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# Influence of comorbidity and markers of atopia on the activity of bronchial asthma in children

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**Abstract—** Bronchial asthma (BA) is an example of a chronic inflammatory process that develops in children in the presence of genetically determined atopy and bronchial hypersensitivity and leads to profound disability in patients 10-24 years [1]. The prevalence of asthma among adults in the world ranges from 1-18%, and among children - 5-10%. In Ukraine, this percentage is only 0.6% -0.56%, which may indicate insufficient diagnosis of this pathology [2]. If children have several diseases that have both acute and chronic course, use the terms "combined pathology", "combined pathology", "concomitant" or "associated" diseases and conditions [3] It should be noted that the term "comorbidity" (comorbidity), used to determine the simultaneous damage of two organs or systems of the body, or the presence of two or the presence of ≥3 comorbidities [4,13],which can be attributed to asthma, because in the vast majority of asthma in children is a primary allergic disease, which causes the development of this pathology with a characteristic comorbid condition, increased blood levels, the main of which are immunoglobulins, erythrocytes, hemoglobin, leukocytes, including eosinophils. and their dependent hematocrit, SaO2. [5].

**Key words:** comorbidity, comorbid conditions, atopic bronchial asthma, eosinophilic leukocytes, IgE, pulse oximetry.

## 1.Introduction

The modern scientific literature actively discusses the need for an integrated assessment of human health, the problem of providing medical care to patients with concomitant and combined pathology, prescribing treatment based on the interaction of drugs on the "multimorbid" condition of a particular patient (multimorbidity) [7,8].

The trend of increasing atopic bronchial asthma and allergic diseases in children, ie the presence of "comorbid conditions", is also observed in many regions of Ukraine, [6] and is 10-40%, according to the World Allergy Organization (WAO), [7,14] . The European Academy of Allergy and Clinical Immunology (EAACI, 2016) predicts that by 2025, half of the population of the European Union will have chronic allergic diseases (multimorbidity). [8,15].

## 2.Aim

Analyze comorbidity as a clinical and laboratory factor of atopic bronchial asthma activity in children.

**3.Materials and methods**

316 school-age children with atopic asthma were under scientific observation and analysis. The methods of high scientific informativeness were used in the work: general - clinical, based on the collection of complaints, anamnesis data, physical examination for objective manifestations, as well as the peculiarities of the course of bronchial asthma; hematological, interpreting clinical and laboratory parameters of peripheral blood and hemogram in patients, also paid attention to the number of eosinophilic leukocytes, erythrocytes, hemoglobin levels, which in turn may indicate disease progression and the development of respiratory failure.

Monitoring of round-the-clock pulse oximetry allowed to study the gas composition of blood (SaO2), the percentage (%) of oxygen saturation of peripheral blood and to establish (%) oxygen saturation of hemoglobin in erythrocytes in different periods of disease exacerbation.

A mandatory range of tests in asthmatics and healthy children as a marker of atopy included determination of total serum IgE levels.

With differential diagnosis, it is mandatory to perform consultative final examinations by a pediatrician, ENT specialist, neurologist, endocrinologist, thoracic surgeon, cardiologist and physicians of the functional diagnostics room.

As a comparative control group, 25 practically healthy children were examined in the absence of complaints and objective signs of hereditary and concomitant (comorbid) conditions, without changes in clinical and laboratory parameters, instrumental studies, with no acute infectious disease.

Statistical processing of the obtained results was performed using methods of variation statistics using a standard application package of multidimensional variational-statistical analysis "STATISTICA 6.0" (owned by CNIT Vinnytsia National Medical University named after MI Pirogov, licensed № AXXR910A374605FA) for Windows'XP (licensed №RKKFD-W8DDF-6PMC4-KX3WW-CR6TI). The nature of the distribution of the obtained data (para- or non-parametric) was determined by the values of excess and asymmetry, and the method of variation statistics (M, SD, m, min - max) was used [48].To assess the significance of the difference between statistical groups (independent samples) used for parametric data Student's test (Studenttest), for non-parametric data - Mann-Whitney U-test (Mann-Whitney), and for the data presented as a percentage - the exact method Fisher. Values of $p < 0.05$ were considered reliable [9].

Under the conditions of parametric distribution of variables, the held data were subjected to computer statistical processing, which resulted in: calculation of the required number of observations to determine the mean M, Student's probability criterion (t), the mean standard error (m). The probability of the difference

was determined by the parametric criterion of Student's probability. The difference was estimated to be significant at $p < 0.05$.

