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## Diagnostic accuracy of mean platelet volume in cirrhotic patients with spontaneous bacterial peritonitis presented to the emergency department

### Abstract

**Background:** The aim of this study was to investigate the diagnostic accuracy of mean platelet volume (MPV) in predicting SBP in cirrhotic patients.

**Methods:** This was an observational, analytical, and retrospective study conducted on cirrhotic patients with abdominal ascites referred to the emergency department (ED) over a 1-year period. The cirrhotic patients with ascites were divided into two groups with or without SBP. The diagnostic accuracy of MPV for detecting SBP was measured and compared with the analysis of the ascites fluid obtained by paracentesis as a gold standard procedure in the absence of any secondary causes of peritonitis. The required data were documented in a checklist.

**Results:** A total of 252 patients, 126 with SBP and 126 without SBP, were included in the study. The mean MPV in these patients was  $8.36 \pm 0.92$  fL. Patients with SBP had a significantly longer duration of cirrhosis, more severe fever and abdominal pain, and higher ascites WBC and PMN counts and higher mean MPV ( $p < 0.001$ ). At the most appropriate cut-off point (i.e., 8.3 fL), MPV provided the sensitivity, specificity, positive predictive value, negative predictive value, and the diagnostic accuracy of 69.84%, 53.97%, 60.27%, 64.15%, and 61.90%, respectively, for the diagnosis of SBP. The receiver operating characteristic (ROC) curve showed that MPV had an acceptable diagnostic accuracy (AUC = 0.677).

**Conclusion:** Mean platelet volume, as a non-invasive, simple, and accessible laboratory parameter, with acceptable diagnostic accuracy in cirrhotic patients with ascites may have a predictive role in the diagnosis of SBP.

**Keywords:** Ascites, Cirrhosis, Mean platelet volume, Spontaneous bacterial peritonitis.

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Approximately 10% to 25% of patients with ascites develop spontaneous bacterial peritonitis (SBP), increasing the in-hospital mortality of these patients to up to 20% (1-3). These patients typically present with fever and abdominal pain; however, these clinical presentations are not adequate diagnostic criteria for SBP. Moreover, it is noteworthy that some patients with SBP do not present with fever and abdominal pain and sometimes are even asymptomatic, in which case SBP may be diagnosed incidentally. Therefore, the diagnosis of SBP cannot be ruled out in asymptomatic patients (4, 5). The diagnosis of SBP is established by analyzing the peritoneal fluid obtained through paracentesis, and the most accurate predictor of SBP is a white blood cell (WBC) count greater than 500 cells/ $\mu$ L of ascitic fluid, with the sensitivity and specificity of 86% and 98%, respectively. When polymorphonuclear (PMN) count in the ascites fluid exceeds 250 cells/ $\mu$ L, the diagnostic sensitivity increases to 93%, while the specificity decreases to 94%. These two thresholds are currently the accepted cut-off points required for the diagnosis of SBP and starting empirical antibiotic therapy (6).



Platelets can be activated in inflammatory and infectious conditions, leading to an increase in the number of their granules, followed by an increase in platelet size and surface area. Consequently, the activation of platelets and an increase in their size leads to an increase in mean platelet volume (MPV). Therefore, MPV is considered a potential predictor of inflammatory and infectious conditions in patients. Several studies have delineated the correlation of MPV with inflammatory status and acute infections (7, 8). In addition, MPV has been suggested as a possible predictor of the severity of infection and even response to treatment (9). This simple laboratory parameter can be obtained by a complete blood count (CBC), requiring a minimally invasive procedure (i.e., venipuncture), and may be able to predict SBP, an inflammatory and infectious condition, in cirrhotic patients presenting with ascites. The present study aimed to investigate the diagnostic accuracy of MPV in predicting SBP in cirrhotic patients who present with ascites referred to the emergency department.

## Methods

This is an observational, analytical, retrospective study on cirrhotic patients who had abdominal ascites and were referred to the emergency department of Afzalipour Hospital, an academic referral center for internal diseases in the southeast of Iran, Kerman City, during a 1-year period from March 2022 to March 2023.

