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Pilot study to determine asthma-like symptoms in the Sverdlovsk region

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Abstract

Introduction. Bronchial asthma (BA) occupies one of the leading places in the structure of chronic nonspecific lung diseases in children. At an early age it develops in a relationship between genetic and environmental factors and often does not have a characteristic clinical picture. Allergic rhinitis (AR) increases the risk of developing and severity of asthma. Assessing the risk of developing BA and AR in children is necessary for timely diagnosis.

Purpose of the study. To identify the prevalence of symptoms of bronchial asthma in children in the Sverdlovsk region using the example of Yekaterinburg and Nizhny Tagil using Russian versions of the Asthma Prediction Tool and ISAAC questionnaires and analyze the data obtained.

Materials and methods. 64 children aged 6-8 years who did not have chronic lung diseases were studied: 30 people - in the Children's Hospital No. 8 of Yekaterinburg and 34 - in kindergarten No. 201 of Nizhny Tagil using Russified versions of the "Asthma Prediction Tool" and ISAAC questionnaires, filled out official representatives of children after informed consent to conduct the study. 64 correctly completed questionnaires were analyzed.

Results. The proportion of children with an average and high risk of developing asthma: in Yekaterinburg 26.67%, in Nizhny Tagil - 35.29%. Symptoms of AR were detected in 60% of children from Yekaterinburg and in 82.35% from Nizhny Tagil, which is 2.5 and 1.6 times more common than the established diagnosis of AR, respectively. In Yekaterinburg, a high risk of asthma is associated with an allergic phenotype based on the frequency of concomitant atopic dermatitis (16.67% compared with 10% in the low-risk group, $p = 0.0159$) or its absence (63.33% and 10%, respectively, $p = 0.0159$), in Nizhny Tagil this relationship was not confirmed when tested by a two-sided Fisher test. The frequency of cases of hereditary predisposition to allergic pathology does not have significant differences between high (medium) and low risk groups in both cities.

Conclusion. In Russia, 4.8 additional cases of asthma and status asthmaticus per 100 thousand children are associated with air quality. In 2021, the Sverdlovsk region is noted as one of the priority subjects of the Russian Federation in terms of the number of asthma diseases associated with the aerogenic factor in the environment of children. Although the observed trend in the predominance of cumulative symptoms of asthma and AR in children in Nizhny Tagil, in comparison with Yekaterinburg, is not statistically significant, it correlates with a higher level of aerogenic air pollution, this indirectly confirms the absence of a statistically significant relationship with a family history of allergic pathology. However, the connection with man-made pollutants is not taken into account in the ISAAC questionnaires. To confirm that the prevalence of asthma and AR symptoms is higher than those obtained in multicenter studies among children of a similar age, a survey of at least 350 people will be required. In any case, it is necessary to study the role of priority

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pollutants in the formation of airway hyperresponsiveness, asthma and AR, in order to find effective preventive measures.

Keywords: Children; Bronchial asthma; Allergic rhinitis; Comorbid diseases; Risk factors; ISAAC

1. Introduction

Bronchial asthma remains a pressing medical, social and economic problem in pediatrics [1], it occupies a leading place in the structure of chronic nonspecific lung diseases in children. In recent decades, there has been a significant increase in the prevalence of this disease, according to a report by The Global Asthma Network, currently about 358 million people suffer from this disease, 14% of them are children [2]. Official data on the prevalence of the disease based on patient visits is an order of magnitude lower than the actual values and does not fully reflect the true scale of the problem. The onset of the disease in 70-80% of cases occurs before the age of 6 years. The start of therapy and the prognosis of the disease are determined by the timely diagnosis of asthma.

The development of asthma in young children is associated with genetic and environmental factors during critical age periods of maturation of the immune system. This dictates the need to conduct epidemiological studies on the prevalence of this pathology, especially in regions with unfavorable environmental conditions that predispose to the development of respiratory diseases.

A study conducted by Naumova V.V. in 2009 in the city of Novouralsk, Sverdlovsk region, revealed a discrepancy between the data on the prevalence of asthma (6.5%) and the overall incidence (1.5% in 2003), which indicates underdiagnosis of asthma [3].

The Sverdlovsk region is a region with developed industry and a high level of urbanization. According to the state report "On the state of the environment in the Sverdlovsk region in 2021," air quality in the Sverdlovsk region has deteriorated sharply over the year. Compared to 2020, the level of air pollution in Nizhny Tagil changed from high to very high, in Yekaterinburg, Krasnoturinsk and Kamensk-Uralsky - from low to high. Emissions of pollutants into the atmosphere increased by 0.05% compared to 2020 and amounted to 784 thousand tons. Constant exposure to aerogenic irritants on the body leads to maladaptation of immune mechanisms, hyperreactivity of the respiratory tract and an increase in the number of diseases of the bronchopulmonary system of allergic etiology [4].

Allergic rhinitis is also a risk factor for the development of asthma and contributes to its more severe course, increasing the frequency and severity of exacerbations. Therefore, it is necessary to identify symptoms of asthma in children suffering from allergic rhinitis [5].

Despite the interest of researchers, there is no valid predictive model for the development of asthma in children. Some predictors of AD development have been identified, but taking into account the heterogeneity of pathogenetic mechanisms, the significance of individual factors of their combinations in its formation requires further study.

