

Procalcitonin as an Indicator of Antibacterial Therapy in Covid-19

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ABSTRACT

The article presents laboratory characteristics as well as the potential of biomarkers to predict disease severity in patients infected with SARS-CoV-2. 120 patients with a new coronavirus infection were examined. All patients had laboratory confirmed SARS-CoV-2 infection. The patients were divided into severe patients (n = 60) and patients with moderate forms (n = 60). The average age was 53 years, of 120 patients 96 (80%) were men. The importance of procalcitonin as a biomarker for assessing the risk of bacterial infection, disease progression, timely administration of antibacterial drugs and the duration of the course of antibacterial therapy was studied.

KEY WORDS: SARS-CoV-2, COVID-19, Gastrointestinal, Neurological, Skin Manifestations, Procalcitonin.

INTRODUCTION

COVID-19 is a disease caused by the novel SARS-CoV-2 coronavirus. [12]. Most patients with COVID-19 develop symptoms of respiratory infection, some of them progress to a more severe systemic disease characterized by persistent fever, acute lung injury with acute respiratory distress syndrome, multiple organ failure, shock and high mortality [3, 4, 5]

Procalcitonin (PCT) has been proposed in highly cited studies as a potentially valuable serum biomarker for the diagnosis of bacterial infections in general [6]. It was found that the level of procalcitonin correlates with the risk of corresponding bacterial infections and decreases after recovery [7]. Prior to COVID-19, serum procalcitonin-based antimicrobial control (AMS) algorithms were shown to be effective in discriminating between bacterial and nonbacterial respiratory tract infections, resulting in increased mortality, less antibiotic use, and reduced risk of infection. side effects of antibiotics [8]. In COVID-19, the previous reports of the benefits of PCT came from hospitalized patients in whom PCT was found to correlate with disease severity, longer intensive care unit (ICU) stay and hospital mortality, as well as a number of other biochemical markers [9, 10, 11].

Procalcitonin in coronavirus infection with damage to the respiratory parts of the lungs is within the reference values [12].

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 for bacterial complications.

Cumulative data show that more than 80% of COVID-19 patients are receiving antibiotic treatment, as it is difficult to identify COVID-19 patients who have no underlying bacterial infection who can safely stop taking antibiotics. However, recent clinical data indicate that procalcitonin can help assess the condition of these patients and reduce unnecessary antibiotic use [13,14,15].

Purpose of the study. Study of serum procalcitonin levels to address initiation and withdrawal of antibiotic therapy, as well as to establish the progression of disease severity in COVID-19 patients.

MATERIALS AND METHODS

This study was a single-center retrospective cohort study. We included all patients with confirmed SARS-CoV-2 infection admitted to an infectious diseases hospital from June 10 to September 12, 2020 in Bukhara. Clinical data were obtained from electronic health records, including demographic data, exposure history, signs and symptoms, and laboratory data at admission. Upon admission to the inpatient emergency department, all patients were assessed using the NEWS scale. The average score was 5.6 ± 1.6 . This made it possible to quickly sort the patients and the most severe ones to be sent to the intensive care unit. All COVID-19 patients included in this study were diagnosed in accordance with the guidelines for the diagnosis and treatment of pneumonia caused by infection with the novel coronavirus. All patients had laboratory confirmed infection with SARS-CoV-2 (real-time RT-PCR specific for SARS-CoV-2 was positive).

From June 10 to September 12, 2020, 120 patients were hospitalized at the Bukhara Regional Infectious Diseases Hospital. The patients were divided into severe patients ($n = 60$) and patients with moderate forms ($n = 60$).

Of these, 12 (20.0%) patients were admitted to the intensive care unit.

The average age was 53 years, of 120 patients 96 (80%) were men. The median time from symptom onset to hospitalization was 2–3 days, and the median time to diagnosis of severe illness was 3–4 days. Routine blood tests: white blood cell count (WBC), lymphocyte count (LYM), mononuclear cell count (MONO), neutrophil count (NEU) were 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 an automatic biochemical analyzer MINDRAY BC-30 (China). PCT concentration was determined by ELISA using reagent kits for enzyme-linked immunosorbent assay for determination of PCT (procalcitonin) concentration in blood plasma PCT-ELISA-BEST. Patients with moderate and severe form used the data of their first laboratory test on the 2nd day of admission, 3 and 5 days of treatment.

