p-ISSN: 0854-4263
e-ISSN: 2477-4685

INDONESIAN JOURNAL OF

Clinical Pathology and Medical Laboratory

Majalah Patologi Klinik Indonesia dan Laboratorium Medik

Diterbitkan oleh Perhimpunan Dokter Spesialis Patologi Klinik Indonesia

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INDONESIAN JOURNAL OF
CLINICAL PATHOLOGY AND MEDICAL LABORATORY
Majalah Patologi Klinik Indonesia dan Laboratorium Medik

2023 March; 29(2): 105-
p-ISSN 0854-4263 e-ISSN 2477-4685
Available at www.indonesianjournalofclinicalpathology.org

Correlation between Platelets Count and C-Reactive Protein in COVID-19 Patient in Jember Regency

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ABSTRACT

The laboratory test for Coronavirus Disease 2019 (COVID-19) is very important for initial treatment and predicting the prognosis of the patients, but there have been reports of false negative COVID-19 diagnostic test results. Another study reported changes in COVID-19 patient biomarkers, namely platelet count and C-Reactive Protein (CRP) levels. This study investigated the correlation between platelet count and CRP in COVID-19 patients. This study was conducted using a cross-sectional analytic observational method, through secondary data analysis of COVID-19 patients hospitalized between June–August 2021 at Dr. Soebandi Hospital and Jember Klinik Hospital. Of 30 patients, there were 16 male patients (53%) and 14 female patients (47%); 18 patients in the 46-59 years old age group (60%) and 12 patients in ≤ 4 years old (40%) age group; and there were 8 patients admitted to ICU (26.67%). There was a negative correlation between platelet count and CRP in COVID-19 patients ($r = -0.733$; $p<0.001$). A strong correlation between platelet count and CRP is related to prognostic and predictive factors of severity in COVID-19 patients. Further studies about the analysis of other biomarkers in COVID-19 are needed to obtain more prognostic and predictive factors of severity in patients.

Keywords: COVID-19, laboratory, biomarkers, platelets, CRP

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is a group of acute respiratory diseases caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), occurring in Wuhan, China for the first time in December 2019. Currently, COVID-19 has spread worldwide very much compared to Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS).[1] Global data of COVID-19 in 2022 has shown 557,917,904 cases including 6,134,953 cases in Indonesia and 21,369 cases in Jember Regency. Cases and deaths are still rising, and the outbreak has become a global public health concern.[2]

The gold standard diagnosis for COVID-19 is a molecular test called Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR), subsequently, the laboratory tests for COVID-19 are complete blood count and inflammation biomarkers such as C-Reactive Protein (CRP).[3] Laboratory testing for COVID-19 is very important for diagnostic purposes but there have been reports of false negative COVID-19 diagnostic test results.[4] The high number of false negatives during the COVID-19 diagnostic tests will affect the initial treatment and prognosis of COVID-19 patients. There are reports of biomarker changes in COVID-19 patients, namely platelet count and CRP levels.[5,6]

Platelets are anucleate disc-shaped cells generated by megakaryocytes in the bone marrow and circulate in the bloodstream. Platelets play a role in hemostasis during vascular injury by stopping bleeding through thrombus formation.[7] Platelets form plugs in vascular injury in response to normal hemostatic adhesion, aggregation, and activation.[8] The normal range of platelets is $(150–450)\times10^3/\mu L$. Thrombocytopenia occurs in 36.2% of cases of COVID-19. Thrombocytopenia is associated with the severity of disease and mortality for COVID-19.[6] In some cases, the significant decrease of platelets is caused by hyper-coagulopathy and Disseminated Intravascular Coagulation (DIC).[9]

C-reactive protein is an acute inflammatory protein produced primarily in liver hepatocytes that plays a role in the complement pathway during inflammation.[10] C-reactive protein is a basic biomarker indicating mortality and can predict the prognosis in patients with sepsis including in COVID-19.[11] CRP increases during inflammation induced by cytokines IL-1 and IL-6. Inflammatory cytokines also increase the formation and activation of platelets, leading to the dissociation of proinflammatory monomeric CRP from its native pentameric form. During COVID-19 infection, CRP in patients has increased on average between 20 to 50

mg/L compared to normal (<10 mg/L).[12]

Recent studies regarding the relationship between platelet count and CRP in COVID-19 patients showed a significant correlation between increased mortality and poor prognosis, but information on a possible correlation between platelet count and CRP is not yet available. This study hypothesized that there is a correlation between platelet count and CRP, indicating that platelet count could be used as both an inflammatory marker and prognostic factor in patients.

