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IMBALANCE BETWEEN IL-2, IL-4 AND IFN-γ AS A MARKER OF SUSTAINABILITY OF PARTLY CONTROLLED ASTHMA IN CHILDREN

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Asthma is one of the most common chronic diseases of childhood and adulthood. The pathogenetic mechanism of asthma is closely related to the functioning of cytokines.

The aim of our study was to improve the knowledge on the assessment of cytokines (IL-2, IL-4, interferon-gamma) in the formation of chronic inflammation in children with partially controlled asthma.

The study included 94 children who met the inclusion and exclusion criteria. The groups were formed depending on the severity of persistent asthma: 59 children with mild asthma - group 1; 10 children with moderate asthma - group 2; 12 children with severe asthma - group 3; 13 children from the control group - group 4. Cytokines were examined in children's serum using specific kits. IL-2, IL-4, and interferon-gamma were measured by a standard enzyme-linked immunosorbent assay.

The study revealed the following data: all children with asthma had elevated levels of IL-2, IL-4 and reduced levels of interferon-gamma in the blood serum compared to the control group. The highest serum levels of IL-2, IL-4 and lowest IFN-γ were observed in patients with severe asthma. The correlation between cytokines and disease duration suggests that IL-2, IL-4 and IFN-γ may be considered as markers of chronic inflammation.

The cytokine profile in children with persistent asthma in the exacerbation stage is characterised by elevated levels of IL-2 and IL-4 and decreased levels of IFN-γ in the blood serum. The data from our clinical study may lead us to the conclusion that there is an imbalance in the Th-1/Th-2 system.

Key words: *asthma, children, cytokines, chronic inflammation.*

Connection of the publication with planned research works.

This article was carried out within the framework of the Department of Paediatrics № 2 of Kharkiv National Medical University «Medical and biological aspects of adaptation of children with somatic pathology in modern conditions. Prediction of asthma control in children taking into account inflammatory markers and the state of the airway barrier of the lungs». State registration number 0120U102471.

Introduction.

Asthma is one of the most common non-communicable diseases that significantly affects the quality of life. Globally, asthma is the 16th leading cause of disability. Around 300 million people worldwide suffer from asthma, and it is likely that another 100 million people may be affected by it by 2025 [1, 2, 3]. The disease usually first appears before the age of 6 years [4,5] and has a significant impact on quality of life in adulthood [6, 7, 8].

Asthma is one of the most common chronic inflammatory diseases of the respiratory tract. It is caused by a significant number of cellular elements and mediators of inflammation, which leads to bronchial hyperreactivity [9].

The obligatory pathogenetic mechanism of asthma is a chronic inflammatory process caused by specific immunological (sensitisation and allergy) or nonspecific mechanisms. This process is not limited to the bronchial tree but is systemic in nature [10].

The formation of inflammation is closely related to the action of cytokines. Proinflammatory interleukins (IL-1, IL-2, IL-6, IL-8, TNF-α, GM-CSF) are the first to be synthesised. Anti-inflammatory interleukins (IL-4, IL-10, IL-13, TGF-b) begin to be synthesised later. Their appearance characterises a chronic inflammatory process leading to airway remodelling with hyperplasia of the smooth muscles of the bronchopulmonary system [11, 12].

The current understanding of the asthma pathogenesis is based on the recognition of the leading role of IgE-mediated allergic reactions that lead to the development of allergic inflammation. The increased IgE production by B lymphocytes under the influence of allergens in patients with asthma is a consequence of proliferation and activation of the Th2 clone of allergen-specific T lymphocytes [11].

T-lymphocytes differentiate into two mutually regulating subsets.

Th1-cells primarily secrete interleukin-2 (IL-2) and interferon-gamma (IFN-γ) and regulate classical cell-mediated immune responses, such as delayed-type hypersensitivity. Th2 cells secreting interleukin-4 (IL-4) contribute to humoral immune responses, including IgE production. Excessive activity of Th1-cells or Th2-cells can lead to an autoimmune disease that damages tissue.

Scientists consider that a number of human diseases, including asthma, are caused by a Th-2 autoimmune response [11, 13].

Researchers studying allergic asthma in mice, using bronchoalveolar lavage as a test material, found a decrease in IFN-γ levels and an increase in IL-4 levels [14, 15].

The mechanism of IL-4 and IL-2 action is well understood, but in recent years the scientific community has been interested in their coordinated interaction rather

than in a single cytokine. In a mouse model of asthma, the content of these cytokines was studied and treatment with the IL-4/IL-2 combination resulted in a decrease in the inflammatory process [16].

