TRENDS IN PREVALENCE OF ASTHMA IN CHILDREN
BY THE EXAMPLE OF THE KYIV REGION OF UKRAINE

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ABSTRACT
Asthma constitute a significant cause of morbidity worldwide and a considerable burden on the health and medical systems of both developed and emerging economies. The article presents the results of the study of the prevalence of asthma symptoms in children of different ages (from 0 to 18 years) in the Kyiv region of Ukraine. Quite high levels of “wheezing in the past 12 months” are noted: 6 month-5 years – 24.6%; 6-7 years – 18.7%; 13-14 years – 12.6%; 15-17 years - 9.2%. But at the same time, the low level of asthma diagnosis remains an important problem in Ukraine. The levels of asthma symptoms, which may indicate a severe course of the disease, are also quite high. The article presents the results of similar studies in other countries for comparison.

KEYWORDS
prevalence of asthma, children, wheezing, Ukraine.

Introduction. The prevalence of asthma has been steadily increasing among children and adults. Globally, asthma is ranked 16th among the leading causes of years lived with disability and 28th among the leading causes of burden of disease [1].

Today, despite the availability of effective therapy and prevention, the economic costs associated with asthma are only increasing worldwide. They are rated as one of the highest among chronic diseases. The greatest economic costs are for children and the elderly, as well as for women compared to men. Among the pediatric population, about 41.3% of the total amount is spent on medicines, which is significantly higher than in adults [2]. Also, the higher costs are spent for patients with comorbid pathology, which significantly complicates the course of asthma, and may also be one of the causes of resistance to anti-inflammatory therapy, which reduces the effectiveness of treatment and worsens the prognosis of the disease [3]. Severe asthma is often associated with comorbidities, including obesity, rhinitis, nasal polyps and food allergies [1]. The high rate of disability of children is usually due to the uncontrolled course of the disease due to poor diagnosis or lack of treatment of the disease or the low effectiveness of standard anti-inflammatory therapy regimens (in 30% of children with asthma) [3].

All these important issues require resolution and settlement. This, in turn, led to the need for large-scale epidemiological studies with unified criteria, which allowed to collate data from around the world. An international epidemiological study was conducted to study the prevalence of allergic diseases in children. An international epidemiological – International Study of Asthma and Allergies in Childhood (ISAAC; http://isaac.auckland.ac.nz/) was conducted to study the prevalence of allergic diseases in children. ISAAC Phase One surveyed about 700,000 children from 156 centers in 56 countries and ISAAC Phase Three surveyed about 1,200,000 children from 233 centers in 98 countries (involving almost 800,000 children aged 13-14 years and almost 400,000 aged 6-7 years) [4, 5]. The study showed not only the true prevalence of asthma in the pediatric population, but also the dynamics of a minimum 5-year interval thanks to Phase Three and had studied the factors influencing the formation of asthma.
The ISAAC affirms that the incidence of allergic diseases has grown into an epidemic. However, there is a large geographical variation in asthma prevalence, severity, and mortality. While asthma prevalence is higher in high income countries, most asthma-related mortality occurs in low-middle income countries [1, 6]. The discrepancy between the incidence and mortality rates of asthma is observed in different countries. There is also an inverse correlation with socioeconomic status. The high prevalence of AD is observed in populations with low socio-economic development, as the population lives in poor conditions (by physical, social and psychological criteria). Due to a number of social, political and economic reasons, some populations become isolated in adverse environmental conditions, which may result in increased exposure to risk factors [4].

In particular, the ISAAC also showed the prevalence of severe asthma symptoms. Severe asthma is associated with the loss of lung function in childhood and is a major determinant of early chronic obstructive pulmonary disease (COPD). Therefore, prevention of severe childhood asthma should be a major component of efforts to reduce premature COPD mortality [1].

An epidemiologic study cannot solve all the problems of interest to the clinician, but it does help to establish a true picture of the prevalence of the disease, outline the range of issues, and identify specific categories of children who need more detailed study.

**Methods and materials.** The standardized questionnaires of the international program ISAAC were used to determine the prevalence of current symptoms of asthma [4]. During 2017-2019, survey was conducted at pre-schools and schools of the Kyiv region among children of the following age categories: 6 months-5 years (Group I - united pre-planned age categories 6 months-3 years and 4-5 years due to low the number of respondents), 6-7 years (Group II), 13-14 years (Group III), and 15-17 years (Group IV).

In accordance to the ISAAC program methodology, to obtain valid results, the sample size of 3000 children for each age group was recommended (in case of individual centers study, a minimum sample of 1000 people was allowed) [4, 7]. To establish a representative sample size, we used the formula for determining the sample size by Lisitsyn Yu. P. (1987) [8], according to which the optimal sample size was 7105 children.

