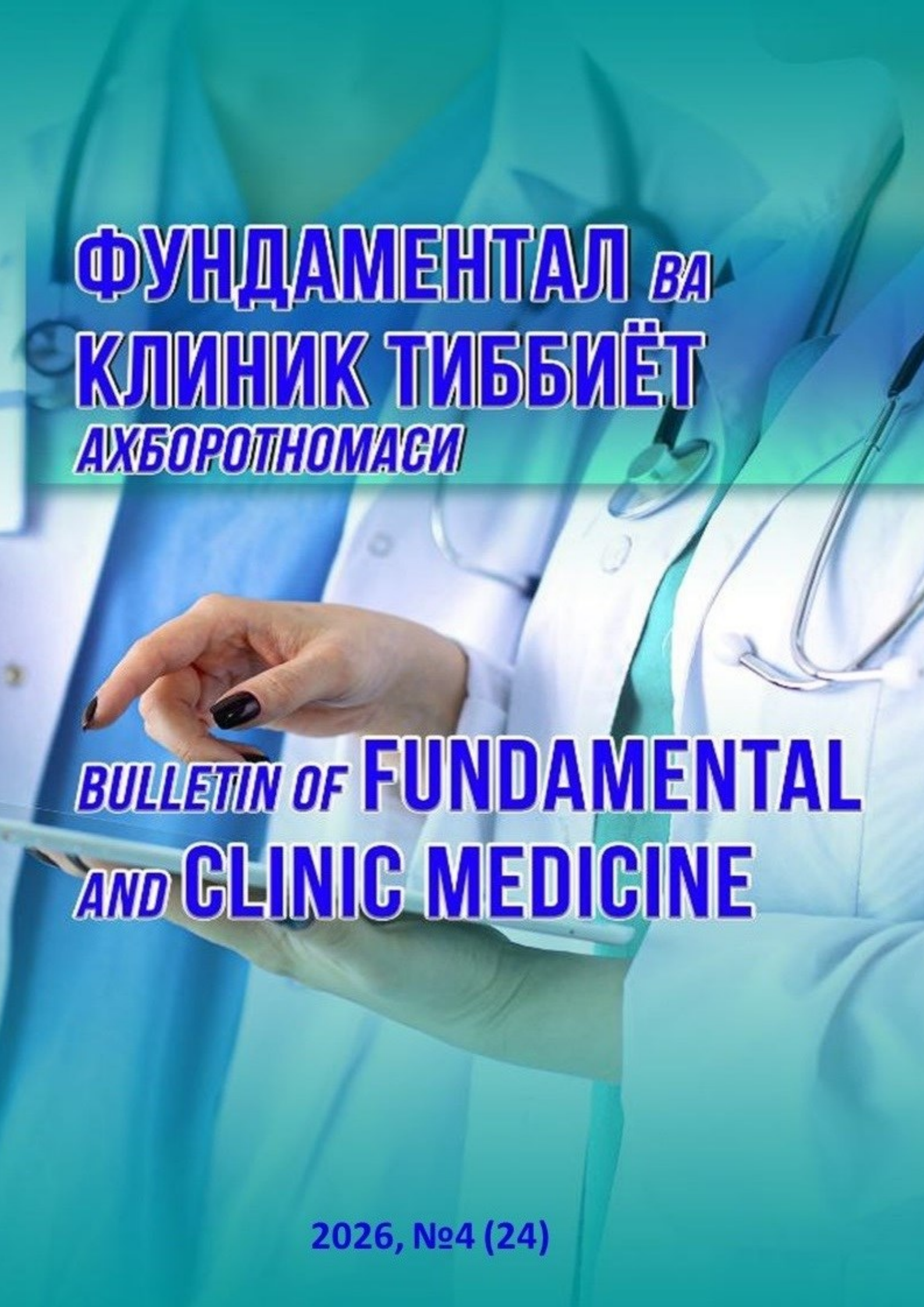

ФУНДАМЕНТАЛ ВА КЛИНИК ТИББИЁТ АХБОРОТНОМАСИ

BULLETIN OF FUNDAMENTAL AND CLINIC MEDICINE

2026, №4 (24)