Thus, it is relevant for study to assess the risk of developing BA and AR in children of preschool and primary school age in areas with increased air pollution using modern standardized questionnaires, the use of which is becoming increasingly widespread throughout the world.

1.1. Purpose of the study

To identify the prevalence of symptoms of asthma and allergic rhinitis in children in the Sverdlovsk region using the example of Yekaterinburg and Nizhny Tagil using Russian versions of the Asthma Prediction Tool and ISAAC questionnaires and analyze the data obtained.

2. Materials and methods

The study was conducted on the basis of the State Autonomous Institution of Children's Hospital No. 8 in Yekaterinburg and in kindergarten No. 201 in Nizhny Tagil using Russian versions of questionnaires: "Asthma Prediction Tool" to identify the risk of developing bronchial asthma in children and ISAAC to assess the prevalence of symptoms and to identify risk factors for the development of allergic rhinitis. These methods are focused on the search for predictive factors, knowledge of which makes it possible to more likely identify a group of children predisposed to the development of bronchial asthma and allergic rhinitis. The questionnaires were completed by official representatives of children aged 3 to 8 years, who signed informed consent for the study. 30 children from Yekaterinburg and 34

children from Nizhny Tagil who did not have respiratory diseases were included. 64 correctly completed questionnaires were analyzed. Among the respondents there were 62.5% (n=40) boys (53.33% (n=16) from Yekaterinburg and 70.59% (n=24) from Nizhny Tagil) and 37.5% (n=24) girls (46.67% (n=14) from Yekaterinburg and 29.41% (n=10) from Nizhny Tagil). Statistical processing of the obtained data was carried out using Microsoft Office Excel 2016 spreadsheets, the chi-square test (χ^2) with Yates' correction for continuity, the calculation of one-sided and two-sided Fisher tests was made using the Statistica 13.0.5.17 application.

3. Results

3.1. Study of the prevalence of symptoms of bronchial asthma and identification of risk factors for the development of the disease

For each child, the total score on the "Asthma prediction tool" questionnaire was determined and the probability of developing bronchial asthma in the future was calculated. Low risk 0-3 points, medium and high risk of developing the disease 4 or more points.

According to the survey results, the proportion of children with a low risk of developing asthma in Yekaterinburg was 73.33% (n=22), in Nizhny Tagil – 64.71% (n=22). The proportion of children with an average and high risk of developing asthma in Yekaterinburg is 26.67% (n=8), in Nizhny Tagil it is higher, 35.29% (n=12). Significance level 2. p=0.6363.

Among children with average and high risk, in comparison with the low-risk group, boys were more likely to develop asthma (62.5% and 50%, respectively), concomitant atopic dermatitis (75% and 4.55%), shortness of breath with wheezing (50% and 0%), wheezing after exercise (62.5% and 13.64%) and hereditary predisposition to allergic diseases (37.5% and 27.27%) (Fig. 1 and Fig. 2)

To the question of the questionnaire about the presence of "episodes of wheezing in the child in the last 12 months without an accompanying cold," 12.5% (n=1) of respondents from Yekaterinburg answered positively, while parents of children from Nizhny Tagil responded positively by 2 times more – 25% (n=3) (Fisher's test p=0.4654).

25% (n=2) of parents of children from Yekaterinburg and 8.33% (n=1) from Nizhny Tagil answered affirmatively about the presence of more than 3 episodes of wheezing in the last 12 months (Fisher test p=0.3439).

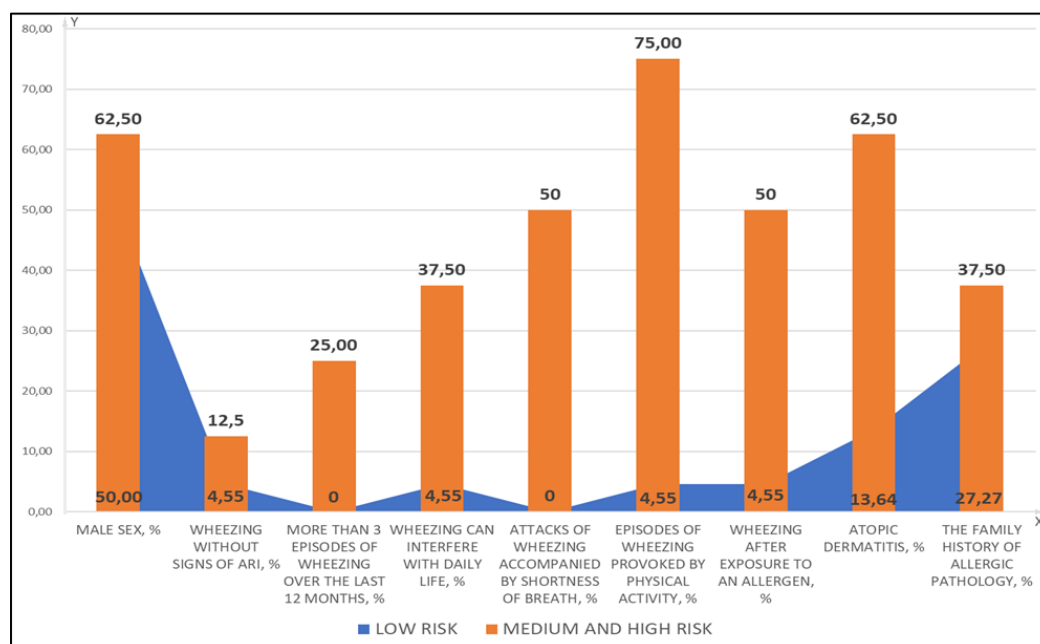


Figure 1 Results of the "Asthma Prediction Tool" questionnaire in Yekaterinburg

Attacks of wheezing were accompanied by shortness of breath in 50% (n=4) of patients from Yekaterinburg and 8.33% (n=1) from Nizhny Tagil. In 75% (n=6) of the examined children from Yekaterinburg and 33% (n=4) from Nizhny Tagil, episodes of wheezing were provoked by physical activity. In 50% (n=4 in Yekaterinburg and n=6 in Nizhny Tagil,

