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T.A. Bobomuratov
Tashkent Medical Academy, Tashkent, 100109, Uzbekistan

U.U. Yusupova
Tashkent Medical Academy, Tashkent, 100109, Uzbekistan

O.A. Sharipova
Tashkent Medical Academy, Tashkent, 100109, Uzbekistan

Sh.S. Bakhronov
Tashkent Medical Academy, Tashkent, 100109, Uzbekistan

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T.A. Bobomuratov, Tashkent Medical Academy
U.U. Yusupova , Tashkent Medical Academy
O.A. Sharipova, Samarkand Medical Institute, Samarkand, Uzbekistan
Sh.S. Bakhronov, Samarkand Medical Institute, Samarkand, Uzbekistan
Zh.N. Abdurakhmonov, Samarkand Medical Institute, Samarkand, Uzbekistan

ABSTRACT

Introduction. Children living in ecologically unfavorable regions often have a risk to acute bronchopulmonary diseases with their own peculiar course. These children have frequent relapses and a complicated course of pulmonary and respiratory diseases. So the present research covers data and analysis of homeostatic system and interleukins level in early age children with acute acquired pneumonia and acute bronchitis, as well as influence of ecological environment on the disease development. **The aim of the research** is to evaluate the features of the clinical course and hemostasis system in children with acute bronchopulmonary diseases with different environmental living conditions. **Materials and methods.** The research involved 42 children with acute acquired pneumonia and 34 children with acute bronchitis (1st group) living in the Aral Sea region (within the territory of Khorezm region) and 40 children with acute acquired pneumonia and 30 children with acute bronchitis aged 1 to 3 years living in the Samarkand region (2nd group). **Results and discussion**. The level of cytokines and indicators of the hemostatic system depended on the severity of the disease. In patients of the 1st group in the acute period of the disease, the levels of pro-inflammatory cytokines IL-1β, IL-6, IL-8 and TNF-α were higher than in patients of the 2nd group. The decrease in the IFN_{γ} content mainly occurred in patients of the 1st group. The level of interleukins in acute pneumonia was higher than bronchitis, 4,1 times in acute pneumonia, 1,5 times higher in acute bronchitis than in control. **Conclusion.** Homeostasis indicators in patients with acute complicated pneumonia living in adverse environmental regions and conditions and having acute pneumonia, showed higher rates of fibrinogen, indicating that the hemostasis system had a high degree of readiness for intravenous blood clotting, hypo-hypercoagulation, thrombinemia, and fibrinolysis. Younger children are characterized by severe and complicated complications of acute pneumonia and bronchitis, as well as compensatory hypercoagulation in the hemostasis system, subcompensative

hypercoagulation, decompensation hypercoagulation (hypercoagulation hypocoagulation, various hemorrhages).
Key words: acute pneumonia, bronchitis, interleukins, hemostatic system, correlation relationship.

Introduction. Despite significant progress in the study of etiology, epidemiology, diagnosis and treatment, acute respiratory diseases occupy the first place in the structure of morbidity in children and the third in the structure of infant mortality. To date, complications, relapses, long duration and chronic respiratory diseases are common [4;11;13].

Recently, due to significant environmental pollution, the problem of the environment and its impact on the health of the child has become one of the most relevant. Children living in ecologically unfavorable regions, have acute bronchopulmonary diseases with their own peculiar course. These are those children who are accompanied by frequent relapses of the disease and a complicated course of respiratory diseases. Such children, constituting a risk group, attract attention as not only a medical, but also a socio- economic problem [2;3;10;12].

