

# Immunological and Biochemical Features in Bronchial Asthma in Children

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## Abstract

The aim of our study was to study the indicators of cytokine status and to determine the features of the hemostasis system and the acid-base state in children with bronchial asthma. We examined 25 children with bronchial asthma aged 7 to 14 years. The study program included: the determination of the level of cytokines: IL-1 $\beta$  and IL-8, the determination of the activity of the acid-base state of the blood. The results of the study showed that the development of bronchial asthma is facilitated by the unfavorable course of the peri- and intranatal periods, aggravated premorbid background, concomitant and past diseases, and significantly high levels of pro-inflammatory cytokines IL-1 $\beta$  and IL-8 were revealed. From the side of biochemical indicators, a very low level of prothrombin time, mild metabolic alkalosis, low partial pressure of oxygen in the blood, and a decrease in the concentration of potassium and calcium ions were detected.

**Keywords:** Bronchial Asthma, Cytokine Status, Hemostasis, Acid-Base State, Children

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## Introduction

Bronchial asthma is one of the most urgent problems of pediatric pulmonology. Despite the positive results in the study of the pathogenesis, diagnosis and treatment of this disease, there is a steady increase in the incidence and life-threatening complications.<sup>[1,2,3]</sup> It is known that the lungs are the central organ of regulation of all parts of hemostasis, control and prevention of thrombogenesis.<sup>[4,5]</sup> In turn, the interaction and activation of blood coagulation factors occurs on the surface of circulating phospholipid membranes.<sup>[6,7,8]</sup> At the same time, the involvement of the hemostasis system in immune-inflammatory processes is beyond doubt, but the complex mechanisms of changes in hemocoagulation and their role in the progression of bronchial asthma in children require further study, since the literature data are very contradictory. In this regard, the disclosure of one of the possible mechanisms that contribute to the prolongation of allergic inflammation in the bronchopulmonary system from the standpoint of studying the coagulo-fibrinolytic link of hemostasis in conjunction with the lipid spectrum, acid-base composition, respiratory and metabolic activity of the lungs, will scientifically substantiate the need to develop a reasonable therapeutic correction in children with bronchial asthma.

Another of the main links in the pathogenesis of bronchial asthma are immune mechanisms.<sup>[9,10]</sup> CD4<sup>+</sup> lymphocytes play a key role in the sensitization of the body. Under the influence of allergenic stimuli, activation and proliferation of the Th2 subpopulation of CD4<sup>+</sup> lymphocytes occurs, followed by the release of cytokines by them, inducing hyperproduction of total and specific IgE. Re-entry of the allergen leads to the release of mediators by cells after non-specific stimulation or binding of allergens to IgE on the

surface of mast cells. These mediators (histamine, leukotrienes) cause the development of an allergic response, manifested by a violation of bronchial patency and an asthma attack.

The participation of the hemostasis system in immune-inflammatory processes is beyond doubt, but the complex mechanisms of changes in hemocoagulation and their role in the progression of bronchial asthma in children require clarification, since the literature data are very contradictory and ambiguous. Identification of the pathogenetic mechanisms of bronchial asthma will help to better understand the pathology and will enable timely development of a set of measures to reduce the frequency of exacerbations of the disease.

The aim of the research is to study of cytokine status indicators and determination of the features of the hemostasis system and acid-base state in children with bronchial asthma.

## Subjects and Methods

We examined 25 children with bronchial asthma in the attack period at the age of 7 to 14 years who received treatment in the department of allergology, the comparison group consisted of 20 patients with bronchial asthma in remission. The diagnosis of AD was based on the 2020 classification adopted by the GINA program. The basis for the diagnosis were: complaints, anamnesis data, results of general clinical, immunological and functional research methods. Immunological studies were carried out at the Institute of Human Immunology and Genomics. The research program included: determination of the level of cytokines: IL-1 $\beta$  and IL-8, by enzyme immunoassay. The conducted biochemical studies include: determination of the activity of the acid-base state of the blood.