respectively) of cases, episodes of bronchial obstruction were provoked by contact with household allergens (Fisher test $p=0.675$).

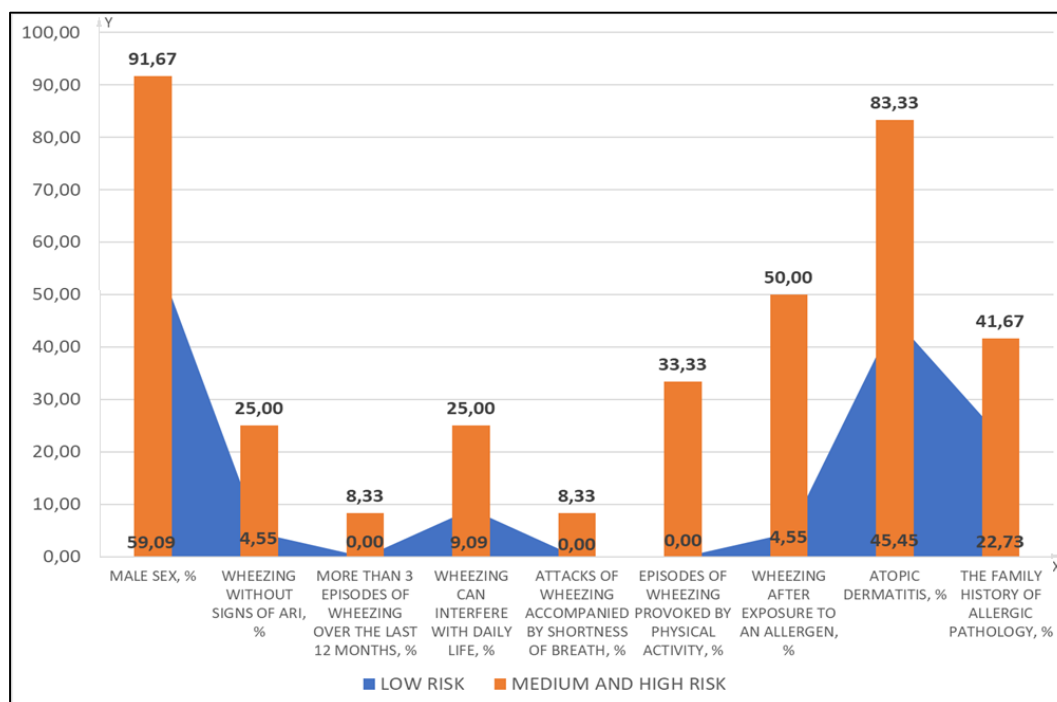


Figure 2 Results of the "Asthma Prediction Tool" questionnaire in Nizhny Tagil

The presence of atopic dermatitis in the anamnesis was confirmed by 62.5% ($n=5$) of respondents from Yekaterinburg and 83.33% ($n=10$) from Nizhny Tagil (Fisher test $p=0.2962$).

The family history of allergic pathology on the part of close relatives in children of average and high risk of developing asthma was 37.5% ($n=3$) in Yekaterinburg, 41.67% ($n=5$) in Nizhny Tagil (Fisher test $p=0,6641$).

Thus, the value of the one-sided Fisher test for the designated predictors is greater than the critically significant level ($p = 0.05$), i.e., no statistically significant difference between cities in their presence or absence in groups of children with an average/high risk of developing AD was found.

Among children in Yekaterinburg with an average/high risk of asthma, compared to the low-risk group, the following signs were significantly more common: "wheezing interferes with life" ($p = 0.0475$), shortness of breath during wheezing ($p = 0.0026$), wheezing after contact with an allergen ($p = 0.0112$), after physical activity ($p = 0.0003$). Probably, in Yekaterinburg, a medium/high risk of developing asthma is associated with an allergic phenotype based on the frequency of concomitant atopic dermatitis (16.67% compared with 10% in the low-risk group, $p = 0.0159$), or its absence (63.33% and 10%, respectively, $p = 0.0159$).

In children of a similar group from Nizhny Tagil, a statistically significant difference, in comparison with children with a low risk of developing asthma, was found in the following signs: wheezing after contact with an allergen ($p = 0.0039$), after physical activity (0.0107). Significant differences in the proportion of children with the absence of atopic dermatitis at a low risk of asthma (35.294%), compared with children from a high-risk group (5.882%), were captured only by the one-sided Fisher test ($p = 0.0352$), however, the more accurate two-sided Fisher test found no differences ($p=0.0662$).

It is noteworthy that the frequency of cases of hereditary predisposition to allergic pathology does not have significant differences between high and medium risk groups in both cities.

