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# Epidemiological Survey 6 Years Apart: Increased Prevalence of Asthma and Other Allergic Diseases in Schoolchildren Aged 13-14 Years in Cluj-Napoca, Romania (Based on Isaac Questionnaire)

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*"I undersign, certificate that we do not have any financial or personal relationships that might bias the content of this work."*

**ABSTRACT**

***Background:*** *The prevalence of asthma and allergy has increased during recent decades.*

***Objective:*** *We investigate the prevalence of asthma and other allergic diseases in children aged 13-14 years and we evaluate the trend of prevalence after an interval of 6 years.*

***Material and methods:*** *We used a core questionnaire designed by the International Study of Asthma and Allergy in Children. In 1991, the questionnaire was administered to 2,866 children from a Romanian city and during 2001 to 1,657 children from the same area.*

***Results:*** *The prevalence of asthma increased from 3.3% in 1995 to 5.5% in 2001 ($p<0.001$). In 1995, 4.3% of children reported asthma-related symptoms, significantly fewer than the percentage 6 years later (13.6%; $p<0.00001$). Similar results were obtained with regard to allergic rhinitis (13.6% versus 20%; $p<0.00001$) and eczema (11.5% versus 16.2%; $p=0.00015$). As far as gender differences are concerned, in the first stage of study all three allergic disorders were found to occur more frequently in females. In the study undertaken in 2001, females proved to have a higher prevalence of asthma ($p=0.226$), but a lower prevalence for allergic rhinitis ($p=0.121$) and eczema ($p=0.064$).*

***Conclusions:*** *The prevalence of asthma and allergy increased significantly during the past 6 years.*

**Keywords:** ISAAC study, asthma prevalence, Romania, children

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## BACKGROUND

Current data published by the World Health Organization reveal that allergic diseases are sixth on the list of causes of morbidity (1). Allergic diseases represent one-third of all chronic diseases in children (2), asthma being the most frequent with a prevalence of between 2 and 25% (1,3). Differences in morbidity can be correlated with genetic and environmental risk factors and also with geographic factors. Over the past 15 years asthma has become a major public health problem, with morbidity due to asthma increasing in many countries during the past two decades. Similar studies 15 to 25 years earlier in Australia (4-6), New Zealand (5,7,8), Switzerland (8), United Kingdom (9,10) and Canada (11) found increased prevalence of asthma and wheezing in children. An increased prevalence of hay fever and eczema in children has also been reported (12,13). Survey data in the United States indicate that the number of children with asthma has more than doubled in the past 15 years. The increased asthma morbidity might be due to a shift in medical practice reflecting the increased awareness and greater readiness to diagnose asthma in wheezing children. Because the genetic features of the population change slowly, genetic susceptibility alone cannot be responsible for the epidemic of asthma that has occurred over the past 15 years. Further research is required into environmental factors such as indoor allergens, tobacco exposure, family size and respiratory infections early in life. Other factors also mentioned as reasons for increased asthma prevalence were: heightened urbanization causing air pollution due to sulphur dioxide, nitrogen dioxide, ozone or vehicle exhausts (1,14-17). Asthma in children is a common part of a more general atopy. It would be interesting to find out if there was a true increase in the prevalence of atopy or if asthma alone had increased in prevalence. ❑

## OBJECTIVES

The aims of this study were to examine the trend of prevalence of asthma, eczema and hay fever between 1995 and 2001 in pupils aged 13-14 years in the city of Cluj Napoca, Romania. ❑

## MATERIAL AND METHODS

**Study areas and population.** The study was undertaken in schoolchildren aged 13-14 years from Cluj-Napoca, a city of approximately 326,000 inhabitants. Surrounded by gentle hills, Cluj-Napoca is situated in Northern Romania, in central Transylvania. The city is moderately industrial but has heavy traffic. Average temperature in July is +22°C and in January is -5°C.

In 1994-1995 the study group consisted of 3,020 pupils aged 13-14 years representing 62.5% of the population of the same age. In 2000-2001, 2,040 pupils of the same age group of schoolchildren from the same schools were enrolled, representing 42.5% of the eligible sample. The schools were selected by simple randomization. Both stages of the study took place between October and March. Parents' consent was obtained prior to the study.