It is also known that IL-2-induced signal transduction during early Th2 cell differentiation is required to maintain increased IL-4 production and increased sensitivity to IL-4, which allows for the creation of an IL-4-positive amplification feedback loop that preserves the Th2 cell phenotype [17].

Studies have shown that two cytokines (IL-4 and IL-2) can interact using the same STAT proteins to either enhance or interfere with each other, producing a different outcome, thus demonstrating the importance of understanding that cytokines can influence each other [18].

Many studies of the above cytokines are conducted in animals, but there are still contradictory data regarding the levels of IFN-γ, IL-4 and IL-2 in children and adults with asthma.

The aim of the study.

To investigate the diagnostic and prognostic significance of IL-2, IL-4 and IFN-γ levels in the blood serum of children with persistent partially controlled asthma of different severity and to assess the relationship between these parameters.

Object and research methods.

This was a cohort study. Patients were recruited at the pulmonology department of a children's clinical hospital.

The study involved 81 children with an existing diagnosis of asthma and 13 children in the control group.

The main condition for participation in this study was compliance with the inclusion and exclusion criteria.

Inclusion criteria: children aged 5 to 17 years with a diagnosis of asthma, persistent mild, moderate, severe (2-4 severity), partially controlled, in the period of exacerbation; 1-2 days of exacerbation; children with signed consent from both parents, and at the age of 14 years, and by the patients themselves.

Exclusion criteria: children under 5 years of age or over 17 years of age; children under 17 years of age whose parents (or one of the parents) did not give written consent to the study; patients aged 14 years and older without written consent to the study; patients with acute bronchitis simple, acute obstructive bronchitis, intermittent asthma, pneumonia; patients diagnosed with asthma in remission and controlled asthma; patients with congenital and chronic cardiopulmonary or neurological diseases; hereditary diseases leading to changes in the functioning of the respiratory tract, including cystic fibrosis; proven immune deficiency; patients with severe somatic conditions and decompensation of vital functions; suspected or confirmed gastrointestinal diseases; patients with neoplasms of any location.

The patients' parents were informed about the scope and methods of the study. The study was performed with minimal psychological distress on the part of the patients.

The control group consisted of healthy children (of similar age/sex) without any signs of chronic or acute illnesses during the previous three months who were referred for age-related control or vaccination. Parents of the control group children were informed about the study objectives and signed a written informed consent before enrolment.

All patients were diagnosed with asthma by a paediatric respiratory specialist (pulmonologist or allergist). The diagnoses and the examination were in line with GINA 2020 criteria and protocols for the treatment of children with asthma No. 868 of 08.10.2013 «On the approval and implementation of medical and technological documents for the standardisation of medical care in asthma».

The examination was carried out in the first days of asthma exacerbation, namely in the presence of dyspnoea, cough, wheezing and before correction of basic therapy.

Patients underwent basic asthma treatment in accordance with the GINA 2020 guidelines [3].

Control was assessed according to the GINA criteria and using c-AST tests: for children aged 4-11 years and 12 years and adolescents [3, 19, 20]. The test results showed partially controlled asthma.

Patients were divided into groups depending on the severity of asthma. The first group included children with mild persistent asthma (n=59), the second group – moderate persistent asthma (n=10), the third group – severe persistent asthma (n=12), and the fourth group was the control group (n=13).

All patients underwent physical and laboratory examination. A thorough study of anamnestic data was carried out, namely: the onset of acute respiratory allergy (in the form of bronchial obstruction), the duration of asthma, a burdened family history of allergic conditions (any and specifically asthma), the presence of atopic dermatitis and allergic rhinitis in the child.

Methods for analysing the cytokine profile of patients peripheral blood.

Blood samples were drawn by a trained paediatric phlebotomist nurse. The biological material was taken during a routine examination and before therapy correction. Physical and emotional stress, overheating and hypothermia, sleep disturbances, air travel, instrumental research methods (ultrasound, X-ray, etc.), physiotherapy procedures, and massage were excluded during the day. Material – blood was taken in the morning, on an empty stomach (8-12 hours of fasting), by venipuncture. The material was collected in special tubes without fillers. Centrifugation to obtain serum was performed at 2000-2500 rpm for 15-20 minutes. After centrifugation, the material was distributed into disposable tubes using a sterile pipette and stored at -70°C. Aliquots of samples were analysed once without a repeated freeze-thaw cycle.