3.2. Study of the prevalence of symptoms of allergic rhinitis in children

Analysis of the questionnaires showed that the frequency of cumulative symptoms of allergic rhinitis prevailed in children from N. Tagil in comparison with children from Yekaterinburg (Fig. 3 and Fig. 4). But a comparison of the

proportion (number of children) of low and medium (high) risk for allergic rhinitis in Yekaterinburg and Nizhny Tagil did not reveal a statistically significant difference (significance level 2· p = 0.7259).

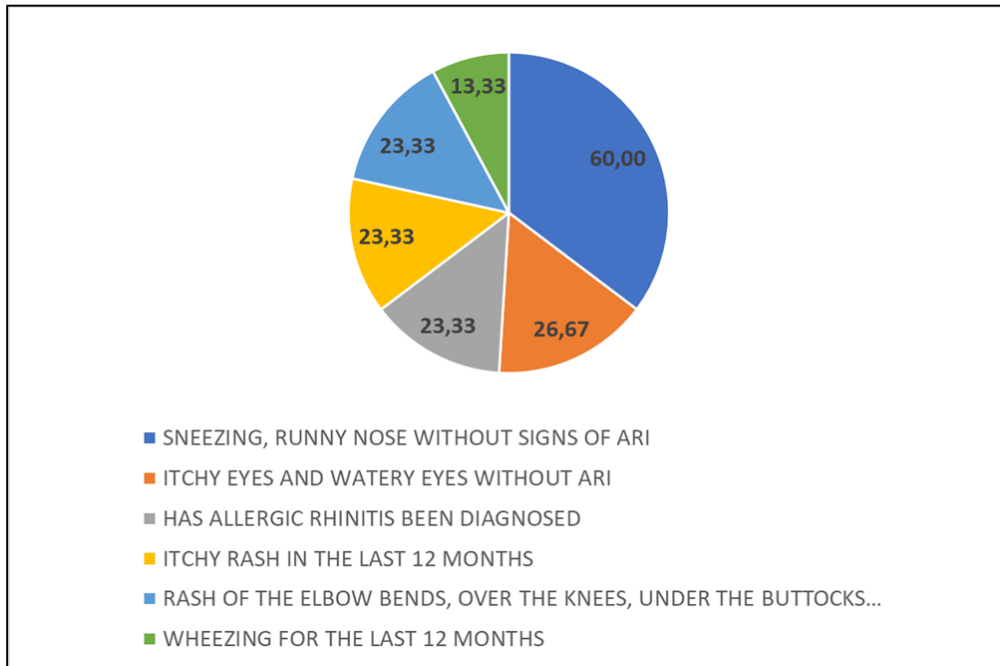


Figure 3 Prevalence of symptoms of allergic rhinitis in children of Yekaterinburg

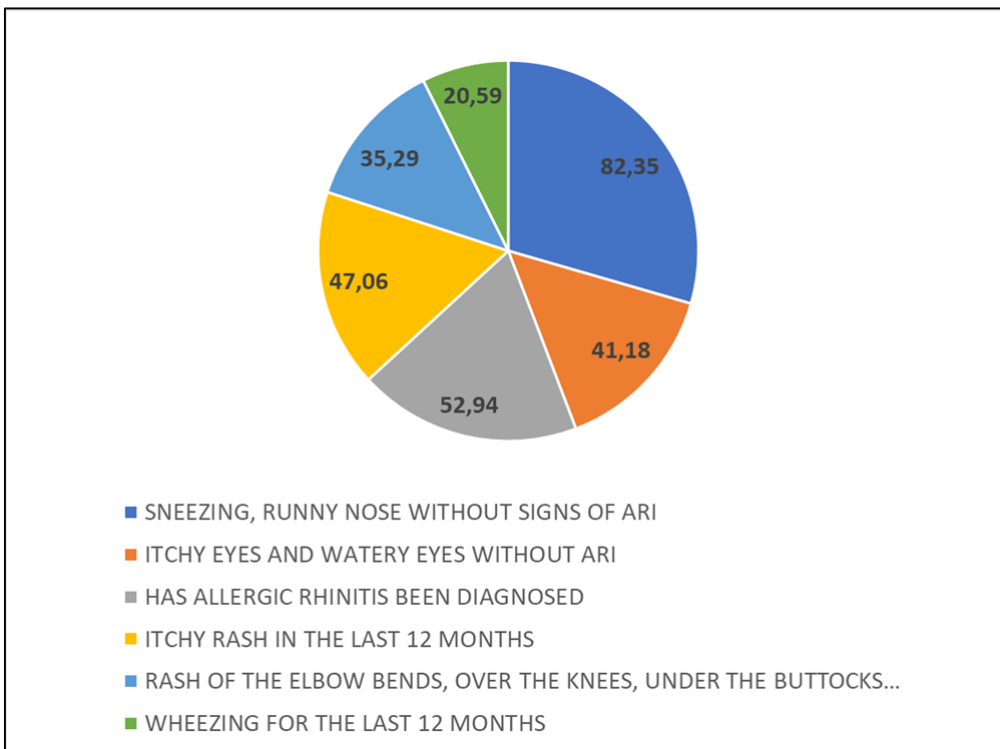


Figure 4 Prevalence of symptoms of allergic rhinitis in children of Nizhny Tagil

“Sneezing, runny nose, nasal congestion in a child over the past 12 months without signs of ARI” occurred in 60% (n=18) of children from Yekaterinburg and 82.35% (n=28) of children from Nizhny Tagil. The combination of these symptoms

with itchy eyes and lacrimation was noted in 26.67% (n=8) of children from Yekaterinburg and 41.18% (n=14) from Nizhny Tagil.