**Study design.** The written questionnaire on asthma, wheezing, allergic rhinitis, and eczema was designed in accordance with the recommendations of the International Study of Asthma and Allergy in Children (ISAAC) (18). The ISAAC questionnaires were translated from English into Romanian by two different people and corrected by an English medical language specialized translator. The translation from Romanian to English was sent to the ISAAC headquarters. Three single page questionnaires were distributed and completed by children under the supervision of a physician who was available to answer any of their questions about the questionnaire. The reproducibility of the questionnaire answers was tested. In those with positive responses to one or more questions, we checked the answers by direct communication with one of the parents after the ISAAC questionnaire had been administered. Included were questions about whether or not asthma had ever been diagnosed, whether wheezing had ever been present or during the previous 12 months, the frequency and severity of symptoms, the presence of a cough during exercise or during the night. Pages two and three of the questionnaire refer to allergic rhinitis and eczema and included similar questions regarding prevalence of symptoms at any time or during the previous 12 months, the diagnosis of the disease made by a physician before the study and the frequency and severity of symptoms. We reported the prevalence of pre-

viously diagnosed asthma based on the answers to the question: "have you ever had asthma?". Positive answers to the first two questions ("wheezing ever" and "wheezing in the past 12 months"), the presence of symptoms during exercise and night cough were used to estimate the prevalence of asthma-related symptoms.

Prior to the questionnaire being administered, pupils were informed about its purpose and agreed to take part in the study, which was approved by the local ethical committee.

**Statistical methods.** The children were randomly sampled and the study groups were homogeneous according to age and sex ratio. We calculated the period prevalence of asthma, wheezing, rhinitis and eczema and the concordance between these allergic diseases in affected children. For comparison of the 1995 and 2001 results, we used $\chi^2$ test with >1 degree of freedom with statistical significance $p<0.05$. We calculated the odds ratio for 95% confidence interval, and applied the same tests to compare allergic disease prevalence within male and female groups. ❑

## RESULTS

Of the total of 3,020 questionnaires distributed during 1995/1996, 2,866 (94.9%) were acceptably answered and analyzed. In 2001/2002 we accepted 1,657 questionnaires out of 1,825 distributed, representing 90.8%. The study groups included 1,459 boys (50.9 %) in 1995/1996 and 777 boys (46.9%) in 2001/2002.

Table 1 summarizes the results of prevalence rates and annual changes in prevalence of asthma, symptoms related to asthma, allergic rhinitis and eczema demonstrating a significant increase of asthma ($p=0.00053$) and of symptoms related to asthma. We also noticed the increase in prevalence of allergic rhinitis (by 7.1%) and eczema (by 4.2%). This increase was significant for both other allergic diseases ($p<0.00001$ for allergic rhinitis and $p=0.0003$ for eczema ever). Wheezing ever, symptoms during exercise and allergic rhinitis presented the highest annual increase in rates.

The increased prevalence of asthma was similar for both males (with 3.5%) and females (with 1.2%). Asthma prevalence was significantly higher in males during the 2001 phase of the study, whereas the prevalence of both allergic rhinitis and atopic eczema were significantly higher in 2001. In 1995 there were no significant differences in the prevalence of either allergic disease with regard to gender. These differences are presented in Table 2. ❑

## DISCUSSION

Our study reveals the increase in asthma prevalence after a period of 6 years in children aged 13-14 years from the city of Cluj-Napoca. The prevalence rate increased from 3.3% in 1995 to 5.5% in 2001, with an annual increase rate of 0.44 percent. The majority of epidemiological studies on the prevalence of asthma reveal the ascendent trend (Table 3). Compared with the prevalence reported by

| | 1995 No=2,866 | 2001 No=1,657 | Percent increase (95% CI) | Annual change of prevalence, % | p |
|---|---|---|---|---|---|
| Asthma ever | 94 (3.3%) | 91 (5.5%) | +2.2% (0.44<OR<0.81) | 0.44 | 0.00053 |
| Symptoms related to asthma: | | | | | |
| -wheezing ever | 153 (5.3%) | 185 (11.2%) | +5.9% (0.38<OR<0.60) | 1.18 | <0.00001 |
| -wheezing during past 12 months | 78 (2.7%) | 136 (8.2%) | +5.5% (0.25<OR<0.44) | 1.1 | <0.00001 |
| -wheezing during exercise | 207 (7.2%) | 274 (16.5%) | +9.3% (0.36<OR<0.53) | 1.86 | <0.00001 |
| -night cough | 111 (3.9%) | 139 (8.4%) | +4.5% (0.35<OR<0.60) | 0.9 | <0.00001 |
| Allergic rhinitis ever | 390 (13.6%) | 343 (20.7%) | +7.1% (0.50<OR<0.77) | 1.42 | <0.00001 |
| Eczema ever | 330 (11.5%) | 260 (15.7%) | +4.2% (0.61<OR<0.87) | 0.84 | 0.0003 |