The upper limit of the norm was taken to be a concentration of 0.05 ng / ml.

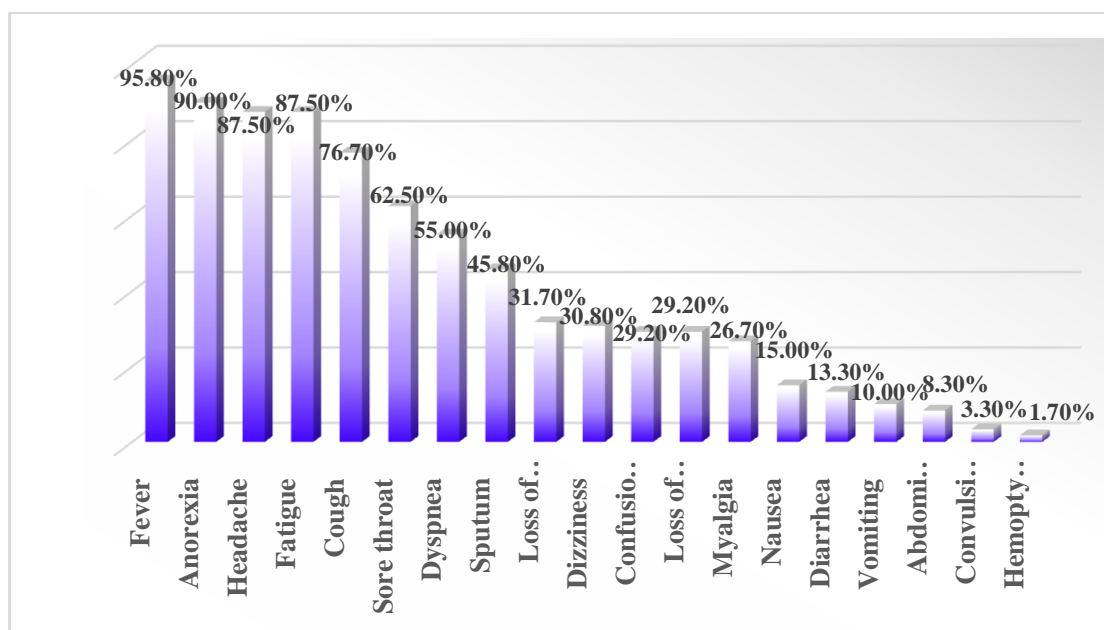
The obtained data were compared with the stock data in the recommendations for the clinical interpretation of the results of determining the PCT (procalcitonin) level in the blood serum: 0.1–0.25 ng / ml - the likelihood of a bacterial infection is very small; 0.25–0.5 ng / ml - local bacterial infection is possible; 0.5–2.0 ng / ml - high probability of bacterial infection, possible systemic bacterial infection; 2.0–10.0 ng / ml - high probability of systemic bacterial infection, severe sepsis is possible; > 10.0 ng / ml - a high probability of severe sepsis [16.].

RESULTS AND DISCUSSION

When studying clinical symptoms, it was found that the most frequent symptom on admission to patients was fever, detected in 115 patients, followed by respiratory symptoms such as cough in 92, sputum in 25, shortness of breath in 66, sore throat in 75. hemoptysis - in 2 patients.

The most common gastrointestinal symptoms in patients with COVID-19 were: anorexia in 108, diarrhea in 16, nausea in 18, vomiting in 12, and abdominal pain in 10 patients.