23.33% (n=7) of children from Yekaterinburg and 52.94% (n=18) of children from Nizhny Tagil answered affirmatively to the questionnaire item about the presence of a confirmed diagnosis of “allergic rhinitis”.

An itchy rash bothered 23.33% (n=7) of children from Yekaterinburg and 47.06% (n=16) of children from N. Tagil over the past 12 months.

3.3. Identification of risk factors for the development of allergic rhinitis in children

The use of a validated ISAAC questionnaire to identify risk factors for the development of AR allowed us to analyze the contribution of numerous hereditary and environmental factors to the development of AR in children. This questionnaire included questions about the presence of allergic diseases in relatives, feeding habits in the first year of life, contact with pets, passive smoking, etc. (Fig. 5 and Fig. 6).

The presence of allergic pathology in the mother was detected in 26.67% (n=8) of children from Yekaterinburg and in 44.18% (n=15) of cases in Nizhny Tagil. Paternal involvement is 13.33% (n=4) of cases in Yekaterinburg and 41.18% (n=14) of cases in Nizhny Tagil. At the present stage, to increase the effectiveness of prognostic criteria, it is proposed to consider parental smoking as additional risk factors for the disease. Smoking in the first year of a child’s life and in the presence of a child was confirmed by 3-4 parents in each of the cities studied.

60% (n=18) of children from Yekaterinburg and 47.05% (n=16) of children from Nizhny Tagil had regular contact with pets in the first year of life.

Particular importance is attached to breastfeeding, which can provide a protective effect against the development of allergic diseases in the first years of a child’s life. Analysis of the questionnaire showed that the proportion of children with an identified high risk of developing asthma and symptoms of AR in preschool age is significantly lower among those who were breastfed for at least 6 months of life (82.81% and 41.11%, respectively).

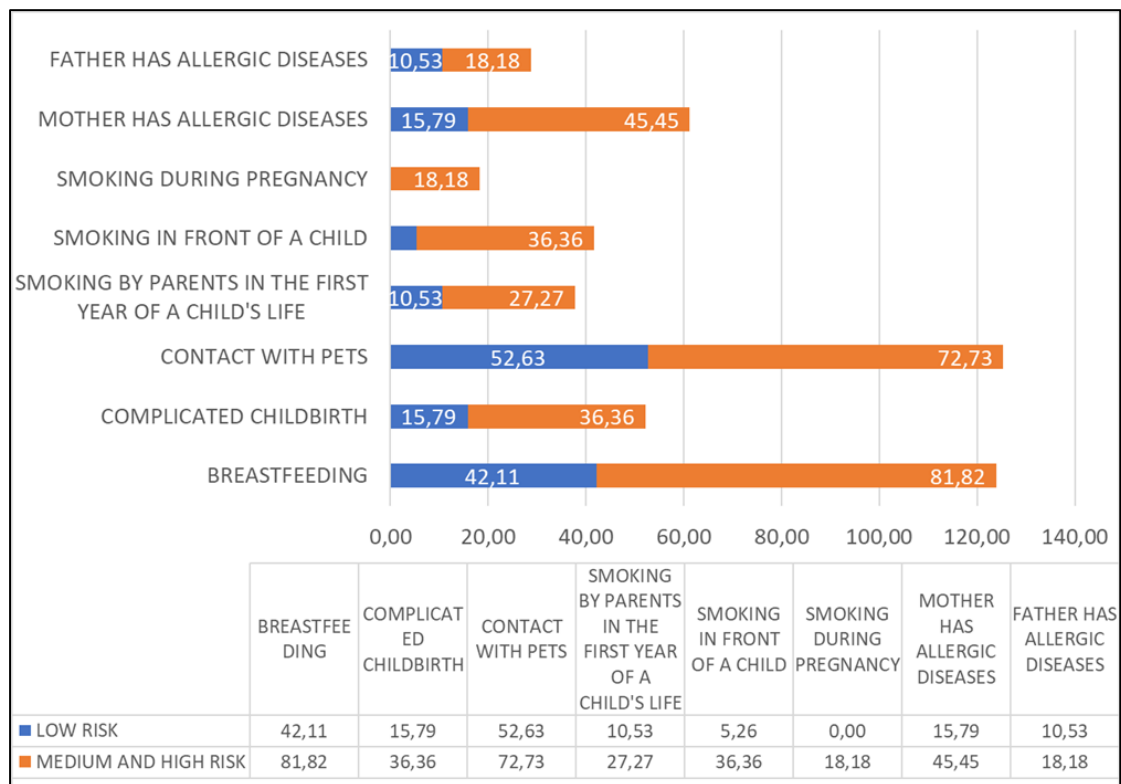


Figure 5 Risk factors for the development of allergic rhinitis in children in Yekaterinburg