The study was carried out by enzyme-linked immunosorbent assay, in strict accordance with the kit instructions: IL-4 – Human IL-4, Vector Best-Ukraine,; IL-2 – Interleukin-2 ELISA-BEST; IFN-γ – Human γ-interferon, Vector Best-Ukraine.

The planned clinical study was carried out after receiving approval by the Ethics and Bioethics Commission of Kharkiv National Medical University on October 2, 2019, protocol № 6 and was conducted in accordance with the principles of the Helsinki Declaration, amended in October 2013

Statistical processing of the study results was performed using the statistical packages EXCELL FOR WINDOWS, StatSoft STATISTICA Version 7 (Tulsa, OK) and MedCalc statistical software (version 17.2). The Shapiro-Wilk test and histogram and q-q plots were used to assess normality. Since the sample distribution differed from the normal one, the median (Me) and interquartile range (Lq – lower quartile; Uq – upper quartile) were determined. For multiple comparisons (the study included 4 groups),

the non-parametric Kruskal-Wallis test (KW) was used. Differences were considered significant after taking into account the Bonferroni correction. The nonparametric Mann-Whitney (MW) test was used to determine the difference between groups. The difference between two parameters was considered statistically significant at $p < 0.05$. The correlation between the parameters was determined using Spearman's rank correlation analysis (r); $p < 0.05$ was considered a statistically significant difference.

Research results and their discussion.

The study involved 81 children with asthma. Analysing the age of the children, the presence of atopic dermatitis or allergic rhinitis, the onset of respiratory pathology (onset of bronchial obstruction in the first year of life or later) and the presence of atopy in close relatives, no differences were found between the groups. The study found that mild asthma was associated with a statistical predominance of boys. The duration of the disease in patients with severe asthma was statistically significant in relation to mild asthma. In patients with severe asthma, the relative number of patients with elevated IgE levels was higher compared to mild asthma. CRP was statistically significantly increased in patients with severe asthma compared with mild asthma **(table 1).**

Serum cytokine levels in children with asthma.

Multiple comparisons using the Kruskal-Wallis test revealed the presence of high significant H-criteria for IL-2, IL-4 and IFN-γ, which allowed us to conclude that there was a significant difference in these indicators in the groups, and their level depends on belonging to one or another group. Given that the group assignment was based on the severity of asthma, it can be assumed that the levels of IL-2, IL-4 and IFN-γ depend on the severity of asthma. In a pairwise comparison using the Mann-Whitney test, we found increased levels of IL-2 and IL-4 in children with asthma compared to the control group, with the highest levels in children with severe asthma. Calculating the differences in IFN-γ levels between the groups, it was determined that this indicator was reduced in children with bronchial asthma compared to the control group, with minimal levels in children with severe asthma **(table 2).**

Correlations between cytokine profile parameters and laboratory and anamnestic data.

A negative correlation was found between the levels of IL-4 and IFN-γ in the blood serum of children with asthma r= - 0.879 p<0.001.

A negative correlation was found between the levels of IL-2 and IFN-γ in the serum of children with asthma r= - 0.833 p<0.001.

A positive correlation was found between the levels of IL-2 and IL-4 in the serum of children with asthma and the duration of the disease r=0.740 p<0.05.

A positive correlation was found between the level of IL-4 in the blood serum of children with asthma and the duration of the disease r=0.695 p<0.05.

A negative correlation was found between the level of IFN-γ in the blood serum of children with asthma and the duration of the disease r= - 0.676 p<0.05.

The asthma pathogenesis is associated with the regulation of a large number of signalling pathways, in which immune and inflammatory regulatory factors play an important role [6].

Our study revealed elevated levels of IL-2 in the blood serum of children with different degrees of partially controlled asthma during exacerbation compared to the control group. These results suggest the presence of an inflammatory process in the body based on the following data. IL-2 is a pro-inflammatory interleukin produced by Th1 cells, which is one of the first to be involved in the inflammatory process. It is also known that IL-2-induced signal transduction during Th2 cell priming is necessary to maintain increased IL-4 production and increased sensitivity to IL-4 [17].

