

The Diagnostic Value of Platelet Count and MPV in Suspected COVID-19 Patient at Dr. Saiful Anwar Hospital

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ABSTRACT

COVID-19 is a disease caused by SARS-CoV-2. Hematology alterations like lymphopenia are common, but study on platelet remains limited. The incidence of thrombocytopenia in COVID-19 patients is 5-53.6%. This study aimed to analyze the diagnostic value of platelet count and MPV in COVID-19. A study with a cross-sectional design took place at Dr. Saiful Anwar Hospital between March and June 2020. Data were collected at first admission. SARS-CoV-2 gene detection with the RT-PCR method was used in this study as a confirmatory test. A total of 115 patients suspected of COVID-19 were involved at the end of the study with 69 positive and 46 negative results. AUROC for platelet was 0.336 (CI: 95%, 0.238–0.435, $p=0.01$); MPV was 0.488 (CI 95%, 0.378–0.598, $p=0.762$). Platelet count and MPV did not have good diagnostic values for COVID-19. This might be due to different conditions that the patient might have at admission. Thrombocytopenia and increased MPV are often caused by the hyperinflammatory condition and severe infection as mentioned in another study. Platelet count and MPV alone can't be used to diagnose COVID-19. Coincide use of another marker such as inflammatory markers might be useful. Future studies with larger samples and serial testing may be needed to further evaluate the diagnostic value of platelet count and MPV.

Keywords: COVID-19, platelet, MPV

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is a disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). This disease was first discovered when a viral pneumonia outbreak happened in Wuhan, China in December 2019. At first, the cause of the disease was unknown, until later on 7th January 2020, the virus was identified as SARS-CoV-2.^{1,2}

COVID-19 is a very contagious disease transmitted via droplets. The symptoms are various, ranging from asymptomatic to severe pneumonia with the need for mechanical ventilation. Fevers, dry cough, and increased work of breathing are the most common symptoms of COVID-19. Consolidation and ground-glass opacities can be found in radiologic tests.^{1,2}

Viral infection has some correlation with hematology parameters changes. Lymphopenia is the most common change found in COVID-19. Increased ferritin, D-dimer, Lactate Dehydrogenase (LDH), and C-Reactive Protein (CRP) seems to be a common finding in a patient with severe infection.¹

Thrombocytopenia is thought to be related to inflammation and its degree is often related to

disease severity and mortality. Incidence of thrombocytopenia in COVID-19 ranges between 5 and 53.6%.² Application of platelet count and its index such as Mean Platelet Volume (MPV) in diagnosing COVID-19 has not been well established. Based on that, this study aimed to analyze the diagnostic value of platelet count and MPV in a patient with suspected COVID-19.

METHODS

This cross-sectional design study took place at Dr. Saiful Anwar Hospital between March and June 2020 and used platelet count and MPV data obtained from the patients with suspected COVID-19 infection that was admitted to the emergency care unit. Patient status was determined by the clinician on duty. Platelet count and MPV were measured at the Central Laboratory of Dr. Saiful Anwar Hospital using the Sysmex XN-1000 series. COVID-19 diagnosis was confirmed by detection of the SARS-CoV-2 gene from naso-and oropharyngeal samples using Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) method. Platelet count and MPV results in this study between confirmed COVID-19 and non-COVID-19 subjects were compared.

Furthermore, the 2 X 2 table was used to determine the sensitivity, specificity, predictive value, and accuracy of the collected data. The receiver operating characteristic curve was also used to determine the Area Under Curve (AUC).

This study was approved by the Ethics Committee for Health Studies Dr. Saiful Anwar Hospital, Malang with the number 400/011/K 3/302/2021.

RESULTS AND DISCUSSION

A total of 115 patient data with suspected COVID-19 was collected at the end of the data collection period, and 69 were confirmed positive and 46 were confirmed negative (Table 1).

