

Prevalence of childhood asthma and allergies in Serbia and Montenegro

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Background: This is the first multi-center epidemiological study on the prevalence of childhood asthma in Serbia and Montenegro. The International Study of Asthma and Allergies in Childhood (ISAAC) phase 3 is a large epidemiological multinational and multicentric study on the prevalence of asthma, allergic rhinitis and eczema in children.

Methods: The 12-month period prevalence of asthma, allergic rhinitis and eczema was calculated using an ISAAC phase 3 questionnaire for two age groups: 6-7 years old and 13-14 years old.

Results: In the 13 485 children from five study centers who responded to the questionnaire, the prevalence for childhood asthma ranged from 2.5% to 9.8%, for allergic rhinoconjunctivitis (hay fever) from 4.6% to 21%, and for eczema from 8.2% to 17.2%. The prevalence of current wheezing was high in both age groups (16.5% and 12.4% respectively).

Conclusions: The prevalence of asthma is higher in 6-7 years old school children in the urban and largest cities of Belgrade and Nis, and in 13-14 years old children in Podgorica. The prevalence of asthma, allergic rhinitis and eczema in the school children of Serbia and Montenegro seems similar to that of other countries in Central and South-Eastern Europe.

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Introduction

The prevalence of asthma and allergies is growing in industrialized and developing countries.^[1,2] Epidemiological surveys in school children in Central and Eastern European countries and Scandinavia have found a lower prevalence (less than 5% in Poland, Estonia, Albania, Romania, Russia, Georgia and Uzbekistan) than in Sweden and Finland (5%-10%).^[3] The studies from Central European countries have mostly been limited to Estonia,^[4] East Germany,^[5] and Poland,^[3] while the prevalence of asthma and childhood allergies in Eastern European countries is generally seldom reported.

The International Study of Asthma and Allergy in Childhood (ISAAC) was developed to provide standardized tools for studies of the worldwide prevalence of wheezing, rhinitis and eczema in school children by a similar study design in all participating centers.^[6]

The ISAAC phase 1 study indicated a higher prevalence of asthma and childhood allergies (15%-35%)^[7,8] in Western Europe or developed countries, but the prevalence was lower (less than 5%) in South-Eastern European countries, probably due to lack of asthma data collected.^[9]

Studies have shown that 1 in 4 children have at least one episode of wheezing in the first seven years of their life in Belgrade (Serbia),^[10] suggesting that the healthcare system is overburdened with direct costs covering physician's visits, diagnostic procedures and treatment. A multicentric national survey, a pilot study for ISAAC phase 3, conducted in several towns in Serbia, such as Belgrade, Nis, Pancevo and Novi Sad, showed a prevalence of 15%-35% for wheezing episodes in school age children. The prevalence of asthma was 7.5% in Belgrade, 9.7% in Nis, 10% in

Pancevo, and 2.5% in Novi Sad.^[10-13]

A clinical study conducted from 2004 to 2006 on asthma management and patient/parent education in Belgrade, Serbia showed that children diagnosed with asthma lost 25 days of school attendance on average within one school year. The same study reported that 70% of the children diagnosed with asthma were hospitalized at least once a year due to asthma attacks, with an average of 2.85 days per hospitalization. Since no survey has been concentrated on economic factors, we assume that the economic loss for the patients, parents, hospitals and the whole society is substantial.^[14]

International data have shown that asthma and allergic rhinitis have an important financial impact on healthcare systems, patients, their families and society as a whole.^[15,16] The increased prevalence of asthma and allergies in Western Europe, New Zealand and Australia has stimulated other regions to collect data for elucidation of the international variations in the prevalence of asthma and allergic diseases.

The ISAAC phase 3 conducted in Serbia and Montenegro was the first multi-center epidemiological study on different geographical regions and socio-demographic areas.

Methods

The present study adhered to the ISAAC phase 3 protocol as described in the manual and the paper concerning rationale and methods.^[17] The core study protocol included children aged 13-14 years. In addition, children aged 6-7 years were grouped in several centers, strictly adhering to the ISAAC phase 3 protocol for this age group.

