

Prognostic value of peripheral blood lymphocytes in community-acquired pneumonia in children

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Abstract

Introduction. Despite a significant decrease in mortality from pneumonia, pneumonia remains the main cause of death in children outside the neonatal period. As a key component of the immune system, CD4⁺ T cells significantly affect lung tissue damage. Prior to the initiation of an adaptive immune response, NK cells not only produce cytokines associated with antiviral immunity, but are also directly involved in the rapid elimination of infected cells.

Objective. To determine changes in lymphocyte subpopulations in peripheral blood in children in different age groups with community-acquired pneumonia and to assess their prognostic significance depending on the severity of community-acquired pneumonia.

Materials and methods. 117 children aged 1 to 18 years with radiologically confirmed diagnosis of community-acquired pneumonia were examined, severe (29 children) and mild (88 children). All children were divided into 4 age groups (1–3 years old, 4–7 years old, 8–12 years old, 13–18 years old). Blood levels of lymphocytes and their subpopulations were determined in all children using flow cytometry.

Results. According to the results of the study, a decrease in the number of NK-lymphocytes in the peripheral blood of children with severe community-acquired pneumonia was revealed compared with children with mild community-acquired pneumonia in all age groups, and an association of NK-lymphocytes and TNK-lymphocytes with the severity of community-acquired pneumonia in children was found.

Conclusions. A decrease in the number of NK-lymphocytes in peripheral blood in children with severe community-acquired pneumonia in all age groups compared with children with mild community-acquired pneumonia, as well as the association between a decrease in the number of NK-lymphocytes and TNK-lymphocytes and the severity of community-acquired pneumonia in children can be considered an independent marker of the severity of this disease.

Keywords: community-acquired pneumonia, children, prognosis, severe pneumonia, lymphocyte subpopulations

Conflict of interest:

The authors declare no conflict of interest related to the publication of this article.

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Прогностическое значение лимфоцитов периферической крови при внебольничной пневмонии у детей

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Аннотация

Актуальность. Несмотря на существенное снижение заболеваемости пневмонией, внебольничная пневмония остается одной из основных причин смерти детей вне неонатального периода. Являясь ключевым компонентом иммунной системы, CD4⁺ Т-клетки значительно влияют на повреждение легочной ткани. До инициации адаптивного иммунного ответа NK-клетки не только продуцируют цитокины, связанные с противовирусным иммунитетом, но также непосредственно участвуют в быстром выведении инфицированных клеток.

Цель. Определить изменения субпопуляций лимфоцитов в периферической крови у детей в разных возрастных группах с внебольничной пневмонией и оценить их прогностическую значимость в зависимости от тяжести внебольничной пневмонии.

Материалы и методы. Было обследовано 117 детей в возрасте от 1 года до 18 лет с рентгенологически подтвержденным диагнозом внебольничной пневмонии тяжелой (29 детей) и нетяжелой (88 детей). Все дети были разделены на 4 возрастные группы (1–3 года, 4–7 лет, 8–12 лет, 13–18 лет). Фенотипирование и дифференцировка субпопуляций лимфоцитов проводились методом проточной цитометрии.

Результаты. По результатам исследования было выявлено снижение количества NK-лимфоцитов в периферической крови у детей с тяжелой внебольничной пневмонией по сравнению с детьми с нетяжелой внебольничной пневмонией во всех возрастных группах, а также обнаружена ассоциация NK-лимфоцитов и TNK-лимфоцитов с тяжестью внебольничной пневмонии у детей.

Заключение. Снижение количества NK-лимфоцитов в периферической крови у детей с тяжелой внебольничной пневмонией во всех возрастных группах по сравнению с детьми с нетяжелой внебольничной пневмонией, а также связь между снижением количества NK-лимфоцитов и TNK-лимфоцитов и тяжестью внебольничной пневмонии у детей может рассматриваться независимым маркером тяжести данного заболевания.