Table 1. Demographic data of the confirmed positive patient

		n	%
Gender	Female	29	42.03%
	Male	40	57.97%
	Total	69	100%
Age	20-30 y.o	6	8.70%
	31-40 y.o	9	13.04%
	41-50 y.o	13	18.84%
	> 50 y.o	41	59.42%
	Total	69	100%
Comorbid (n=62)	Diabetes mellitus	16	
	Hypertension	19	
	Heart failure	18	
	Coronary artery disease	2	
	Other	7	
	> 2 Comorbid	21	

The age of confirmed positive population in this study ranged from 22 to 79 years old, with 41 subjects (59.42%) over 50 years old. Twenty-nine subjects (42.03%) of the total population were females and 40 subjects (57.97%) were males. In addition, this study found 62 subjects with comorbid disease. Sixteen people suffered from diabetes and 11 of them had other concurrent diseases such as heart failure and hypertension.

Table 2. Performance of platelet count and MPV for COVID-19 diagnosis

		COVID-19 Diagnosis Based on RT PCR Test Result		Total
		Positive	Negative	
Platelet count	< 150,000/μL	11	1	12
	≥ 150,000/μL	58	45	103
Total		69	46	115
MPV value	>10.5 fl	19	15	34
	≤ 10.5 fl	50	31	81
Total		69	46	115

Table 2 shows the performance of platelet count and MPV in the diagnosis of COVID-19. This study found that sensitivity, specificity, positive predictive value, and negative predictive value for platelet count were 15.94%, 97.82%, 91.67%, and 43.69% respectively. Accuracy of 48.69% was also determined in Table 2. In addition, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for MPV was 27.93%, 67.39%, 55.88%, 38.27%, and 43.48%, respectively. By using Levene's test, platelet count and MPV were found homogenous (p>0.05). It was found that there was a significant difference in platelet count (p=0.01) but no significant difference in MPV between the COVID-19 and non-COVID-19 groups (p=0.762).

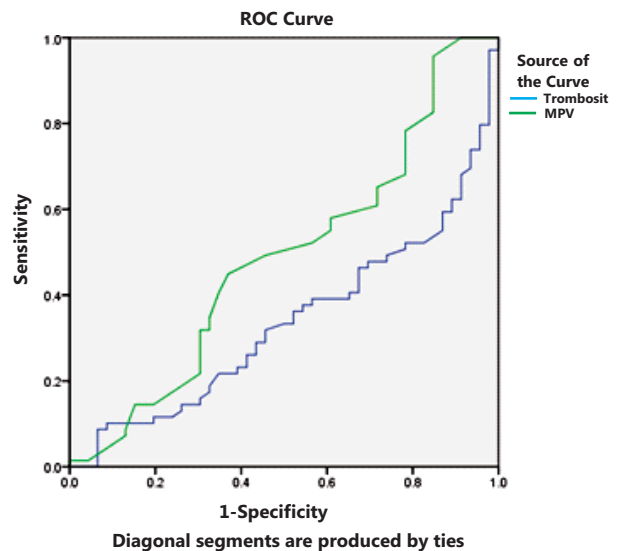


Figure 1. ROC of platelet count and MPV

The ROC analysis for the platelet count and MPV (Figure 1) shows the Area Under ROC (AUROC) of 0.336 for the platelet count and 0.488 for the MPV (Table 3).

Table 3. AUROC value of platelet count and MPV

Test Result Variable(s)	AUC	Std.Error	Asymptotic Sig.	Asymptotic 95% CI	
				Lower Bound	Upper Bound
Platelet count	.336	.050	.003	.238	.435
MPV	.488	.056	.056	.378	.598

Changes in hematological parameters are very common in COVID-19 patients. Lymphopenia is one of the main findings and is often associated with more severe infections as noted in one study conducted by Fan *et al.*^{3,4}

