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THE IMPORTANCE OF C-REACTIVE PROTEIN, PROCALCITONIN, AND CYTOKINES IN DETERMINING THE PROSPECT OF SARS-COV-2 – ASSOCIATED PNEUMONIA

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Abstract

Introduction. 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.

Purpose of the study. This study highlights the importance of CRP, PCT, and cytokines such as IL-6 – In determining the prognosis of SARS-CoV-2-associated pneumonia. This 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 study 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 Materials and Methods

This retrospective study included 120 patients diagnosed with COVID-19 (SARS-Cov-2 associated pneumonia) From June 10 to September 12, 2021, 120 patients were admitted to the Bukhara Regional Infectious Diseases Hospital 120. Patients were divided into severe cases 60/120 – 50 % and moderate cases 60/120 – 50 %. Of these, 12/120 – 20.0 % patients were admitted to the intensive care department. 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 IL-6 have been studied as potential predictors of the severity and outcome of SARS-CoV-2 – associated pneumonia. Studies that investigated the use of biomarkers 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). To study the predictor value of CRP) and PCT in patients with COVID-19 the inflammatory response plays a critical role in COVID-19, the



ability of CRP and PCT to predict moderate and severe cases of COVID-19. PCT is secreted by various cell types from numerous organs in response to pro-inflammatory stimulation.

Results

The study population was divided into two groups depending on the severity of the disease: the medium severe group 83/120 - 69.17 % and the severe group 37/120 - 30.83 %. Data on demographic characteristics, basic clinical characteristics, and levels of CRP and PCT at admission were collected. Among 120 patients, CRP and PCT levels increased in 85/120 - 70.83 % and 103/120 – 85.83 % patients upon admission accordingly. Serum PCT levels were increased in the average severe patients 17/83 - 20.5 % less than 0.05 ng/ml, 44/83 - 53.0 % in 0.05-0.5 ng/ml, 22/83 - 26.5 %, and severe patients 28/37 - 75.7 % 0.5-2.0 ng/ml, 9/37 - 24.3 % more 2.0 ng/ml. Based on the results of laboratory data, it was found that in 64/120 - 53.33 % of the 120 observed patients. the PCT content was 0.05-0.1 ng/ml in 46/120 - 38.33 % patients, 0.1-0.25 ng/ml in 10/120 - 8.33 %, 0.25 - 0.5 ng/ml in 35/120 - 29.18 %, 0.5-2.0 ng / ml in 19/120 - 15.83 %, and more than 2.0 ng/ml in 10/120 - 8.33 %. These tests were obtained within the first 48-72 hours after the onset of the disease. The upper limit of the norm was assumed to be the concentration of 0.05 ng/ml. Therefore, tracking inflammatory markers such as CRP becomes definitely important. Normally, the level of CRP in the blood does not exceed 5 mg/l. According to studies examining the clinical parameters of patients with COVID-19, there was a significant increase in CRP levels (on average from 20 to 50 mg/l). In patients with severe COVID-19, CRP values were significantly higher compared to patients with mild disease. An increase in CRP was observed up to 112/120 -93.33 % in severe cases of COVID-19. In all 40 critically ill patients, a causative agent of 1-10 and above the IL-6 level norm was found. An indicator of 1-5 times was observed in 23/40 -57.5 %, 5 to 10 times in 14/40 - 35 %, and even higher than 10 times in 3/40 - 7.5%. IL-6 norm has a blood plasma concentration of 0-7-pg/ml. Serum CRP levels were increased in the average severe patients 5/83 - 6.02 % less than 0.5 mg/ml, 9/83 - 10.84 % in 10.0-20.0 mg/ml, 69/83 -83.1 % in 20.0- 40.0 mg/l, and severe patients 11/37 – 29.73 % 40.0-60.0 mg/ml, 26/83 – 70.27 % more than 60 mg/ml. Clinically, a concentration of CRP > 10 mg/l and PCT > 0.1 ng/ml indicates a bacterial infection requiring antibiotic treatment, while a PCT concentration of more than 0.5 ng/ml indicates a risk of severe sepsis or septic shock in patients. In recent years, PCT has been considered as a specific and early biomarker for the diagnosis of systemic bacterial infection. The proportion of patients with elevated CRP and PCT levels was significantly higher. The proportional risk model (Cox Regression) has shown that CRP and PCT can be used as independent factors to predict the severity of COVID-19. In addition, patients with CRP >40.0 mg/l (normal CRP level <5 mg/L) or PCT >2.0 ng/ml (normal PCT level <0.05 ng/L) were more likely to have severe complications. CRP, PCT, and IL-6 are valuable biomarkers in predicting the prognosis of 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. Further research is needed to determine the optimal use of these biomarkers in the management of COVID-19 patients. Additionally, the development of rapid and accurate methods for measuring these biomarkers will improve their utility in clinical practice. Biomarkers 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