**TABLE 1.** Prevalence of asthma, asthma-related symptoms, allergic rhinitis and eczema

| | 1995 study No=2,866 | p* | 2001 study No=1,657 | p** | Percent increase |
|---|---|---|---|---|---|
| Asthma ever | | | | | |
| • males | 49 (3.3%) | 0.809 | 53 (6.8%) | 0.026 | +3.5% |
| • females | 45 (3.1%) | | 38 (4.3%) | | +1.2% |
| Wheezing ever | | | | | |
| • males | 72 (4.9%) | 0.327 | 90 (11.6%) | 0.649 | +6.7% |
| • females | 81 (5.7%) | | 95 (10.8%) | | +5.1% |
| Wheezing during past 12 months | | | | | |
| • males | 28 (1.9%) | 0.008 | 66 (8.5%) | 0.713 | +6.6% |
| • females | 50 (3.5%) | | 70 (7.9%) | | +4.4% |
| Wheezing during exercise | | | | | |
| • males | 98 (6.7%) | 0.286 | 111 (14.3%) | 0.021 | +7.6% |
| • females | 109 (7.7%) | | 163 (18.5%) | | +10.8% |
| Night cough | | | | | |
| • males | 42 (2.8%) | 0.004 | 58 (7.4%) | 0.205 | +4.6% |
| • females | 69 (4.9%) | | 81 (9.2%) | | +4.3% |
| Allergic rhinitis | | | | | |
| • males | 192 (13.1%) | 0.534 | 144 (18.5%) | 0.033 | +5.4% |
| • females | 198 (14.1%) | | 199 (22.6%) | | +8.5% |
| Eczema | | | | | |
| • males | 150 (10.3%) | 0.061 | 102 (13.1%) | 0.006 | +2.8% |
| • females | 180 (12.8%) | | 158 (17.9%) | | +5.1% |

**TABLE 2.** Gender differences in the prevalence of asthma, related symptoms and other allergic diseases
p* - differences between genders in 1995 study; p** - differences between genders in 2001 study.

these studies, our data indicate low rates of increase from 0.35 to 0.46 (10,19-22). Other studies (22-27) report a higher increase in annual rate, with values between 1.22 and 2.08%. There are studies that indicate the stabilization trend of asthma during the last few years. The study by Toelle G et al (28) in children aged 8-11 years mentions the increase in asthma prevalence between 1982-1992 and the decrease in prevalence of this disease, although the hyperreactivity of airways remains the same in the period 1992-2002.

Parallel to the increase in prevalence of asthma we noticed the increase in prevalence of current wheezing (during the past 12 months) from 2.72% in 1995 to 8.22% in 2001, with an annual rate of increase of 0.9 percent. In our study the increase in prevalence of current wheezing is much higher compared with the increase in asthma prevalence. In a meta-analysis, Magnus P et al (29) reports only two (23,24) of 8 studies in which the trend of current wheezing has a higher annual rate than in our study (1,22 respectively 1,24). The other studies (10,19,20,30-34) reveal annual increase in the prevalence of current wheezing ranging from 0.14 to 0.65 percent. The increase in prevalence of current wheezing indicates an increasing trend of exacerbation episodes or the apearence of new cases, although some recent studies do not confirm this interpretation. Sunderland R et al (35) revealed a decreasing trend in the frequency of asthma episodes during the period 1993-1999. Since 1999, up to 2002, various authors have reported the stabilization of the prevalence of acute episodes. Dobson R (36) showed that the number of new cases of asthma decreased from 160 at 100,000 consultations in 1993 to 60 in 2002.

Increase in prevalence of asthma and other allergic diseases during the past decades, especially in developed countries, is correlated with changes in life style – the hygiene hypothesis (37). The modern life style produced changes of diet, reducing the frecquency of infections and of contacts with allergens during infancy and the first few years of life. The changes of diet, with a reduction of fruit and vegetables and increase in the polyunsaturated fatty acids may alter the immune response (38,39). The reduction of infections during the first years of life (38,40) produces an imbalance in the Th1/Th2 response, the Th2 being favoured with the release of allergic reaction mediators (41). In children who have one or more older brothers (42) or who went to a crèche at an early age (43) or who have a pet (44) there is a degree of

