

**COVID-19 PATSIENTLARIDA IMMUNOLOGIK  
KO'RSATKICHLARNING O'ZGARISHLARI VA ULARNING  
PROGNOSTIK QIYMATI.**

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Annotatsiya. Yuqumli kasalliklar patologiyasida organizmning umumiy immunoreaktivligi bilan bog'liq jarayonlar muhim o'rin tutadi, shu boisdan COVID-19 ning turli klinik shakllarida immunologik o'zgarishlar namoyon bo'lishini o'rganish kasallik kechishini prognozlash va og'ir holatlar rivojlanish xavfini baholash nuqtai-nazaridan muhim ilmiy-amaliy ahamiyat kasb etadi.

Kalit so'zlar: Koronavirus, immunologik, laborator, epidemiologiya, profilaktika.

**CHANGES IN IMMUNOLOGICAL INDICATORS IN COVID-19  
PATIENTS AND THEIR PROGNOSTIC SIGNIFICANCE**

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Abstract. Immune reactivity plays a key role in the pathogenesis of infectious diseases. Studying immunological changes in different clinical forms of COVID-19 is of significant scientific and practical importance for predicting disease progression and assessing the risk of severe complications.

Keywords: coronavirus, immunological, laboratory, epidemiology, prevention.

The analysis indicates that COVID-19 primarily affects T-lymphocytes, leading to a significant reduction in their number, particularly CD3+CD4+ and CD3+CD8+ T-cells. Consequently, as the severity of the disease increases, lymphopenia deepens, demonstrating a direct correlation between disease progression and lymphopenia. Additionally, the conducted analysis revealed that in most cases among patients in the third group, there was a decrease in the B-lymphocyte population and in the absolute number of natural killer (NK) cells.

The above findings indicate that assessing these cellular immunological parameters from the earliest days of symptom onset is critically important for predicting severe and critical courses of the disease.

As a result of the conducted study, due to pronounced lymphopenia, patients in Group 3 showed significant differences compared to patients in Groups 1 and 2 in the absolute counts of activated T-lymphocytes, B-lymphocytes, activated NK cells, and activated CD25+ T-lymphocytes expressing the  $\alpha$ -chain of the IL-2 receptor.

Analysis of the cytokine levels in blood serum samples showed that the TNF- $\alpha$  concentration in patients with mild, moderate, and severe COVID-19 remained within the reference range.

Assessment of IL-6 levels in serum revealed that, compared to samples from patients in Group 1, this parameter was approximately 2 times higher in samples from patients in Group 2 and 4 times higher in samples from patients in Group 3. The significant increase in IL-6 levels correlated proportionally with the severity of the patients' condition ( $p < 0.05$ ).

Since the clinical criteria for assessing the severity of COVID-19 are broad and do not fully reflect the dynamics of changes in patient condition, the informativeness and prognostic value of the coefficients were evaluated by calculating the ratio of the absolute number of lymphocytes expressing CD3+CD4+, CD3+CD8+, and CD3-CD56+ markers to the number of neutrophils in the study groups.

The significance of differences between the indicators in the group with severe disease and those in other groups (patients with mild and moderate disease) was determined as follows: significant –  $p < 0.05^*$ ; highly significant –  $p < 0.05^{**}$ ; very highly significant –  $p < 0.05^{***}$ .

In the ICU cohort, compared with patients with moderate disease, the ratios of CD4+ lymphocytes to neutrophils were 3.5 times lower, CD8+ lymphocytes to neutrophils were 2.6 times lower, and NK cells to neutrophils were 5 times lower ( $p < 0.05$ ).

In the next phase of the study, changes in the humoral branch of the immune system during different courses of the disease were examined. During the first 10 days of COVID-19 onset (first assessment), antibodies of the IgM, IgG, and IgA classes were detected in 6.3%, 5.5%, and 21.4% of cases, respectively. It is noteworthy that during the first 10 days of disease onset, there was no significant difference in the frequency of detection between IgM and IgG antibodies ( $p > 0.05$ ), meaning that antibodies of both classes begin to be synthesized almost simultaneously from the first 10 days of illness and at nearly the same frequency. In contrast, during the first 10 days of disease onset, the frequency of detection of IgA antibodies was significantly higher than that of IgM and IgG antibodies ( $p < 0.05$ ).

During days 15–21 of illness, in the second set of samples, the detection frequencies of antibodies of the IgM, IgG, and IgA classes increased markedly, reaching 45.3%, 33.0%, and 91.7%, respectively. At this time point, the frequency of IgA antibody detection remained significantly higher than that of IgM and IgG antibodies ( $p < 0.05$ ).

The obtained results indicate that the humoral immune response in COVID-19 progressively increases and reaches high levels during the late stages of the infection. In samples collected on days 25–30 of illness (third time point), the detection frequencies of IgM, IgG, and IgA antibodies—reflecting seroconversion—were 92.8%, 99.5%, and 93.9%, respectively. In these third-time-point plasma

samples, IgM, IgG, and IgA antibodies were not detected in 181 (7.2%), 13 (0.5%), and 151 (6.1%) patients, respectively. This absence can be explained by the fact that, at the time of testing (25–30 days after illness onset), the antibody titers were lower than the diagnostic threshold. Additionally, it should be considered that IgM antibody levels may decline during the convalescent period.

The majority of patients (77.2%) exhibited IgG antibody titers in the range of 1:800–1:1600, indicating that these titers were detected with a significantly higher frequency compared to other titer levels. Minimal seropositive titers of 1:100 and 1:200 were observed in patients with mild COVID-19 (10.9% and 18.5%, respectively) and moderate disease (1.4% and 5.8%, respectively). In contrast, among patients in intensive care units (severe and critical cases), IgG antibodies were reliably detected at high titers, with 90.6% of cases showing a titer of 1:1600. Meanwhile, a titer of 1:1600 was observed in 30.3% of patients with mild disease and 32.4% of patients with moderate disease ( $p < 0.05$ ).

The obtained results indicate that, from a public health perspective, the analysis of both humoral and cellular immunity parameters in clinical practice is essential for the diagnosis, treatment, and prevention of the spread of COVID-19. It is crucial that clinicians fully understand the significance and necessity of determining patients' immune status, and possess well-developed skills in interpreting and assessing immunological indicators.

By the convalescent phase, the frequency of detection of virus-neutralizing antibodies (IgM, IgG, and IgA classes) reaches a high seroconversion level, and in the majority of patients (77.2%), IgG antibody titers are high (1:800–1:1600). This supports the preparation of concentrated immunoglobulin fractions from convalescent plasma, which can be incorporated into therapeutic regimens as an immunotherapeutic intervention in severe cases of COVID-19 or in the presence of prognostic markers indicating a risk of disease aggravation.

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