## Results & Discussion

Important factors that determine the state of health of the child and its development are the features of the obstetric history, the condition of the child at birth and its development before the onset of this disease. Analyzing the complete information on the anamnesis of the examined children, we identified the risk factors that were most common in them. 22 (48.8%) patients with bronchial asthma were born from the first pregnancy, 25 (37.7%) from II-III pregnancies, from IV or more - 6 (13.3%) children. 39 (86.6%) mothers had various complications during pregnancy. The threat of abortion was in 19 (42.2%) mothers, acute respiratory infections during pregnancy were suffered by 36 (80.0%) mothers, anemia - in 37 (82.2%), pathological course of labor - in 34 (75.5%) cases, prematurity and birth in asphyxia - in 6 (13.3%) and 23 (51.1%), respectively. Upon admission to the hospital, the main complaints of children with bronchial asthma in 100.0% of cases were cough with a small amount of predominantly mucous sputum, especially on awakening, shortness of breath in 100.0% of children, loss of appetite in 80.0%, lethargy in 40, 0%, asthma attacks in 80.0% of the examined, oral wheezing in 80.0%, sweating in 50.0%, headache in 45.0% of patients.

The development of a disease with an immunopathogenetic basis should be considered from the point of view of the effector links of the immune system, whose participation in pathological processes is largely due to the cytokine cascade. To identify the features of the immune status and its role in the pathogenesis of bronchial asthma, it seemed interesting to us to study the cytokine status. The study of cytokines showed that in practically healthy children, the production of IL-1 $\beta$  fluctuated slightly (14–69 pg/ml) and averaged  $52.4 \pm 3.5$  pg/ml. In patients with bronchial asthma during the attack period, IL-1 $\beta$  values were significantly increased and reached  $96.8 \pm 5.7$  pg/ml ( $P < 0.01$ ). Indicators of IL-8 in the group of children with bronchial asthma during remission amounted to  $19.8 \pm 1.4$  pg/ml. The study of cytokines showed that in patients with bronchial asthma during the attack period, the levels of IL-1 $\beta$  and IL-8 were significantly increased compared with the indices in the group of children with bronchial asthma during the period of remission ( $P < 0.01$ ). According to our data, spontaneous production of IL-8 in patients is 3.7 times higher than in controls ( $P < 0.001$ ). The study of the coagulogram showed that in the study group there was a high level of prothrombin index ( $125.48 \pm 1.57$ ), and in the control group it did not exceed the norm ( $P < 0.01$ ). The study of the acid-base composition showed that the result of bronchial obstruction was a change in the activity of the reaction of the internal environment, the main manifestation of which was arterial hypoxemia. So, in patients with bronchial asthma during the attack period, PO<sub>2</sub> ( $55.5 \pm 6.16$  mm Hg), SO<sub>2</sub> ( $83.9 \pm 5.13\%$ ) were significantly lower ( $P < 0.05$ ) of similar indicators in children from the control group (RO<sub>2</sub> =  $82.4 \pm 2.9$  mm Hg; SO<sub>2</sub> =  $93.6 \pm 4.2\%$ ). Along with this, the blood pH in children during the attack period was slightly above the norm ( $7.45 \pm 0.02$ ), and in the control group it was within the normal range ( $7.38 \pm 0.04$ ), ( $P < 0.01$ ).

There were also changes in the electrolyte composition of the blood. The level of potassium (K<sup>+</sup>) in the study group was ( $3.09 \pm 0.159$  mmol/l), which is below the norm, and in the control group ( $4.43 \pm 0.2$  mmol/l), ( $P < 0.01$ ). The level of calcium (Ca<sup>++</sup>) in the study group was almost two times lower than normal ( $1.01 \pm 0.05$  mmol/l), and in the control group ( $2.1 \pm 0.3$  mmol/l), ( $P < 0.01$ ).

## Conclusion

Thus, the development of bronchial asthma is facilitated by the unfavorable course of the peri- and intranatal periods, aggravated premorbid background, concomitant, and past diseases, which significantly aggravate the course of the underlying pathology, and revealed significantly high levels of pro-inflammatory cytokines IL-1 $\beta$  and IL-8 in the blood serum. According to biochemical parameters, in patients with bronchial asthma, on the part of the coagulogram, a high level of the prothrombin index was detected, on the part of the acid-base balance, mild metabolic alkalosis, a low level of oxygen partial pressure in the blood, a decrease in the concentration of potassium and calcium ions was noted in the electrolyte composition of the blood. This suggests that disturbances in the hemostasis system are caused by long-term persistent inflammation in the bronchopulmonary system and severe hypoxia.

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