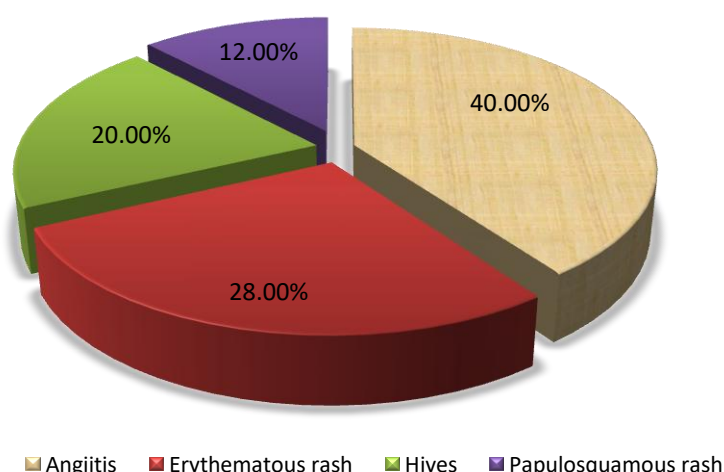
Of the neurological symptoms, such as headache were recorded in 105, fatigue - in 104, dizziness - in 37, loss of taste - in 35, loss of smell - in 38, myalgia - in 32, confusion - in 35, convulsions - in 4 patients (Pic 1.).



Pic. 1. Frequency of symptoms in patients with COVID-19 (%).

Also, ophthalmological manifestations were recorded, such as conjunctivitis - in 48, lacrimation from the eyes - in 12.

According to the results of the obtained data on 120 patients, it turned out that skin manifestations were found in 25 patients (20.8%). In 18 (20.8%) patients, they manifested themselves together with the manifestation of other symptoms, in 7 (28%) patients - after hospitalization. Among the skin manifestations were angitis in 10 patients, erythematous rash in 7 patients, widespread urticaria in 5 patients, as well as vesicles, papulosquamous rashes in 3 patients (Pic. 2.)



Pic. 2. The proportion of elements among skin manifestations in patients with COVID-19 (%)

According to the results of laboratory data, it was found that 40 patients (33.3%) had leukopenia, 56 patients (46.7%) had leukocytosis; in 88 patients (73.3%) lymphocytopenia was revealed, in 24 patients (15.0%) - an increase in the number of lymphocytes.

Platelet count and coagulation parameters were analyzed in this study. Of the 120 patients included in the study, thrombocytopenia was found in 23 (24.2%), thrombocytosis - in 18 (15.0%). In 64 (53.3%) of 120 observed patients, the PCT content was 0.05-0.1 ng / ml, in 46

(38.3%) patients - 0.1-2.0 ng / ml, in 10 (8.4%) - more than 2.0 ng / ml. These analyzes were obtained within the first 48-72 hours from the onset of the disease. And on the basis of the PCT content in the blood serum, they were conditionally divided into 3 groups. Subsequently, the analyzes were repeated on the 3rd, 5th day, in severe patients, the PCT (procalcitonin) level was investigated on the 7th day of treatment. Patients whose PCT (procalcitonin) count was higher than 0.1 ng / ml were regarded as co-infection and they were recommended for treatment with antibiotics (a combined preparation of amoxicillin and clavulanic acid, cephalosporins of 2-3 generations), severely ill meropenem and respiratory fluoroquinolones (levofloxacin). The effectiveness of the treatment was assessed as insufficient if after 3 days of treatment there was no decrease in the PCT level in the blood serum by 50%. In such cases, where there was no decrease in the PCT (procalcitonin) level, it can be assumed that the treatment does not give the expected effect. Therefore, change the tactics of antibiotic therapy. If the PCT (procalcitonin) level decreases, this will mean that the treatment has given the expected result. As soon as there is a decrease in the amount of PCT(procalcitonin) by about 80-90% of the peak level, it is recommended to discontinue antibiotic 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 PCT (procalcitonin) level, which did not differ from the norm, in 8 (12.5%) patients, the PCT content remained unchanged. Whereas in 10 (15.6%) patients, an increase in the PCT (procalcitonin) level in the blood serum was observed and they were prescribed antibiotic therapy.