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CLINICAL SIGNIFICANCE AND USE OF PROCALCITONIN FOR GUIDING ANTIBIOTIC THERAPY IN SARS-COV-2 INFECTION

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Resume. *This article highlights the importance of C-reactive protein (CRP) and procalcitonin (PCT), and cytokines in determining the prognosis of SARS-CoV-2-associated pneumonia. The article discusses the methods used to measure these biomarkers and the results of studies that have investigated their use in predicting the severity and outcome of SARS-CoV-2-associated pneumonia. The article concludes with a discussion of the implications of these findings and suggestions for future research.*

Keywords: *SARS-CoV-2, pneumonia, C-reactive protein, procalcitonin, cytokines, biomarkers, prognosis.*

SARS-COV-2 ИНФЕКЦИЯСИДА АНТИБИОТИК ТЕРАПИЯСИНИ БОШҚАРИШДА ПРОКАЛЬЦИТОНИННИНГ КЛИНИК АҲАМИЯТИ ВА ҚЎЛЛАНИЛИШИ

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Резюме. *Ушбу мақолада SARS-CoV-2 билан боғлиқ пневмонияни истиқболини аниқлашда с-реактив оқсил (CRO) ва прокальцитонин (ПКТ) ва цитокинларнинг аҳамияти таъкидланган. Мақолада биомаркерларни аниқлаш усуллари ва SARS-CoV-2 билан боғлиқ пневмониянинг оғирлиги ва натижаларини башорат қилишда улардан фойдаланишни ўрганган тадқиқотлар натижалари муҳокама қилинади. Мақола ушбу натижалар ва келажакдаги тадқиқотлар учун таклифларнинг натижаларини муҳокама қилиш билан якунланади.*

Калит сўзлар: *SARS-CoV-2, пневмония, С-реактив оқсил, прокальцитонин, цитокинлар, биомаркерлар, башорат*

КЛИНИЧЕСКОЕ ЗНАЧЕНИЕ И ПРИМЕНЕНИЕ ПРОКАЛЬЦИТОНИНА ДЛЯ ВЫБОРА АНТИБИОТИКОТЕРАПИИ ПРИ ИНФЕКЦИИ SARS-COV-2

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Резюме*. В этой статье подчеркивается важность С-реактивного белка (СРБ) и прокальцитонина (ПКТ), а также цитокинов в определении прогноза пневмонии, связанной с SARS-CoV-2. В статье обсуждаются методы, используемые для измерения этих биомаркеров, и результаты исследований, в которых изучалось их использование для прогнозирования тяжести и исхода пневмонии, связанной с SARS-CoV-2. Статья завершается обсуждением последствий этих выводов и предложениями для будущих исследований.*

Ключевые слова*: SARS-CoV-2, пневмония, С-реактивный белок, прокальцитонин, цитокины, биомаркеры, прогноз*

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Introduction. Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has had a strong impact on health systems around the world [1,2]. Patients with severe pneumonia have a high mortality rate due to the large number of complications they face [3].

It is reported, that in COVID-19, the prevalence of community-acquired bacterial respiratory coinfections (hereinafter referred to as bacterial coinfection) during hospitalization is less than 5% [4,5,6,7]. Although the impact of this complication on mortality is still widely debated, almost three-quarters of patients with COVID-19 receive antibiotics, so the number of prescriptions significantly exceeds the estimated prevalence of bacterial co-infection [8]. Excluding bacterial co-infection at hospital admission in these patients may potentially limit overuse of antibiotics and thus reduce hospital admission costs, potential side effects, and the development of multidrug-resistant infections [9]. PCT is a serum biomarker that has shown promising results in distinguishing between viral and bacterial infections [10, 11, 26], and it is

commonly used in conjunction with clinical data as a guideline for de-escalation with prescribing of antibiotics in critically ill patients [12, 13, 14]. The role of PCT in community-acquired pneumonia (CAP) has been evaluated in several studies, but There is no scientific consensus on its usefulness for the diagnosis or administration of antibiotics [15,27]. C-reactive protein (CRP), another well-known systemic marker of inflammation and tissue damage, is widely used by clinicians to monitor infections [16,22]. In patients with COVID-19, CRP at admission correlated with disease severity and was generally a good predictor of an adverse outcome [16,17].

