

Peculiarities of immune status in children with chronic bronchitis**Nilufar Irgashevna Karimova^{a*}, Furkat Mukhitdinovich Shamsiev^b**^a Tashkent State Medical University, Department of Children's Diseases in Family Medicine^b Republican Specialized Scientific and Practical Medical Center of Pediatrics Ministry of Health of the Republic of Uzbekistan, Tashkent, Uzbekistan

Received 4 July 2024

Accepted 28 Jul. 2025

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ABSTRACT: The aim of the study was to determine the state of the immune and cytokine status in chronic bronchitis in children. The results of the study showed that chronic bronchitis occurs in 10.4% of the total number of children with bronchopulmonary pathology and develops against the background of unfavorable perinatal factors, concomitant and past diseases affecting the development, course and outcome of the disease. The clinical picture and course of chronic bronchitis depend on the nature and degree of bronchial damage. The data obtained by us on the indicators of the immune status in different age groups in children with chronic bronchitis indicate suppression of indicators of cellular immunity and phagocytosis of neutrophils, activation of the humoral link of immunity, the most informative diagnostic markers of chronic diseases of the lower respiratory tract in children, manifested by overproduction of pro- and anti-inflammatory cytokines indicating chronic inflammation.

KEYWORDS: chronic bronchitis, children, immune status, history, clinical manifestations.

Chronic lung diseases remain a serious public health problem in all countries of the world and reach 10–40% among all pathologies of the bronchopulmonary system [1,2]. They lead to frequent, prolonged exacerbations, a decrease in the quality of life of patients, disability at a young working age. The main place in the structure of chronic diseases of the lower respiratory tract belongs to chronic bronchitis [3,4,5]. Chronic bronchitis is a common disease, and the number of patients continues to increase, which, in all likelihood, is explained by the difficulties in identifying pathology due to the blurred clinical manifestations, the frivolous attitude of this contingent to the mild symptoms of the disease [6,7]. Immunological dysfunctions are an important factor contributing to the formation of chronic bronchitis in children. The failure of the immune system can be caused by genetic factors, immunodeficiency state, as well as unfavorable exogenous influence of the environment [8,9,10].

Purpose of the study. Determine the state of the immune and cytokine status in chronic bronchitis in children.

MATERIALS AND METHODS

The study was carried out in 172 children with

chronic bronchitis for the period 2020–2021, who were inpatient treatment at the pulmonology department. The comparison group consisted of 40 children with acute bronchitis. The control group consisted of 24 apparently healthy children of the same age. The diagnosis of chronic bronchitis was verified on the basis of complex clinical and instrumental studies: a carefully collected anamnesis, clinical, laboratory and instrumental (chest x-ray). The immunological study included the determination of CD3+, CD4+, CD8+, CD16+, CD20+ lymphocytes, the concentration of immunoglobulins of classes A, M, G, phagocytic activity of neutrophils, which was performed at the Institute of Human Immunology and Genomics.

RESULTS

Analysis of anamnestic data in the examined children showed that the majority of children with chronic bronchitis were born from an unfavorable pregnancy with symptoms of toxicosis – 75.0% (129), 77.0% (132) of mothers of children with chronic bronchitis were diagnosed with anemia during pregnancy I and II degrees, which significantly ($P < 0.01$) differs from the indicators of the comparison group. \

Mothers of children with chronic bronchitis during this pregnancy suffered acute respiratory infections in 60.4% (104) cases, bronchitis 34.3% (59) had endocrine diseases 32.5% (56), which differs markedly from the indicators of the comparison group ($P < 0.01$). Most mothers had foci of chronic infection - diseases of the upper respiratory tract (rhinitis, tonsillitis) 69.7% (120), which differs markedly from the indicators of the comparison group ($P < 0.01$). It is known that the severity of chronic bronchitis in children is significantly influenced by an unfavorable premorbid background [11,12]. Analysis of the data showed that anemia of I-II degrees was determined in 94.7% (163) children, which differs from the indicators of the comparison group ($P < 0.001$); this, as is known, aggravates oxygen starvation in the child. Residual effects of rickets were detected in 54.0% (93), which complicates ventilation of the lungs.