METHODS

This study used a cross-sectional analytic observational method, subjects were patients who were confirmed with COVID-19 from June until August 2021 at Dr. Soebandi Hospital and Jember Klinik Hospital in Jember Regency. Health Research Ethics Commission, Faculty of Medicine, University of Jember has approved this research with article number 1577/H25.1.11/ KE/2022. The study was conducted from January 2022 to April 2022. Medical histories of COVID-19 patients with positive RT-PCR tests, under 60 years old, with laboratory findings for platelet count and CRP levels were acquired from medical records of Dr. Soebandi Hospital and Jember Klinik Hospital. The exclusion criteria were patients with a history of immunocompromised disease and incomplete medical records. The study sample was taken using simple random sampling, and 30 patient data was acquired. The correlation test of numerical data was performed using the Pearson test using SPSS version 24.

RESULTS AND DISCUSSIONS

A total of 30 patients with COVID-19 were included in this study, the overall mean value of platelet count was 179.7×10^3/µL (Standard Deviation [SD] 39.7), and the mean value of CRP was 54 mg/L (SD 28). These patients were 53% male and 47% female, showing females had a lower mean platelet count and higher mean CRP than males. The age group of 46-59 years old (60%) had lower mean platelets count and higher mean CRP than the ≤ 45 years old (40%) age group. Patients admitted to the ICU (26.67%) had lower platelet counts and higher mean CRP than patients admitted to isolation wards (73.33%). The basic characteristics of the study sample can be seen in Table 1.

The result of the correlation between platelets count and CRP of patients can be seen in Table 2. There was a negative correlation with strong correlation strength between platelet count and CRP (r = -0.733; p<0.001).

There were more males (53%) than females in this study. Female patients had lower mean platelet counts and higher mean CRP compared to male patients. This is not in line with a study by Widjaja *et al.* in Immanuel Hospital Bandung, which found that female COVID-19 patients (54.2%) were more common than males. Various results in these studies were caused by the imbalance of the number of samples involved in the related studies.[13] A study by Maryati *et al.*, obtained similar results finding more male COVID-19 patients (55.9%) than females.[14] These results are based on a study by Raza *et al.*, stating females are more superior in innate and adaptive immunity in responding to viral

Table 1. Clinical characteristics of patients according to platelets and CRP levels

Variable	n	Percentage %	Platelets (10^3/µL)		CRP (mg/L)	
			Mean	SD	Mean	SD
Gender						
Males	16	53	198.8	39.9	43.6	31.8
Females	14	47	157.7	26.7	66	19
Age group						
= 45 y.o	12	40	198.1	36.2	44.3	23.4
46-59 y.o	18	60	167.3	38	60.5	30.3
Wards						
a. Non-ICU	22	73.33	187.5	42.5	47.3	28
b. ICU	8	26.67	158.2	20.2	72.5	22
Total sample	30	100	179.7	39.7	54	28

CRP: C-Reactive Protein; ICU: Intensive Care Unit

Table 2. Pearson correlation of platelets count and CRP

Pearson Correlation	n	p-value	Coefficient Correlation
Platelets count and CRP	30	0.001	-0.733

infections. Cytokines that play a role in modulating the immune system are linked to the X chromosome, which is more commonly found in females. While the Y chromosome has more ability to increase the expression of TMPRSS2, which assists in the fusion of SARS-CoV-2 to host cells. Hormones also play a role in immunity, estrogen assists the recruitment of monocytes and macrophages and regulates proinflammatory cytokines such as IFN-α. Various immune system responses in males and females can affect the response to inflammation and cause a more persistent presence of the virus, thereby the risk factors for COVID-19 cases are higher in male patients compared to female patients.[15]