In 38 (82.6%) patients of the 2nd group who received antibacterial drugs, as in cases of coinfection, the PCT (procalcitonin) content decreased by 50%, and in 8 (17.4%) patients, the PCT (procalcitonin) level remained significantly high. Only 3 (30%) patients out of 10 seriously ill patients had a positive result. When, against the background of antibiotic therapy on the 3rd day of treatment, there was no decrease in the PCT (procalcitonin) level, and then another combination of 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, in 18 patients of group 1, the PCT (procalcitonin) level significantly decreased and returned to normal. In 6 (13%) patients of the 2nd group, the PCT (procalcitonin) level remained significantly high and continued treatment with antibacterial drugs. In 2 (20%) patients of the 3rd group, despite the administration of antibacterial drugs, the PCT (procalcitonin) level remained high, the disease was fatal.

CONCLUSION

1. Procalcitonin is a biomarker for assessing the risk of bacterial infection and disease progression.
2. The level of procalcitonin can serve as biomarkers of bacterial infection adherence to COVID-19 and determines the timely prescription of antibacterial drugs and the duration of the course of antibiotic therapy.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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REFERENCES

1. Ibrakhimova H.R., Oblokulov A.R. (2020). Pathogenetic Bases And Prevalens Of Parasitic Infections In Children: Literature Review. The American Journal Of Medical Science And Pharmaceutical Research, 2(10),87-95
2. Lu H., Stratton C.W., Tang Y.-W.: Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. J. Med. Virol., 2020; 92: 401–402.
3. Zhu N., Zhang D., Wang W.: A novel coronavirus from patients with pneumonia in China, 2019. N. Engl. J. Med., 2020; 382: 727–733.]
4. Oblokulov, A. R.; Niyozov, G.E. (2020) Clinical and epidemiological characteristics of patients with COVID-19. International Journal of Pharmaceutical Research; 12(4):3749-3752.
5. Oblokulov A.R., Musaeva D.M., Elmurodova A.A. (2020) Clinical and epidemiological characteristics of the new coronavirus infection (COVID-19). // New Day in Medicine. №2 (30/2) p.110-115.
6. Cao Y., Liu X., Xiong L. et al. Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2: a systematic review and metaanalysis. J. Med. Virol., 2020; doi: 10.1002/jmv.25 822.
7. Uzzan B, Cohen R, Nicolas P, Cucherat M, Perret GY (2006) Procalcitonin as a diagnostic test for sepsis in critically ill adults and after surgery or trauma: a systematic review and meta-analysis. Crit Care Med 34(7):1996–2003.
8. Kutz A, Briel M, Christ-Crain M, et al. Prognostic value of procalcitonin in respiratory tract infections across clinical settings. Critical Care (London, England) 2015;19 (1):74.
9. Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest. 2020;130(5):2620-9.
10. Heesom L, Rehnberg L, Nasim-Mohi M, Jackson AIR, Celinski M, Dushianthan A, et al. Procalcitonin as an antibiotic stewardship tool in COVID-19 patients in the intensive care unit. J Glob Antimicrob Resist. 2020;22:782-4.
11. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020;368:m1091.
12. Guan, W., Ni, Z., Hu, Y. et al. Clinical characteristics of 2019 novel coronavirus infection in China // N Engl J Med. 2020; 382 (18): 1708-1720.
13. Williams EJ et al. (2020) Routine measurement of serum procalcitonin allows antibiotics to be safely withheld in patients admitted to hospital with SARS-CoV-2 infection. medRxiv. doi. org/10.1101/2020.06.29.20136572.
14. Niyazov G.E., Oblokulov A.R., Pondina A.I. et al. (2020) Clinical and epidemiological characteristics of COVID-19 patients // New Day in Medicine. №4 (32) 110-115 p.
15. Ikhtiyarova G.A., Aslonova M.Zh., Sadullaeva M. Diagnosis and treatment of COVID - 19 for pregnancy// A new day in medicine. - 2020. - №2 (30/2). - P. 98 - 103.
16. Meisner M. Procalcitonin – biochemistry and clinical diagnosis. Bremen: UNI-MED; 2010. 128 p.
17. Oblokulov A.R., Oblokulov Z.I., Elmurodova A.A., Farmanova M.A. (2020) Virologic response in the treatment of infection with antiviral drugs. // World Journal of Pharmaceutical Research. Volume 9, Issue 9, 87-92.