**Ethics:** This study was approved by the Ethics Committee of Kerman University of Medical Sciences under the ethics code of IR.KMU.AH.REC.1402.090. The data collection checklist included the ID of patients' files but not their names to ensure confidentiality. Also, the collected data remained confidential with the researchers and were used only for research purposes. The authors were committed to report their results with utmost honesty, accuracy, and integrity.

**Study participants:** Cirrhotic patients presenting with abdominal ascites referred to the emergency department who met our eligibility criteria as follows were enrolled:

### Inclusion criteria:

- Patients aged <18 years.
- Patients with confirmed prior diagnosis of cirrhosis based on clinical, laboratory, and ultrasound findings presenting with ascites.
- Patients should have undergone ascites fluid paracentesis in the emergency department
- Patients had complete data related to the analysis of the ascites fluid, CBC and MPV in their clinical records.

### Exclusion criteria:

- Patients aged <18 years.
- Patients with abdominal ascites secondary to other diseases (e.g., hemorrhagic ascites, pancreatitis-related ascites, lymphatic chain defects, etc.).
- Patients with secondary bacterial peritonitis caused by acute intra-abdominal infections.
- Patients with sepsis, chronic lung disease, diabetes, hypertension, heart failure, anemia, deep vein thrombosis, pulmonary embolism, malignancies, pregnancy, rheumatic disorders.
- Patients with incomplete clinical records for the main outcome variables.

**Data retrieval:** The required data were collected using an information collection checklist, including demographic information (age and sex), clinical data (symptoms on admission, such as fever, abdominal pain, hepatic encephalopathy, and gastrointestinal bleeding, as well as the duration of cirrhosis, the presence or absence of SBP based on ascites fluid analysis), and MPV, which was determined by reviewing CBC results obtained within the shortest interval after ascites fluid paracentesis. All CBC results were obtained from the reports of the central laboratory of the Afzalipour Hospital using a Sysmex KX-21N autoanalyzer to homogenize for any possible source of bias and laboratory error.

**Definitions:** The gold standard diagnosis of SBP was established by the analysis of the ascites fluid obtained by paracentesis and the presence of at least 500 WBC/ $\mu$ L in this fluid, including at least 250 cells/ $\mu$ L of PMNs, regardless of the result of ascites fluid culture and in the absence of secondary causes of peritonitis, including tuberculosis-related peritonitis and hemorrhagic ascites (5, 6).

**Outcome measurement:** Cirrhotic patients were divided into two groups, with and without SBP. The diagnostic accuracy of MPV for the detection of SBP was then investigated using appropriate statistical models.

**Sample size calculation:** For sample size calculation, we used the PASS statistical software Version 2023 according to the findings of Osman (10), who conducted ROC curve analysis and estimated the AUC value between 0.643 and 0.798 for the diagnostic accuracy of SBP based on ascitic fluid paracentesis. Therefore, the minimum sample size required to determine the diagnostic accuracy of MPV, considering >0.8 as the power threshold, was determined to be  $n = 252$  (126 subjects per group).

**Data curation and analysis:** The data collected were analyzed using SPSS Version 27 software. To describe the data, descriptive statistics such as frequency, relative frequency, mean, and standard deviation were utilized. A  $p$ -value of <0.05 was considered statistically significant. The

diagnostic accuracy of MPV for SBP was perused by receiver operating characteristic (ROC) curve analysis. The Youden index was used to designate the optimum cut-off value, according to which sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

## Results

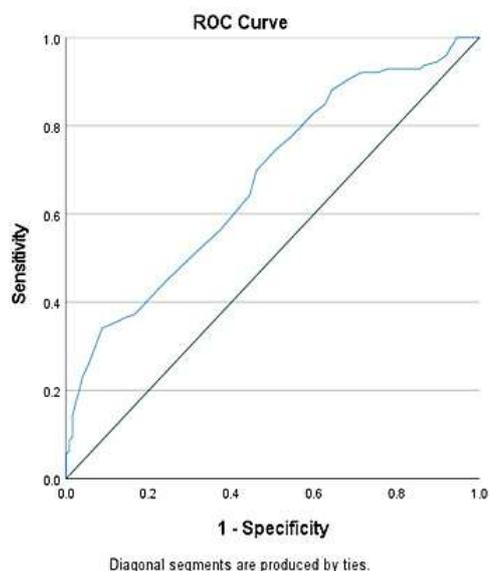
A total of 252 patients with liver cirrhosis-associated ascites (126 patients with SBP and 126 patients without SBP) were analyzed. The mean age of the patients was  $59.77 \pm 12.25$  years, and most of them were men (58.73%). The average time since the diagnosis of cirrhosis in these patients was  $2.96 \pm 1.19$  years. At the time of admission, most patients were feverless (55.16%), had no abdominal pain (59.52%), hepatic encephalopathy (81.75%), and gastrointestinal bleeding (84.92%). The average counts of WBC and PMN in the ascites fluid were  $793.59 \pm 622.91$  and  $471.62 \pm 391.66$ , respectively. The mean MPV in our patients was  $8.36 \pm 0.92$  fL (table 1).