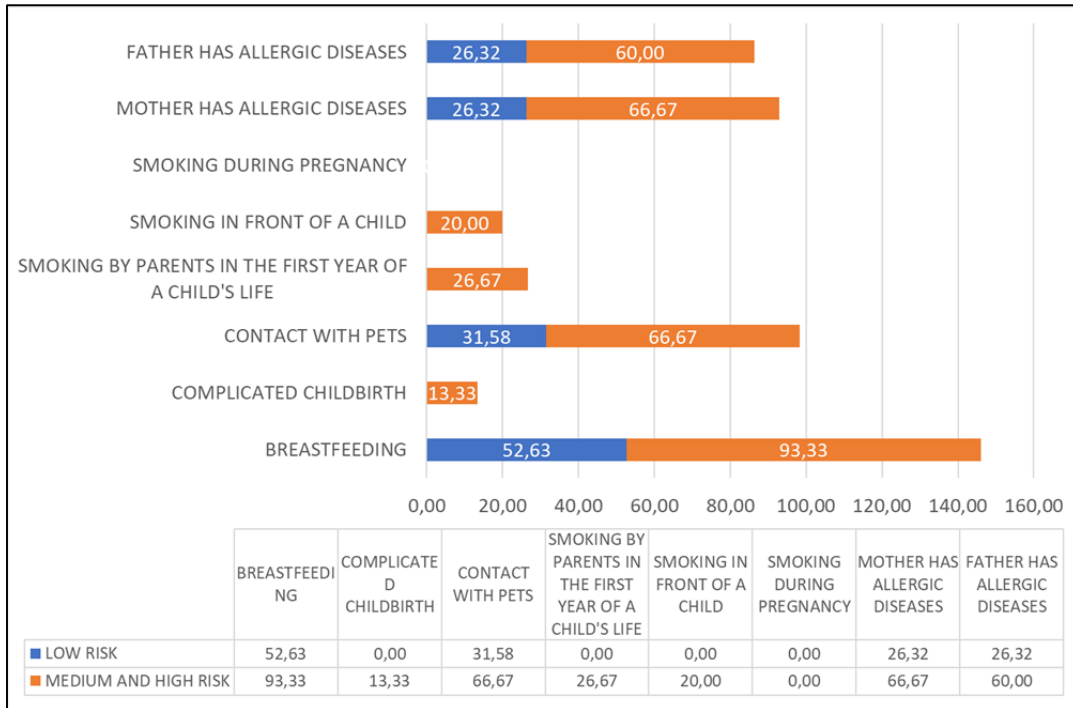


Figure 6 Risk factors for the development of allergic rhinitis in children of Nizhny Tagil

3.4. Symptoms of bronchial asthma in combination with allergic rhinitis in children

When analyzing questionnaires, the combination of the prevalence of asthma symptoms with allergic rhinitis was identified in 20% (n=6) of children from Yekaterinburg and 29.4% (n=10) of children from Nizhny Tagil (Fig. 7 and Fig. 8) According to Andreeva’s study E.A. the specificity of HLA-DRB1*01, on the one hand, marks resistance to the development of allergic rhinitis, and on the other hand, its presence in the HLA phenotype of a patient with AR is a marker of a high risk of developing an allergic form of bronchial asthma [6].

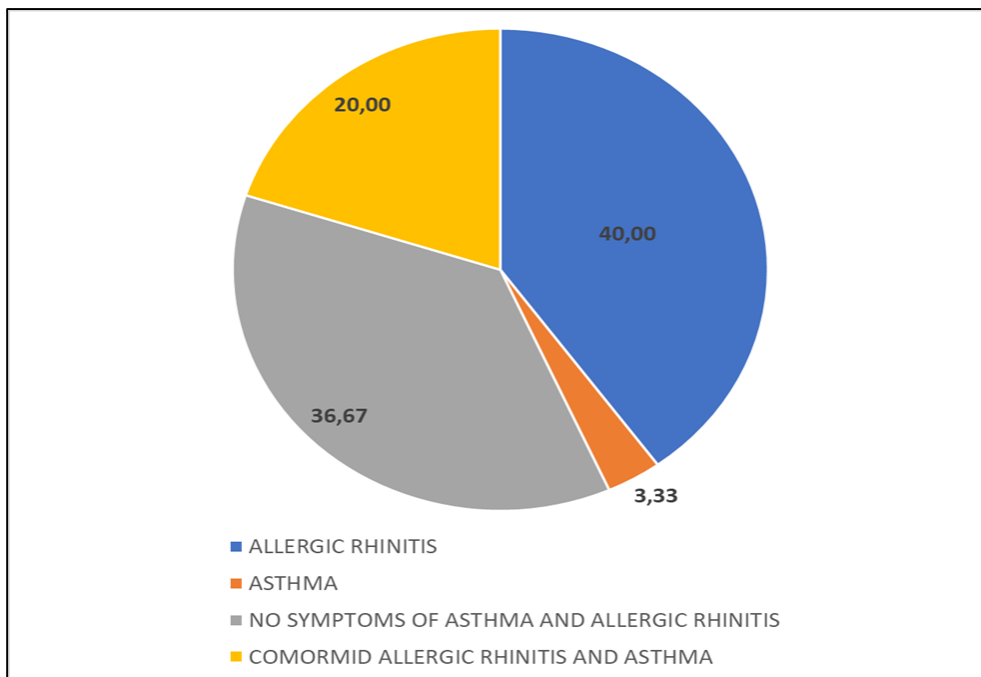


Figure 7 Combination of prevalence of asthma and AR symptoms in children in Yekaterinburg