| Study | Period | Sample | Lifetime asthma | Yearly change rate |
|---|---|---|---|---|
| Mitchell et al (19) | 1968<br>1982 | 952<br>858 | 7.1<br>13.5 | 0.46 |
| Burr et al (10) | 1973<br>1988 | 818<br>965 | 5.5<br>12 | 0.43 |
| Shaw et al (20) | 1975<br>1988 | 715<br>435 | 8<br>13.3 | 0.38 |
| Mitchell et al (7) | 1985<br>1991 | 1084<br>1901 | 14.2<br>16.3 | 0.35 |
| Peat et al (23) | 1982<br>1992 | 1487<br>1668 | 11<br>31.8 | 2.08 |
| Omran et al (24) | 1989<br>1994 | 3403<br>4034 | 10.2<br>19.6 | 1.88 |
| Downs et al (25) | 1982<br>1992<br>1997 | 768<br>850<br>1016 | 12.9<br>30.5<br>38,6 | 1.78<br><br>1,62 |
| Ng Man Kwoget (26) | 1991<br>1999 | 4543<br>4806 | 17.9<br>27.7 | 1.22 |
| Selnes et al (22) | 1985<br>1995 | 10093<br>8676 | 5.1<br>8.6 | 0.35 |
| Al Frayh AR (27) | 1986<br>1995 | 2123<br>1008 | 8<br>23 | 1.6 |

**TABLE 3.** The evolution of asthma prevalence and the annual changes in prevalence

protection against the development of atopy. Under these circumstances the infections during the first months or years of life, and the early allergenic contact stimulates the immune system to produce a normal response (Th1). Another cause incriminated in the increase in prevalence of asthma and other allergic diseases is represented by the frequent use of chemical products for children's hygiene, chemical products that might precipitate or exacerbate the respiratory and allergic symptoms (45,46).

Several critical analyses on asthma epidemiology suggest a possibly false interpretation of the results (biases symptoms) that indicate the increase in prevalence (28,31,47). Different studies, some performed in the same country and during the same period, report very different annual rates of increase in the prevalence, varying from 0.35% to 2.08% (29). There are very few studies that use objective criteria (determination of airways reactivity, testing skin sensitivity for allergens) to study the trend of the prevalence of asthma and other allergic diseases (10,23). The great majority of studies only use clinical data that might be influenced by errors due to educational methods addressed to a population which required a better knowledge of the diseases. Continued medical education and the new antiasthma drugs have contributed to a transfer of the diagnosis from bronchitis/wheezing to asthma. On the other hand, in some studies, changing diagnostic criteria and study questionnaires might also produce errors in interpretation of results (23,48, 49).

In our study, we recorded the increase in prevalence of allergic rhinitis concomitent with the increase in prevalence of asthma (from 13.6% in 1995 to 20.7% in 2001) and also in the prevalence of atopic dermatitis (from 11.5% in 1995 to 15.7% in 2001). The ascending trend for the 3 diseases indicates indirectly the real increase in the prevalence of allergy. A national survey was underwent in Romania between 2006-2007, in 200 schools from all regions, using a simplified ISAAC questionnaire. A number of 47.695 questionnaires were analysed and the data revealed a prevalence of asthma of 7.2% in children aged 13-14 years and of 6,4% in younger children of 6-7 years of age (50). These data were reported at international meetings. In a study carried out in pupils over a period of 20 years (1978-1998) Anthrocopoulos M et al considered that the increase in prevalence of asthma is real because the ratio between current asthma diagnosed by the physician / current wheezing diagnosed by the physician was simillar during 1991-1998, which shows that there was no diagnostic transfer from bronchitis to asthma (47). The real increase in prevalence is demonstrated by studies that used objective criteria to prove hyperreactivity of the airways and of atopy. Peat JK et al (23) studied the trend of prevalence of airway hyperreactivity in 2 regions from Australia and noticed increasing rates of

1.4- and 2-fold during a 10-year period (1982-1992). The increases were higher in atopic children. Two epidemiological studies that also used the skin prick test method revealed the increase in prevalence of allergy. Downs et al (25) showed a significant 6.7 % increase of atopy between 1992 and 1997. Von Mutius E et al (50) proved an increase in atopy prevalence from 19.3% in 1991/1992 to 26.7% in 1995/1996 in children aged 9-11 years from Leipzig. The authors correlate these change in prevalence with the introduction of a new life style in the former East Germany. ❑

## CONCLUSION

Based on our epidemiological data we conclude that the prevalence of asthma, of allergic rhinitis and of eczema increased significantly during the past decade. The ascending trend of allergic diseases in Romania is simillar with those in developed countries worlwide. ❑

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