An increase in PCT indicates the addition of a bacterial infection and correlates with the severity of the course, the prevalence of inflammatory infiltration, and the prognosis of the progression of bacterial complications.

Accumulating data indicate that more than 80% of patients with COVID-19 are treated with antibiotics, as it is difficult to identify patients with COVID-19 without a concomitant bacterial infection who can было бы safely stop taking antibiotics. However, recent clinical data show that procalcitonin can help assess the condition of these patients and reduce unnecessary use of antibiotics [18,19,25]. Therefore, we sought to determine the role of PCT and CRP in detecting bacterial co-infection in patients with COVID-19 pneumonia. Serum levels of CRP and PCT have a significant correlation with the severity of COVID-19 and can be used to as independent factors for predicting disease risk. Serum levels of CRP and PCT can effectively assess the severity of the disease and predict the outcome in patients with COVID-19. The study of the level of CRP in the blood serum is a mandatory laboratory study. Since the level of CRP correlates with the severity of the course, the prevalence of inflammatory infiltration and the prognosis for pneumonia. PCT is a well-known diagnostic marker of bacterial infection. [20, 28].

Purpose of the study. Study of serum procalcitonin levels to decide whether to start or discontinue antibiotic therapy, as well as to determine the progression of disease severity in COVID-19 patients.

Materials and methods: This study was a single-centre, retrospective cohort study. We included all patients with confirmed SARS-CoV-2 infection admitted to the Infectious diseases hospital from June 30, 2021 to September 14, 2022 in Bukhara. Clinical data was obtained from electronic medical records, including demographic data, exposure history, signs and symptoms, and laboratory data at admission. Upon admission to the inpatient emergency department, all patients were evaluated on the NEWS2 scale. The average score was 5.7±1.4. This made it possible to quickly sort out patients and send the most severe cases to the intensive care unit. All patients with COVID-19 included in this study were diagnosed in accordance with the guidelines for the diagnosis and treatment of pneumonia caused by a novel coronavirus infection. All patients were laboratory-confirmed to have SARS-CoV-2 infection (the result of real-time RT-PCR specific for SARS-CoV-2 was positive).

From June 30, 2021 to September 14, 2022, 120 patients were admitted to the Bukhara Regional Infectious Diseases Hospital. 120 patients were divided into severe cases (n=67) and moderate cases (n=53). Of these, 12 (20.0%) patients were admitted to the intensive care unit. The median age was 51 years, 120 patient and 74 (61.67%) of the 120 patients were male. The average time from the onset of symptoms to hospitalization was 2-3 days, and the average time to the diagnosis of a serious illness was 3-4 days.

A general blood test with determination of the number of white blood cells (WBC), lymphocytes (LYM), mononuclear cells (MONO), and neutrophils (NEU) was performed on blood samples. Blood biochemistry parameters: aspartate aminotransferase (AST), alanine aminotransferase (ALT), glucose (GLU), urea, creatinine, and C-reactive protein (CRP) were measured using the MINDRAY BC–30 automatics biochemical analyzer (China). The concentration OF PKT was determined using the ELISA method using reagent kits for enzyme-linked immunosorbent assay OF PKT CONCENTRATION in blood plasma PKT-ELISA-BEST. In patients with moderate and severe forms, the study was performed on the 2nd day of admission, the 3rd and 5th days of treatment. The upper limit of the norm was assumed to be the concentration of 0.05 ng/ml. The obtained data were compared with the recommendations for clinical interpretation of the results of determining the level of PCT in blood serum: 0.1-0.25 ng/ml–the probability of bacterial infection is very low; 0.25-0.5 ng/ml–local bacterial infection is possible; 0.5-2.0 ng/ml–high probability of bacterial infection, systemic bacterial infection is possible; 2.0-10.0 ng/ml–high probability of systemic bacterial infection, possible severe sepsis; >10.0 ng/ml–high probability of severe sepsis[15, 21, 23, 24].