The study was conducted in compliance with the current Ukrainian legislation and meets the international ethical requirements. The approval of bioethical expert commission is received. The permits issued by the Department of Education and Science and the Department of Health of the Kyiv region were obtained. Written questionnaires were completed by children’s parents and by senior students on a voluntary basis. Educational institutions have been chosen randomly.

Data analysis was performed using “R” version 3.6.0. software using nonparametric statistical processing methods to determine the significant difference between the two independent groups.

**Research results.** As a result of the study, 7106 correctly completed questionnaires were received at this stage, which is 98.6% of the respondents. The distribution by the age categories is following: Group I has 1787 children (, Group II – 2080 children, Group III – 1909 children, Group IV – 1330 children. The gender distribution of the sample is about 1:1.

The prevalence of asthma symptoms among the surveyed pediatric population, namely the index «wheezeing in the past 12 months», which corresponds to question # 2 in each block of the questionnaire (were selected as the most sensitive criterion, based on the international experience of colleagues) has the rank of 16.8% (1192/7106), and among them is reliably higher in boys – 18.9% (645/3418), and in girls – 14.8% (547/3688) (χ²=20.439; p=0.000).

The distribution by age categories is following: Group I has 24.6% (440/1787), Group II – 18.7% (388/2080), Group III – 12.6% (241/1909), Group IV – 9, 2% (123/1330) – with a significant difference between the groups (p = 0.000) (Table 1). The highest rates of asthma symptoms prevalence are observed among children of the youngest age group, which, of course, is due to age-related anatomical and physiological features and features of the autonomic nervous system in young children. There is a gradual decrease in asthma incidence over the years, but they remain quite high. The same trends persist for «wheezing at any time in the past». Another indicator that may also indicate asthma in a child – "dry cough at night, apart from a cough associated with a cold or chest infection" - is quite high in Group I and II children, accounting for 17.2% and 18.0 % respectively.

Table 2 and 3 presents the prevalence of wheezing by gender distribution. The prevalence of wheezing among boys is significantly higher than girls in Group I (χ²=20,453; p=0,000).
Table 1 The prevalence of symptoms of asthma in children in the Kyiv region (Ukraine), frequency, %

| symptoms of asthma | Age groups          | P       |
|--------------------|---------------------|---------|
|                    | 6 months – 5 years  | 6-7 years | 13-14 years | 15-17 years |
|                    | (n=1787)            | (n=2080) | (n=1909)    | (n=1330)    |
| 1. wheezing at any time in the past | 31.6 | 28.3 | 26.2 | 20.3 | <0,000 |
| 2. wheeze in the past 12 months | 24.6 | 18.7 | 12.6 | 9.2 | <0,000 |
| 3. attacks of wheezing in the past 12 months | | | |
| 1 | 7.7 | 6.5 | 4.2 | 5.0 | <0,000 |
| 2 to 3 | 11.1 | 8.0 | 5.4 | 5.0 | <0,000 |
| 4 to 12 | 5.0 | 3.5 | 1.8 | 1.2 | <0,000 |
| > than 12 | 1.1 | 0.9 | 1.3 | 0.6 | 0.239 |
| 4. How often, on average, has your child’s sleep been disturbed due to wheezing? | | |
| never | 11.3 | 10.8 | 8.6 | 6.4 | <0,000 |
| < than 1 per week | 7.9 | 5.6 | 3.6 | 2.6 | <0,000 |
| 1 or > per week | 1.6 | 1.3 | 1.0 | 1.0 | 0.274 |
| 5. Has wheezing ever been severe enough to limit your child’s speech to only one or two words at a time between breaths? | 4.0 | 1.8 | 2.2 | 1.9 | <0,000 |
| 6. Has your child ever had asthma? | | |
| 0.8 | 1.9 | 3.7 | 2.8 | <0,000 |
| 7. Has your child’s chest sounded wheezy during or after exercise? | 5.1 | 5.2 | 7.9 | 8.0 | <0,000 |
| 8. Has your child had a dry cough at night, apart from a cough associated with a cold or chest infection? * | 17.2 | 18.0 | 12.9 | 10.5 | <0,000 |

Table 2 The prevalence of “wheezing in the past 12 months” among boys (symptom of asthma, as the most sensitive criterion)

| AGE (YEARS) | N | %     | 95% CI       |
|-------------|---|--------|--------------|
| ALL         | 645 | 18.9  | 17.6-20.2    |
| 0-5         | 265 | 29.2  | 26.3-32.3    |
| 6-7         | 210 | 19.6  | 17.3-22.1    |
| 13-14       | 127 | 14.0  | 11.8-16.5    |
| 15-17       | 43  | 8.1   | 5.9-10.7     |

