CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS OF CHILDREN WITH COVID-19 DUE TO CYSTIC FIBROSIS

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Relevance: The study of clinical and immunological characteristics of children with COVID-19 against the background of cystic fibrosis is becoming highly relevant in light of the pandemic. Cystic fibrosis, as a chronic disease, poses special challenges to the immune system, which makes patients in this group vulnerable to the SARS-CoV-2 virus.

Methods: To achieve the goals of the study, clinical data and analysis of cytokine levels (IL-6, IL-8, TNF-α) in children with cystic fibrosis and COVID-19 of varying severity were used.

Results: The study found that children with cystic fibrosis have different clinical and immunological characteristics depending on the severity of cystic fibrosis and the course of COVID-19. Elevated levels of cytokines, especially IL-6, IL-8 and TNF-α, correlate with severe disease in both diseases. Cytokine levels provide important information for prognosis, selection of treatment strategies and monitoring of the condition.

Conclusion: This study underscores the need for deeper exploration of clinical and immunological aspects of this issue and the development of personalized care approaches for children with cystic fibrosis amidst the COVID-19 pandemic.

Relevance: This study highlights the need to better understand the clinical and immunological aspects of this problem and develop individualized approaches to caring for children with cystic fibrosis during the COVID-19 pandemic.

Key words: cystic fibrosis, COVID-19, cytokine, immunology.

INTRODUCTION: COVID-19, caused by the coronavirus SARS-CoV-2, has become a major health and social problem worldwide. However, for some patient groups, such as children with chronic diseases, the risk of developing severe disease may be higher (2). One such group is children with cystic fibrosis, a genetic disorder that affects the respiratory and digestive systems.

Cystic fibrosis, also known as cystic fibrosis, is an inherited genetic disorder that affects the exocrine glands, such as the salivary, sweat, and stomach glands (3). The main characteristic of cystic fibrosis is the high viscosity and density of the secretions that are secreted by these glands, which makes it difficult to remove them. The respiratory and digestive systems are predominantly affected (1).

COVID-19 is caused by the SARS-CoV-2 virus and is an acute respiratory disease that can occur in various forms, from asymptomatic cases to severe complications (6).

Both cystic fibrosis and COVID-19 affect the respiratory system, and may be accompanied by: an increased risk of infections; inflammation; potential complications. Understanding these commonalities and similar mechanisms may help develop more effective treatment and support strategies for children suffering from COVID-19 due to cystic fibrosis (4).

The interaction between COVID-19 and cystic fibrosis in children is a complex process involving a variety of immunological, molecular and pathophysiological mechanisms. Research into the interactions between COVID-19 and cystic fibrosis will provide insight into how the two diseases interact with each other and what tailored approaches can be developed to treat and support children with cystic fibrosis when they become infected with COVID-19 (1, 5).

OBJECTIVE OF THE STUDY: To gain a deeper understanding of the clinical and immunological characteristics of children with COVID-19 against the background of cystic fibrosis, we decided to conduct a comprehensive immunological study.

MATERIAL AND METHODS: This study included 56 children aged 1 to 18 years suffering from cystic fibrosis and infected with COVID-19 and 15 children for the control group. Patients were selected from clinical databases of various medical institutions. Clinical characteristics of patients were assessed based on medical history, symptoms, physical examination, and laboratory results. Attention was paid to the presence of fever, cough, difficulty breathing and other symptoms.

To carry out immunological analysis, levels of cytokines such as interleukins (IL-6, IL-8), tumor necrosis factor (TNF-α) and other inflammatory markers were measured from the patients' serum. Lymphocytes and monocytes were also analyzed to assess the state of the immune system.

The obtained data were subjected to statistical analysis using the SPSS software package. For quantitative variables, means and standard deviations were used; for categorical variables, absolute and relative frequencies were used.

Statistical differences between groups were assessed using analysis of variance (ANOVA) and Student's t test. Differences were considered statistically significant at $p<0.05$.

RESULTS: In this study, 56 children suffering from various forms of cystic fibrosis were divided into groups depending on the severity of the underlying disease. This made it possible to more accurately study the influence of the severity of cystic fibrosis on the clinical and immunological characteristics of children with COVID-19.

Group 1 - group with mild cystic fibrosis (n = 26). children diagnosed with cystic fibrosis, but with a relatively mild course of the underlying disease.

Group 2 with moderate severity of cystic fibrosis (n = 17): children with more moderate severity of cystic fibrosis.

Group 3 - with severe cystic fibrosis (n = 13): Children with severe cystic fibrosis who have been diagnosed with serious complications and symptoms.

This division into groups allowed for a more differentiated assessment of the impact of the severity of cystic fibrosis on the clinical and immunological characteristics of children with coronavirus infection.