Results. The time from symptom onset to hospital admission averaged 3–4 days for patients with moderate disease and 5–7 days for those with severe disease. The duration of hospitalization in the respective wards was 7±2.3 days and 13±3.2 days, with the overall treatment period recorded as 10.5±5.7 days.

Clinical manifestations observed in the patients were analyzed according to organ systems. The results were as follows:

Respiratory system: cough was reported in 85.83% of patients (103/120), including dry cough in 54.17% (65/120), productive cough in 28.33% (34/120), and hemoptysis in 3.33% (4/120); sore throat was observed in 70.0% (84/120); shortness of breath in 69.17% (83/120); sneezing in 19.17% (23/120); nasal congestion in 16.67% (20/120); and rhinorrhea in 13.33% (16/120) (figure 1).

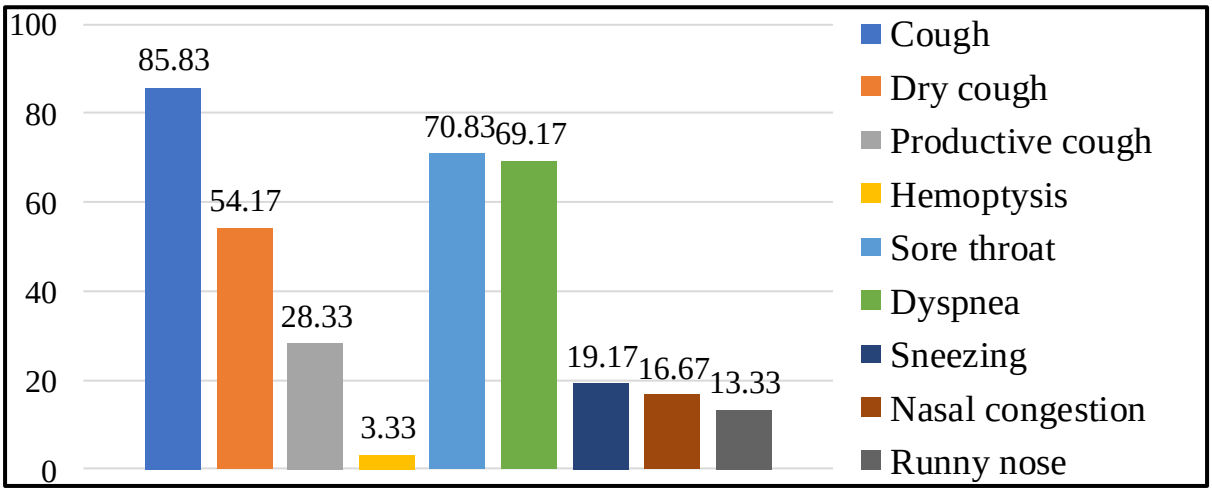

Figure 1. Clinical manifestations observed in the respiratory system of patients (%)

Central nervous system: headache was reported in 85.83% of patients (103/120); loss of appetite in 89.17% (107/120); fatigue in 74.17% (89/120); fever in 72.5% (87/120); loss of smell (anosmia) in 54.17% (65/120); dizziness in 37.5% (45/120); loss of taste (ageusia) in 51.67% (62/120); myalgia (muscle pain) in 50.83% (61/120); sleep disturbances in 46.67% (56/120); impaired attention in 18.33% (22/120); memory impairment in 5.83% (7/120); tingling sensations (paresthesia) in 4.17% (5/120); and photophobia in 3.33% (4/120) (figure 2).