The highest IL-2 levels in our study were obtained in severe asthma. This may indicate that the more severe the inflammatory process, the higher the levels of IL-2. Scientists have demonstrated similar data in their studies. Some show a difference in IL-2 levels at different degrees of severe asthma control (poorer control is associated with higher IL-2 levels), while others demonstrate high

Table 1 – The main group clinical and laboratory data

Sign	Mild asthma (Group 1)	Moderate asthma (Group 2)	Severe asthma (Group 3)	Control (Group 4)	p
Number	n=59	n=10	n=12	n=13	
Gender, M/F	23/36	4/6	6/6	7/6	**P_1<0,05** $P_{2,3,C}$ > 0,05
Child's age, years Me (Lq; Uq)	11,0 (7,0;15,0)	10,0 (10,0;11,0)	12,5 (11,0;14,0)	8,0 (6,0;10,0)	p_{1-2} – 0,798 p_{1-3} – 0,253 p_{2-3} – 0,129
The presence of atopic dermatitis, %	71,2% (42/59)	80,0% (8/10)	66,7 (8/12)		p_{1-2} – 0,302 p_{1-3} – 0,410 p_{2-3} – 0,282
The presence of allergic rhinitis, %	49,2% (29/59)	70,0% (7/10)	50% (6/12)		p_{1-2} – 0,162 p_{1-3} – 0,482 p_{2-3} – 0,238
Onset of bronchial obstructive syndrome in the first year of life, %	25,4% (15/59)	20,0% (2/10)	66,7% (8/12)		p_{1-2} – 0,439 **p_{1-3} – 0,031** p_{2-3} – 0,131
Disease duration, years Me (Lq; Uq)	2,0 (1,0;6,0)	3,0 (2,0;4,0)	6,5 (3,5;10,0)		p_{1-2} – 0,213 **p_{1-3} – 0,002** p_{2-3} – 0,075
Presence of allergic diseases in the family (atopic dermatitis and/or allergic rhinitis), %.	16,9% (10/59)	20,0% (2/10)	25% (3/12)		p_{1-2} – 0,460 p_{1-3} – 0,380 p_{2-3} – 0,452
The presence of asthma in the family, %.	39,0% (23/59)	30,0% (3/10)	58,3 (7/12)		p_{1-2} – 0,651 p_{1-3} – 0,293 p_{2-3} -0,262
Elevated IgE levels, %.	74,5% (44/59)	100% (10/10)	91,6% (11/12)		p_{1-2} – 0,034 **p_{1-3} – 0,003** p_{2-3} – 0,391
Elevated CRP levels, %.	16,9 % (10/59)	40,0% (4/10)	66,7% (8/12)		p_{1-2} – 0,246 **p_{1-3} – 0,007** p_{2-3} – 0,291

Table 2 – Indicators of cytokines in patients with asthma, Me (Lq; Uq)

Sign	Mild asthma (Group 1) n=59	Moderate asthma (Group 2) n=10	Severe asthma (Group 3) n=12	Control (Group 4) n=12
IL-2, pg/ml	13,04 (11,15;16,17)	20,62 (20,05;22,06)	27,92 (27,22;29,94)	5,37 (5,15;5,64)
KW: H=69.4637; p<0.001 MW: p_{1-2}<0,001; p_{1-3}<0,001; p_{2-3}<0,001; p_{1-c}<0,001; p_{2-c}<0,001; p_{3-c}<0,001.				
IL-4, pg/ml	7,11 (6,14;9,34)	19,01 (18,15;20,06)	30,61 (27,38;32,92)	3,20 (2,96;3,71)
KW: H=69.4627; p<0.001 MW: p_{1-2} <0,001; p_{1-3}<0,001; p_{2-3}<0,001; p_{1-c}<0,001; p_{2-c}<0,001; p_{3-c}<0,001.				
IFN-γ, pg/ml	86,12 (83,96;89,72)	80,59 (79,05;81,50)	68,15 (59,25;77,92)	125,15 (124,70;130,10)
KW: H=69.1081; p<0.001 MW: p_{1-2}<0,001; p_{1-3}<0,001; p_{2-3}<0,001; p_{1-c}<0,001; p_{2-c}<0,001; p_{3-c}<0,001.				

Notes: Me (Lq; Uq) — median (lower quartile; upper quartile); KW — Kruskal-Wallis test; MW— Mann-Whitney test; p significant with the Bonferroni correction.

levels of IL-2 in adults with severe and moderate asthma compared to mild asthma [21, 22].

Researchers have also shown that elevated levels of IL-2 are associated with both acute and chronic respiratory tract pathologies [23].