**4.Results of research and discussion.**

Analysis of clinical, laboratory and statistical results shows that inpatient treatment was received mainly by patients with persistent asthma (253 children; 80.06%), and intermittent asthma was only 19.94% (63 patients). This distribution of children with asthma can be justified by the severity of asthma, which required treatment in a pulmonary hospital.

The peculiarity of clinical observations of school-age children with asthma who were hospitalized was that atopic "comorbid" comorbidities dominated, which determined the general "multimorbid" condition of the patient (allergic rhinitis, atopic dermatitis, household allergies, obesity). curvature of the nasal membrane and others) (table 1).

**Table 1** - Distribution of the frequency of comorbid pathology in children with asthma, depending on the severity of the disease

| Comorbid pathology | The severity of Bronchial asthma | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Persistent (n=253; 80,06%) | | | | Intermittent (n=63; 19,94%) | | | |
| | Boysn=193 | | Girls n=60 | | Boys n=43 | | Girlsmn=20 | |
| | n | % | n | % | n | % | n | % |
| Allergic rhinitis | 113 | 24,62* | 35 | 7,63 | 31 | 6,75* | 10 | 2,18 |
| Atopic dermatitis | 11 | 2,4 | 7 | 1,53 | 3 | 0,65 | 2 | 0,44 |
| Household allergy | 76 | 16,55* | 26 | 5,67 | 19 | 4,14* | 7 | 1,53 |
| Adiposity | 17 | 3,7 | 3 | 0,65 | 7 | 1,52 | 1 | 0,22 |
| Curvatureofthe nasalmembran e | 5 | 1,09 | 2 | 0,44 | 6 | 1,31 | 1 | 0,22 |
| Others | 46 | 10,02 | 15 | 3,26 | 14 | 3,05 | 2 | 0,44 |
| Total: | 268 | 58,38* | 88 | 19,18 | 80 | 17,42* | 23 | 5,02 |

**Notes:** * - $p < 0,05$ - the difference is significant between groups of indicators of children withpersistent and intermittent asthma.

It is known that allergic rhinitis, or rather its long course, often leads to asthma attacks. One pathology in this case generates the development of another, or prolongs it [10]. Therefore, we analyzed theconcomitant (allergic) pathology in asthma in children, both in persistent and intermittent course as in boys and girls with asthma. Comorbid pathology was found in 316 patients (268 boys -75.82% and girls 24.18%).

With high reliability (p <0.05) allergic rhinitis and allergy were common in boys with persistent asthma (allergic rhinitis: 113 - 4.62% and 76 - 16.55%, respectively, household allergies) and with intermittent asthma. (allergic rhinitis: 31 - 6.75% and 19 - 4.14%, respectively, household allergies).

Among patients with asthma, non-traumatic curvature of the nasal septum was observed in 14 children (4.43%), and, in persistent and intermittent courses - with the same frequency (respectively: 7 (2.21%) and 7 (2.22%). it is possible to consider that disturbance of nasal breath can lead to deterioration of a course of any lung disease, including also BA.

Almost all children (293 - 92.6%) had a comorbid inherited predisposition to allergic diseases and only 23 patients (7.4%) had no factors that would indicate the genetic nature of the pathology.

Because, one of the leading markers of atopy is IgE, which is actively involved in the activation of the synthesis of inflammatory mediators and plays a leading role in the pathogenesis of the immune stage of allergy, as well as the fact that IgE overproduction in asthma due to activation of cytokine and progression of the severity of pathological changes in this pathology [12], we conducted a study to determine its content in children with on bronchial asthma (tab. 2).

**Table 2** - The content of total IgE in children with asthma, depending on the severity of the disease

| Indexes | Theseverityofbronchialasthma | | |
|---|---|---|---|
| | General group n =316 | Intermittent n = 63 | Persistent n = 253 |
| | M±m | M±m | M±m |
| IgE, IU/ml | 892,00±29,46 | 838,89±113,8* | 982,67±32,51* |
| Almosthealthychildren | 37,82±8,45 | | |

**Notes:*** - p <0.001 - thedifferenceissignificantbetweengroupsofindicatorsandalmosthealthychildren.

Obtainedas a resultofthestudyinthebloodplasmaIgEinpatientswithasthmaofthegeneralgroup, showed a statisticallyhighcontentrelativetotheindicatorsofalmosthealthychildrenin 23.59 times (p <0,001).