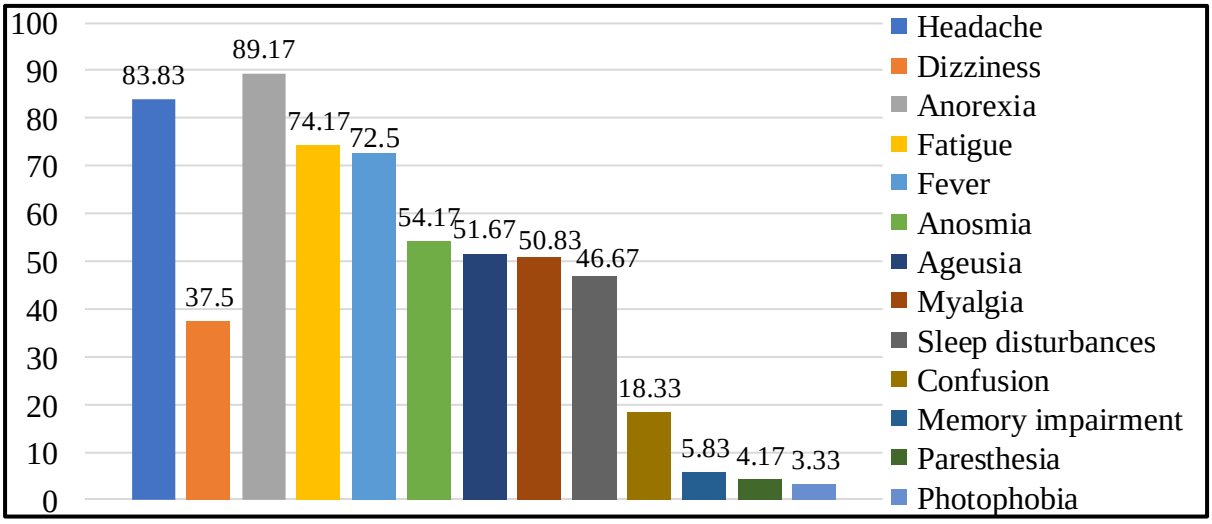

Figure 2. Clinical manifestations observed in the CNS of patients (%)

In COVID-19, gastrointestinal symptoms are often associated with the direct effects of the virus, immune response, and disruption of the gut microbiota. Among the clinical manifestations related to these changes, abdominal pain was frequently observed. In patients with moderate disease, 4 individuals reported abdominal pain, while among those with severe disease, 13 patients experienced this symptom. Another common clinical manifestation was nausea, reported in 7 patients with moderate disease and 12 patients with severe disease. Diarrhea was also documented in patient histories, occurring in 10 patients with moderate disease and 16 patients with severe disease. Additionally, vomiting was observed in 5 patients with moderate disease and in 9 patients with severe disease.

SARS-CoV-2 infection also caused several ophthalmologic changes in patients due to its effects on various organs and tissues. Observed clinical signs included conjunctivitis, pathological lacrimation (exces-

sive tearing), eyelid itching, and blurred vision. Conjunctivitis was reported in 6 patients with moderate disease and 11 patients with severe disease. Pathological lacrimation was observed in 4 patients with moderate disease and 9 patients with severe disease. Eyelid itching occurred in 3 patients with moderate disease and 5 patients with severe disease. Blurred vision was a rare manifestation, not observed in moderate cases, but reported in 3 patients with severe disease.