The study consisted of 1000-2999 children of 6-7 and 13-14 years old. They were selected randomly from schools in a specified geographic area. The teachers in the selected schools were informed in writing and verbally about the study, and written information was then distributed to the pupils and their parents. The questionnaires underwent the forward and backwards translation process. In all, 93.5% of questionnaires were translated into Serbian and 6.5% into Hungarian language (Sombor). The Serbian and Hungarian language have no exact equivalents for the word "wheezing", so the appropriate term was identified in a pilot study including children and their parents with recurrent wheezing, as recommended in the ISAAC core protocol.

Childhood asthma was defined as recurrent wheezing episodes, clinically confirmed by a physician, exactly a pediatrician or a pediatric pulmonologist. Wheezing was defined as: any episodes of wheezing (life-time wheezing) or any wheezing episodes for the last 12 months (current wheezing). Allergic rhino-

conjunctivitis was defined clinically by a physician as sneezing, itchiness and waterish secretion, and upon seasonal variations during the pollen season. Allergic rash was defined as a skin rash with itchiness by typical flexural localization, confirmed by a physician. We calculated the prevalence of rhinitis/rash during their lifetime, prevalence of rhinitis/rash for the last 12 months (current symptoms) and prevalence of doctor's diagnosed hay fever/eczema.

The ISAAC phase 3 was conducted and completed at the time when Serbia and Montenegro were formed into one country. Serbia was divided into three regions: Central Serbia, Vojvodina, and Kosovo and Metohija. The latter was not included in the study due to political conflicts in this region.

As seen on the map (Fig. 1), we selected the following regional centers: from Vojvodina, Sombor and Novi Sad, the capital of Vojvodina; from Serbia, Belgrade, the capital of Serbia and Montenegro, and Nis as the largest city of South Serbia; and Podgorica, the capital of Montenegro. Belgrade, Nis and Novi Sad have been chosen as large cities with urban lifestyle. Sombor is situated in the far North of Serbia, with low environmental air-pollution and mostly rural lifestyle. Podgorica is the only center in Montenegro with a population of school age children large enough to fulfill the criteria (only for 13-14 years old). Podgorica is located in the continental area, but close to the Adriatic coast.

Centers with sample sizes ranging from 1000 to 2999 were valid for the prevalence comparisons.^[17] Although the study population of Podgorica for the 6-7 year old group did not fulfill these criteria and did not meet inclusion criteria for the international study, the data were reported and presented in this paper.

Data management and analysis

The data were entered exactly as recorded on the questionnaire at the study centers and checked for



Fig. 1. Geographical location of participating centers in Serbia and Montenegro.

coding errors, omissions and inconsistencies at the ISAAC Data Centre in Auckland, New Zealand (T. Clayton). The data were transferred using the protocol described in the ISAAC Coding and Data Transfer Manual to the ISAAC International Data Center. The data from the 6-7 and 13-14 years age groups were analyzed separately. A written report was sent back to the collaborator who responded to the issues and made corrections as needed. A final document on all aspects of the methodology actually used was completed for each center and checked by the ISAAC International Data Center and the regional coordinator. This document included information about the sampling frame, the sampling method, the participation rate of schools and of children within schools, the data entry method and the details of translation.

For each of the core symptoms of asthma, allergic rhinoconjunctivitis and eczema, a 12-month period prevalence was calculated by dividing the number of positive responses to each question by the number of completed questionnaires.^[17]

Results

The number of 6-7 year old children participating in the study varied from 933 to 2309 and the response rate to the questionnaire varied from 89.2% to 98.2%. There was a distinctive variation in the prevalence of wheezing, allergic rhinitis and eczema among the 6-7 year old children in the five study centers.