Researchers draw attention to the study of the immune regulation of physiological functions. In this regard, the hemostatic system is no exception. It is known that immunocompetent cells carrying receptors for the active factor of blood coagulation are able to realize afferent. In the literature there are data on the effect of cytokines on vascular-platelet hemostasis, blood coagulation and fibrinolysis [1;7]. It is also known that coagulation factors are able to affect the production of certain cytokines [5]. However, the study of the mechanism of cytokines action in the field of medicine practically did not affect the underlying problems of the study of the hemostatic system. Simultaneously, the study of the relation between immunogenesis and hemostasis with the direct participation of interleukins allows to understand at the molecular-cellular level the mechanisms of regulation of blood coagulation and fibrinolysis in the development of DIC and other disorders of the hemostasis system in acute respiratory diseases.

In addition, a new direction in the study of this pathology is the analysis of clinical features and the role of cytokines in the regulation of the hemostatic system of the ADBL system in children with different environmental living conditions. Identifying and analysis of these features would expand the data on the pathogenesis of acute bronchopulmonary diseases. And they would also allow us to develop new ways of predicting, diagnosing, treating disorders in the hemostatic system, which often occur in acute bronchopulmonary diseases in ecologically unfavorable regions.

The aim of the study. To evaluate the features of the clinical course and hemostasis system in children with acute bronchopulmonary diseases with different environmental living conditions.

Materials and methods. The research involved 42 children with acute acquired pneumonia and 34 children with acute bronchitis (1st group) living in the

Aral Sea region (within the territory of Khorezm region) and 40 children with acute acquired pneumonia and 30 children with acute bronchitis aged 1 to 3 years living in the Samarkand region (2nd group). The examined children were at a stationary distance.

The diagnostic algorithm for verifying pneumonia and bronchitis is based on generally accepted clinical symptoms and according to the Protocol for the treatment of pneumonia and bronchitis in children. Pneumonia was diagnosed in the presence of a complex of symptoms of general intoxication, fever, catarrhal manifestations (productive cough), respiratory failure (shortness of breath, assisted muscles in breathing, acrocyanosis, etc.), percussion (local shortening of percussion tone) and auscultatory (hard or bronchial crepitus, asymmetric moist finely bubbling rales) changes in the lungs. The presence of pulmonary infiltrates is confirmed according to x-ray studies of the chest in a straight line, if necessary - in a lateral projection.

Hemostasis systems included determination of prothrombin time (PT), fibrinogen concentration (FC), partial thromboplastin time activity (PTTA), prothrombin index (PTI) on the device (HUMAN CLOT DUO plus), platelet count using an analyzer - “Couiter MD”, coagulability of blood by Fonio.

The concentration of cytokines TNF-α, IL-1β, IL-6, IL-8 in blood serum was carried out by the method of enzyme-linked immunosorbent analysis using the ELISA test system IFA-TNF-α, IL-1β, IL-6 (Vector -Best”, Russia, 2009), the interferon level y (IFL_γ) - by enzyme-linked immunosorbent analysis. The study of various parts of the hemostatic system and the concentration of cytokines was carried out at admission and before of the patient discharge (if necessary, more often).

Statistical processing of the research results was carried out using modern computer systems with application of the standard software package "Excel". To identify the relationships between the analyzed indicators, a correlation analysis was carried out using the correlation coefficient r and checking its significance using the t-student and Pearson $\chi 2$ criteria.

Results and discussion. The results of the study showed that the high incidence of complicated forms of pneumonia was observed in children of the 1st group (81%), compared with the 2nd group (25%) living in the Samarkand region. In patients of the 1st group, the most frequent complications were carditis, which was determined in 45% (19), broncho-obstructive syndrome was detected in 26% (11) and DIC syndrome 9.5% (4). Whereas in patients of the 2nd group carditis was revealed in 3 (7,5%), and bronchial obstructive syndrome was identified in 6 (15%) patients. When analyzing cases of bronchitis, acute obstructive bronchitis was often detected in 24 (71%) patients of the 1st group, recurrent course was detected in 14 (41,2%) patients, while acute obstructive bronchitis was found in 6 patients of the 2nd group (20%) either, recurrent 4 course (13,3%).