Ключевые слова: внебольничная пневмония, дети, прогноз, тяжелая пневмония, субпопуляции лимфоцитов

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INTRODUCTION

Despite a significant reduction in overall child mortality, community-acquired pneumonia (CAP) remains one of the causes of death in children beyond the neonatal period. It can also cause exacerbation of chronic diseases and worsen long-term lung health by reducing lung function [1].

The etiologic structure of pneumonia in children is very diverse and depends on the child's age. Data on the etiology of community-acquired pneumonia

in children vary greatly, which can be explained by the different epidemic conditions in which the studies were conducted. Various bacteria and viruses are the most common causative agents of CAP in children, but in most cases the etiology of CAP remains unidentified [2]. According to a large population-based study in the United States, viruses were detected in 66.2% of children under 18 years of age who were hospitalized with CAP, had radiologic confirmation of CAP, and from whom samples for etiologic

testing were obtained ($n = 2222$) [3]. The severity of clinical manifestations of community-acquired pneumonia varies considerably. Consequently, both differentiation of viral and bacterial infection and accurate assessment and prediction of disease severity are critical for effective management of patients with community-acquired pneumonia, including the decision to prescribe antibiotics and hospitalization. Both of these goals are much easier to achieve in adults than in children, especially in the early years of life. The limited ability to obtain lower respiratory tract secretions or sputum from young children, given their poor expectorative capacity and inability to expectorate sputum, is the most important obstacle to obtaining sufficient respiratory specimens for etiologic identification by microbiologic methods in young patients [4].

One of the easiest ways to monitor pneumonia patients is through a general blood count, which usually measures the white blood cell count, neutrophil count, monocyte count, and lymphocyte count. Among these, neutrophils, lymphocytes and monocytes are common indicators of human inflammation and immune status [5]. Total leukocyte counts fluctuate in the pediatric population, especially in early life. Consequently, reference values differ between age groups. In general, a value greater than $11 \times 10^9/L$ is considered leukocytosis [2, 6]. Some studies have emphasized that leukocytes had the lowest positive predictive value compared with serum levels of procalcitonin and C-reactive protein [7]. In a study by Zhu F. et al. it was noted that the percentage of neutrophils compared to the total leukocyte count reflected the presence of bacterial infection better [8].

Given the viral-bacterial etiology of pneumonia, especially in children under 5 years of age, cellular and humoral immunity plays a key role in the body's defense against viral infections, and activation and impairment of immune function have a significant impact on disease progression and prognosis. In recent years, it has been found that respiratory viral infections often cause a decrease in the number of lymphocytes in peripheral blood [9]. Previous studies have suggested that this may be due to virus-induced destruction of T cells. For example, Liu B. et al. demonstrated that, influenza A (H1N1) infection can induce thymus cell apoptosis and atrophy [10].

As a key component of the immune system, $CD4^+$ T-cells significantly influence lung damage caused by viral infection. $CD4^+$ T-cells stimulate the activation and differentiation of B-cells. $CD4^+$ T cells also promote the differentiation of $CD8^+$ T-cells into cytotoxic effectors and memory cells, as well as the localization of $CD8^+$ memory T-cells in infected airways. In addition, cytotoxicity, which has the potential to directly destroy infected cells, is an increasingly proven function of $CD4^+$ T-cells. $CD8^+$ cytotoxic T cells recognize virus-infected cells, induce apoptosis, and produce pro-inflammatory cytokines to inhibit viral replication, such as $IFN\gamma$. In a study by Liu B. et al. 2023 there was a significant decrease in NK cells in children with severe influenza B virus-induced pneumonia [9].

To date, there is little information on the status of lymphocytes and their subpopulations in viral-bacterial pneumonias in children in different age groups, which was the purpose of this study.

STUDY OBJECTIVE — Determine changes in lymphocyte subpopulations in peripheral blood in children in different age groups with community-acquired pneumonia and assess their prognostic significance depending on the severity of community-acquired pneumonia.

MATERIALS AND METHODS

The work was carried out at the Department of Microbiology, Virology and Immunology, the Department of Propaedeutics of Children's Diseases and Pediatrics and at the Research Institute of Immunology of the South Ural State Medical University of the Ministry of Health of the Russian Federation.