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can help in the early intervention and management of SARS-CoV-2-associated pneumonia. Future research should focus on the development of biomarkers that can predict the development of severe disease and mortality in COVID-19 patients. The use of biomarkers can help guide the use of immunomodulatory therapies and improve patient outcomes. Additionally, more research is needed to understand the pathogenesis of cytokine storms in COVID-19 patients and develop effective treatments to mitigate their effects. The presented study showed that PCT can serve as a reliable biomarker for the early diagnosis and treatment of patients with SARS-Cov-2-etiology pneumonia. 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. Biomarkers 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.

Discussion

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-2associated pneumonia were reviewed. 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

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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. CRP and PCT are acute-phase reactants that are produced in response to inflammation and infection. Elevated levels of CRP and PCT have been observed in COVID-19 patients and studies have shown that high levels of these parameters at admission are associated with poor outcomes. Both CRP and PCT can be used as prognostic markers in COVID-19 patients to identify those at higher risk of severe disease and poor outcomes. Cytokines are a group of proteins that regulate the immune response. During an infection, cytokines are produced to fight the infection. However, in some cases, the body can produce too many cytokines, leading to a cytokine storm. Cytokine storms have been observed in some COVID-19 patients and are associated with severe disease and mortality. Elevated levels of cytokines, such as IL-6 have been observed in severe cases of COVID-19. Measuring cytokine levels can help identify patients at risk of developing a cytokine storm and guide the use of immunomodulatory therapies. This metaanalysis has several limitations. First, all included studies were retrospective except one, so the data were prone to confounding factors. Second, the included studies had a considerable level of heterogeneity. The number of included articles and the total number of patients were limited, so publication bias, subgroup, and sensitivity analyses could not be performed. More high-quality studies may be needed to elucidate the role of PCT in coinfections with COVID-19 and identify optimal cut-offs. In summary, although PCT has a limited ability to diagnose coinfections in patients with COVID-19, low levels of PCT seem to be a good indicator for excluding coinfections. We remain skeptical about the ability of PCT to help clinicians detect coinfections early; more research is needed to validate the usefulness of PCT so that clinicians can initiate effective management quickly and reduce the overall mortality of COVID-19. Further research is needed to develop accurate predictive models and diagnostics for coinfections in patients with COVID-19.



Conclusions:

CRP, PCT, and cytokines are valuable biomarkers in predicting the prognosis of SARS-CoV-2associated pneumonia. Thus, serum CRP and PCT levels have a significant correlation with the severity of COVID-19 and can be used as independent factors to predict disease risk. Serum CRP and PCT levels can effectively assess the severity of the disease and predict the outcome in patients with COVID-19. These biomarkers can help identify patients with a higher risk of developing severe pneumonia and those who may benefit from more aggressive treatment. PCT 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 for stopping antibacterial therapy. Further research is needed to determine the optimal use of these biomarkers in the management of COVID-19 patients. Additionally, the development of rapid and accurate methods for measuring these biomarkers will improve their utility in clinical practice. CRP, PCT, and cytokines are important laboratory parameters that can help in the diagnosis and prognosis of SARS-CoV-2associated 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. Future research should focus on the development of biomarkers that can predict the development of severe disease and mortality in COVID-19 patients. The use of biomarkers can help guide the use of immunomodulatory therapies and improve patient outcomes. Additionally, more research is needed to understand the pathogenesis of cytokine storms in COVID-19 patients and develop effective treatments to mitigate their effects.

References

- 1. Lanzavecchia A. Antigen-specific interaction between T and B cells // Nature. –1985. –Vol. 314, no. 11. –P. 537–539.
- 2. 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).
- 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.
- 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.
- 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.
- 6. Oblokulov A.R., Oblokulov A.A., Ergashov M.M. (2021) Clinical And Laboratory Criteria for spontaneous Bacterial Peritonitis In Liver Cirrhosis Of Viral Etiology // Central asian journal of medical and natural sciences. P. 172-177.