The main risk factors for the development of acquired pneumonia and acute bronchitis in patients living in adverse zones was premorbid background. The data obtained showed that in the stationary group of children with 58% (76,3%). At the

same time, 53 (69,7%) children were diagnosed with rickets, 43 (56,6%) children had protein-energy deficiency, anemia was found in 68 (89,5%) children, 2 and 3 concomitant diseases occurred in 42 (55,3%) children of the 1st group. In the 2nd group, the presence of concomitant diseases was determined in 42 (60%) children. The diagnosis of rickets was determined in 28 (40%) children, BEN in 32 (45.7%) children, the diagnosis of anemia was revealed in 57 (81,4%) children. In this case, 2 or more concomitant diseases in children of the 2nd group were detected in 34 (48,6%) children.

The results of the study showed that both in 1st and 2nd groups in the acute period of the disease in the cytokine status, as well as in the hemostatic system, significant changes were identified. The results of studies on the cytokine system are of greatest interest. Changes in cytokine levels characteristic of varying severity corresponded to the volume of lung tissue lesion.

Table 1

Indicators of cytokine state in patients of the 1st and 2nd groups (M ± m)

Indicators	Acute pneumonia I group (n=42)	Acute pneumonia II group (n=40)	Bronchitis I group (n=34)	Bronchitis II group (n=30)	Healthy children (n=30)
IL-1β, пг/ml	186,0±6,9***	141,9±5,6***	72,6±3,8*	54,6±3,4*	44,8±2,8
TNF-α, пг/ml	204,8±9,0***	159,8±8,9***	88,5±2,7***	59,8±2,2***	54,5±2,4
IL-6, пг/ml	24,1±2,1***	15,2±2,2**	13,8±0,5*	8,2±0,6	6,5±0,2
IL-8, пг/ml	109,6±4,2***	84,3±2,2***	79,3±2,4**	63,3±2,2**	54,3±3,3
INF_{γ}, пг/ml	21,2±1,3***	44,0±1,7***	32,1±2,4***	64,1±2,8**	86,2±4,6

*Note. The statistical significance of the difference with the indices of the control group: * p <0.05, ** p <0.01, *** p <0.001.*

As can be seen from the Table 1, in patients of the 1st group in the acute period of the disease, the levels of pro-inflammatory cytokines IL-1β, IL-6, IL-8 and TNF-α were higher than in patients of the 2nd group. The decrease in the INF_{γ} content mainly occurred in patients of the 1st group. Mostly occurred in patients of the 1st group. The level of bronchopulmonary system lesion 4.1 times with acute pneumonia, 1.5 times higher with acute bronchitis. Normalization during the period of clinical remission in patients of the 1st group does not occur. The high level of pro-inflammatory cytokines observed in the period of clinical remission causes less adaptive capabilities of these children. At the beginning and in the midst of acute pneumonia process, a normalization of the inflammatory activity of IL-8 was detected in both groups. However, in patients with a severe form of the disease, the value of regulatory IL-6 remained significantly high. In patients of the 1st group, who have frequent complications, there were more pronounced changes (Table 1).

Thus, a change in the cytokine status, severe, often complicated course of acute pneumonia and bronchitis in the period of clinical remission in the 1st group

of patients, causes inflammation to persist, preservation of the infectious agent during clinical remission.

Laboratory indicators of hemostasis at admission to the hospital in patients of the 1st and 2nd groups are presented in the Table 2**.**

Table 2

Indicators of hemostasis in patients of the 1st group (M ± m)

Criterion	Acute pneumonia I group (n = 32)	Acute pneumonia I group (n = 32)	Bronchitis I group (n = 24)	Bronchitis II group (n = 30)	Healthy children group (n = 30)
Platelets ($X10^9$/l)	379±15,3	330±15,9	234±8,3	239±11,6	205,0 ± 16. 9
AChTV (sec)	47,7±1,9*	33,9±2,1	33,8±1,9	33,4±1,9	33± 0,7
TV (sec)	9,7±1,1*	9,8±1,1	9,3±1,2	9,5±1,4	17,2 ± 1,2
PTV (sec)	15,7±1,2*	14,7±1,2	14,4±1,3	14,4±1,23	16,8 ± 2,5
Fibrinogen (g / l)	4,49±0,32*	3,9±0,32	2,9±0,37	3,29±0,34	2-4 г/л

