

## Prevalence of Asthma and Allergic Diseases in Croatian Children Is Increasing: Survey Study

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**Aim.** To estimate the prevalence of asthma, allergic rhinitis, and atopic dermatitis among school children in the region of Primorsko-goranska County in Croatia, and compare the results with data from other countries.

**Methods.** The study was conducted during the 2001-2002 school year, in complete adherence to the Phase One protocol of the International Study of Asthma and Allergies in Childhood (ISAAC). The target population comprised two age groups (6-7 and 13-14 years) in the region of Primorsko-Goranska County in Croatia. Data were collected using standardized ISAAC written questionnaire and asthma video questionnaire.

**Results.** There were 1,634 participating children in the 6-7 age group (response rate 80.3%) and 2,194 participating children in the 13-14 age group (response rate 89.8%). Estimated 12-month prevalence rates of symptoms were: wheezing 9.7% and 8.4%, allergic rhinitis symptoms 16.9% and 17.5%, allergic rhinoconjunctivitis symptoms 5.6% and 6.7%, and atopic dermatitis symptoms 5.4% and 3.4%, for younger and older age group, respectively.

**Conclusion.** Results suggest an increase in the prevalence of atopic disease symptoms in north-west part of Croatia over the last few decades when compared to prior studies. The results are suitable for international comparison, suggesting that this part of Croatia is a county with a moderate prevalence of atopic diseases in the pediatric population. The results represent a baseline for further epidemiological research of asthma and allergic diseases.

**Key words.** asthma; respiratory sounds; rhinitis, allergic, perennial; dermatitis, atopic; child; epidemiology; prevalence

Allergic diseases related to atopy, such as asthma, allergic rhinitis, and atopic dermatitis, have now become the most common chronic childhood medical conditions in developed countries. They have a comprehensive impact on each affected child, its family, and society as a whole. There are disturbing epidemiological data confirming a worldwide increase in the prevalence of asthma and allergic diseases affecting children over the last few decades (1,2). The exact reason for this increase is not known and it can not be explained solely by the improved criteria for recognizing and diagnosing these diseases (3). Environmental factors, rather than genetic predisposition seem to be the major determinants of their increasing prevalence in a community (4,5). Demographic, geographic, and temporal comparison of descriptive epidemiological data is a potentially useful approach to studying distribution and determinants of asthma and allergic diseases in populations. Despite many previous attempts to elucidate risk factors by epidemiologic studies, there has been little insight into the etiology due to a lack of methodological uniformity (6).

Therefore, a global epidemiological project named the International Study of Asthma and Allergies in Childhood (ISAAC) was initiated ten years ago (7). ISAAC provided standardized epidemiological methodology suitable for international comparison of asthma, allergic rhinitis, and atopic dermatitis prevalence rates. ISAAC was planned to be carried out in three phases. The objective of ISAAC Phase One was to obtain baseline descriptive epidemiological data – the prevalence and severity of these diseases. More than 150 centers in 56 countries participated in ISAAC Phase One. The results showed wide international differences in the prevalence of their symptoms with generally lower rates in developing than in wealthy countries (8). These results became a framework for the ongoing ISAAC Phases Two and Three analyses. Their objectives comprise etiological research into the genetic and environmental determinants of asthma and allergic diseases, and assessment of further trends in their prevalence and severity.

The aim of this study was to determine the prevalence rates of these diseases among a population of

**Table 1.** Prevalence rates of asthma symptoms calculated from the written questionnaire

| Age group (years) | No. of participants | Prevalence (%) reporting   |                                   |                               |               |             |
|-------------------|---------------------|----------------------------|-----------------------------------|-------------------------------|---------------|-------------|
|                   |                     | wheezing in last 12 months | exercise wheeze in last 12 months | night cough in last 12 months | wheezing ever | asthma ever |
| 6-7               | 1,634               | 9.7                        | 4.2                               | 11.1                          | 26.2          | 3.9         |
| 13-14             | 2,194               | 8.4                        | 12.6                              | 17.3                          | 19.9          | 5.2         |

**Table 2.** Prevalence rates of asthma symptoms in the 13-14 years old age group (n=2,194) calculated from the video questionnaire

| Appearance of asthma symptoms | Prevalence (%) reporting |                 |              |             |               |
|-------------------------------|--------------------------|-----------------|--------------|-------------|---------------|
|                               | wheezing                 | exercise wheeze | night wheeze | night cough | severe wheeze |
| Last 12 months                | 4.6                      | 6.7             | 1.4          | 6.7         | 2.1           |
| Ever in life                  | 9.1                      | 10.2            | 3.9          | 12.3        | 4.3           |

school children in the region of Primorsko-Goranska County in Croatia, using standardized methodology recommended by ISAAC. We hypothesized that the results would confirm a general impression that there was an increasing trend of prevalence of atopic diseases among Croatian children. The results obtained should be suitable for international comparison and represent a baseline for further epidemiological research.