We have identified reduced IFN-γ levels in children with asthma. The lowest levels are associated with severe asthma compared to the control group. Our findings suggest that the degree of IFN-γ reduction depends on the severity of asthma. Our data are in line with the results of other researchers who have demonstrated reduced levels of IFN-γ in frequently ill children [24] and in mice with asthma [14, 15, 23]. In their work, they show how the levels of IFN-γ change under the influence of medicines, which leads to an improvement in the clinical and laboratory parameters of patients with asthma.

In our study, we found elevated levels of IL-4 in the blood serum of all children with different degrees of partially controlled asthma at the height of clinical manifestations compared to the control group. These data indicate the presence of allergic inflammation. This fact is supported by the ability of IL-4 to stimulate increased IgE production, which in turn contributes to the accumulation of eosinophils in the peripheral blood and tissues [25, 26]. This is reflected in studies of atopic dermatitis [27] and allergic rhinitis [28] in children, and asthma in adults [29]. Taking into account these studies, it can be assumed that elevated levels of IL-4 in patients with asthma indicate an allergic nature of chronic inflammation.

The highest levels of IL-4 were observed in patients with severe asthma, and given that the groups were formed depending on the severity of asthma, it can be assumed that the inflammatory process increases with increasing severity of asthma.

Our study demonstrated strong positive correlations between IL-2 and IL-4, which supports the thesis that IL-2 is involved in the early differentiation of Th2 cells, resulting in increased IL-4 production [17].

A negative correlation was found between IL-4 and IFN-γ levels in the serum of children with asthma, reflecting the regulatory role of Th1-induced signals in inhibiting Th2 cell differentiation.

Similar results have been reported in animal studies of asthma: scientists have studied this combination of interleukins in bronchoalveolar lavage in allergic asthma in remission and have shown that asthma is associated with an increase in IL-4 and a simultaneous decrease in IFN-γ [14, 15].

Studies have shown that in patients with asthma, the immunological pathogenesis of this disease is not only excessive differentiation of Th2 cells and excessive secretion of Th2 cytokines, but also an imbalance of Th1/Th2 in CD4+ Th cell subpopulations [30]. This is also confirmed by the fact that medical correction of Th1/Th2 imbalance leads to better asthma control.

Our study revealed a positive correlation between serum IL-4 levels in children with asthma and the duration of the disease. This suggests that increased chronicity of the inflammatory process corresponds to increased IL-4 production.

Modern studies show a link between elevated levels of IL-4 in exhaled air condensate and the formation of chronic inflammation in children with diagnosed asthma and at the stage of its formation [31]. These studies made it possible to see dynamic changes in IL-4 at the height of clinical manifestations of asthma and repeated bronchial obstruction in children, and in the period outside of exacerbation.

A negative correlation was found between the level of IFN-γ in the blood serum of children with asthma and the duration of the disease. This indicates a decrease in the functional capabilities of IFN-γ in the Th1/Th2 immune balance regulation system in patients with chronic disease. We interpreted such data as a likely manifestation of not just inflammation, but chronic allergic inflammation.

Conclusions.

The cytokine profile in children with asthma in the midst of clinical manifestations is characterised by elevated levels of IL-2 and IL-4 and decreased levels of IFN-γ in the blood serum. The levels of IL-2, IL-4 and IFN-γ depend on belonging to different groups, which were divided into according to the severity of asthma. Thus, we found that during exacerbations of asthma in children, with increasing severity of the disease, the Th1/Th2 imbalance deepens, which can be considered a marker of the formation of a more severe degree of asthma.

Prospects for further research.

Our study has shown that higher levels of IL-2, IL-4 and lower levels of IFN-γ in the serum during exacerbation of asthma are associated with an increased risk of developing more severe asthma and subsequently having a risk of complications.These observations are important for patient assessment and treatment. It makes sense to continue this study in order to deepen the knowledge about the involvement of IL-2, IL-4 and IFN-γ in the pathophysiology of inflammatory processes, which may represent a new way to treat chronic respiratory diseases.

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ПОРУШЕННЯ БАЛАНСУ МІЖ IL-2, IL-4 ТА IFN-γ, ЯК МАРКЕР ТЯЖКОСТІ ЧАСТКОВО КОНТРОЛЬОВАНОЇ БРОНХІАЛЬНОЇ АСТМИ У ДІТЕЙ

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Резюме. Астма це одне з найпоширеніших хронічних неінфекційних захворювань серед дорослих та дітей. Дослідження патогенетичних механізмів бронхіальної астми бере початок з перших нагадувань про це захворювання, але не закінчилось і до нині. Астма хронічний запальний процес, який тісно пов'язаний з дією цитокінів. В останні роки вчені приділяють особливу увагу саме участі цитокінів в формуванні бронхіальної астми.

