two studies 8 years apart, a modest increase in the prevalence of allergic disorders among Estonian schoolchildren was found. The increase was

more pronounced for symptoms of eczema, while most of the asthma symptoms did not change or the prevalence of rhinitis did (28). Lastly, most ISAAC centers showed a change in prevalence of allergic diseases with increases being more common than decreases and occurring more commonly in the younger age group than the older age group (29). According to the data of our study, symptoms of asthma and allergies in our 6–7-year-old population continue to show an increasing trend. Similar trends were reported in German 6–7- and 13–14-year olds (16). This trend is likely to reflect real change in the morbidity from all three allergic conditions within our population as it spans the whole spectrum of symptoms and severity levels.

Having such reliable data is instrumental in the generation of valid concepts about possible intervention strategies and for the assessment of costs of asthma and allergies within the society.

Conclusions

1. The prevalence of diagnosed asthma and atopic dermatitis as well as their symptoms increased significantly in 6–7-year-old children.

2. The prevalence of diagnosed allergic rhinitis increased significantly, though the prevalence of allergic rhinitis symptoms did not increase.

3. The prevalence of asthma and allergic rhinitis, allergic rhinitis and atopic dermatitis combinations increased significantly in 6–7-year-old children.

4. Our data showed male predominance of symptoms and diagnosis of all three allergic disorders.

5. An increase of current asthma, allergic rhinitis, and atopic dermatitis symptoms and prevalence of asthma and atopic dermatitis was more marked in boys.

6. Discrepancy between reporting the symptoms and diagnosis of all three allergic disorders reflecting possible untreatment of children was found.

Vaikų bronchų astmos, alerginio rinito ir atopinio dermatito bei jiems būdingų simptomų paplitimo kaita tarp 6–7 metų Kauno miesto moksleivių (ISAAC tyrimo I ir III fazės rezultatai)

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Santrauka. *Tyrimo tikslas.* Nustatyti bronchų astmos, alerginio rinito ir atopinio dermatito bei šioms ligoms būdingų simptomų paplitimo kaitą per septynerius metus tarp 6–7 metų Kauno miesto moksleivių, naudojant ISAAC klausimyną.

Tyrimo medžiaga ir metodai. Tyrimai atlikti 1994–1995 ir 2001–2002 mokslo metais. Tirti 6–7 metų vaikai. Abiejų apklausų metu naudoti identiški standartizuoti ISAAC klausimynai bronchų astmos, alerginio rinito ir atopinio dermatito simptomų paplitimui bei jo kaitai nustatyti. Tyrimai atlikti tuo pačiu metų laiku, tose pačiose mokyklose (klausimynus pildė tėvai namuose).

Rezultatai. 1994–1995 metais tyrime dalyvavo 1879–2000 (93,95 proc.), 2001–2002 metais 2772–3000 (92,4 proc.) 6–7 metų Kauno miesto moksleivių. Per septynerius metus statistiškai reikšmingai padidėjo bronchų astmos (nuo 0,9 iki 2,6 proc.), alerginio rinito (nuo 1,4 iki 2,4 proc.) ir atopinio dermatito (nuo 1,4 iki 3,5 proc.) paplitimas tarp 6–7 metų Kauno miesto moksleivių. Padidėjo bronchų astmai ir atopiniam dermatitui būdingų simptomų paplitimas. Simptomų ir ligų paplitimo padidėjimas žymesnis tarp berniukų. Tarp 6–7 metų vaikų alerginėmis ligomis dažniau serga berniukai nei to paties amžiaus mergaitės. Per septynerius metus statistiškai reikšmingai padidėjo bronchų astmos ir alerginio rinito (nuo 0,1 iki 0,4 proc.), alerginio rinito ir atopinio dermatito (nuo 0,1 iki 0,4 proc.) derinių paplitimas.

Išvados. Per septynerius metus (1994–2002) statistiškai reikšmingai padidėjo bronchų astmos, atopinio dermatito bei šių ligų simptomų paplitimas 6–7 metų vaikų grupėje. Alerginio rinito paplitimas padidėjo statistiškai reikšmingai, tačiau simptomų paplitimas nepadidėjo. Tarp 6–7 metų vaikų bronchų astmos ir alerginio rinito bei alerginio rinito ir atopinio dermatito derinių paplitimas padidėjo statistiškai reikšmingai. Visos trys alerginės ligos bei jų simptomai labiau paplitę tarp berniukų.

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