The prevalence of wheezing, rhinitis and rash over the child's life in the past 12 months, and the overall prevalence in children of 6-7 years old are presented in Table 1. The prevalence of wheezing ever in life varied from 18.8% in Podgorica (the lowest) to 35% in Nis (the highest). The prevalence of 12-month (current)

wheezing among the 6-7 year old children varied from 8.7% in Podgorica and Novi Sad (the lowest) to 16.5% in Nis (the highest). The prevalence of asthma in the 6-7 year old children was 2.5% in Novi Sad, 3.6% in Podgorica, 4.6% in Sombor, 7.5% in Belgrade, 9.8% in Nis. The overall prevalence of asthma in 6-7 year old children in Serbia and Montenegro was 5.6%. The prevalence of rhinitis over the child's life in 6-7 year old children varied from 14.8% in Nis (the lowest) to 20.8% in Novi Sad (the highest). The 12-month (current) prevalence of rhinitis varied from 11.0% in Podgorica (the lowest) to 19.4% in Belgrade (the highest). The prevalence of hay fever in 6-7 year old children was 4.6% in Novi Sad, 5.3% in Sombor, 5.9% in Podgorica, 8.3% in Nis, and 9.4% in Belgrade. The overall prevalence of allergic rhinitis for the 6-7 year old children in Serbia and Montenegro was 6.7%. The prevalence of rash over the child's life in 6-7 year old children varied from 2.8% in Podgorica (the lowest) to 15.4% in Nis (the highest). The 12-month (current) prevalence of rash in the 6-7 year old children varied from 2.2% in Podgorica (the lowest) to 11.0% in Nis (the highest). The prevalence of eczema over the child's life in the 6-7 year old children was 9.5% in Podgorica, 11.2% in Nis, 11.6% in Novi Sad, 13.1% in Sombor, and 17.2% in Belgrade. The overall prevalence of eczema for the 6-7 year old children in Serbia and Montenegro was 12.5%.

The prevalence of wheezing, rhinitis and rash over the child's life in the past 12 months and the overall prevalence in children of 13-14 years old are presented in Table 2. The prevalence of wheezing over life in the 13-14 year old children varied from 14.0% in Novi Sad (the lowest) to 24% in Nis (the highest). The prevalence of 12-month (current) wheezing among the 13-14 year old children varied from 5.8% in Novi Sad (the lowest)

Table 1. Prevalence (%) of wheezing, rhinitis and skin symptoms in 6-7 year old children participating in the ISAAC study

	Belgrade	Nis	Novi Sad	Sombor	Podgorica
Wheezing					
Wheezing ever	26.5	35.0*	21.6	20.5	18.8†
12-month wheezing	10.7	16.5*	8.7†	11.1	8.7†
Asthma ever	7.5	9.8*	2.5†	4.6	3.6
Rhinitis					
Rhinitis ever in life	20.4	14.8*	20.8*	16.4	15.9
12-month rhinitis	19.4*	12.3	16.8	12.5	11.0*
Hay fever	9.4*	8.3	4.6†	5.3	5.9
Eczema					
Rash ever	14.0	15.4*	8.7	8.0	2.8†
12-month rash	9.8	11.0*	6.5	6.1	2.2†
Eczema ever	17.2*	11.2	11.6	13.1	9.5†

*: the highest prevalence in percentage; †: the lowest prevalence in percentage.

Table 2. Prevalence (%) of wheezing, rhinitis and skin symptoms in 13-14 year old children participating in the ISAAC study

	Belgrade	Nis	Novi Sad	Sombor	Podgorica
Wheezing					
Wheezing ever	19.0	24.0*	14.0†	18.0	19.6
12-month wheezing	8.7	12.4*	5.8†	10.9	10.3
Asthma ever	6.0	6.0	3.2†	4.7	7.2*
Rhinitis					
Rhinitis ever in life	33.2	42.3*	27.3	25.0†	37.0
12-month rhinitis	24.6	31.8*	18.1	17.8†	23.7
Hay fever	14.6	21.0*	13.2†	13.2†	17.7
Eczema					
Rash ever	14.5*	12.3	5.7†	7.1	6.9
12-month rash	10.1*	9.7	4.4†	5.1	4.7
Eczema ever	15.6	16.2*	8.2†	9.3	9.1

*: the highest prevalences in percentage; †: the lowest prevalence in percentage.