Our results revealed that cirrhotic patients with and without SBP were comparable in terms of age ( $P=0.68$ ) and

gender ( $P=0.60$ ); however, the mean duration of cirrhosis was significantly longer in patients with SBP ( $p<0.001$ ). In terms of clinical symptoms, the frequencies of encephalopathy ( $P=0.51$ ) and gastrointestinal bleeding ( $p=0.48$ ) were not significantly different between patients with and without SBP.

However, patients diagnosed with SBP had significantly higher rates of fever and abdominal pain ( $p<0.001$ ), as well as higher WBC and PMN counts in the ascites fluid ( $p<0.001$ ). Also, mean MPV was significantly higher in cirrhotic patients with SBP than their peers without SBP ( $p<0.001$ ) (table 2). Evaluation of the diagnostic accuracy of MPV for SBP showed that this biomarker had acceptable diagnostic accuracy, evidenced by ROC analysis (AUC = 0.677) (figure 1).

The sensitivity, specificity, PPV, NPV, and diagnostic accuracy of MPV were finally calculated at different cut-off values. The most suitable MPV cut-off point for separating cirrhotic patients with SBP from patients without SBP was found to be 8.3 fL, delivering the sensitivity, specificity, PPV, and NPV of 69.84%, 53.97%, 60.27%, and 64.15%, respectively. Also, at this cut-off value, MPV offered a diagnostic accuracy of 61.90% (table 3).



**Figure 1. ROC curve for prediction of SBP by MPV; Area Under Curve (AUC): 0.677**

**Table 1. Baseline characteristics of cirrhotic patients with ascites**

Variables	N=252
Age (year), Mean±SD	59.77±12.25
Sex, n (%)	
Men	148 (58.73%)
Women	104 (41.27%)
Duration of cirrhosis (year), Mean±SD	2.96±1.19

Variables	N=252
<b>Fever, n (%)</b>	
Yes	113 (44.84%)
No	139 (55.16%)
<b>Abdominal pain, n (%)</b>	
Yes	102 (40.48%)
No	150 (59.52%)
<b>Encephalopathy, n (%)</b>	
Yes	46 (18.25%)
No	206 (81.75%)
<b>GI Bleeding, n (%)</b>	
Yes	38 (15.08%)
No	214 (84.92%)
<b>WBC<sup>1</sup> in ascites fluid, Mean±SD</b>	793.59±622.91
<b>PMN<sup>2</sup> in ascites fluid, Mean±SD</b>	471.62±391.66
<b>MPV<sup>3</sup>, Mean±SD</b>	8.36±0.92

White Blood Cell<sup>1</sup>, Polymorphonuclear leukocytes<sup>2</sup>, Mean Platelet Volume<sup>3</sup>