### Participants and Methods

#### Participants

The target population comprised two age groups of school children aged 6-7 years and 13-14 years within the Primorsko-Goranska County in Croatia, using schools as the sampling units. The sample size of at least 1,000 per age group was estimated to provide sufficient statistical power for the calculation of prevalence rates.

There were a total number of 56 elementary schools on this geographical area with a total of 2,670 children in the 6-7 years age group and 3,437 children in the 13-14 years age group. All 56 schools were randomly arranged on a list, and were surveyed in this order until a satisfactory sample size was obtained. The study comprised 34 randomly selected elementary schools located in the surveyed geographical region. The total numbers of children selected to participate in these schools were 2,036 in the 6-7 year old group and 2,442 in the 13-14 year old group. The final number of children that participated in the study was 1,634 in the younger age group and 2,194 in the older age group (80.3% and 89.8% response rate, respectively).

The survey was conducted during the 2001/02 school year.

#### Methods

The study was conducted in complete adherence to the Phase One protocol of the published ISAAC rationale and methods (7). Data were collected using the standardized written questionnaire, developed by the ISAAC group, about the presence of symptoms or conditions related to asthma, allergic rhinitis/conjunctivitis, and atopic dermatitis (7). The questionnaire was com-

pleted by the 13-14 year-old children and by the parents of the 6-7 year olds. It was translated from English into Croatian language by a pediatrician pulmonologist. According to ISAAC guidelines (9), back-translation into English was performed by an independent professional translator to make sure that the certain key symptoms were correctly translated.

In addition to the written questionnaire, 13-14 year old children completed a video asthma questionnaire. The European version of audiovisual presentation of the questionnaire included five scenes of asthma symptoms in different situations: wheezing at rest, wheezing due to exercise, night wheeze, night cough, and severe wheeze (7). After each scene, the children ticked the answer whether or not they experienced the same problems with breathing as the child in the video in the past 12 months or ever in life. The terms asthma and wheezing were not mentioned in the video questionnaire in order to avoid problems of translation.

Recorded data were transferred to the ISAAC International Data Center in Auckland, New Zealand where the two age groups were analyzed separately. Symptom prevalences were calculated by dividing the number of positive responses to each question by the number of completed questionnaires.

### Results

According to the 12-month prevalence of wheezing, estimated current prevalence rates of asthma in the younger and in the older age groups were 9.7% and 8.4%, respectively. Amongst asthma symptoms, the highest prevalence was recorded for "wheezing ever", and the lowest prevalence was recorded for "asthma ever", in both age groups (Table 1).

The cumulative (ever in life) and current (last 12 months) prevalence rates of asthma symptoms reported on the video questionnaire were all lower than that of comparable variables reported on the written questionnaire (Table 2).

The prevalence rates of allergic nasal symptoms were all higher in the older age group. Their 12-month prevalence in the younger and in the older age groups was 16.9% and 17.5%, respectively. The nasal symptoms with eyes affected showed much lower prevalence (Table 3).

In contrast to nasal symptoms, the prevalence rates of eczema symptoms were all higher in the younger age group. According to the 12-month prevalence of itchy rash affecting flexural areas, estimated current prevalence rates of atopic dermatitis in the

**Table 3.** Prevalence rates of allergic rhinitis symptoms calculated from the written questionnaire

| Age group (years) | No. of participants | Prevalence (%) reporting         |                                 |                     |                |
|-------------------|---------------------|----------------------------------|---------------------------------|---------------------|----------------|
|                   |                     | nasal symptoms in last 12 months | eyes affected in last 12 months | nasal symptoms ever | hay fever ever |
| 6-7               | 1,634               | 16.9                             | 5.6                             | 19.8                | 5.3            |
| 13-14             | 2,194               | 17.5                             | 6.7                             | 25.4                | 10.5           |

**Table 4.** Prevalence rates of atopic dermatitis symptoms calculated from the written questionnaire

| Age group (years) | No. of participants | Prevalence (%) reporting     |                |                 |             |
|-------------------|---------------------|------------------------------|----------------|-----------------|-------------|
|                   |                     | itchy rash in last 12 months | flexural areas | itchy rash ever | eczema ever |
| 6-7               | 1,634               | 6.1                          | 5.4            | 9.2             | 10.6        |
| 13-14             | 2,194               | 4.8                          | 3.4            | 8.6             | 8.5         |

younger and in the older age groups were 5.4% and 3.4%, respectively (Table 4).