Skin changes were also documented in patients with COVID-19. Among the 120 patients, 23 reported skin-related complaints. Observed dermatological manifestations included mainly angiitis, erythematous rashes, purpura, and, less frequently, vesicular lesions. According to the study results, some COVID-19 patients exhibited cutaneous changes, confirming the systemic nature of the infection. Among patients with moderate disease, angiitis was observed in 3 individuals, erythematous rashes in 2, purpura in 1, and vesicular lesions in 1. In the severe disease group, skin changes were more frequent, with angiitis in 7 patients, erythematous rashes in 4, purpura in 3, and vesicular lesions in 2. These findings indicate that skin manifestations are more common in severe cases of SARS-CoV-2 infection. This may be related to the virus's tropism for vascular endothelial cells and associated microcirculatory disturbances. Cutaneous angiitis and erythematous rashes likely result from vascular wall inflammation, increased cytokine levels, and immune complex reactions, while purpura and vesicular lesions are often explained by hypersensitivity reactions or an exaggerated immune response to the virus.

According to the results of laboratory data, it was found that 40 patients (3,3,3%) had leukopenia, 56 patients (46.7%) had leukocytosis; 88 patients (73.3%) had lymphocytopenia, and 24 patients (15.0%) had an increase in the number of lymphocytes.

Platelet counts and coagulation parameters were analyzed in the present study. Of the 120 patients included in the study, thrombocytopenia was detected in 23 (24.22%), thrombocytosis - in 18 (15.0%).

In the study, an interval-based distribution analysis of procalcitonin (PCT) concentrations was performed in the examined patients. The obtained results clearly demonstrate the characteristics of PCT levels within the patient cohort (figure 3).

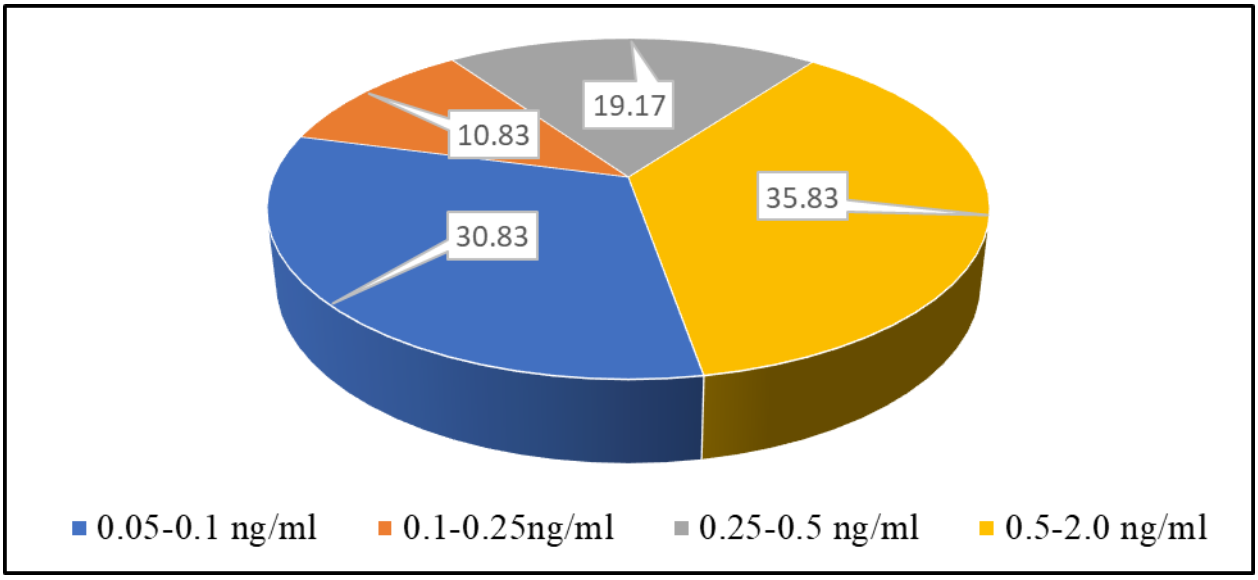

Figure 3. Serum procalcitonin concentrations in patients

According to the presented data, the majority of patients exhibited moderate to high concentrations of the biomarker (0.25–2.0 ng/mL), indicating clinically significant inflammatory activity. This finding supports the applicability of PCT as a marker for assessing disease severity and as a prognostic indicator. The largest proportion of patients fell within the 0.5–2.0 ng/mL range (35.83%), suggesting an active or complicated inflammatory process in a substantial number of cases. The 0.05–0.1 ng/mL interval accounted for 30.83% of patients, reflecting a relatively mild disease course or a favorable response to therapy. PCT levels of 0.25–0.5 ng/mL were observed in 19.17% of patients, corresponding to a moderate degree of inflammatory activity. The smallest proportion (10.83%) was represented by patients with PCT concentrations in the 0.1–0.25 ng/mL range, indicating that relatively few patients had low-to-moderate biomarker levels.