This study obtained a mean value of 250.800 for platelet counts in the group of patients who were confirmed positive ($p=0.05$). This figure was still within the normal platelet range of 150.000-400.000/ μ L. This was consistent with studies conducted in China. Thrombocytopenia is not always found in COVID-19 patients. A study conducted in Wuhan at the start of the pandemic showed that only 5% of COVID-19 patients had thrombocytopenia when they were admitted to the hospital. However, serial platelet examinations performed in several studies have shown that 5-41.7% incidence of thrombocytopenia was found in patients with severe infections.^{3,5}

A decreased platelet count accompanied by a decreased leukocytes and neutrophils count can indicate COVID-19 infection. However, there are limitations that different cut-offs of platelet counts were found between the positive and negative groups. For example, in a study conducted by Usul *et al.*, a cut-off value of 211.000/ μ L was obtained in patients who were confirmed positive. This result was still within the normal range of platelet counts. Thrombocytopenia followed by a decreased leukocytes and neutrophils count might be caused by COVID-19 with pneumonia.⁶

Cytokine storms are one of the causes of thrombocytopenia in COVID-19 patients. Dysregulation of the immune system causes hyperinflammatory conditions in which excessive production of cytokines such as IFN can suppress the expression of transcription factors involved in megakaryopoiesis. Damage to lung endothelial cells can also trigger platelet activation, increasing platelet consumption leading to thrombocytopenia.⁵

Hyperinflammation due to the overproduction of cytokines is often associated with high morbidity and mortality rates in COVID-19 patients. The natural immune response as a front line of defense against viral infection under normal conditions may become

uncontrolled, especially in severe infections. An in-vitro study on patients with COVID-19 showed that cytokines and chemokines were largely produced by respiratory epithelial cells, dendritic cells, and macrophages during the early stages of the disease. This was followed by increased production of proinflammatory cytokines such as Interleukin (IL)-1 β , IL-6, Tumour Necrosis Factor (TNF)- α , and antiviral factor interferon (IFN) along with disease progression.⁷

The inflammation that occurs also causes a decreased production of thrombopoietin (TPO). The binding between SARS-CoV-2 and the ACE2 receptor in the liver can affect the hepatic function and reduce the production of TPO. Proinflammatory cytokines such as IL -1 β and TNF- α can also affect the function of ACE2 on the cell surface.⁵ These findings results showed that the platelet count has a poor diagnostic value, similar to the finding in a study conducted by Khartabil *et al.* This study found that several severely symptomatic patients had lower platelet counts on admission, but there were also severely symptomatic patients with normal platelet counts. It was reported that a decreased number of new platelets was found when serial examinations were carried out during hospitalization and there was a significant difference in the group with worsening symptoms and the group with improvement. Several drugs such as enoxaparin, azithromycin, and hydroxychloroquine, which are used in the treatment of COVID-19 also have side effects of thrombocytopenia.⁸

This study found no significant relationship between the increase in MPV values and the positive confirmed group. This was similar to a study conducted by Aktas *et al.*⁹

Mean platelet volume correlates with platelet activation; an increase in MPV can indicate inflammatory and prothrombotic conditions.⁹ The serial MPV examination in one of the studies demonstrated the usefulness of MPV for predicting mortality in COVID-19 patients. An increase in the MPV value by 1 fl between the first and third days increased the mortality 1.76 times. This was thought to occur because the inflammatory process that

continues to be triggered by high viral replication has contributed to the increase in proinflammatory cytokines.⁸

Analysis of eleven study groups of COVID-19 patients conducted by Khartabil *et al.* found that there might be an increase in MPV that accompanies thrombocytopenia. This was thought due to an increase in the number of young platelets in response to the body's response to the increased platelet consumption.¹⁰ A decrease in the number of platelets will trigger the production of platelets by the bone marrow; therefore, the lower platelet count will lead to a higher response to produce platelets, which causes an increase in MPV as one of the platelet indexes.⁸

The MPV is one of the newer indices of inflammatory markers. The high and low MPV values can be influenced by tumors, diabetes, coronary heart disease, and connective tissue disease.¹¹ Studies on the clinical value of MPV in COVID-19 patients with various types of comorbid are still being conducted.

