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Clinical And Laboratory Features And Their Correlation In Children With Bronchial Asthma In The Post-Covid Period

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Abstract: The COVID-19 pandemic has significantly altered the clinical course of many chronic pathologies. Despite the relatively mild course of infection in the majority of children, in the post-COVID period patients with bronchial asthma increasingly demonstrate persistent functional impairments, immune imbalances, and biochemical shifts, which may affect disease severity, the frequency of exacerbations, and the effectiveness of baseline therapy. The aim of the study is to identify clinical and laboratory features and their correlation in children with bronchial asthma in the post-COVID period. Materials and methods of research. For the purpose of a comprehensive assessment of the immune status in children suffering from bronchial asthma (BA) who had previously contracted coronavirus infection, a clinical and laboratory study was conducted, involving 135 children aged 7 to 15 years. All patients were under observation in pediatric inpatient and outpatient settings, which ensured the reliability and completeness of clinical data collection. Depending on the history of COVID-19, the examined children were divided into two main groups: Group I – 60 children with a confirmed diagnosis of bronchial asthma of varying severity (mild, moderate, severe) who had a documented history of COVID-19. Group II – 65 children with bronchial asthma of comparable severity who had not contracted coronavirus infection. Results and discussion: An average correlation $r=+0.57$ was found between the duration of wheezing and K^+ , while a weak correlation with Ca^{++} was found ($r= -0.37$). The correlation between the frequency of exacerbations per

year and Ca^{++} was $r=-0.42$, but a strong correlation was found with K^+ ($r=+0.8$) and P ($r=+0.71$). The revealed changes show that there is a direct correlation between the clinical manifestation of bronchial asthma and ME (potassium and phosphorus), which can aggravate the course of the disease. The correlation between Phosphorus and Potassium was positive in all groups, and in severe bronchial asthma the coefficients were higher ($r=0.78$ and $r=0.65$, respectively). Zinc in all children, regardless of the severity of the disease, had a pronounced negative correlation, which increased as bronchial asthma worsened (from $r=0.68$ for mild asthma to $r=0.88$ for severe asthma). A study of the relationship between magnesium and calcium also revealed a negative correlation, particularly pronounced in children with severe asthma. Eosinophils and IgE in children with severe asthma and COVID-19 showed a moderate positive correlation ($r=0.36$). Conclusion. Thus, the identified changes in the level of ME confirm their significance in the pathogenesis of bronchial asthma, especially in conditions of viral infection, and can be considered as additional markers of the severity of the condition and the effectiveness of therapeutic interventions.

Keywords: Bronchial asthma; children; COVID-19; post-COVID period; clinical and laboratory parameters; immune status; correlation analysis.

Introduction: Bronchial asthma (BA) is one of the most common chronic diseases of childhood and is characterized by a multifactorial pathogenesis, including genetic predisposition, immune and metabolic disorders, and environmental factors. According to international epidemiological studies, the prevalence of BA in children ranges from 5 to 15%, with a trend toward an increase in severe and comorbid forms of the disease [1, 10].

The COVID-19 pandemic has significantly altered the clinical course of many chronic conditions. Despite the relatively mild course of the infection in most children, in the post-COVID period, patients with bronchial asthma are increasingly experiencing persistent functional impairments, immune imbalances, and biochemical shifts that can impact the severity of the disease, the frequency of exacerbations, and the effectiveness of standard therapy [2, 5, 7, 9].

Current research indicates that SARS-CoV-2 induces the activation of proinflammatory cytokines, alters metabolic and micronutrient parameters, and may also enhance apoptosis and airway remodeling. In children

with asthma, this leads to additional stress on the already altered immune system and impaired regulation of bronchial patency. However, data on the nature and relationships of clinical and laboratory changes in the post-COVID period remain limited and fragmented [3, 4, 6, 10].

Identifying correlations between clinical manifestations and laboratory parameters in children with asthma who have had COVID-19 is extremely important for understanding the pathogenetic mechanisms of the disease, developing individualized diagnostic criteria and optimizing therapeutic strategies [8, 10].