**Table 2. Comparing demographics and clinical features between SBP and non-SBP groups**

Variables	SBP <sup>1</sup> Group	Non-SBP Group	p-value
<b>Age (year), Mean±SD</b>	60.08±11.62	59.45±12.89	0.68
<b>Sex, n (%)</b>			
Men	72 (57.14%)	76 (60.32%)	0.60
Women	54 (42.86%)	50 (39.68%)	
<b>Duration of cirrhosis (year), Mean±SD</b>	3.56±1.14	2.37±0.91	<0.001
<b>Fever, n (%)</b>			
Yes	108 (85.71%)	5 (3.97%)	<0.001
No	18 (14.29%)	121 (96.03%)	
<b>Abdominal pain, n (%)</b>			
Yes	89 (70.63%)	13 (10.32%)	<0.001
No	37 (29.37%)	113 (89.68%)	
<b>Encephalopathy, n (%)</b>			
Yes	25 (19.84%)	21 (16.67%)	0.51
No	101 (80.16%)	105 (83.33%)	
<b>GI Bleeding, n (%)</b>			
Yes	21 (16.67%)	17 (13.49%)	0.48
No	105 (83.33%)	109 (86.15%)	
<b>WBC<sup>2</sup> in ascites fluid, Mean±SD</b>	1329.92±437.99	257.25±85.96	<0.001
<b>PMN<sup>3</sup> in ascites fluid, Mean±SD</b>	822.56±239.08	120.67±50.73	<0.001
<b>MPV<sup>4</sup>, Mean±SD</b>	8.66±0.89	8.06±0.86	<0.001

Spontaneous Bacterial Peritonitis<sup>1</sup>, White Blood Cell<sup>2</sup>, Polymorphonuclear leukocytes<sup>3</sup>, Mean Platelet Volume<sup>4</sup>

**Table 3. Diagnostic Tests of MPV1 in cirrhotic patients with SBP2 in different cut-off**

Cut-off (fL)	Sensitivity% (95%CI)	Specificity% (95%CI)	PPV <sup>3%</sup> (95%CI)	NPV <sup>4%</sup> (95%CI)	Accuracy% (95%CI)
8.3	69.84 (61.34-77.17)	53.97 (45.28-62.42)	60.27 (52.17-67.85)	64.15 (54.67-72.64)	61.90 (55.77-67.68)
8.4	64.29 (55.61-72.12)	55.56 (46.84-63.94)	59.12 (50.75-67)	60.87 (51.74-69.3)	59.92 (53.76-65.78)
8.5	56.35 (47.63-64.69)	62.70 (54-70.65)	60.17 (51.15-68.55)	58.96 (50.49-66.92)	59.52 (53.36-65.40)
8.6	51.59 (42.94-60.14)	68.25 (59.69-75.74)	61.90 (52.35-70.62)	58.50 (50.42-66.15)	59.92 (53.76-65.78)
8.7	44.44 (36.06-53.16)	76.19 (68.05-82.78)	65.12 (54.59-74.35)	57.83 (50.23-65.08)	60.32 (54.17-66.16)
8.8	39.68 (31.57-48.41)	80.95 (73.22-86.85)	67.57 (56.27-77.14)	57.30 (49.96-64.34)	60.32 (54.17-66.16)

Mean Platelet Volume<sup>1</sup>, Spontaneous Bacterial Peritonitis<sup>2</sup>, Positive predictive value<sup>3</sup>, Negative predictive value<sup>4</sup>

## Discussion

This study's findings disclosed that even though cirrhotic patients with or without SBP were comparable in terms of liver failure complications such as hepatic encephalopathy and gastrointestinal bleeding, those with SBP have significantly higher rates of fever and abdominal pain. Additionally, patients suffering from SBP exhibit significantly elevated WBC and PMN counts in their ascites fluid compared to their counterparts without SBP. Moreover, patients with SBP had a higher mean MPV than those without SBP. MPV demonstrated acceptable diagnostic accuracy (>60%) in distinguishing these groups at a cut-off of 8.3 fL, but its performance was less optimal compared to the gold standard method.

Although SBP is not a fatal complication in cirrhotic patients with ascites if they receive proper treatment, timely detection of this condition is crucial to prevent sepsis development. Direct analysis of the ascites fluid provides the most accurate diagnosis, but this procedure carries potential risks including abdominal visceral perforation, hematoma, infection, and intense pain. Thus, paracentesis-associated complications can be prevented if an alternative, less invasive diagnostic test with comparable accuracy is introduced (11). Various studies have reported the association between MPV and inflammatory conditions, acute infection, and even sepsis (7-9). In a study by Suvak *et al.*, the role of MPV as an indicator of systemic inflammation was investigated in 135 cirrhotic patients with ascites fluid infections, reporting significantly increased MPV values in cirrhotic patients with concomitant ascites

