PREDICTIVE VALUES OF PROCALCITONIN FOR SECONDARY BACTERIAL INFECTIONS IN PATIENTS WITH COVID-19

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ANNOTATION. 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.

Introduction. The COVID-19 pandemic caused by the SARS-CoV-2 virus has affected millions of people worldwide and resulted in a significant number of deaths. One of the severe complications of COVID-19 is pneumonia, which can lead to respiratory failure and death. Early identification of patients with severe pneumonia and predicting their prognosis is critical in the management of COVID-19 patients. Biomarkers such as CRP, PCT and cytokines have been studied as potential predictors of the severity and outcome of SARS-CoV-2-associated pneumonia. Studies that investigated the use of CRP, PCT, and cytokines in predicting the prognosis of SARS-CoV-2-associated pneumonia were reviewed. These studies used different methods to measure the levels of these biomarkers in the blood of COVID-19 patients, including enzyme-linked immunosorbent assay (ELISA), chemiluminescence assay (CLIA), and electrochemiluminescence assay (ECLIA). Several studies have demonstrated the importance of CRP, PCT, and cytokines in predicting the severity and outcome of SARS-CoV-2-associated pneumonia. Elevated levels of these biomarkers have been associated with a higher risk of developing severe pneumonia and a worse prognosis. In addition, these biomarkers have been used to monitor the response to treatment and predict the risk of complications, such as acute respiratory distress syndrome (ARDS) and sepsis. SARS-CoV-2 is a novel coronavirus that emerged in Wuhan, China, in late 2019. Since then, it has spread rapidly around the world, causing a pandemic. The disease caused by SARS-CoV-2 is called COVID-19 and can range from mild to severe respiratory illness. SARS-CoV-2-associated pneumonia is one of the severe forms of

the disease and can be life-threatening in some cases. CRP, PCT and cytokines are all laboratory parameters that can help in the diagnosis and prognosis of SARS-CoV-2-associated pneumonia. In this article, we will discuss the importance of these parameters and their role in determining the prospect of SARS-CoV-2-associated pneumonia. CRP is a protein produced by the liver in response to inflammation in the body. Its levels in the blood can rise within hours of the onset of infection or inflammation. CRP levels can be measured using a simple blood test. Elevated CRP levels have been found in patients with severe COVID-19 and are associated with poor outcomes. Studies have shown that CRP levels can be used as a prognostic marker in COVID-19 patients. A high CRP level at admission is associated with a higher risk of severe disease, ICU admission, and mortality. PCT is a peptide hormone produced by the thyroid gland in response to bacterial infections. PCT levels can be measured in the blood, and elevated levels are usually indicative of bacterial infection. However, recent studies have shown that PCT levels can also be elevated in viral infections, including SARS-CoV-2. Elevated PCT levels have been found in COVID-19 patients with severe disease and are associated with poor outcomes. PCT levels can be used as a prognostic marker in COVID-19 patients. A high PCT level at admission is associated with a higher risk of severe disease, ICU admission, and mortality. Cytokines are a group of proteins produced by cells of the immune system that regulate the body's immune response. During an infection, the body produces cytokines to fight the infection. However, in some cases, the body can produce too many cytokines, leading to a cytokine storm. The cytokine storm is a severe immune response that can cause widespread inflammation and tissue damage. Cytokine storms have been observed in some COVID-19 patients and are associated with severe disease and mortality. Cytokine levels can be measured in the blood, and elevated levels are usually indicative of a cytokine storm. In conclusion, CRP, PCT and cytokines are important laboratory parameters that can help in the diagnosis and prognosis of SARS-CoV-2-associated pneumonia. Elevated levels of these parameters are usually indicative of severe disease and poor outcomes. Early identification of patients with elevated levels of these parameters can help in the early intervention and management of SARS-CoV-2-associated pneumonia. Discussion: The measurement of CRP, PCT, and cytokines is a valuable tool in the management of patients with SARS-CoV-2-associated pneumonia. These biomarkers can help identify patients with a higher risk of developing severe pneumonia and those who may benefit from more aggressive treatment. They can also be used to monitor the response to treatment and predict the risk of complications. However, the use of these biomarkers in clinical practice should be carefully evaluated, and their limitations should be considered. Further research is needed to investigate the use of these biomarkers in the management of COVID-19 patients.