*Note. M - arithmetic mean; m is the error of the average value; n is the number of patients; Statistical significance of the difference with the indices of the control group: * - significant intergroup differences (p ≤ 0.05; p ≤ 0.01).*

In acute pneumonia, the inflammatory process cannot be described as separate, without changes in the hemostasis, since the effects of the clotting and coagulation system are of particular importance in the pathogenesis of the disease. Analysis of laboratory observations of our observations shows that, especially in the 1st group, patients had increased fibrinogen content (4,49 + 0,32g/l), increased platelet time (AChTV 47,7 + 1,9 sec), increased platelet number, prothrombin index, and time was reduced. Normal or significant changes were not detected in 9% of the patients analyzed, 22% had compensatory hypercoagulation, 55% had subcompensated hypercoagulation, 14% had decompensated hypercoagulation (hypercoagulation hypocoagulation, various hemorrhages). Changes in the system of hemostasis in acute pneumonia are more pronounced than in uncomplicated forms, and a dramatic increase in platelet count is the compensatory response of platelets to the occurrence of intracranial clotting. It has also been shown that a number of coagulation joints of hemostasis in complicated pneumonia are at high thrombotic readiness for intravenous coagulation. Failure of timely correction of hypercoagulation syndrome in sick children leads to the worsening of the general condition of patients and the decompensation of hypercoagulation.

In acute armor in different groups of changes in coagulation hemostasis, significant hypercoagulation (AChTV 34 ± 2,1; 33,8 ± 1,9) are distinguished

against the background of inhibition of the final stage of coagulation (TB 9,9 ± 1,1; 9,3 ± 1, 2), fibrinogenemia (fibrinogen 3,2 ± 0,34; 2,9 ± 0,37), fibrinemia (127,2 ± 5,3; 118,2 ± 4,3), inhibition of fibrinolysis and an increase in blood levels of products fibrin degradation. The revealed changes are due to severe thrombinemia (199,2 ± 12,3; 134,9 ± 4,7) and activation of intravascular coagulation to a greater extent. decompensation of the current intravascular coagulation. All this is an indication for the correction of the blood coagulation system.

To make the relationship between cytokines and the hemostatic system, a correlation analysis of their indicators was conducted. The greatest effect in the pathogenesis of acute bronchopulmonary diseases is characteristic of IL-6 and IL-8, which are important triggers of hypercoagulation [8]. In children of the 1st group (vulnerable zone), a high positive correlation was observed between the levels of IL-6, IL-1 and fibrinogen concentration (r = 0,42), compared with the 2nd group (r = 0,48). This can be explained by the fact that a high level of pro-inflammatory cytokines, especially IL 6, acting on hepatocytes, stimulate the cleavage of proteins of the acute phase (α1 – antitrypsin, α2 – macroglobulin and fibrinogen) [6;8]. An average positive correlation was observed between the content of IL-6, TNF-α and RFMC (r = 0,32; r = 0,49), which reflects hypercoagulation and a decrease in fibrinolytic activity in the examined patients.

Between IFNu and indicators of the hemostatic system revealed a close negative correlation. This can be explained by the "immune mechanisms of hemostasis regulation." According to this theory, how low the number of immunocompetent cells will be, so the coagulation ability of the blood will be prone to increase [9].

A human body has a single integrated cellular-humoral defense system, including immunity, hemostasis and nonspecific resistance of the body [5]. Changes in one of the functional links of this system lead to the shifts in others.