These tests were obtained within the first 48-72 hours after the onset of the disease. And based on the content of PCT in the blood serum, they were conditionally divided into 3 groups. Further tests were

repeated on the 3rd and 5th days, and in severe patients, the level of subcutaneous fat was also studied on the 7th day of treatment. Patients with a PCT level of more than 0.1 ng/ml were considered co-infected and were recommended for treatment with antibiotics (a combined drug of amoxicillin and clavulanic acid, cephalosporins of 2-3 generations), severe patients with meropenem and respiratory fluoroquinolones (levofloxacin). The effectiveness of treatment was assessed as insufficient if after 3 days of treatment there was no decrease in the level of PCT in the blood serum by 50%. In such cases, it can be assumed that the treatment does not give the expected effect. Therefore, it is necessary to change the tactics of antibacterial therapy. If the level of PCT decreases, it will mean that the treatment gave the expected result. As soon as there is a decrease in the number of PCT by about 80-90% from the peak level, it is recommended to stop antibacterial therapy.

The results of the study showed that in 46 (71.9%) patients of the first group under observation, there was a significant decrease in the level of PCT, which did not differ from the norm, in 8 (12.5%) patients, the content of PCT remained unchanged. While 10 (15.6%) patients had an increase in the level of PCT in the blood serum and were prescribed antibacterial therapy.

In 38 (82.6%) patients of group 2 who received antibacterial drugs, as in cases of co–infection, the content of PCT decreased by 50%, and in 8 (17.4%) patients, the level of PCT remained significantly high. Only 3 (30%) patients out of 10 seriously ill patients showed a positive result. When there was no decrease in the level of PCT on the 3rd day of treatment against the background of antibacterial therapyче, another combination of antibacterial drugs was prescribed for the treatment of these patients.

The data of our study, obtained on the 5th day of treatment, showed that according to the results of the first stage, the level of PCT significantly decreased and normalized in 18 patients of group 1. In 6 (13%) patients of group 2, the PCT level remained significantly high and continued treatment with antibacterial drugs. In 2 (20%) patients of group 3, despite the introduction of antibacterial drugs, the PCT level remained high, and the disease ended fatally.

For dynamic assessment, patients were conditionally divided into three groups, and plasma PCT levels were measured three times: on day 1, day 3, and day 7 of observation (figure 4).