The onset of the disease was acute in 29.0% (9) children with chronic bronchitis aged 3-6 years, in 31.2% (44) children aged 7-15 years, gradual in 71.0% (22) children in at the age of 3-6 years, in 68.8% (97) at the age of 7-15 years. The severity of the general condition was determined by the severity of clinical manifestations or complications. At the time of the present hospitalization, the general condition of the patients was severe in 28.5% (49) of children with chronic bronchitis, of moderate severity in 71.5% (123). Upon admission to the hospital, the main complaints of parents of children, patients were cough in 100.0% (172), shortness of breath - in 28.5% (49), fever - in 41.8% (72) children, decreased appetite - in 91.8% (158), lethargy - in 84.8% (146), pallor - in 92.4% (159). X-ray examination showed an increase and deformation of the bronchopulmonary pattern in 62.4% (88) children with chronic bronchitis, the process was more often localized in both lungs, in 167 (97.1%) patients there was an increase in the pulmonary pattern and in 85 (60.3%) deformation of the bronchopulmonary pattern was revealed in children. The carried out complex of immunological studies made it possible to assess the state of cellular and humoral immunity in chronic bronchitis. The results of the study of the immune status of

the examined patients made it possible to establish a different severity of the immunodeficiency state (mainly due to the cellular link of immunity) with signs of tension in the humoral link of immunity and the multidirectional nature of immunological changes (Table 1). As can be seen from the presented data, in patients with chronic bronchitis in the phase of exacerbation of the disease, the following deviations were revealed: a significant decrease in CD3+ lymphocytes, in relation to the comparison group ($41.6 \pm 0.7\%$ with $61.5 \pm 2.2\%$ in children of the control group, $P < 0.001$, in relation to the comparison group ($50.2 \pm 2.5\%$, $P < 0.01$). The indicators of children with chronic bronchitis exceeded those of children with acute bronchitis by 1.2 times. A significant decrease in CD3+ lymphocytes up to $36.8 \pm 0.6\%$ at $61.5 \pm 2.2\%$ in practically healthy children, $P < 0.001$, in relation to the comparison group ($50.2 \pm 2.5\%$; $P < 0.001$). CD4+ lymphocytes belong to regulatory cells. Without them, transformation of CD20+ lymphocytes into plasma cells that form antibodies is impossible. A study of the number of CD4+ lymphocytes revealed their deep deficiency. The content of CD4+ lymphocytes was reduced to $28.9 \pm 281.0\%$ in relation to the comparison group ($P < 0.01$) in children with chronic bronchitis, which exceeded the acute bronchitis data by 1.3 times.

The number of CD8+ lymphocytes, which play an important role in antiviral immunity, in children with chronic bronchitis was increased by 1.3 times in comparison with the indicators of practically healthy children. There was a significant increase in CD8+ lymphocytes ($25.8 \pm 0.5\%$ at $19.5 \pm 1.8\%$; in children of the control group, $P < 0.001$, in relation to the comparison group ($18.9 \pm 1.2\%$; $P < 0.01$). It was revealed a decrease in the immunoregulatory index in patients with chronic bronchitis by 1.8 times due to a more significant increase in the number of CD8+ cells compared to CD4+. There was a significant increase in natural killer cells - CD16+ lymphocytes in comparison with children of the control group and amounted to $14.2 \pm 0.4\%$ ($10.2 \pm 1.3\%$ in practically healthy children; $P < 0.001$), in relation to the comparison group ($P < 0.05$). There was a significant decrease in neutrophil phagocytosis to $39.8 \pm 1.2\%$ in relation to the comparison

Table 1.