The study involved 117 children aged 1 to 18 years with radiologically confirmed diagnosis of severe (29 children) and non-severe (88 children) community-acquired pneumonia hospitalized in respiratory infections departments of MBHI CCCH No. 7 and CHCH No. 8 in Chelyabinsk. All children were divided into 4 age groups (1-3 years, 4-7 years, 8-12 years, 13–18 years) and comparable by sex and age. Inclusion criteria of patients in the study: age from 1 year to 17 years 11 months and 30 days, diagnosis of community-acquired pneumonia made according to the criteria specified in the 2015 Clinical Guidelines for

Community-acquired Pneumonia in Children, edited according to the 2022 guidelines adopted in the Russian Federation [2].

Exclusion criteria: parental refusal to participate in the proposed study, history of chronic diseases, including bronchial asthma, allergic rhinitis, juvenile rheumatoid arthritis, diffuse connective tissue diseases, diabetes mellitus, HIV infection, cancer, central nervous system pathology.

Phenotyping and differentiation of lymphocyte subpopulations were performed by flow cytometry using Navios 6/2 (Beckman Coulter, USA). Blood was collected in tubes with anticoagulant K2 EDTA on the 1st day after hospitalization in the morning on an empty stomach. Markers of subpopulations were determined: T-lymphocytes ($CD3^+$), T-helper ($CD3^+CD4^+$), T-cytotoxic ($CD3^+CD8^+$), TNK-lymphocytes ($CD3^+CD16^+CD56^+$), NK-lymphocytes ($CD3^-CD16^+CD56^+$), B-lymphocytes ($CD3^-CD19^+$).

The results were processed using statistical programs in IBM SPSS package (v. 23). The Kruskal-Wallis and Mann-Whitney criteria were used to judge the reliability of differences in quantitative features in independent groups. In case of 3 or more repeated observations, the Friedman criterion was used, followed by pairwise comparison in two related or dependent groups using the Wilcoxon test. To assess the differences between the main group and the comparison group, the data were summarized in contingency tables, which were analyzed using the likelihood ratio criterion (chi-square of maximum likelihood). In case of low saturation of conjugacy table cells (minimum expected less than 4), statistical significance was assessed using the exact permutation method in Cytel Studio StatXact (version 7.0; Cytel Software Corporation). Correlation analysis was performed using the Spearman rank correlation method.

In all cases, the detected effects were considered statistically significant at $p \leq 0,05$.

STUDY RESULTS AND THEIR DISCUSSION

The results of the study showed a decrease in the absolute number of TNK-lymphocytes ($CD3^+CD16^+CD56^+$) in children with severe CAP in all age groups, with the exception of children from 13 to 18 years of age, compared to children with mild community-acquired pneumonia. When comparing the level of NK-lymphocytes ($CD3^-CD16^+CD56^+$) in the peripheral blood of children with CAP, a decrease in both relative and absolute values of these indicators was found in children with severe CAP in all age groups. The relative number of B-lymphocytes ($CD3^-CD19^+$) was higher in the group of children with severe CAP in the age group from 4 to 7 years and from 8 to 12 years in relation to children with mild community-acquired pneumonia. In addition, a decrease in the number of T-helper cells ($CD3^+CD4^+$) was observed in children from 1 to 3 years of age with severe CAP compared with children with mild CAP (Table 1).

The correlation analysis between the severity of pneumonia and immunologic indices revealed negative correlations with the number of TNK-lymphocytes and NK-lymphocytes (Table 2).