Thus, a comprehensive analysis of immunological and biochemical changes in children with bronchial asthma after COVID-19 represents a highly relevant and timely area of research. The data obtained will contribute to a deeper understanding of the disease's pathogenesis, the development of individualized approaches to treatment and rehabilitation, and improved quality of medical care for children.

The aim of the study is to identify clinical and laboratory features and their correlation in children with bronchial asthma in the post-COVID period.

Methods

To comprehensively study the immune status of children with bronchial asthma (BA) who had recovered from COVID-19, a clinical and laboratory study was conducted involving 135 children aged 7 to 15 years. All patients were monitored in a pediatric inpatient and outpatient setting.

Based on their history of COVID-19, the subjects were divided into two main groups: Group I – 60 children diagnosed with bronchial asthma of varying severity (mild, moderate, severe) who had a confirmed history of COVID-19. Group II – 65 children with bronchial asthma of similar severity who had not recovered from COVID-19.

To compare the obtained data, a control group was formed, consisting of 30 apparently healthy children of the corresponding age, without chronic respiratory disease and without a history of COVID-19.

All study participants underwent a clinical assessment (frequency and severity of exacerbations, respiratory distress patterns, and allergic history), as well as laboratory and instrumental examinations. The tests included: clinical and biochemical blood tests, urinalysis, immune status testing (including determination of the

levels of key lymphocyte subsets, cytokines, and immunoglobulins), and respiratory function tests.

This study design allowed us not only to determine the nature of clinical and immunological changes in children with asthma after COVID-19, but also to conduct a comparative analysis with children who did not have a coronavirus infection, which significantly increased the reliability of the results obtained.

Results And Discussion

Our research has shown that children with asthma, especially those who have had a coronavirus infection, experience significant changes in their blood macro- and microelement composition.

To identify the relationship between the clinical course of the disease and laboratory data, we conducted a correlation analysis of macro- and microelement status with respiratory function parameters (e.g., FEV1, SOC25-75, OLV, TLC), inflammatory marker levels (C-reactive protein), and immunological parameters (IgE, eosinophil activity) (Table 1).

Table 1

The relationship between clinical, functional, and laboratory parameters of macro- and microelement composition in children with bronchial asthma who had COVID-19 (n=78)

ME I	Mg++	Ca++	P	K+	Zn
Frequency of exacerbations per year		-0,42	+0,8	+0,71	
Duration of wheezing		-0,37		+0,57	
C-reactive protein	-0,4				-0,43
Eosinophils, %					
IgE mg/%	-0,37				
PSV1		+0,52	-0,67	-0,71	
FEV1	+0,77		-0,46	-0,56	+0,32
FVC			-0,51	-0,68	+0,28
OLV	-0,82		+0,91	+0,78	
OEL		-0,48	+0,71		
OEL/OEL				+0,81	-0,25
Designations:					
	- significant strong positive relationship				
	- significant strong negative relationship				
	- significant moderate positive relationship				
	- significant moderate negative relationship				

According to Table 1, there are two positive and five negative moderate correlations, as well as seven positive and two strong negative correlations, between the clinical and laboratory-functional parameters of children with asthma and COVID-19.

A moderate correlation of $r=+0.57$ was found between wheezing duration and K+, while a weak correlation

with Ca++ was found ($r=-0.37$). The correlation between the annual exacerbation rate and Ca++ was $r=-0.42$, while a strong correlation was found with K+ ($r=+0.8$) and P ($r=+0.71$). These changes indicate a direct link between the clinical manifestations of asthma and ME (potassium and phosphorus), which may worsen the course of the disease.

Next, we studied the correlation relationships between laboratory and instrumental data and the severity of bronchial asthma in children who had coronavirus infection (n=78) (Fig. 1).