## Discussion

There is a small number of asthma prevalence surveys conducted in the Croatian pediatric population (10-14). If we ignore the fact that different methodologies, including the use of self-created non-standardized questionnaires or just searching through medical records for diagnosed asthma, and study designs were applied by investigators, a crude comparison of their results suggests a substantial increase of asthma prevalence over the last 25 years (Table 5). The results of the penultimate study listed in the table attracted our attention because data collection was also performed using the written questionnaire recommended by ISAAC, thus potentially being comparable to our study (14). The survey of an urban population of school children in the city of Zagreb revealed slightly lower prevalence rates of asthma symptoms in comparison to our results (12-month wheezing 6.02%; exercise wheeze 3.44%; night cough 8.69%; wheezing ever 20.34%; asthma ever 4.39%). Since the Zagreb and our study concern geographically different parts of Croatia, which also differ in climate and vegetation, we believe the results of both studies are representative of the country as a whole.

The global ISAAC Phase One asthma report demonstrated large worldwide variations in the prevalence of asthma symptoms among 156 collaborating centers in 56 countries, with a total of 721,601 participating children. There were more variations between countries than within countries (15). The highest asthma prevalence rates were recorded in United Kingdom, New Zealand, and Australia followed by the countries in North America. The lowest asthma prevalence rates were reported from several eastern European countries, China, and some other countries in Southeast Asia. Generally, asthma was less prevalent in developing countries than in more affluent countries (16). The strong northwest to southeast gradient in asthma prevalence has been noticed in Europe (17). The results of our study fit into this pattern (Fig. 1A) and, together with the results of the survey conducted in the city of Zagreb (14), suggest that Croatia is a country with a moderate prevalence of childhood asthma (range of 5 to <10%).

ISAAC collaborators agreed that the current prevalence of asthma symptoms is best reflected by 12-month prevalence of wheezing (15). In our study, "12-month wheezing" was more prevalent in the younger than in the older age group. It is probably a

consequence of the fact that many young children suffer from wheezy bronchitis which occurs during the winter months in response to viral infections, and in most cases it resolves relatively rapidly during early school age (18). In contrast to our results, 57 of 90 (63%) ISAAC Phase One participating centers reported to have a lower 12-month prevalence of wheezing in the younger age group (15).

In our study, like in other ISAAC participating centers (17), "wheezing ever in life" showed the highest prevalence in comparison to all other variables regardless of age, suggesting that responses to this question were related not only to asthma but also to other conditions associated with wheezing.

The global ISAAC Phase One asthma study reported a considerable variation in the prevalence of a positive response to the question on whether the child had ever had asthma. In some countries 12-month prevalence of wheezing was higher than prevalence of asthma ever in life, whereas in other countries there was much more asthma ever than 12-month wheeze (15). In our study, the prevalence of "asthma ever in life" was the lowest among all variables, including "12-month wheezing," regardless of age. Most studies found that only 50% or fewer of those with recurrent wheezing consistent with asthma have been given that diagnosis, and that those so diagnosed generally have more severe disease. Hence, the prevalence of "asthma ever in life" indicates physician-diagnosed asthma which is influenced by the parents' or the children's perception of their symptoms, physician practice, and the availability of health care (19).

Almost all of the ISAAC Phase One participating countries reported that "12-month prevalence of exercise wheeze" differed from "12-month prevalence of wheezing" in both age groups, being consistently higher in older group and lower in younger group (15). The results of our study followed the same pattern. There may be several reasons for such differences between self reporting and parental reporting of symptoms related to exercise wheeze. Parents may report more serious symptoms and they might be less aware of occasional symptoms occurring following exercise. On the other hand, teenagers may have difficulties in differentiating exercise induced wheezing from other poor conditioning forms of breathlessness that may result in over-reporting (20).