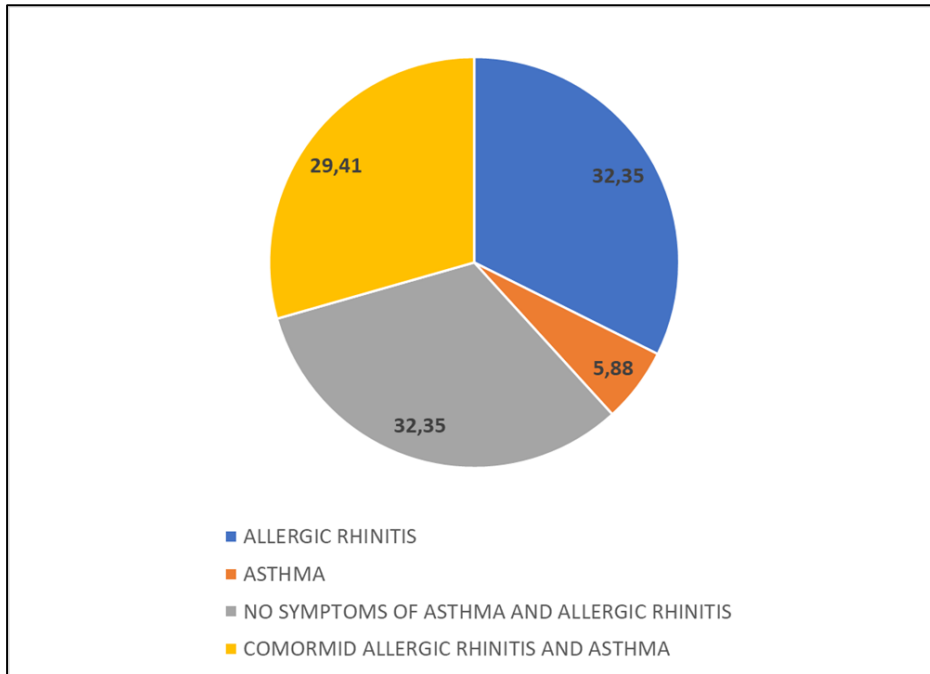


Figure 8 Combination of prevalence of asthma and AR symptoms in children in Nizhny Tagil

Despite the fact that no significant differences were obtained between the cities in the proportion of children with a high (average) and low risk of developing AR and BA, Figure 9 shows a tendency towards an increase in children at high risk of developing this pathology in Nizhny Tagil.

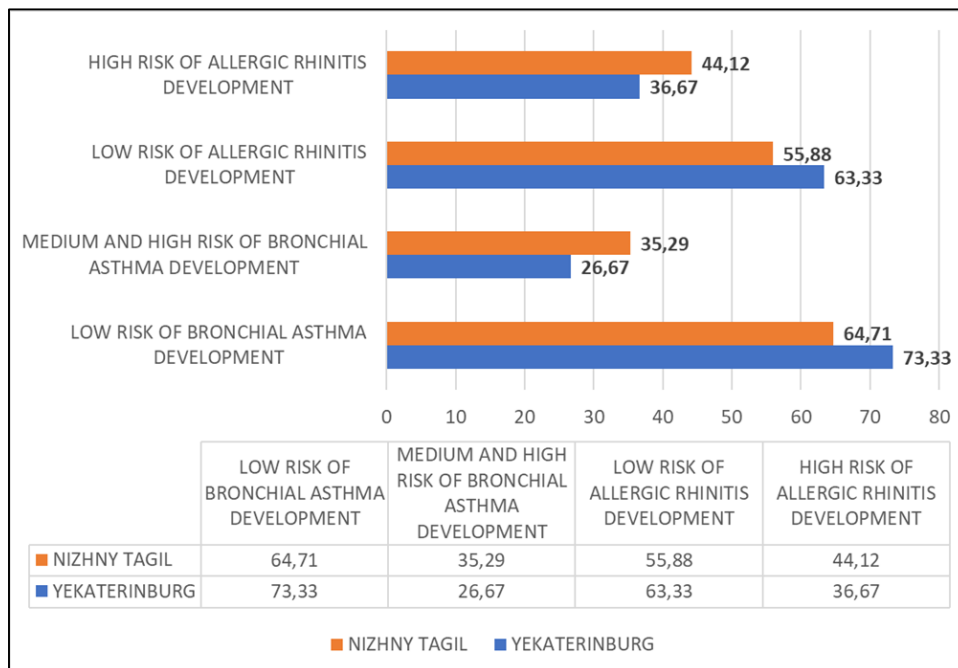


Figure 9 Comparison of final indicators of Yekaterinburg and Nizhny Tagil

4. Discussion

According to some data, the diagnosis of asthma is made in children with a delay of 4-5 years and only during the period of manifestation [9]. Many primary care doctors do not know the diagnostic criteria, which is the main reason why the true prevalence of asthma exceeds official statistics. This fact is confirmed by epidemiological studies [7,8].

Based on population studies, numerous experts from the Global Initiative for Asthma (GINA) concluded that episodes of wheezing are widespread among young children, but asthma does not develop in all cases, but such children are already at risk for developing asthma. Late diagnosis leads to untimely initiation of preventive and therapeutic measures, in connection with which epidemiological studies carried out in the region become important.