The study revealed changes in T-lymphocytes, in particular, a decrease in T-helper cells ($CD3^+CD4^+$) in children aged 1-3 years with severe CAP compared to children with mild CAP. Effector $CD4^+$ cells are able to provide the assistance needed by both $CD8^+$ T-cells and B cells to reach their full functional potential, as well as to exert direct effector functions through cytotoxicity of virus-infected cells. After virus infection, $CD4^+$ T-cells persist long term with an increased ability to protect against secondary infec-

Table 1. Indicators of lymphocyte subpopulations in children with community-acquired pneumonia, severe and mild, at different age periods, Me ($Q_{0,25}$ – $Q_{0,75}$) (author's table)

Таблица 1. Показатели субпопуляций лимфоцитов у детей с внебольничной пневмонией тяжелой и нетяжелой в различные возрастные периоды, Me ($Q_{0,25}$ – $Q_{0,75}$) (таблица автора)

Age group, years	Mild pneumonia (n = 29, 21, 20, 18)	Severe pneumonia (n = 12, 9, 4, 4)	Significance of differences <i>p</i>
T-lymphocytes ($CD3^+$), %			
1–3	70,0 (47,8–80,3)	68,7 (44,4–80,2)	$p_{1-2}=0,4$ $p_{1-3}=0,5$ $p_{2-3}=0,9$
4–7	68,4 (51,7–83,8)	67,2 (49,1–81,5)	$p_{1-2}=0,1$ $p_{1-3}=0,02$ $p_{2-3}=0,9$

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T-lymphocytes (CD3 ⁺), %			
8–12	70,4 (61,9–88,1)	68,7 (76,5–68,7)	$p_{1-2}=0,1$ $p_{1-3}=0,1$ $p_{2-3}=0,4$
13–18	73,9 (63,8–80,5)	68,4 (68,2–79,4)	$p_{1-2}=0,3$ $p_{1-3}=0,5$ $p_{2-3}=0,2$
T-lymphocytes (CD3 ⁺), abs			
1–3	1950,0 (757,0–3996,0)	1267,0 (374,0–3993,0)	$p_{1-2}=0,1$ $p_{1-3}=0,8$ $p_{2-3}=0,05$
4–7	1667,0 (755,0–3424,0)	1267,0 (968,0–4050,0)	$p_{1-2}=0,02$ $p_{1-3}=0,008$ $p_{2-3}=0,9$
8–12	1659,0 (768,0–3974,0)	1267,0 (1267,0–2234,0)	$p_{1-2}=0,9$ $p_{1-3}=0,2$ $p_{2-3}=0,5$
13–18	1207,5 (680,0–2401,0)	1222,0 (977,0–1374,0)	$p_{1-2}=0,07$ $p_{1-3}=0,06$ $p_{2-3}=0,4$
T-helpers (CD3 ⁺ CD4 ⁺), %			
1–3	35,7 (21,8–50,6)	33,0 (17,7–40,3)	$p_{1-2}=0,009$ $p_{1-3}=0,001$ $p_{2-3}=0,3$
4–7	34,3 (24,2–54,4)	33,0 (22,7–49,2)	$p_{1-2}=0,3$ $p_{1-3}=0,06$ $p_{2-3}=0,6$
8–12	36,5 (19,1–62,4)	33,0 (33,0–50,9)	$p_{1-2}=0,05$ $p_{1-3}=0,1$ $p_{2-3}=0,4$
13–18	44,0 (29,4–51,6)	45,7 (33,0–48,7)	$p_{1-2}=0,01$ $p_{1-3}=0,1$ $p_{2-3}=0,6$
T-helpers (CD3 ⁺ CD4 ⁺), abs			
1–3	1022,0 (393,0–3083,0)	610,0 (149,0–1788,0)	$p_{1-2}=0,4$ $p_{1-3}=0,3$ $p_{2-3}=0,021$
4–7	805,0 (401,0–2257,0)	655,0 (610,0–2428,0)	$p_{1-2}=0,03$ $p_{1-3}=0,005$ $p_{2-3}=0,8$
8–12	880,5 (322,0–1997,0)	610,0 (610,0–1675,0)	$p_{1-2}=0,3$ $p_{1-3}=0,2$ $p_{2-3}=0,3$
13–18	758,0 (11,0–1544,0)	654,0 (610,0–844,0)	$p_{1-2}=0,3$ $p_{1-3}=0,1$ $p_{2-3}=0,4$
T-cytotoxic (CD3 ⁺ CD8 ⁺), %			
1–3	26,3 (10,9–44,3)	25,3 (20,1–36,8)	$p_{1-2}=0,008$ $p_{1-3}=0,001$ $p_{2-3}=0,7$
4–7	26,0 (18,7–42,8)	25,3 (20,9–29,4)	$p_{1-2}=0,3$ $p_{1-3}=0,3$ $p_{2-3}=0,8$
8–12	25,5 (15,3–43,1)	25,3 (12,1–25,3)	$p_{1-2}=0,9$ $p_{1-3}=0,5$ $p_{2-3}=0,3$