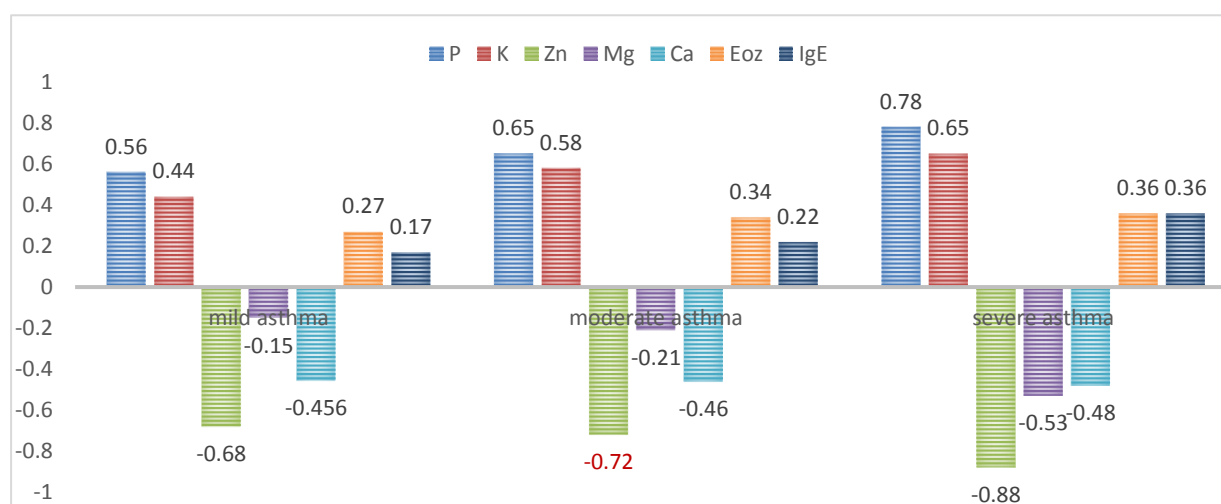


Figure 1. Correlation between laboratory parameters and the severity of bronchial asthma, group 1 (n=78)

We also found a significant, strong negative correlation between disease severity and zinc levels in children ($r=-0.68$, $r=-0.72$, and $r=-0.88$, respectively). In children with asthma who had not had COVID-19, the correlations with these elements were weak.

Phosphorus and Potassium correlations were positive in all groups, with higher coefficients in severe asthma ($r=0.78$ and $r=0.65$, respectively). Zinc showed a significant negative correlation in all children, regardless of disease severity, which increased with asthma severity (from $r=-0.68$ for mild asthma to -0.88 for severe asthma).

A study of the relationship between elements such as magnesium and calcium also revealed a negative correlation, particularly pronounced in children with severe asthma.

Eosinophils and IgE in children with severe asthma combined with COVID-19 showed a moderate positive correlation ($r=0.36$).

As severity progressed, children in the first group showed increasing positive correlations between phosphorus, potassium, and immune parameters (IgE,

eosinophils), which may indicate their role in the pathogenesis of the disease. Meanwhile, the negative correlation with zinc, magnesium, and calcium increased, suggesting possible metabolic disturbances associated with the disease

In children with asthma who had not recovered from COVID-19, correlations were also found between laboratory and instrumental tests and asthma severity ($n = 92$) (Fig. 2).

The analysis revealed that in mild asthma, there was a positive correlation with phosphorus, potassium, and IgE, with phosphorus ($r = 0.54$) and potassium ($r = 0.42$) demonstrating the highest values. However, there was a negative correlation between zinc ($r = -0.48$), magnesium ($r = -0.15$), and calcium ($r = -0.456$). As the disease worsened, the correlations changed: with moderate asthma severity, phosphorus ($r=0.56$), potassium ($r=0.54$), calcium ($r=0.55$) and IgE ($r=0.47$) continued to show a positive correlation, but an increase in the negative correlation was noted for zinc ($r=-0.56$) and magnesium ($r=-0.21$).