We also noted an increase in levels of total immunoglobulin - E depending on the severity of the disease. In the intermittent course of asthma, total IgE exceeded the levels of immunoglobulin - E in almost healthy children by 22.18 times (p <0.001). In sick children, the persistent course of IgE pathology was increased 25.98 times compared to normal.

Given the importance of IgE in the pathogenesis of asthma, we studied its age levels, both in patients with intermittent and persistent asthma, as well as in almost healthy children (table 3).

**Table 3** - The content of total IgE in patients with asthma, depending on age and severity of the disease

| Agegroups | Theseverityofbronchialasthman=316 | | Almost healthy children |
|---|---|---|---|
| | Intermittent asthma n=63 | Persistentastma n=253 | |
| | M±m | M±m | M±m |
| 6 -7 years | 218,45±36,90* | 1693,77±171,69* | 25,05±3,05** |
| 8-12 years | 762,48±170,13* | 1260,08±102,00* | 35,41±3,20** |
| 13–16 years | 974,82±169,40* | 1396,95±139,30* | 45,42±2,90** |
| 17-18 years | 532,7 | 724,8±87,34 | 56,16±3,14** |

**Note:** * - p <0.05 - the difference is significant between groups of children with intermittent and persistent asthma;

** - p <0.05 - the difference is significant between groups of indicators and practically healthy children.

In the case of persistent asthma, the levels of total IgE on admission to the hospital were statistically significantly higher in patients of all ages.

Thus, in children 6-7 years of age the level of total IgE in the intermittent course of asthma was statistically lower compared to older age groups and was 7.75 times lower than in the same age group of children with persistent disease.

In patients aged 8-12 years, total IgE prevailed in the persistent course of asthma in 1.68 times the level of indicators in intermittent asthma, in 13-16 years - in 1.43, in 17-18 years - 1.36 times (p <0,05).

The results of the study of total immunoglobulin-E depending on the level of control of asthma (Table 4) also showed a statistical increase in its levels relative to almost healthy children (p <0,001). At the controlled course - in 29,11 times, partially-controlled - in 37,4 times, uncontrolled - in 25,82 times.

**Table 4** - The content of total IgE in children with asthma, depending on the level of disease control

| Indexes | Levels of control of bronchial asthma | | |
|---|---|---|---|
| | Controlledn = 44 | Partially controlledn = 68 | Uncontrolledn = 141 |
| | M±m | M±m | M±m |
| IgE, МО/мл | 1101,1±120,9* | 1414,2±124,3* | 976,6±44,24* |
| Almost healthy childrenn = 25 | 37,82±8,45 | | |

**Note:** * - p <0.001 - the difference is significant between groups of indicators and almost healthy children.

After analyzing the atopic comorbid pathology found in each child with asthma, and statistically calculating the rate of atopy, which is IgE, depending on age, severity and level of disease control, we conducted another scientific step - to determine the level of eosinophilic leukocytes in general. clinical blood tests of sick and

healthy children, school age. It is known that eosinophils play an important role in the development of airway inflammation in asthma [10]. They are determined in the bronchoalveolar lavage fluid and in the biopsy material not only during exacerbation, but also during remission of the disease. [16].

Eosinophils are also markers of allergy, tissue damage by inflammation, increased sensitivity of class E immunoglobulins, accumulation and stimulation of the release of inflammatory mediators, absorption and binding of inflammatory mediators, primarily histamine [11,12].

Therefore, the determination of the content in the blood of children with asthma, eosinophils was very important to determine their role in the pathogenetic mechanisms of development and the nature of the course of asthma in children (Table 5).