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T-cytotoxic (CD3 ⁺ CD8 ⁺), %			
13–18	25,7 (16,6–47,6)	22,6 (19,9–26,7)	$p_{1-2}=0,02$ $p_{1-3}=0,7$ $p_{2-3}=0,4$
T-cytotoxic (CD3 ⁺ CD8 ⁺), abs			
1–3	827,0 (252,0–1797,0)	466,0 (195,0–1865,0)	$p_{1-2}=0,01$ $p_{1-3}=0,2$ $p_{2-3}=0,1$
4–7	636,0 (328,0–1395,0)	466,0 (286,0–1429,0)	$p_{1-2}=0,2$ $p_{1-3}=0,3$ $p_{2-3}=0,9$
8–12	625,5 (229,0–1530,0)	466,0 (399,0–466,0)	$p_{1-2}=0,9$ $p_{1-3}=0,1$ $p_{2-3}=0,2$
13–18	448,5 (240,0–861,0)	374,0 (284,0–466,0)	$p_{1-2}=0,9$ $p_{1-3}=0,7$ $p_{2-3}=0,3$
Immunoregulatory index Tx/Tz			
1–3	1,3 (0,6–4,1)	1,3 (0,7–1,6)	$p_{1-2}=0,001$ $p_{1-3}=0,001$ $p_{2-3}=0,1$
4–7	1,3 (0,7–2,7)	1,3 (0,9–2,1)	$p_{1-2}=0,1$ $p_{1-3}=0,08$ $p_{2-3}=0,6$
8–12	1,3 (0,4–3,2)	1,3 (1,3–4,2)	$p_{1-2}=0,6$ $p_{1-3}=0,7$ $p_{2-3}=0,5$
13–18	1,6 (0,6–2,9)	2,0 (1,3–2,3)	$p_{1-2}=0,01$ $p_{1-3}=0,8$ $p_{2-3}=0,4$
TNK-lymphocytes (CD3 ⁺ CD56 ⁺), %			
1–3	1,1 (0,1–50,4)	0,2 (0,2–1,4)	$p_{1-2}=0,7$ $p_{1-3}=0,1$ $p_{2-3}=0,014$
4–7	2,8 (0,9–7,2)	1,0 (0,2–23,0)	$p_{1-2}=0,6$ $p_{1-3}=0,1$ $p_{2-3}=0,006$
8–12	2,8 (0,2–6,8)	0,2 (0,0–0,2)	$p_{1-2}=0,7$ $p_{1-3}=0,01$ $p_{2-3}=0,004$
13–18	2,9 (0,5–9,6)	1,3 (0,2–5,3)	$p_{1-2}=0,01$ $p_{1-3}=0,06$ $p_{2-3}=0,2$
TNK-lymphocytes (CD3 ⁺ CD56 ⁺), abs			
1–3	40,0 (6,0–17,82)	7,5 (4,0–46,0)	$p_{1-2}=0,06$ $p_{1-3}=0,08$ $p_{2-3}=0,003$
4–7	73,0 (9,0–306,0)	19,0 (4,0–752,0)	$p_{1-2}=0,7$ $p_{1-3}=0,1$ $p_{2-3}=0,037$
8–12	61,5 (3,0–205,0)	4,0 (1,0–4,0)	$p_{1-2}=0,7$ $p_{1-3}=0,04$ $p_{2-3}=0,004$
13–18	52,0 (17,0–148,0)	19,0 (4,0–93,0)	$p_{1-2}=0,3$ $p_{1-3}=0,01$ $p_{2-3}=0,1$