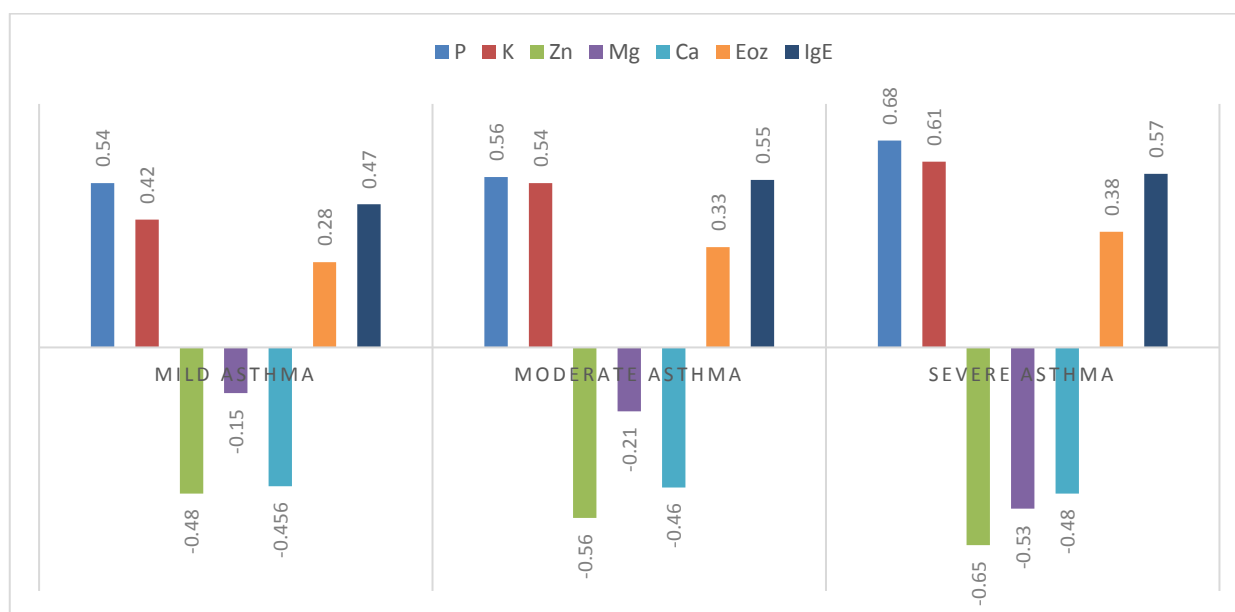


Figure 2. Correlation between laboratory parameters and the severity of bronchial asthma, 2 groups (n=96)

In severe asthma, the correlations became even more pronounced. The positive correlations between phosphorus ($r=0.68$), potassium ($r=0.61$), calcium ($r=0.57$), and IgE ($r=0.57$) increased significantly, indicating a stronger influence on the course of the disease. Meanwhile, zinc ($r=-0.65$), magnesium ($r=-0.53$), and calcium ($r=-0.48$) demonstrated the most pronounced negative correlations.

Thus, the correlation between micro- and macronutrient status and clinical and laboratory parameters in children with bronchial asthma highlights the importance of a comprehensive approach to diagnosis and treatment. These data can be used to develop personalized treatment regimens aimed at improving patients' quality of life and reducing the frequency of exacerbations.

Early diagnosis of electrolyte imbalances allows for the adjustment of therapeutic approaches and the reduction of the risk of asthma complications, especially in children who have had a coronavirus infection.

The strong positive correlation between phosphorus and potassium levels and severe asthma, and a moderate positive correlation with moderate asthma, highlights the importance of monitoring these parameters. This opens new opportunities for improving diagnostics and developing more targeted therapeutic strategies.

We further examined the correlation between the levels of apoptotic cells and apoptotic cells (Table 2).

Table 2.

Correlation relationships between the average content of apoptotic cells

Indicators	Correlation coefficient (r)	Significance level (p)	Type of correlation
sCD95 ↔ sCD30	0,34	<0,05	Direct
sFAS ↔ Caspase-1/ICE	0,28	<0,05	Direct
sFAS ↔ Annexin V	0,29	<0,05	Direct
sCD95 ↔ sFASL	-0,31	<0,05	Reverse
sCD30 ↔ sCD40	-0,30	<0,05	Reverse
sCD95 ↔ Caspase-1/ICE	-0,34	<0,05	Reverse
sCD95 ↔ Annexin V	-0,36	<0,05	Reverse