**Table 5** - The level of eosinophilic leukocytes in children with bronchial asthma, depending on the severity of the disease

| Indexes | The severity of asthma | | |
|---|---|---|---|
| | General group, n=316 | Intermittentasthma n=63 | Persistentasthma, n=253 |
| | M±m | M±m | M±m |
| The level of eosinophils in the peripheral blood, % | 16,29±0,31* | 13,06±0,82* | 17,08±0,31* |
| Almost healthy children, % | 1,64±0,05 | | |

**Note:** * - p <0.001 - the difference is significant between groups of indicators and almost healthy children.

Immediately during the attack of asthma in the general group of patients there was an increase in the activity of eosinophils to the level of moderate eosinophilia (16.29 ± 0.32%), which exceeded the indicators of almost healthy children by 9.93 times (p <0.001), and depended on the severity disease. Thus, the content of eosinophils in the peripheral blood of children with persistent asthma was 17.08 ± 0.31% and was 10.41 times higher (p <0.01) compared with almost healthy children. In the intermittent course of the disease there was also moderate eosinophilia, which exceeded the levels of eosinophils compared with a group of almost healthy children in 7.93 times.

It should be noted that moderate eosinophilia was observed in all variants of asthma (Table 6). Thus, in the controlled course it was 14.83 ± 0.76%, in the partially controlled - 17.20 ± 1.4%, in the uncontrolled - 17.73 ± 0.44% and was statistically significantly higher than in healthy children. (p <0.001). We observed an increase of 2.9% (p <0.05) in the number of eosinophils in the uncontrolled course of asthma compared with patients in the controlled course of the disease.

**Table 6** - The level of eosinophilic leukocytes in children with bronchial asthma, depending on the level of disease control

| Indexes | Levels of control of bronchial asthma | | |
|---|---|---|---|
| | Controlled, n = 44 | Partially controlled, n = 68 | Uncontrolled, n = 141 |
| | M±m | M±m | M±m |
| Eosinophilic leukocytes,% | 14,83±0,76* | 17,20±1,4* | 17,73±0,44* |
| Almost healthy children | 1,64±0,05 | | |

**Note:** * - p <0.05 – the difference is significant between groups of indicators and almost healthy children.

Eosinophil levels are directly related to the severity and level of asthma control. The content of eosinophils in the peripheral blood of children with persistent asthma was statistically significantly higher (p <0.01), compared with the intermittent course of the disease and 9.93 times compared with almost healthy children. The number of eosinophils in the uncontrolled course of asthmais 2.9% (p <0.05) higher compared to the controlled level of the disease.

Thus, the results are due to the fact that atopic asthma in children is a multifactorial disease, and its clinical course depends on both a set of genetic factors and comorbid pathology, adverse environmental factors.

Determination of levels of total IgE and leukocyte eosinophils can be a prognostic marker of the occurrence and features of atopic asthma in children. Elevated levels of total IgE and leukocyte eosinophils are associated with an increased risk of developing asthma in children, the development of persistent and uncontrolled disease.

**5. Conclusions:**

**1.** Concomitant (comorbid) pathologycanbe a factor in the negative impact on the severity of asthma in children. Allergic rhinitis and allergy are much more common inpersistent asthma (allergicrhinitis: 113 - 24.62% and 76 - 16.55%, respectively, householdallergy) compared with intermittent disease (allergicrhinitis: 31 - 6.75% and 19 - 4.14%, respectively, householdallergies; p <0,001).

**2.** A marker of atopic asthma activity in children is a high level of IgEinthe blood plasma, which exceeds the indicators of almost healthy children by 23.59 times (p <0.001). In the intermittent course -, 22.18 times (p <0.001), inpersistent - 25.98 times (p <0.001) and depends on ageand level of control.

**3.** Inchildren 6-7 years, the level of total IgE in the intermittent course of asthma is lower compared to older age groups by 7.75 times relative to the same age group of children with persistent disease (p <0.001). Inpatients aged 8-12 years, total IgE prevailed in the persistent course of asthma in 1.68 times the level of indicators in intermittent asthma, in 13-16 years - in 1.43, in 17-18 years - 1.36 times (p <0, 05).

**4.** Depending on the level of asthma control, the indicators of total IgE in the controlled course of the disease incomparison with almost healthy children were 29.11 times higher, in the partially controlled - 37.4, uncontrolled - 25.82 times.

**5**. The criterion for the activity of asthma in children may be the content of eosinophils in the peripheral blood. In patients with persistent asthma, it is higher ($p < 0.01$), compared with the intermittent course of the disease and 9.93 times – compared with almost healthy children. The content of eosinophils in the uncontrolled course of asthma is 2.9% ($p < 0.05$) higher than in the controlled course of the disease.

**Prospects for further research** are the role of comorbid pathology and the immune status of patients with asthma, is extremely important for the develop ment of effective measures to prevent the disease and increase the effectiveness of the irtreatment.

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