	Volume 2, Issue 6, June 2024 ISSN (E): 2938-376	
	7.	Guan WJ, et al. Clinical characteristics of coronavirus disease 2019 in China. N. Engl. J. Med. 2020; 382:1708–1720. doi: 10.1056/NEJMoa2002032.
Web of Medicine: Journal of Medicine, Practice and Nursing	8.	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.
	9.	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 - N ¹ /2021. P 62-66.
	10.	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. P480-483.
	11.	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.
	12.	Lanzavecchia A. Antigen-specific interaction between T and B cells // Nature. – 1985. – Vol. 314, no. 11. – P. 537–539.
	13.	Westblade LF, Simon MS, Satlin MJ (2021) Bacterial coinfections in coronavirus disease 2019. Trends Microbiol 29:930–941.
	14.	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.
	15.	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
	16.	Lopez L.A., et al. Importance of conserved cysteine residues in the coronavirus envelope protein // J. Virol. – 2008. – Vol. 82, no. 6. – P. 3000–3010.
	17.	Schoeman, D. Coronavirus envelope protein: current knowledge // Virol. J. – 2019. – Vol. 16, no. 1. – P. 69.
	18.	Эргашов М.М., Бомомуратова М.Н. (2023) Прокальцитонин – перспективный диагностический маркер для управления антибактериальными терапии при COVID-19 // Лучшие интеллектуальные исследования. Часть-6, Том-1, ст89-94.
	19.	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.
	20.	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.
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ISSN (E): 2938-3765

- 21. 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.
- 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.
- Lopez L.A., et al. Importance of conserved cysteine residues in the coronavirus envelope protein // J. Virol. –2008. –Vol. 82, no. 6. –P. 3000–3010. 7.Schoeman, D. Coronavirus envelope protein: current knowledge // Virol. J. –2019. –Vol. 16, no. 1. –P. 69.
- 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.
- 25. Escher R, Breakey N, Lammle B. Severe COVID-19 infection associated with endothelial activation. Thromb Res.2020; 190:62. doi: 10.1016/j.thromres.2020.04.014.
- 26. 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
- Ergashov M.M. (2023) The importance of C-reactive protein, Procalcitonin, and cytokines in determining the prospect of SARS-COV-2-associated pnumonia // Horizon Journal of Humanity and Artificial Intelligence. Volume: 02 Issue: 06 | 2023, ISSN: 2835-3064. P. -167-171.
- 28. Langford BJ, So M, Simeonova M, et al. (2023) Antimicrobial resistance in patients with COVID-19: a systematic review and meta-analysis. Lancet Microbe 4: e179–e191.
- 29. 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.
- 30. Hermans C, Lambert C. Impact of the COVID-19 pandemic on therapeutic choices in thrombosis-hemostasis. J Thromb Haemost. 2020 doi: 10.1111/jth.14845.
- 31. 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.
- 32. Облокулов А.Р., Нарзиев И.И., Облокулов А.А., Эргашов М.М., Бадиева Б.М. (2021) Пандемия шароитида фаолят кўрсатган тиббиёт ходимларида юзага келаган рухий ўзгаришлар // "Инфекция, имунология, фармакалогия" научно-практический журнал. №1/2021. Ст. -58-62.
- Xiaomin Luo and others, Prognostic Value of C-Reactive Protein in Patients with Coronavirus 2019, Clinical Infectious Diseases, Volume 71, Issue 16, 15 October 2020, Pages 2174–2179.





- 34. Хусенова З.З., Облокулов А.Р. Эргашов М.М. (2021) Клинико эпидемиологическая характеристика пациентов с SARS CoV 2 инфекцией // Tibbiyotda yangi kun, №2(34/3)202. Ст. 270-273.
- Эргашов М.М. (2021). Ролъ прокальцитонинового теста в диагностике и лечении COVID – 19 // Ш Международное книжное издание – Лучший молодой ученый. Ст.40-42.
- 36. 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.
- 37. Облокулов А.Р., Хусенова З.З., Эргашов М.М. (2021) Значимость уровня прокальцитонина при терапии пациентов с COVID 19 // ВЕСТНИК ТМА Ташкетской медициской академии, Ст. 42-43.
- 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.
- 39. Облокулов А.Р., Хусенова З.З., Эргашов М.М. (2021) Значимость уровня прокальцитонина при терапии пациентов с COVID 19 // Новый день в медицина 2(34)3. Ст. 267-270.
- 40. Эргашов М.М. (2023) Прогностическое значение прокальцитонина при COVID 19 // Ta'lim innovatsiyasi va integratsiyasi. 11-son, 3-to'plam, ст. -122-128.