The increase in the prevalence of asthma and AR is confirmed by the results of the International Study of Asthma and Allergies in Childhood (ISAAC), which is based on a standardized methodology recommended and approved by WHO [10]. The publication of a validated ISAAC questionnaire in Russian made it possible to conduct research in many regions of Russia and improve the diagnosis of asthma in children. In Russia, studies were carried out in 17 regional centers. Phase I of the ISAAC study involved 39,056 children aged 7–8 years from 13 regional centers in Russia. The variability in the prevalence of asthma symptoms in the regions of the country ranges from 5.0% to 11.1%: in Novosibirsk (11.1%), Vladivostok (10.1%) and the mountainous regions of Dagestan (10.8%). In Russia, stage III of the ISAAC study was carried out only in Novosibirsk, according to the results of which, over a 6-year observation period, a decrease in the prevalence of wheezing in children aged 7–8 years was noted from 11.1% to 10.8% [11].

Analysis of the results of the implementation of the ISAAC program in Russia shows that the data obtained through questionnaires can be used to identify risk groups for the development of asthma. Despite the fairly high specificity and sensitivity of each question, an in-depth clinical, functional and allergological examination of patients is necessary to make a final diagnosis. Domestic experts came to the conclusion (2022) that there are still no valid diagnostic criteria for establishing the diagnosis of “bronchial asthma” in children of early and preschool age [12], therefore, the search for ways to predict the risk of development, diagnose BA at the preclinical stage in of young children using simple, inexpensive, non-invasive diagnostic questionnaires does not lose its relevance.

The Asthma Prediction Tool questionnaire [13] used in the study is focused on searching for predictive factors that make it more likely to identify a group of children predisposed to developing asthma. The questionnaire contains 10 questions regarding the gender and age of the child, family history of asthma, the presence of atopic dermatitis, episodes of wheezing without concomitant acute respiratory viral infection and their number in the last 12 months, including with shortness of breath, or provoked by physical activity, inhalation allergens (house dust, grass, pets) [14]. This diagnostic approach significantly reduces time and increases prognostic value when used in combination with other methods, since the results of questionnaires reflect only the prevalence of disease symptoms and provide only a subjective assessment. Children with an average and high level of risk for the development and prevalence of symptoms of asthma and AR require clinical observation in order to verify the diagnosis and carry out treatment and preventive measures.

If the questionnaire data is incorrectly interpreted, one can come to the conclusion that the existing underdiagnosis of BA in Russia will be replaced by unjustified overdiagnosis. Thus, up to 11% of primary care patients receive inhaled glucocorticosteroids inappropriately. [15].

According to WHO, the incidence of asthma is an indicator disease in relation to air quality. The formation of additional cases of asthma is likely associated with abnormal levels of hydroxybenzene, dihydrosulfide, sulfur dioxide, fluorine compounds, etc. in the air. In 2021, the incidence rate of children (0–14 years) with asthma and asthmatic status associated with atmospheric air quality in general The Russian Federation was at the level of 4.8 additional cases per 100 thousand children of the corresponding age (or 5.6% of the actual incidence for this reason). In the state report “On the state of sanitary and epidemiological well-being of the population in the Russian Federation in 2021,” the Sverdlovsk region was noted as one of the priority subjects of the Russian Federation in terms of the number of children with asthma, probably associated with the aerogenic factor of the environment. However, international questionnaires assessing the risk and prevalence of asthma and AR do not contain items related to industrial air pollution.

5. Conclusions

A study conducted using the Russian version of the ISAAC questionnaire showed that the proportion of children aged 3–8 years with an average and high risk of developing asthma in Yekaterinburg was 26.67%, in Nizhny Tagil - 35.29%. The prevalence of symptoms of allergic rhinitis in children in Yekaterinburg exceeds the established diagnosis by 2.5 times, in Nizhny Tagil – by 1.6 times.

The results can be correlated with the high and different levels of air pollution in the 2 cities, given the lack of a statistically significant relationship with a family history of allergic pathology, but the connection with man-made pollutants is not taken into account in the ISAAC questionnaires.

To confirm that the prevalence of asthma and AR symptoms is higher than those obtained in multicenter studies among children of a similar age, a survey of at least 350 people will be required.

In any case, it is necessary to study the role of priority pollutants in the formation of airway hyperresponsiveness, asthma and AR, and to search for effective preventive measures aimed at preventing the development of the latter.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

Authors' contribution to the work

- Inga Albertovna Plotnikova: Design development, general control of the study, analysis of results and interpretation of data, final editing of the article.
- Anastasia Dmitrievna Kataeva: Conducting research, collecting material, filling out information cards, creating a database, creating charts and graphs in Microsoft Office Excel, working with literary sources, participating in writing an article.
- Natalya Ganizhonovna Grushina: Statistical data processing using the Statistica application: using the chi-square test (χ^2) with Yates' continuity correction, calculating one-sided and two-sided Fisher tests.
- Vera Leonidovna Zelentsova: Approval of the design, editing of the “discussion of results” section.
- Timofey Viktorovich Babin: Participation and control in the research in Yekaterinburg, editing the text of the article.
- Irina Borisovna Chirkova: Organization of research in Nizhny Tagil.
- Oksana Konstantinovna Khodko: Organization of research in Yekaterinburg

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