The age distribution of COVID-19 patients in this study is higher in the 46-59 years old age group (60%), which had a lower mean platelet count and higher mean CRP. Similar results were also obtained in a study by Ernawati, which reported the distribution of COVID-19 patients by age group in Pati Regency was dominated by the 46-59 years old age group (36.59%). The 26-59 years old age group is included in the productive age population, where there is higher mobility and more activities out of the house, which increases the risk of contact with COVID-19.[16] The age in this range also has frequent contact with the elderly, who are more vulnerable and have higher risk factors when in contact with COVID-19. According to Bayram *et al*., the immune response is compromised in old age due to changes in the maturation process and B cells and T cells lymphocytes function, increasing the frequency of COVID-19 infections.[11]

Based on the type of wards, most patients were hospitalized in non-ICU COVID-19 rooms (73.33%), and patients admitted in ICU wards had lower mean platelet counts and higher mean CRP levels compared to non-ICU. This result is similar to the study conducted by Zeng *et al*. at the Shenzen Third People's Hospital China, which stated that the most types of hospitalization were in the non-ICU COVID-19 room at 91.58%.[17] This observation contradicted a study done by Antinori *et al*. at Luigi Sacco Hospital, Milan, Italy, where more COVID-19 patients (51.4%) were admitted to the ICU.[18] The difference in the results of these researches where due to the imbalance of the number of samples involved in the related study.

The mean platelet count was 179.7±39.7.16 × 10^3/μL. This is not much different from research conducted by Arentz *et al*. at Evergreen Hospital, Washington, United States on 21 COVID-19-positive ICU patients that had a mean platelet count of 235×10^3/μL. The mean CRP in this study was 54.08±28.07 mg/L. This is similar to a study by Chen *et al*. at Jinyintan Hospital Wuhan, China, with an average CRP of 51.4 mg/L.[19]

Several things can underlie the negative correlation between platelet count and CRP levels in COVID-19 patients, which means that the lower the platelet count, the higher the CRP levels ($r = -0.733$; $p<0.001$). Thrombocytopenia in COVID-19 patients is associated with infections in the bone marrow, thereby interrupting the forming process of megakaryocytes that will differentiate into platelets in the peripheral blood, also SARS-CoV-2 induces immune system regulation, triggering autoantibodies complexes that will destroy platelets.[20] Proinflammatory cytokines such as IL-6 will induce hepatocytes to produce acute phase reactants, namely CRP. C-reactive protein is initially produced by the liver in form of native CRP (nCRP). nCRP will be converted into activated CRP, namely monomer CRP (mCRP) by binding to phosphocholine. Phosphocholine is highly expressed on cell membranes around the injury caused by SARS-CoV-2 inflammation, especially on activated platelets that form plaques around the vascular injury, nCRP will dissociate followed by increased mCRP levels. mCRP in the inflammatory phase will induce the expression of P-selectin, CD63, and GPIIb/IIIa on platelets, which will increase platelet recruitment, platelet aggregation, and platelet activation. Platelets have increased production but are also used excessively used due to endothelial injury and autoantibody complexes in COVID-19 patients causing a decrease in platelet count and an increase in CRP levels.[21]

CONCLUSIONS AND SUGGESTIONS

There was a significant correlation between the platelet count and CRP of COVID-19 patients. These biomarkers are related to prognostic and predictive factors of severity in COVID-19 patients. As there is still a lot to be understood about laboratory findings of COVID-19, further studies about the analysis of other biomarkers in COVID-19 are needed to obtain more prognostic and predictive factors of severity in patients.

REFERENCES

1. Yüce M, Filiztekin E, ¨Ozkaya KG. COVID-19 diagnosis- A review of current methods. Biosens Bioelectron J, 2021; 172: 112752.
2. Kemenkes RI. Situasi terkini perkembangan Coronavirus Disease (COVID-19). 2022. Available from https://infeksiemerging.kemkes.go.id/document/situasi-terkini-perkembangan-coronavirus-disease-covid-19-17-juli-2022.pdf (accessed July 20, 2022).

3. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, *et al.* Hematological findings and complications of COVID-19. Am. J. Hematol, 2020; 95(7): 834-847.
4. Pfoh ER, Hariri EH, Misra-Hebert AD, Deshpande A, Jehi L, Rothberg MB. Late Diagnosis of COVID-19 in Patients Admitted to the hospital. J. Gen. Intern. Med, 2020; 35(9): 2829-2831.
5. Ali N. Elevated level of C-reactive protein may be an early marker to predict risk for severity of COVID-19. J. Med. Virol, 2020; 92(11): 2409-2411.
6. Mei H, Luo L, Hu Y. Thrombocytopenia and thrombosis in hospitalized patients with COVID-19. J. Hematol. Oncol, 2020; 13(1): 13-15.
7. Ziegler M, Wang X, Peter K. Platelets in cardiac ischaemia/reperfusion injury: A promising therapeutic target. Cardiovasc. Res, 2019; 115(7): 1178-1188.
8. Suryana D, Widaningsih Y, Mangarengi F, Muhadi D. Analysis of Platelet indices and proteinuria in primary hypertensive patients. Indonesian Journal of Clinical Pathology and Medical Laboratory, 2022; 28(2): 105-110.
9. Asakura H, Ogawa H. COVID-19-associated coagulopathy and disseminated intravascular coagulation. Int. J. Hematol, 2021; 113(1): 45-57.
10. Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. Front. Immunol, 2018; 9: 1-11.
11. Bayram M, Yildrim O, Ozmen RS, Soylu B, Dundar AS, *et al.* Prognostic nutritional index and crp, age, platelet count, albumin level score in predicting mortality and intensive care unit admission for COVID-19. Biomark. Med, 2021; 15(18): 1733-1740.
12. Francesca C, Luca C, Laura C, Flavia M, Mario R. The cytokine storm in COVID-19: An over view of the involvement of the chemokine/chemokine-receptor system. Cytokine Growth Factor Rev, 2020; 53: 25-32.
13. Widjaja JT, Kwee L, Giantara AK, Suabgiyo HA, Edwin C, Putri RL. Karakteristik pasien COVID-19 rawat inap di RS Immanuel Bandung, Indonesia. J. Med. Heal, 2021; 3(2): 164-175.
14. Maryati W, Widyastuti A, Pinta A, Rizky K, Ika P, Aryanti FD. Analisis karakteristik pada pasien rawat inap kasus COVID-19. INFOKES, 2022; 12(1): 20-25.
15. Raza HA, Sen P, Bhatti OA, Gupta L. Sex hormones, autoimmunity and gender disparity in COVID-19. Rheumatol. Int, 2021; 41(8): 1375-1386.
16. Ernawati A. Overview of COVID-19 cases by gender, age group, and population density in Pati Regency. Jurnal Litbang, 2021; 17(2): 131-146.
17. Zeng JH, Wu WB, Qu JX, Wang Y, Dong CF, *et al.* Cardiac manifestations of COVID-19 in Shenzhen, China. Infection, 2020; 48(6): 861-870.
18. Antinori S, Cossu MV, Ridolfo AL, Rech R, Bonazzetti C, *et al.* Compassionate remdesivir treatment of severe COVID-19 pneumonia in Intensive Care Unit (ICU) and non-ICU patients: Clinical outcome and differences in post-treatment hospitalisation status. Pharmacological Research, 2020; 158: 104899.
19. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y. Epidemiological and clinical characteristics of 99 cases of 2019 novel Coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet, 2020; 395(10223): 507-513.
20. Gowda SB, Gosavi S, Rao AA, Shastry S. Prognosis of COVID-19?: Red cell distribution width, platelet distribution width, and C-reactive protein. Cureus, 2021; 13(2): e13078.
21. Melnikov IS, Kozlov SG, Saburova OS, Avtaeva NY, Prokofieva LV, Gabbasov ZA. Current position on the role of monomeric C-reactive protein in vascular pathology and atherothrombosis. Current Pharmaceutical Design, 2020; 1-7.