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NK-lymphocytes (CD3 ⁺ CD56 ⁺), %			
1–3	10,0 (4,2–20,6)	5,8 (3,4–28,4)	$p_{1-2}=0,06$ $p_{1-3}=0,3$ $p_{2-3}=0,001$
4–7	14,5 (5,1–26,9)	5,8 (3,4–8,3)	$p_{1-2}=0,06$ $p_{1-3}=0,1$ $p_{2-3}<0,001$
8–12	12,2 (3,3–24,5)	5,8 (3,6–5,8)	$p_{1-2}=0,6$ $p_{1-3}=0,5$ $p_{2-3}=0,002$
13–18	9,1 (3,0–23,0)	5,8 (4,8–5,8)	$p_{1-2}=0,1$ $p_{1-3}=0,005$ $p_{2-3}=0,009$
NK-lymphocytes (CD3 ⁺ CD56 ⁺), abs			
1–3	313,0 (113,0–650,0)	107,0 (89,0–318,0)	$p_{1-2}=0,5$ $p_{1-3}=0,6$ $p_{2-3}<0,001$
4–7	392,0 (46,0–938,0)	107,0 (84,0–272,0)	$p_{1-2}=0,6$ $p_{1-3}=0,1$ $p_{2-3}=0,003$
8–12	284,0 (50,0–1234,0)	107,0 (107,0–119,0)	$p_{1-2}=0,6$ $p_{1-3}=0,3$ $p_{2-3}=0,013$
13–18	201,0 (67,0–501,0)	84,0 (84,0–107,0)	$p_{1-2}=0,02$ $p_{1-3}=0,005$ $p_{2-3}=0,013$
B-lymphocytes (CD3 ⁺ CD19 ⁺), %			
1–3	17,5 (10,7–34,3)	22,5 (13,3–33,0)	$p_{1-2}=0,5$ $p_{1-3}=0,08$ $p_{2-3}=0,1$
4–7	14,5 (7,0–32,4)	22,5 (10,7–43,8)	$p_{1-2}=0,9$ $p_{1-3}=0,005$ $p_{2-3}=0,01$
8–12	13,8 (6,5–29,1)	22,5 (19,3–22,5)	$p_{1-2}=0,3$ $p_{1-3}=0,004$ $p_{2-3}=0,007$
13–18	13,8 (7,5–26,9)	23,8 (13,4–25,1)	$p_{1-2}=0,7$ $p_{1-3}=0,7$ $p_{2-3}=0,05$
B-lymphocytes (CD3 ⁺ CD19 ⁺), abs			
1–3	601,0 (190,0–1171,0)	415,0 (222,0–1351,0)	$p_{1-2}=0,1$ $p_{1-3}=0,2$ $p_{2-3}=0,1$
4–7	336,0 (85,0–765,0)	415,0 (360,0–1453,0)	$p_{1-2}=0,2$ $p_{1-3}=0,1$ $p_{2-3}=0,08$
8–12	278,0 (106,0–766,0)	415,0 (415,0–639,0)	$p_{1-2}=0,5$ $p_{1-3}=0,01$ $p_{2-3}=0,1$
13–18	251,0 (81,0–920,0)	362,0 (234,0–416,0)	$p_{1-2}=0,1$ $p_{1-3}=0,9$ $p_{2-3}=0,1$

Note: p_{2-3} — statistically significant differences between children with severe and mild community-acquired pneumonia and in the comparison group ($p < 0.05$).