Purpose of the study. Study of serum procalcitonin (PCT) levels to decide whether to start or discontinue antibiotic therapy, as well as to determine the progression of disease severity in COVID-19 patients. The study of PCT levels is performed to diagnose bacterial infection, sepsis, septic complications, purulent-inflammatory pathologies and clarify the cause of inflammation.

Materials and methods. From June 10 to September 12, 2021, 120 patients were admitted to the Bukhara Regional Infectious Diseases Hospital120. Patients were divided into severe cases (n=60) and moderate cases (n=60). Of these, 12 (20.0%) patients were admitted to the intensive care unit. The concentration PCT was determined using the ELISA method using THE PCT–ELISA-BEST reagent kits. 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.

Results. Based on the results of laboratory data, it was found that in 64 (53.3%) of the 120 observed patients, the PCT content was 0.05-0.1 ng / ml in 46 (38.33%) patients, 0.1-0.25 ng/ml in 10 (8.33%), 0.25 – 0.5 ng/ml in 35 (29.18%), 0.5-2.0 ng / ml – in 19 (15.83%), and more than 2.0 ng/ml-in 10 (8.33%). 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%. 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.

Conclusion: This study demonstrates that PCT overexpression can strongly predict poor outcomes in COVID-19 patients; evaluating PCT at the time of admission may help clinicians identify potentially severe cases early. Nevertheless, further well-designed, and high methodological quality multicentric studies from different populations are needed to obtain precise predictive accuracy of PCT for mortality and disease severity in COVID-19 patients. Future studies should report the predictive accuracy of PCT with a predefined cut-off value at 0.1 ng/ml to obtain homogenous findings.P rocalcitonin is a biomarker for assessing the risk of bacterial infection and disease progression. PCT levels can serve as biomarkers of bacterial infection joining COVID-19 and determine the timely administration of antibacterial drugs and the duration of the course of antibacterial therapy. A decrease in the level of PCT by 80-90% from the peak level is one of the markers of discontinuation of antibacterial therapy.

References:

1. Arsenault, C., Gage, A., Kim, M.K. *et al.* COVID-19 and resilience of healthcare systems in ten countries. *Nat Med* 28, 1314–1324 (2022).
2. Oblokulov, A.R., Husenova, Z. Z., & Ergashev, M. M. (2021). Procalcitonin as an indicator of antibacterial therapy in covid-19. Annals of the Romanian Society for Cell Biology, 5220-5224.
3. Scaglioni V., Soriano E.R. Are super antigens the cause of cytokine storm and viral sepsis in severe COVID-19? Observations and hypothesis // Scand. J. Immunology –2020. –Vol. 92, no. 6. – P. 1–5.
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. Gorbalenya A.E., et al. The species Severe acute res piratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2 // Nat. Microbiol. –2020. –Vol. 5, no. 4. –P. 536–544.
6. Encyclopaedia Britannica, Inc. – URL: https://www.britannica.com (date of viewing: 12.01.2021).
7. Mahendra M, Nuchin A, Kumar R, *et al.* (2021) Predictors of mortality in patients with severe COVID-19 pneumonia—a retrospective study. Adv Respir Med 89:135–144.
8. Bosch B.J., et al. The coronavirus spike protein is a class I virus fusion protein: structural and functional characterization of the fusion core complex // J. Virol. – 2003. –Vol. 77, no. 16. –P. 8801–8811.