Diabetes Mellitus (DM) is comorbid that is often found in COVID-19 patients and is associated with increased mortality. Patients with DM have a prothrombotic tendency and increased platelet activity. Several studies have shown significantly higher MPV values in patients with DM.¹¹

The diagnostic value of platelet count and MPV was not good enough in this study. This might be because data were only collected when the patient was admitted for the first time and no retrieval of serial data. Patients in this study also had multiple and comorbid conditions that could affect platelet counts and MPV. The difference in cut-offs obtained in each study also needs to be considered. In addition, simultaneous analysis of both parameters also did not yield good results. This might be caused by many factors that influence these two parameters and the inability to rule it out in this study.

CONCLUSIONS AND SUGGESTIONS

Platelet count and MPV have poor diagnostic values for COVID-19 patients; with AUC, sensitivity, specificity of 0.336, 15.94%, 97.82% for platelet count and AUC, sensitivity, specificity of 0.488, 27.93%, and 67.39% for MPV. Based on the data, both parameters

can't be used alone for supporting the diagnosis of COVID-19. Coincidence use of another marker such as inflammatory markers might be useful.

Future studies with larger sample sizes and serial examinations are needed to further evaluate the diagnostic value of platelet count and MPV. In addition, comorbidities and the therapy given to patients must be considered in the interpretation of platelet counts and MPV in COVID-19 patients.

REFERENCES

1. Ragab D, Salah Eldin H, Taeimah M, Khattab R, Salem R. The COVID-19 cytokine storm; What we know so far?. *Front Immunol*, 2020; 11:1446.
2. Cheung CKM, Law MF, Lui GCY, Wong SH, Wong RSM. Coronavirus Disease 2019 (COVID-19): A haematologist's perspective. *Acta Haematol*, 2020; 1-14.
3. Xu P, Zhou Q, Xu J. Mechanism of thrombocytopenia in COVID-19 patients. *Ann Hematol*, 2020; 99(6): 1205-8.
4. Fan BE, Chong VCL, Chan SSW, Lim GH, Lim KGE, *et al.* Hematologic parameters in patients with COVID-19 infection. *Am J Hematol* [Internet]. 2020. Available from: <https://onlinelibrary.wiley.com/doi/abs/10.1002/ajh.25774> (accessed Oct 3, 2020).
5. Zhang Y, Zeng X, Jiao Y, Li Z, Liu Q, *et al.* Mechanisms involved in the development of thrombocytopenia in patients with COVID-19. *Thromb Res*, 2020; 193: 110-5.
6. Usul E, Şan İ, Bekgöz B, Şahin A. The role of hematological parameters in COVID-19 patients in the emergency room. *Biomark Med*, 2020; bmm-2020-0317.
7. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the 'cytokine storm' in COVID-19. *J Infect*, 2020; 80(6): 607-13.
8. Güçlü E, Kocayigit H, Okan HD, Erkorkmaz U, Yürümez Y, *et al.* Effect of COVID-19 on platelet count and its indices. *Rev Assoc Médica Bras*, 2020; 66(8): 1122-7.
9. Aktas A. Is mean platelet volume useful for predicting the prognosis of COVID-19 diagnosed patients?. *Int J Res Stud Med Health Sci*, 2020; 5(7): 8-11.
10. Khartabil TA, Russcher H, van der Ven A, de Rijke YB. A summary of the diagnostic and prognostic value of hemocytometry markers in COVID-19 patients. *Crit Rev Clin Lab Sci*, 2020; 57(6): 415-31.
11. Ozder A. A novel indicator predicts 2019 novel Coronavirus infection in subjects with diabetes. *Diabetes Res Clin Pract*, 2020; 166: 108294.