A great majority of ISAAC Phase One participating countries reported that "12-month prevalence of night cough" was consistent in both age groups showing higher prevalence than "12-month wheezing"

**Table 5.** Chronological overview of the present and other studies investigating asthma prevalence in Croatian children

| Author/s                      | Study year | Region studied            | Sample (No.) | Age (years) | Prevalence (%) |
|-------------------------------|------------|---------------------------|--------------|-------------|----------------|
| Kolbas V, et al (10)          | 1978/79    | Zagreb                    | 88,673       | 7-18        | 1.3            |
| Restović-Sirotković M (11)    | 1982/83    | Split                     | 510          | 6-14        | 2.8            |
| Banac S (12)                  | 1988/89    | Cres-Lošinj               | 1,201        | 7-14        | 5.9            |
| Aberle N, et al (13)          | 1990       | Slavonski Brod            | —*           | 2-15        | 3.6            |
| Radonić M (unpublished)       | 1998       | Dubrovnik                 | 1,778        | 9-15        | 6.9            |
| Stipić-Marković A, et al (14) | —*         | Zagreb                    | 1,047        | 10-11       | 6.0            |
| Present study                 | 2001/02    | Primorsko-Goranska County | 2,194        | 13-14       | 8.4            |
| Present study                 | 2001/02    | Primorsko-Goranska County | 1,634        | 6-7         | 9.7            |

\*Not reported.

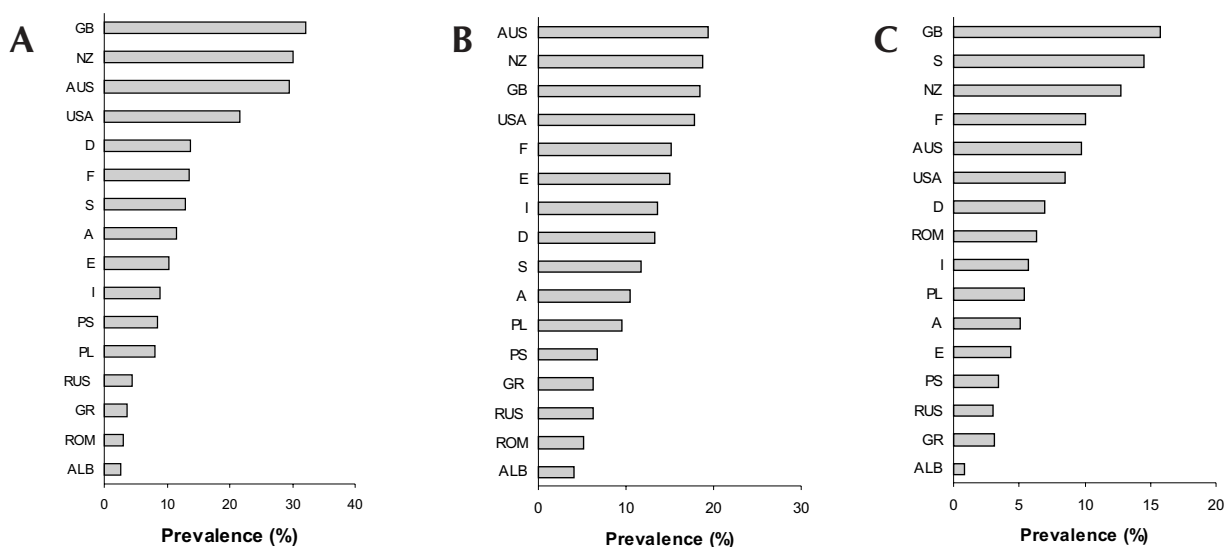


**Figure 1.** Current prevalence rates in the 13-14 years old age group of symptoms of: (A) asthma, (B) allergic rhinoconjunctivitis, and (C) atopic dermatitis, reported in the present study and compared with prevalence of these diseases reported by some ISAAC participating countries (15,24,27). PS – present study; A – Austria; ALB – Albania; AUS – Australia; D – Germany; E – Spain; F – France; GB – United Kingdom; GR – Greece; I – Italy; NZ – New Zealand; PL – Poland; ROM – Romania; RUS – Russia; S – Sweden; USA – United States of America.

(15). Again, analogous results were obtained in our study. According to ISAAC collaborators, such higher prevalence of night cough suggests that this question may be measuring other respiratory conditions as well as that parents may have a higher awareness of child's night cough because it disturbs their own sleep (15).

There is much debate over which methods are the most valid and practicable for asthma prevalence studies. It seems that standardized written questionnaires of self-reported symptoms have become the method of choice for large prevalence surveys, including international comparative studies. However, due to cultural and language differences between the countries being compared, great care must be taken when translating questionnaires. There are many language groups which have no colloquial term for wheezing that is directly equivalent to the English term (21). Therefore, a video questionnaire was developed to try to circumvent the discrepancies of language. However, the ISAAC pilot study, our study, and the great majority of the ISAAC Phase One participating countries found video prevalence estimates lower than written estimates for comparable questions (22). A possible explanation is that visible and audible scenes on a video are likely to represent more severe symptoms than the full spectrum from mild to severe asthma covered by the written questionnaire (15).