Comparative analysis of indicators of cellular immunity in children with chronic bronchitis, ($M \pm m$)

Indicators	Control group n = 24	Acute bronchitis n = 40 (I)	Chronical bronchitis n = 172 (II)	P
Leukocytes, abs.	6677,8 \pm 167,9	7048,5 \pm 125,9	6924,8 \pm 102,5	>0,05
Lymphocytes,%	33,5 \pm 0,5	35,2 \pm 0,6	38,2 \pm 0,5	<0,01
CD3 ⁺ - Lymphocytes,%	61,5 \pm 2,2	50,2 \pm 2,5	41,6 \pm 0,7	<0,01
CD4 ⁺ - Lymphocytes,%	39,1 \pm 2,1	37,9 \pm 1,3	28,9 \pm 1,0	<0,01
CD8 ⁺ - Lymphocytes,%	19,5 \pm 1,8	18,9 \pm 1,2	25,8 \pm 0,5	<0,001
(CD4 ⁺ /CD8 ⁺) - immunoregulatory index	2,0 \pm 0,2	2,0 \pm 0,2	1,1 \pm 0,06	<0,01
CD16 ⁺ - Lymphocytes,%	10,2 \pm 1,3	9,8 \pm 0,8	14,2 \pm 0,4	<0,01
Phagocytosis of neutrophils, %	58,5 \pm 2,3	52,1 \pm 1,1	39,8 \pm 1,2	<0,001

Note: P - reliability of differences between indicators of I and II groups of patients;

Table 2.

Comparative analysis of indicators of humoral immunity in the examined children, ($M \pm m$)

Indicators	Control group (n = 24)	Acute bronchitis n = 40 (I)	Chronical bronchitis n = 172 (II)	P
CD20 ⁺ - Lymphocytes,%	16,4 \pm 0,5	18,1 \pm 0,8	32,4 \pm 0,7	<0,001
IgG, mg/%	938,3 \pm 17,6	908,7 \pm 18,4	1360,5 \pm 36,5	<0,001
IgA, mg /%	107,9 \pm 3,6	104,6 \pm 2,8	149,7 \pm 5,8	<0,001
IgM, mg /%	90,7 \pm 2,8	102,5 \pm 3,4	126,8 \pm 2,5	<0,01

Note: P - reliability of differences between indicators of I and II groups of patients;

group (52.1 \pm 1.1%, $P < 0.01$). The change in neutrophil phagocytosis was more pronounced in the group of children with chronic bronchitis compared with acute bronchitis ($P < 0.001$). of these children, there was also a tendency to an increase in CD20⁺ lymphocytes (32.4 \pm 0.7% at 16.4 \pm 0.5% in children of the control group, $P < 0.001$, in relation to the comparison group ($P < 0.01$) (table 2).

The activation of the humoral link of immunity was evidenced by the increased concentration of immunoglobulin IgM in patients; their increase was 1.4 times, on average, up to 126.8 \pm 2.5 mg /%, in relation to the comparison group by 1.2 times (102.5 \pm 3, 4mg /% $P < 0.01$). The IgG content in the group of patients with chronic bronchitis showed an increase in this indicator by 1.5 times compared with the data of practically healthy children and averaged

1360.5 \pm 36.5 mg /% ($P < 0.001$), in relation to the comparison group it was increased 1.5 times (908.7 \pm 18.4 mg /%, $P < 0.001$). In the examined children with chronic bronchitis, an increase in the IgA level was also noted by 1.4 times compared with the indicators of practically healthy children and on average was 149.7 \pm 5.8 mg /% ($P < 0.001$), it was increased in relation to the comparison group 1.4 times (104.6 \pm 2.8 mg /%, $P < 0.001$).

CONCLUSION

Thus, summarizing the results of the study, we can conclude that chronic bronchitis occurs in 10.4% of the total number of children with bronchopulmonary pathology and develops against the background of unfavorable perinatal factors, concomitant and transferred

diseases affecting the development, course and outcome of the disease. The clinical picture and course of chronic bronchitis depend on the nature and degree of bronchial damage. The data obtained by us on the indicators of the immune status in different age groups in children with chronic bronchitis indicate suppression of indicators of cellular immunity and phagocytosis of neutrophils, activation of the humoral link of immunity, the most informative diagnostic markers of chronic diseases of the lower respiratory tract in children, manifested by overproduction of pro- and anti-inflammatory cytokines indicating chronic inflammation.

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