9. Lanzavecchia A. Antigen-specific interaction between T and B cells // Nature. – 1985. – Vol. 314, no. 11. – P. 537–539.
10. Scaglioni V., Soriano E.R. Are superantigens the cause of cytokine storm and viral sepsis in severe COVID-19? Observations and hypothesis // Scand. J. Immunol. – 2020. – Vol. 92, no. 6. – P. 1–5.
11. Gorbalenya A.E., et al. The species Severe acute res piratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2 // Nat. Microbiol. – 2020. – Vol. 5, no. 4. – P. 536–544.
12. Encyclopaedia Britannica, Inc. – URL: https:// www.britannica.com (date of viewing: 12.01.2021).
13. Schoeman, D. Coronavirus envelope protein: current knowledge // Virol. J. – 2019. – Vol. 16, no. 1. – P. 69.
14. Williams EJ et al. (2020). Routine measurement of serum procalcitonin allows antibiotics to be safely with held in patients admitted to hospital with SARS-CoV-2 infection. medRxiv. doi. org/10.1101/2020.06.29.20136572.
15. Oblokulov A.R., Kholov U.A., Niyozov G.E., Khusenova Z.Z., Ergashov M.M. (2021) Extrapulmonal manifestations of COVID – 19 // “Infection, immunity and pharmacology –scientific and practical journal - №1/2021. P. - 62-66.
16. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020; 395:1033–1034. doi: 10.1016/S0140-6736(20)30628-0.
17. Облокулов А.Р., Хусенова З.З., Эргашов М.М. (2021) Значение Уровня Прокальцитонина при назначении и мониторинга антибактериальной терапии пациентов с COVID – 19 // Журнал гепато – гастроэнтерологических исследований. Том №1, Специалый выпуск. Ст. -115-117
18. Nahum J, et al. Venous thrombosis among critically ill patients with coronavirus disease 2019 (COVID-19) JAMA Netw. Open. 2020;3: e2010478. doi: 10.1001/jamanetworkopen.2020.10478.
19. Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. J. Thromb. Haemost. 2020; 18:1421–1424. doi: 10.1111/jth.14830.
20. Zhou F, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395:1054–1062. doi: 10.1016/S0140-6736(20)30566-3.
21. Guan WJ, et al. Clinical characteristics of coronavirus disease 2019 in China. N. Engl. J. Med. 2020; 382:1708–1720. doi: 10.1056/NEJMoa2002032.

22. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020;395(10229):1054–1062. doi: 10.1016/S0140-6736(20)30566-3.

23. Wesley H. Self and others, Procalcitonin as a Marker of Etiology in Adults Hospitalized with Community-Acquired Pneumonia, *Clinical Infectious Diseases*, Volume 65, Issue 2, 15 July 2017, Pages 183–190.

24. Clyne B, Olshaker JS (1999) The C-reactive protein. J Emerg Med 17:1019–1025.

25. Авдеева М.Г., Облокулов А.Р., Эргашов М.М. (2022) Прокальцитонин как предиктор антибактериальной терапии при Covid-19 // Новый День в Медицине Том 2 (40) 2022. Ст. -323-327.

26. Williams EJ et al. (2020) Routine measurement of serum procalcitonin allows antibiotics to be safely with held in patients admitted to hospital with SARS-CoV-2 infection. medRxiv. doi. org/10.1101/2020.06.29.20136572.

27. Ergashov M.M. (2023) The importance of C-reactive protein, procalcitonin, and cytokines in determining the prospect of SARS-COV-2-associated pneumonia // Galaxy International Interdisciplinary Research Journal (GIIRJ) ISSN (E): 2347-6915. Vol. 11, Issue 04, April. P.-480-483.

28. Rothe K, Feihl S, Schneider J, *et al.* (2021) Rates of bacterial co-infections and antimicrobial use in COVID-19 patients: a retrospective cohort study in light of antibiotic stewardship. Eur J Clin Microbiol Infect Dis 40:859–869