Метою дослідження було удосконалити знання з оцінки участі прозапальних (IL-2), протизапальних (IL-4) інтерлейкінів та інтерферону-гамма (IFN-γ) в формуванні хронічного запального процесу у дітей із частково контрольованою астмою.

Об'єкт і методи дослідження. У дослідженні взяли участь 94 дитини, які лікувалися у пульмонологічному відділенні. Пацієнтів розподілили на 4 групи: 1 група — діти з легкою персистуючою БА (n=59), 2 група — середньо важкою персистуючою БА (n=10), 3 група — важкою персистуючою БА (n=12) та четверта група – група контролю (n=13). На момент дослідження всі пацієнти мали ознак загострення астми. Дослідження проводи-

лося до початку корекції базисної терапії. IL-2, IL-4 та інтерферон-гамма досліджували за методом імуноферментного аналізу, з використанням наборів «Вектор Бест-Україна». Проведено аналіз даних за допомогою Statsoft Statistica версії 8 (Tulsa, OK) та статистичної програми MedCalc версії 17.2.

Результати. Було встановлено, що у дітей з бронхіальною астмою (1 – 3 групи) вірогідно підвищувалися рівні IL-2, IL-4 та знижувалися рівні інтерферону-гамма у сироватці крові порівняно із групою контролю. Найвищі показники IL-2, IL-4 та найнижчі IFN-γ у сироватці крові були виявлені у пацієнтів з важкою астмою. Отримані кореляційні зв'язки між рівнями IL-2, IL-4 та IFN-γ та тривалістю бронхіальної астми, вірогідніше за все говорить про їх участь у хронічному запальному процесі.

Висновки. Цитокіновий профіль у дітей з бронхіальною астмою в розпалі клінічних проявів характеризується підвищеними рівнями ІЛ-2 та ІЛ-4 та зниженими рівнями IFN-γ сироватці крові. Це приводить до висновків про порушення балансу в системі Th-1 /Th-2.

Ключові слова: астма, діти, цитокіни, хронічний запальний процес.

IMBALANCE BETWEEN IL-2, IL-4 AND IFN-γ AS A MARKER OF SUSTAINABILITY OF PARTLY CONTROLLED ASTHMA IN CHILDREN

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Abstract. Asthma is one of the most common chronic non-communicable diseases among adults and children. The study of the pathogenetic mechanisms of asthma dates back to the first reports of the disease but has not ended to this day. Asthma is a chronic inflammatory process that is closely related to the action of cytokines. In recent years, scientists have been paying special attention to the involvement of cytokines in the formation of asthma.

The aim of the study was to improve knowledge on the role of proinflammatory (IL-2), anti-inflammatory (IL-4) interleukins and interferon-gamma (IFN-γ) in the formation of chronic inflammation in children with partially controlled asthma.

Object and research methods. 94 children treated in the pulmonology department took part in the study. Patients were divided into 4 groups: Group 1 – children with mild persistent asthma (n=59), Group 2 – moderately severe persistent asthma (n=10), Group 3 – severe persistent asthma (n=12) and Group 4 – control group (n=13). At the time of the study, all patients had signs of asthma exacerbation. The study was conducted before the start of correction of baseline therapy. IL-2, IL-4, and interferon-gamma were measured by enzyme-linked immunosorbent assay using Vector Best-Ukraine kits. Data were analysed using Statsoft Statistica version 8 (Tulsa, OK) and MedCalc statistical software version 17.2.

Results. It was found that children with asthma (groups 1 – 3) had significantly increased levels of IL-2, IL-4 and decreased levels of interferon-gamma in the blood serum compared with the control group. The highest levels of IL-2, IL-4 and the lowest IFN-γ in the blood serum were found in patients with severe asthma. The obtained correlations between the levels of IL-2, IL-4 and IFN-γ and the duration of asthma most likely indicate their involvement in the chronic inflammatory process.

Conclusions. The cytokine profile in children with asthma in the midst of clinical manifestations is characterised by elevated levels of IL-2 and IL-4 and decreased levels of IFN-γ in the blood serum. This leads to conclusions about the imbalance in the Th-1/Th-2 system.

Key words: asthma, children, cytokines, chronic inflammatory process.

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