Thus, in acute bronchopulmonary diseases in children with complicated forms of acute bronchopulmonary diseases, there was a hemostasis reaction in the form of thrombinemia, inhibition of fibrinolysis. Changes in the cytokine state and hemostasis system may be one of the factors that determine the complicated and recurrent course of the pathological process. Those changes were more pronounced in children, living in the Aral Sea region (in the Khorezm region) compared with those living in the Samarkand region.

Conclusions.

1. Background diseases play a significant role in the development and progression of acute bronchial pulmonary diseases in children living in the background diseases were revealed in 55.3% of patients. Those background diseases caused severe and prolonged development of acute pneumonia and bronchitis in children, complications, profound changes in the immune system and hemostasis.

2. In the acute period of bronchopulmonary diseases, the level of cytokines and indicators of the hemostatic system depended on the severity of the disease: in all patients, the level of pro-inflammatory cytokines IL-1β, IL-6, IL-8 and TNF-α

increases and the concentration of interferon in both groups reduces, but it was noted more in children living in the Khorezm region compared to healthy children.

3. Younger children are characterized by severe and complicated complications of acute pneumonia and bronchitis, as well as compensatory hypercoagulation in the hemostasis system, subcompensative hypercoagulation, decompensation hypercoagulation (hypercoagulation hypocoagulation, various hemorrhages). Living in adverse conditions and having acute pneumonia, patients showed increased hemostasis, mainly with increased readiness for intravenous blood clotting, increased fibrinogen levels, decreased hypercoagulation, thrombinemia, and fibrinolysis. These changes in acute pneumonia in young children indicate the presence of thrombogenic risk, which in turn requires effective correction and prevention of hemostasis.

4. The established correlation between cytokines and hemostasis indicates immune regulation of blood coagulation. Changes in one of the functional links of this system lead to the shifts in others. At the same time, cytokines are informational molecules that adapt protective mechanisms to maintain homeostasis of the body.

References:

1. Arai K. Cytokines: coordinators of immune and inflammatory responses. Ann. Rev. Biochem. 2006; 59: 783.
2. Baranov A.A., Albitsky V.Yu. Social and organizational problems of pediatrics. M.:Dynasty. 2003; 233-252.
3. Bellanti J. Recurrent respiratory tract infection in pediatric patient. Drugs 2006; 54 (suppl. 1): 1-4.
4. Bobomuratov T.A. Studying the hemostatic system and evaluating the effectiveness of lymphotropic anticoagulant therapy in young children with acute pneumonia. Lymphology. 2000; 1-2: 9-13.
5. Emelyanova A.N., Vitkovsky Yu. A. Lymphocyte- platelet adhesion and pro-inflammatoru cytokines contents in patients with erysipelas. Siberian medical journal. 2012; 27(1): 57-59.
6. Gusev E.Yu., Yurchenko L.N., Chereshnev V.A. et al. Options for the development of acute systemic inflammation. Cytokines and inflammation. 2008; 7 (2): 9–17.
7. Kashtalyan O.A., Ushakova L. Yu. Cytokines as universal regulation system. Medical news. 2017; 9: 3-7.
8. Ketlinsky S.A., Simbirtsev A.S. Cytokines. St. Petersburg: Foliant. 2008; p.552
9. Kuznik B. I., Tsybikov N. N. Autoimmune mechanisms of regulation of the hemostatic system. J. Siberian oncology, 2005; 13 (1): 88-95.
10. Mamatkulova D.Kh., Bobomuratov T.A. Clinical and pathogenetic significance of changes in hemostatic disorders and their correction in chronic pneumonia in children. Medical sciences. 2004; 2: 29-30.

11. Samsygina G.A. The issues of frequently ill children in pediatrics. Pediatric Journal after the name of G.N. Speranskiy. 2015; 94 (1): 167-169.
12. Uchaykin V.F. Recurrent respiratory infections in children: the use of immunomodulators for treatment and prevention. Pediatrics. 2009; 87 (1): 127-132.
13. Zaitseva OV Recurrent respiratory infections: is it possible to prevent? Pediatrics. 2015; 94 (2): 185-192.