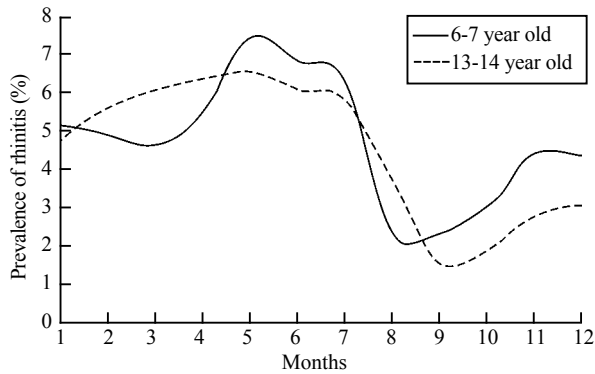


Fig. 2. Seasonal variations in the prevalence of rhinitis in 6-7 year and 13-14 year old children.

to 12.4% in Nis (the highest). The prevalence of asthma for the 13-14 year old children was 3.2% in Novi Sad, 4.7% in Sombor, 6% in Belgrade, 6% in Nis, and 7.2% in Podgorica. The overall prevalence of asthma for the 13-14 year old children in Serbia and Montenegro was 5.4%. The prevalence of rhinitis over life in the 13-14 year old children varied from 25.0% in Sombor (the lowest) to 42.3% in Nis (the highest). The 12-month (current) prevalence of rhinitis varied from 17.8% in Sombor (the lowest) to 31.8% in Nis (the highest). The prevalence of hay fever in the 13-14 year old children was 13.2% in Novi Sad and Sombor, 14.6% in Belgrade, 17.7% in Podgorica, and 21.0% in Nis. The overall prevalence of allergic rhinitis for the 13-14 year old children in Serbia and Montenegro was 15.9%. The prevalence of rash over life in the 13-14 year old children varied from 5.7% in Novi Sad (the lowest) to 14.5% in Belgrade (the highest). The current 12-month prevalence of rash in the 13-14 year old children varied from 4.4% in Novi Sad (the lowest) to 10.1% in Belgrade (the highest). The prevalence of eczema over life in the 13-14 year old children was 8.2% in Novi Sad (the lowest) to 16.2% in Nis (the highest). The overall prevalence of eczema for the 13-14 year old children in Serbia and Montenegro was 11.68%.

In Belgrade, the largest study center, the highest prevalence of rhinitis was reported in March-May for the 6-7 year old children, and February-April for the 13-14 year old children. The lowest prevalence of rhinitis in Belgrade was detected in June-August for the 6-7 year old children, and in July-September for the 13-14 year old children (Fig. 2).

Discussion

The prevalence of asthma symptoms was the highest in Nis and the lowest in Novi Sad among the 6-7 year old children. The prevalence of symptoms of current rhinitis and allergic rhinitis were the highest in Belgrade

and the lowest in Podgorica and Novi Sad. The highest prevalence of current eczema was in Nis and the highest prevalence of eczema over the child's lifetime was in Belgrade. The lowest prevalence of eczema and current eczema was in Podgorica.

The prevalence of symptoms of current wheezing and asthma among the 13-14 year old school children was the highest in Nis and Podgorica respectively. The lowest prevalence of asthma was observed in Novi Sad. The highest prevalence of current rhinitis and allergic rhinitis was seen in Nis and the lowest prevalence was in Novi Sad and Sombor. The highest prevalence of current eczema was recorded in Belgrade, and the highest prevalence of ever presented eczema was in Nis. The lowest prevalence of current eczema and ever presented eczema was in Novi Sad. The prevalence of asthma obtained from ISAAC phase 3 was in accordance with that of the pilot study conducted in three main cities, Belgrade, Nis and Novi Sad and one additional, Pancevo, located north 30 km from Belgrade. The high prevalence was seen in the main cities of Serbia (Belgrade and Nis) and Montenegro (Podgorica).