Table 2. **The relationship between the severity of community-acquired pneumonia and the number of TNK-lymphocytes, NK-lymphocytes in children with community-acquired pneumonia (author's table)**
 Таблица 2. **Взаимосвязи между степенью тяжести внебольничной пневмонии и количеством TNK-лимфоцитов, NK-лимфоцитов у детей с внебольничной пневмонией (таблица автора)**

Children with severe and mild community-acquired pneumonia (n = 117)		
Indicator	Correlation coefficient (ρ)	p
Severity of community-acquired pneumonia — TNK-lymphocytes (CD3 ⁺ CD16 ⁺ CD56 ⁺), abs	-0,468	<0,001
Severity of community-acquired pneumonia — NK-lymphocytes (CD3 ⁺ CD16 ⁺ CD56 ⁺), abs	-0,511	<0,001

tion due to their ability to respond more rapidly and robustly upon antigen exposure. In addition, unlike naive cells, which remain in the lymphoid tissue, memory cells are localized in peripheral sites, ready to respond to a secondary challenge in the focus of infection [11, 12].

The decrease in NK-lymphocytes in all age groups in children with severe community-acquired pneumonia obtained in our study is consistent with similar studies in adult patients. Numerous studies on influenza A virus have shown that a decrease in peripheral blood leukocytes, lymphocytes and lymphocyte subsets is an immune process of the body in the early stages of the disease [13, 14].

Previous studies have also shown that total CD3⁺, CD4⁺ and CD8⁺ T-cell counts were significantly reduced in the acute phase in adults with influenza B virus-induced pneumonia [15].

In recent years, respiratory viral infections have also been found to frequently cause a decrease in the number of lymphocytes in the peripheral blood. A large number of studies have shown that the number of CD4⁺, CD8⁺ T-cell and NK-cell counts were

significantly reduced in patients with COVID-19 and were associated with COVID-19 severity and prognosis, and both CD8⁺ and CD4⁺ T-cell counts were diagnostic markers of COVID-19 and predictors of disease severity, which is consistent with the findings of our study [16, 17].

Natural killer cells (NK-cells) are an early line of defense against infection. Before the initiation of the adaptive immune response, NK-cells not only produce cytokines associated with antiviral activity, but also directly participate in the rapid removal of virus-infected cells and interact with dendritic cells to directly regulate the adaptive immune response [9].

A study by Ma L. et al. showed that in the early stage of pneumonia caused by influenza B virus, the level and percentage of NK-cells were significantly lower in the group of patients with severe infection. Clinical symptoms were more pronounced in the severe patient group, causing organ dysfunction in addition to pneumonia, providing further evidence that NK-cells play an important role in the progression of infection [9].

One important function of humoral immunity in viral infection is antibody-mediated neutral-

ization of the virus. In a study by Xu et al. 2013, it was shown that B-lymphocyte counts, although decreased in adult patients after influenza B virus infection, were similar between the mild and severe groups. In the total lymphocyte count, the percentage of B-lymphocytes was higher in severe patients than in the mild group, a consequence of a greater decrease in T-lymphocytes and NK-cells in the severe group. In our study, the percentage content of B-lymphocytes was higher in the group of children 4-7 and 8-12 years old in severe community-acquired pneumonia, which may be due to the peculiarities of immune system activation in different age groups [18].

Patients with severe influenza A (H1N1) infection are thought to have high levels of functional humoral

immune response and low levels of antibody affinity, and it has been hypothesized that antibody levels increase with disease severity and that high viral load may enhance the humoral immune response [19].

CONCLUSION. Thus, the analysis revealed a decrease in the number of NK-lymphocytes in peripheral blood in children with severe community-acquired pneumonia in all age groups compared to children with mild community-acquired pneumonia. The association between the decrease in the number of NK-cells and TNK-cells with the severity of community-acquired pneumonia may be related to the direction of disease progression and may be considered an independent risk factor for the development of severe pneumonia in children.

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THE AUTHORS' CONTRIBUTION TO THE WORK

Natalia V. Iziurova — review of publications on the topic of the article, design development, data analysis and interpretation, responsibility for the integrity of all parts of the article, writing and formatting of the article.

Albina Yu. Savochkina — discussion and editing of the article, final approval for the submission of the manuscript.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Prior to carrying out the prescribed procedures, the child’s legal representative has signed an informed consent. The study was approved by the local ethics committee of the Federal State Budgetary Educational Institution of Higher Education “South-Ural State Medical University” of the Ministry of Healthcare of the Russian Federation (protocol No. 1 dated 15.01.2015).

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