The first group included children diagnosed with cystic fibrosis, whose underlying disease had a relatively mild course. Levels of mucosal secretions in the respiratory tract were not as high as in more severe cases. The clinical appearance was characterized by less severe symptoms of respiratory disorders and infections. Levels of the cytokines IL-6 and IL-8 were elevated in this group of children with mild cystic fibrosis and COVID-19 compared with the control group. IL-6 was 17.28 ± 1.93 pg/ml ($P < 0.05$), which was 4.6 times higher than the control group (3.76 ± 0.32 pg/ml). at the same time, the concentration of IL-8 increased by 3.4 times (in group 1 it was 64.1±2.73 pg/ml ($P<0.05$), in the control group it was 19.01±2.51 pg/ml). the level of TNF-α did not show statistically significant differences between the control group, it was slightly increased and amounted to 10.21 ± 1.08 pg/ml, in the control group it was 9.47 ± 1.12 pg/ml. This may indicate the specificity of changes in IL-6 and IL-8 in cystic fibrosis in association with COVID-19.

The second group included children with more moderate severity of cystic fibrosis. They had more noticeable respiratory symptoms, such as cough, difficulty breathing, and increased levels of mucosal secretions. The levels of IL-6 and IL-8 cytokines in this group were also increased (26.19 ± 2.42 pg/ml ($P<0.05$), 94.57 ± 4.51 pg/ml ($P<0.05$) respectively) and perhaps even more significantly compared to the group with mild cystic fibrosis. IL-6 was increased by 7 times, IL-8 was 5 times higher than the control group. This may be due to a more active inflammatory response due to disruption of the airway structure and higher accumulation of mucosa. The cytokines IL-6 and IL-8, in addition to their role in inflammation, may also promote phagocyte activation and the migration of leukocytes to the site of infection. In the second group, the level of TNF-α was significantly increased to

24.17 ± 2.17 pg/ml (P<0.05), which was 2.2 times more than in the control group. Increased TNF-α levels in children with moderate cystic fibrosis infected with coronavirus (COVID-19) may have several explanations and clinical implications: Inflammatory response: TNF-α is an anti-inflammatory cytokine that is involved in regulating inflammatory processes in the body, increasing TNF-α levels may indicate the presence of a strong inflammatory response, which can be caused by both COVID-19 and cystic fibrosis, in which case elevated TNF-α levels may be part of the body's attempt to fight inflammation; Cystic fibrosis and inflammation: Cystic fibrosis is characterized by chronic inflammatory processes in the airways, these inflammatory processes can increase TNF-α levels as part of the body's overall inflammatory response.

Children with severe cystic fibrosis infected with COVID-19 represent a special group of patients who are at high risk for developing serious complications such as bronchial dilation and pulmonary fibrosis. In the third group, cytokine levels were significantly elevated and differed sharply from the other groups; here, the increase in cytokine levels may be associated with higher levels of inflammation caused by pre-existing changes in the lungs. The IL-6 level was 39.71 ± 4.59 pg/ml (P<0.05), which was 10.6 times higher than the control group. At the same time, the level of IL-8 was increased by 5.8 times and amounted to 109.61 ± 7.09 pg/ml (P<0.05). The cytokine IL-6, in particular, plays a key role in the regulation of inflammation, the mobilization of immune cells and the induction of other cytokines. It is possible that increased levels of IL-6 and IL-8 indicate increased activation of the immune system to fight the virus and restore the airways.

COVID-19 also causes inflammation, especially in the airways. In children with cystic fibrosis who already have chronic inflammation, COVID-19 infection may increase inflammation and therefore increase TNF-α levels. In this group, the TNF-α level was 40.46 ± 4.29 pg/ml (P < 0.05). Elevated levels of TNF-α may help enhance the immune response and fight viral infection.

DISCUSSION: Discussion of the results and the importance of the level of cytokine measurement when considering the clinical and immunological characteristics of children with COVID-19 against the background of mild, moderate and severe cystic fibrosis is important for understanding the characteristics of this group of patients. Children with mild cystic fibrosis and COVID-19 may have smaller changes in cytokine levels. This may indicate that their immune systems are more successful at fighting off viral infection without a significant inflammatory response (5). This can be a positive aspect, since too much of an inflammatory response can worsen the airway.

The study has its limitations, including limited sample size and retrospective nature. Future studies may include larger cohort studies with prospective long-term monitoring of patients. It is also important to study in more detail the mechanisms of immunological dysfunction in children with cystic fibrosis and COVID-19 to develop effective methods to support immunity and manage the inflammatory response.

CONCLUSION: Measuring cytokine levels is an important tool for assessing the clinical and immunological characteristics of children with COVID-19 associated with cystic fibrosis of varying severity. This data helps clinicians better understand patients' conditions, make informed decisions about treatment and monitoring, and determine the risk of complications.

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