The variations in the prevalence of asthma, rhinitis and eczema between the study centers could be due to variations in healthcare institutions providing asthma care between urban and rural centers. There could be a difference in recognition of asthma symptoms, particularly when mild to moderate, which could be the reason for many cases of undiagnosed asthma. Clearly, in large cities, asthma can be more easily recognized with better diagnostic tools.

The inter-city variations reported for asthma among school children could be explained by unequal healthcare and availability of pediatric pulmonologists. Also, it may be related to severe environmental pollution in urban centers.^[18] Additionally, in urban and residential areas, children are exposed frequently to respiratory infections since they attend the daycare centers from an early age.^[19]

Evidently, in all our participating centers there was a significant difference between the prevalence of current wheezing and asthma diagnosis; approximately twice as many children had wheezing episodes over 12 months in comparison to the established diagnosis of asthma. It is possible that general physicians taking care of children of Serbia and Montenegro are reluctant to diagnose asthma or the diagnosis is denied by patients and their parents as well.

Doubled prevalence of current symptoms of rhinitis in relation to allergic rhinoconjunctivitis is obtained when rhinitis has been analyzed. It is definitely the result of neglecting the symptoms of allergic rhinitis by physicians and patients as well.

However, the same difference was not detected regarding symptoms of eczema. It is possible that eczema is less embarrassing for patients and their parents, thus they find it more comfortable to accept the diagnosis. That is perhaps the explanation for the consistently higher prevalence of eczema over a child's lifetime at all the centers and both age groups as compared to the presence of rash over lifetime or current symptoms of eczema. It is also possible that children with symptoms of eczema visit the dermatologists more often than pediatricians, since there is a tendency to ignore the diagnosis of eczema if the skin lesions are mild.

The symptoms of rhinitis may be caused by allergies to some extent or by respiratory infections. The seasonal variations of symptoms of allergic rhinitis in both age groups highlight a higher prevalence in winter and spring with peak prevalence in early spring.

It should be mentioned that one study center is in an area with low air pollution, Sombor in northern Serbia. Although none of the northern cities is heavily polluted in comparison with some southern cities, the findings indicate that air pollution can explain the observed regional differences. However, the similarity of the results from Sombor from the northern Serbia, and Podgorica from the continental part of Montenegro might be explained by the rural lifestyle of Sombor and the mild, beneficial climate in Podgorica.

Looking at the data from countries in the surrounding geographic area, that are comparable in population (Greece, Western Turkey, Republic of Macedonia), social, political and economic status (Croatia and Republic of Macedonia), we found similar results in our study. The ISAAC Study conducted in Croatia's northern regions (corresponding to the continental area of our country) found current wheezing in 5.11%, allergic rhinitis in 10.87% and eczema in 5.34% of school children.^[19] An article on the prevalence of allergies in childhood in Greece together with time trends in prevalence has reported similar data as mentioned and increased prevalence in preadolescent children.^[20] The prevalence of asthma, hay fever and eczema in school children in the Republic of Macedonia is low according to the ISAAC study.^[21] The prevalence of allergic rhinitis and conjunctivitis similar to ours was 14.5% and 13% respectively in the ISAAC in Western Turkey. The rate of physician-diagnosed asthma was 7.9%, which was similar to ours.^[22]

Global variation of rhinitis in ISAAC phase 3 was observed, with a rate of 14.6% for current rhinitis in 13-14 year old children and 8.5% in 6-7 year old children.^[23] Comparing the prevalence of wheezing and asthma in our study to the results from Western European countries showed similar results of wheezing over lifetime and current wheezing.^[23,24] However, the difference in the

prevalence of asthma in Serbia and Montenegro and West European countries was pronounced.^[25] The prevalence of asthma in Serbia and Montenegro and South Eastern European was more consistent.^[26]

In conclusion, the prevalence of asthma is higher in the 6-7 year old school children in urban areas and the largest cities of Belgrade and Nis, and in the 13-14 years old children in Podgorica. The prevalence of asthma, allergic rhinitis and eczema in school children of Serbia and Montenegro seems to be similar to that of the countries of Central and South-Eastern Europe.^[27-29]

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