The data about the prevalence of allergic rhinitis in Croatian pediatric population is even more lacking than the data related to the prevalence of asthma. There have been two studies conducted among children, 10-20 years ago, which reported the prevalence rates of hay fever to be 1.17% and 1.37%, respectively, and the prevalence rate of perennial allergic rhinitis to be 2.94% (11,23). A recent study conducted among 10-11 years old children in the city of

Zagreb using the ISAAC questionnaire (14), reported much higher prevalence of allergic nasal symptoms than the former two older studies (12-month nasal symptoms 12.13%; nose and eyes affected 7.55%; nasal symptoms ever 14.42%; hay fever ever 9.84%). The results obtained in our study showed even higher 12-month and lifetime prevalence rates of allergic nasal symptoms and hay fever, particularly in the older age group. Temporal comparison of all these epidemiological data suggests that the prevalence of allergic rhinitis in the Croatian pediatric population has increased over the past few decades.

The global ISAAC Phase One study reported a more than fourfold worldwide variation in the prevalence of allergic nasal symptoms in both age groups (24). The prevalence of allergic rhinoconjunctivitis symptoms estimated in our study, together with the results of the survey conducted in the city of Zagreb (14), suggest that Croatia is a country with a moderate prevalence of these symptoms among the pediatric population (range 5 to < 10%). Generally, the grouping of ISAAC participating centers with a lower prevalence of allergic rhinoconjunctivitis was similar to those for asthma symptoms (Fig. 1B).

As might be expected, our results showed that all the answers in the rhinitis questionnaire were higher in the older age group because the majority of nasal symptoms in young children tend to be attributed to infection. In fact, the results of the global ISAAC Phase One report confirmed that questionnaire based differentiation between allergic and infective rhinitis may be a difficult task (24). According to the objective indicators of allergic sensitization in European populations, the combination of nasal and eyes symptoms was found to be the most reliable indicator for epidemiological identification of allergic rhinitis because it correlates better with positive skin prick test in ISAAC

Phase Two (25). However, we believe that 12-month prevalence of nasal symptoms (not the combination of nasal symptoms with eyes affected) would best reflect current prevalence of allergic rhinitis in our population. Since the great majority of children living in the surveyed region are sensitized to house dust mite it may be expected that many of them have perennial allergic rhinitis without associated significant conjunctival symptoms (26). Furthermore, the results of our study showed much higher prevalence of "hay fever ever" than that of "nasal symptoms with eyes affected" in the older age group. This finding suggests that current prevalence of allergic rhinitis would be underestimated in our population if represented with the latter question.

To our knowledge, with the exception of the survey conducted in the city of Zagreb (14), there are no other published studies about the prevalence of atopic dermatitis in the Croatian pediatric population. In the above mentioned study, data collection was performed using ISAAC eczema questionnaire, and the reported results showed slightly higher prevalence rates than the results in our study (atopic eczema symptoms in the last 12 months 7.83%; atopic eczema symptoms ever 18.82%; reported atopic eczema ever 11.27%).

In the global ISAAC Phase One report atopic eczema symptoms were defined as "itchy rash affecting flexural areas". Among European countries, the highest prevalence rates (> 10%) were found in Scandinavia and the United Kingdom, moderate rates (5-10%) in Western Europe, and low rates (< 5%) in former socialist Europe (27). Our results, together with the results of the survey conducted in the city of Zagreb (14), suggest that Croatia is a country with moderate prevalence of atopic dermatitis among the pediatric population (range 5 to < 10%) (Fig. 1C). However, the question considering itchy rash in the last 12 months may slightly overestimate the true prevalence of atopic dermatitis. On the other hand, the definition of the disease in the global ISAAC Phase One report seems to overemphasize flexural forms of eczema.

In conclusion, the results of this study support an increasing prevalence of atopic diseases in Croatia as compared to prior studies. The results were recognized by ISAAC Data Center in Auckland, New Zealand and are suitable for the international comparison. Considering the values estimated in the present study and in the study conducted in the city of Zagreb (14), Croatia is a country with moderate prevalence of atopic diseases among the pediatric population. The results obtained are a baseline for further analytic epidemiological researches.

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