Table 3 The prevalence of “wheezing in the past 12 months” among girls (asthma symptom, as the most sensitive criterion)

| AGE (YEARS) | N  | %     | 95% CI       |
|-------------|----|--------|--------------|
| ALL         | 547 | 14.8  | 13.7-16.0    |
| 0-5         | 175 | 19.9  | 17.3-22.7    |
| 6-7         | 178 | 17.6  | 15.3-20.1    |
| 13-14       | 114 | 11.4  | 9.5-13.5     |
| 15-17       | 80  | 10.1  | 8.0-12.4     |

Severe asthma symptoms (representative questions #3 (had had> 4 attacks of wheezing in the past 12 months; > than 12 attacks of wheezing), #4 (had had> 1 night per week sleep disturbance from wheeze), #5 (have had wheeze affecting speech) are more clearly presented at Figure 1. Presented asthma symptoms, which may indicate the severity if this disease, are high enough.
According to the obtained data, there are quite low levels of asthma confirmed by specialists in all age categories. Diagnosed asthma at the time of the survey: in Group I - 0.8% (0.4-1.3), Group II - 1.9% (1.3-2.6), Group III - 3.7% (2.9-4.6), Group IV - 2.8% (2.0-3.8). While the prevalence of wheezing is much higher in all groups (Figure 2). Wheezing is not considered by doctors as an equivalent of the asthma attack, as a possible version of mild or moderate asthma.

ISAAC has demonstrated, by means of simple standardized questionnaires, that there are large variations in the prevalence of asthma symptoms throughout the world. The prevalence of asthma symptoms in different regions of Ukraine with neighboring countries, European countries and the world average can be compared using the data given in Table 3 and 4 [7, 8, 9]. We will continue to use for further analysis only the results from two age groups – Group II (6-7 years) and Group III (13-14 years) as provided by the methodology of the international ISAAC program [7].

High rates of wheezing in the past 12 months are observed, even compared to Kharkiv region (Ukraine) and neighboring countries, while at the same time low level of diagnostics compared to Europe, especially in the younger age category.

| Region                          | wheeze in the past 12 months | diagnosis of asthma at any time | wheeze during or after exercise | dry cough at night |
|---------------------------------|------------------------------|---------------------------------|---------------------------------|-------------------|
| Ukraine, Kyiv region            | 18.7                         | 1.9                             | 5.2                             | 18.0              |
| Ukraine, Kharkiv region         | 4.5                          | 0.3                             | 1.3                             | 5.5               |
| Republic of Belarus (Grodno region) | 9.3                         | 2.9                             | 1.7                             | 8.2               |
| Russia                          | 5.9-13.2                     | 0.66-9.6                        | 2.8-21.8                        | 7.8-13.6          |
| Western Europe                  | 8.1                          | 7.2                             | 3.7                             | 16.1              |
| Northern and Eastern Europe     | 8.8                          | 3.2                             | 3.6                             | 11.4              |
| World average                   | 4.1-32.1                     | 1.4-27.2                        | 1.6-16.5                        | 5.9-39.5          |
Table 4 Prevalence of current symptoms of asthma, by region among 13-14 years age children, %

| Region                                      | wheeze in the past 12 months | diagnosis of asthma at any time | wheeze during or after exercise | dry cough at night |
|---------------------------------------------|------------------------------|---------------------------------|---------------------------------|-------------------|
| Ukraine, Kyiv region                        | 12.6                         | 3.7                             | 7.9                             | 12.9              |
| Ukraine, Kharkiv region                     | 3.3                          | 0.7                             | 2.9                             | 4.7               |
| Republic of Belarus (Grodno region)         | 9.1                          | 4.1                             | 12.8                            | 14.6              |
| Russia                                      | 5.3-16.9                     | 0.66-8.9                        | 7.1-23.4                        | 6.2-17.8          |
| Western Europe                              | 16.7                         | 13.0                            | 20.0                            | 27.1              |
| Northern and Eastern Europe                 | 9.2                          | 4.4                             | 12.3                            | 12.2              |
| World average                               | 2.1-32.2                     | 1.6-28.2                        | 2.3-43.4                        | 4.0-42.3          |

Conclusions. The results of the study indicate a fairly high levels of asthma symptoms prevalence in Kyiv region of Ukraine, which is consistent with global trends. Wherein, low rates of diagnosed asthma in all age categories were detected. Asthma underdiagnosis remains super important problem in Ukraine. This lack of proper recognition often results in a lack of, or incorrect, diagnosis resulting in sub-optimal disease management, negative effects on quality of life, increased morbidity and mortality, and considerable additional direct and indirect costs [10]. The conducted study should inform doctors and public health care institutions first and urge scientists to further address the issues raised.

Conflict of interest. None declared.

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