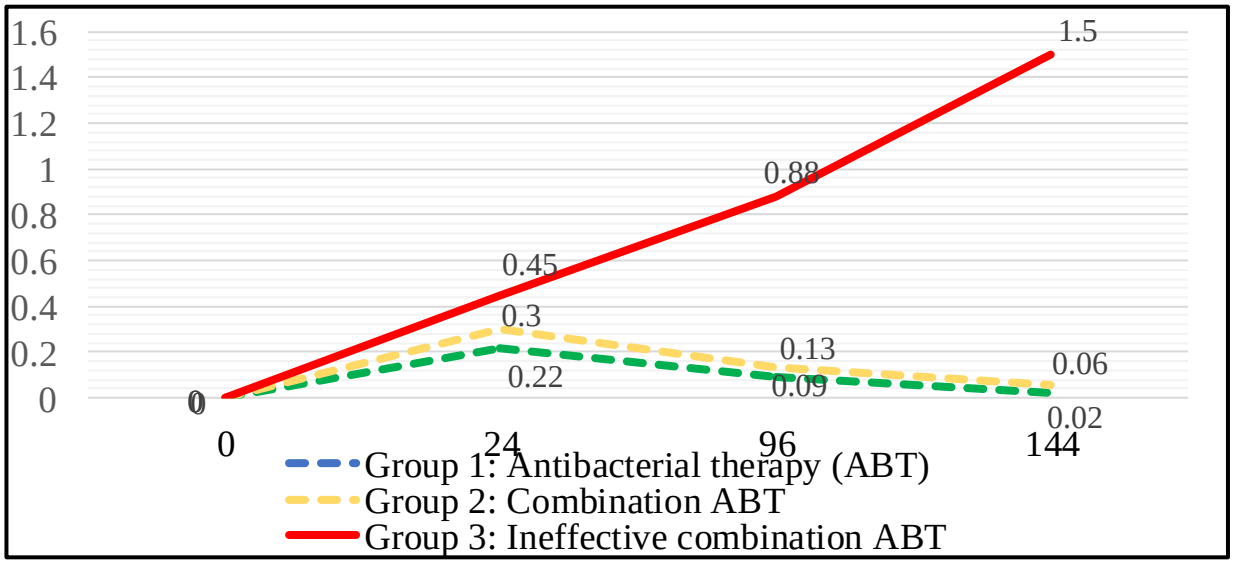

Figure 4. Guidance of antibacterial therapy based on the dynamics of procalcitonin levels

The data presented in the figure clearly illustrate the dynamic changes of the investigated marker in evaluating therapeutic efficacy. In groups where antibacterial therapy (ABT), particularly combination therapy, was effective, a decreasing trend in PCT levels was observed. In contrast, in cases of ineffective treatment, a consistent increase in PCT concentration was recorded. These findings confirm the value of PCT as an important prognostic marker for assessing disease severity and treatment effectiveness.

In Group 1 (patients receiving ABT), the baseline PCT level was 0.22 ng/ml. At subsequent stages, the indicator showed a steady decline, reaching a minimal value (≈0.02 ng/ml) by the end of follow-up, indicating stable control of the inflammatory process under antibacterial therapy.

In Group 2 (patients receiving combination ABT), the initial PCT level reached 0.3 ng/ml. During follow-up, a gradual decrease was observed, with the level declining to 0.06 ng/ml by the end of observation.

This trend demonstrates the effectiveness of combination antibacterial therapy in reducing inflammatory activity.

In Group 3 (patients with ineffective therapy), PCT levels showed a persistent upward trend from the initial stage, increasing from 0 to 0.45 and subsequently to 0.88 ng/mL during follow-up, and reaching the highest value (≈1.5 ng/ml) by the end of the observation period. The absence of a decreasing trend reflects progression of the inflammatory process and the clinical ineffectiveness of the administered therapy.

Conclusion:

1. PCT is a highly informative biomarker for evaluating the likelihood of bacterial co-infection and monitoring the progression of infectious diseases. Its serum concentration reflects the host's systemic inflammatory response to bacterial pathogens, making it a valuable tool in distinguishing bacterial infections from viral or non-infectious inflammatory conditions.

2. In patients with COVID-19, elevated procalcitonin levels can serve as a reliable indicator of concurrent bacterial infection, thereby guiding clinical decision-making regarding the initiation and duration of antibiotic therapy. By integrating PCT measurements into the management of SARS-CoV-2 infection, clinicians can optimize the timing of antibacterial interventions, avoid unnecessary antibiotic exposure, and tailor the course of therapy based on objective biomarker trends, ultimately improving patient outcomes and reducing the risk of antimicrobial resistance.

3. ABT - It is recommended that the initiation, continuation, or discontinuation of antibiotic therapy be guided by an algorithm based on PCT results. This approach enhances the effectiveness of ABT against secondary concomitant bacterial infections and ensures the rational use of antibiotics. A decrease in the level of PCT by 80-90% from the peak level is one of the markers for stopping antibacterial therapy.

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