As can be seen from the data in Table 5.1.2. a weak direct relationship was found between the levels of sCD95 and sCD30 ($r=0.34$; $p<0.05$), sFAS and Caspase-1/ICE ($r=0.28$; $p<0.05$), sFAS and Annexin V ($r=0.29$; $p<0.05$), an inverse correlation between the content of sCD95 and sFASL ($r=-0.31$; $p<0.05$), sCD30 and sCD40 ($r=-0.30$; $p<0.05$), sCD95 and Caspase-1/ICE ($r=-0.34$; $p<0.05$), sCD95 and Annexin V ($r=-0.36$; $p<0.05$), which characterizes the possible pathogenetic relationships of these indicators in the process of development of allergic inflammation and may indicate a violation of the ratio between activation and elimination of immunocompetent and proinflammatory cells in children who have had coronavirus infection against the background of bronchial asthma.

The identified correlations demonstrate an imbalance between the activation and elimination of immune and proinflammatory cells, which is characteristic of children with asthma. The findings confirm the role of apoptosis in the development of allergic inflammation and may serve as a basis for the search for new biomarkers for the diagnosis and prognosis of asthma in children who have recovered from COVID-19.

Conclusion: The results of the studies presented in this chapter suggest that asthma, as well as asthma plus COVID-19, are characterized by a longer duration of shortness of breath, wheezing, wet cough, and wheezing. With severe bronchospasm, symptoms of intoxication and respiratory failure become more pronounced, leading to prolonged clinical manifestations.

Decreased levels of these macro- and micronutrients may be associated with the body's increased needs under conditions of chronic inflammation, activation of antioxidant defenses, and changes in cell membrane permeability. Furthermore, an imbalance of magnesium and potassium can affect bronchial tone and neuromuscular conduction, which may contribute to increased bronchial reactivity and worsening of the disease.

Thus, the identified changes in the level of ME confirm their significance in the pathogenesis of bronchial asthma, especially in conditions of viral infection, and can be considered as additional markers of the severity of the condition and the effectiveness of therapeutic interventions.

Correlation analysis revealed a significant relationship between the concentration of macro- and microelements (Ca, Mg, Zn, P, K) and a number of immunological parameters, indicating their important

role in the pathogenesis of bronchial asthma in children who have recovered from COVID-19. A deficiency or imbalance of these elements can contribute to increased inflammation, decreased antioxidant protection, and impaired regulation of the immune response, which, in turn, increases bronchial hyperreactivity and increases the risk of frequent exacerbations of the disease.

The identified correlations also reflect the degree of stress on compensatory and adaptive mechanisms, indicating the persistence of the pathological process. This may contribute to the chronicity of inflammation and airway remodeling, which has important diagnostic and prognostic implications. Thus, assessing serum micronutrient levels can be used as an additional marker of disease severity and the effectiveness of therapy in children with bronchial asthma following COVID-19 infection.

Conclusions

1. Children with asthma have decreased levels of magnesium and zinc, and increased levels of potassium and phosphorus compared to healthy children. Children who had COVID-19 with asthma had a significant decrease in zinc levels ($p<0.005$). All children with asthma had increased serum potassium and phosphorus levels, which may indicate their involvement in the formation of the neurotransmitter acetylcholine, which plays a significant role in the development of bronchoconstriction, sputum hyperproduction, and bronchial mucosal edema.
2. Dyselementosis depended on the severity of the disease, with levels of the studied macronutrients significantly lower in children with severe disease compared to children with moderate disease. Persistent homeostasis disturbances during remission, most pronounced in patients with severe disease, indicate a prolongation of the inflammatory process in the bronchopulmonary system.
3. The conducted correlation analysis between dyselementosis and the severity of bronchial asthma showed that there is a direct correlation between the level of Phosphorus and Potassium in the blood serum ($r=+0.78$ and $r=+0.65$; $p<0.0001$), and an inverse correlation between the values of Zinc, Magnesium and Calcium ($r=-0.88$, $r=+0.53$ and $r=-0.51$; $p<0.005$).

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