fluid infection compared to healthy individuals, as well as their counterparts without ascites fluid infection. In this study, ROC curve analysis showed that at the cut-off point of 8.45 fL, MPV delivered the sensitivity, specificity, NPV, and PPV of 70.7%, 67.5%, 75.4%, and 62.1%, respectively, for detecting ascites fluid infection in cirrhotic patients, with an AUC of 0.768 and diagnostic accuracy of 68.8% for SBP (12). Gálvez-Martínez investigated the role of MPV as a novel predictor of systemic inflammatory response in cirrhotic patients with culture-negative neutrocytic ascites. The findings of the recent study have shown that out of 51 patients diagnosed with ascites fluid infection, 48 (94.1%) patients had culture-negative neutrocytic ascites; 2 (3.9%) patients were diagnosed with bacterial ascites, and one (2%) patient had SBP. Also, WBC and PMN counts in the ascites fluid and MPV were found to be suitable predictors for ascites fluid infections in cirrhotic patients, and at the cut-off point of > 0.8 fL under ROC curve analysis, MPV was able to best separate cirrhotic patients with ascites fluid infections from those without infection with the sensitivity, specificity, PPV, and NPV of 84%, 82%, 83%, and 84%, respectively, and diagnostic accuracy of 83% (13). In another study, Abdelmoez Amal evaluated 198 patients and reported that MPV had diagnostic accuracy of 79.3% for detecting SBP in cirrhotic patients, delivering the sensitivity, specificity, PPV, and NPV of 73%, 85.7%, 75.7%, and 83.9%, respectively, at the cut-off point of 8.4 fL, with an AUC of 0.84 (14). In their study, Khorshed enrolled 41 patients to investigate the predictive value of MPV in identifying SBP and found that at the threshold of

>8.3 fL, this index offered the sensitivity, specificity, PPV, NPV, diagnostic accuracy, and AUC of 85.7%, 75%, 78.3%, 83.3% 80.5%, and 0.87, respectively (15). In a pilot study on 40 cirrhotic patients, Khalil *et al.* declared that MPV at the threshold of 8.4 fL had the sensitivity, specificity, PPV, and NPV of 73%, 85.7%, 83.9%, and 75.7%, respectively, for the diagnosis of SBP, with AUC = 0.84 (16). Rafi *et al.* studied 180 patients and identified that 8.3 fL was the optimal cut-off of MPV for predicting SBP in patients with hepatitis C infection developing cirrhosis, at which the sensitivity, specificity, PPV, NPV, and diagnostic accuracy were obtained as 75.1%, 55.8%, 84.4%, 41.3%, and 70.5%, respectively (17). Lashin also examined the predictive role of MPV in the diagnosis of SBP in cirrhotic patients and declared the sensitivity, specificity, PPV, and NPV 68.75%, 80%, 54.8%, and 87%, respectively, at the cut-off point of 8.71 fL (18). In a similar study, Abdel-Razik studied 150 patients and observed the significant increase in MPV along with a significant increase in CRP, PDW, and WBC in cirrhotic patients with ascites fluid infection compared to their peers without infection, as well as healthy individuals. In the recent report and at the cut-off point of 8.77 fL, MPV delivered sensitivity and specificity of 95.9% and 91.7%, respectively, for the diagnosis of ascites fluid infection with an AUC of 0.964 (19). In their study, Abudeif announced that MPV had a diagnostic accuracy of 62% for detecting SBP, as well as sensitivity, specificity, PPV, NPV, and AUC of 62%, 63%, 47%, 75%, and 0.678, respectively, at the threshold of 8.8 fL (20). In accordance, Huynh Cao *et al.* introduced MPV as a non-invasive diagnostic biomarker for detecting SBP in cirrhotic patients, with the sensitivity, specificity, PPV, NPV, and AUC of 84%, 82%, 83%, 84%, and 0.9, respectively (21). In another investigation on 106 patients with decompensated viral hepatitis-associated cirrhosis suffering from SBP, Hamed *et al.* stated that patients with SBP had significantly higher values of MPV, the neutrophil to lymphocyte ratio, platelet distribution width (PDW), and the platelet to lymphocyte ratio compared to patients without SBP and healthy controls (22).

As shown in several studies, MPV with a cut-off value of 8.3 fL seems to provide a reasonable diagnostic accuracy for the detection of SBP and ascites infections in cirrhotic patients. Consistent with this, our results showed that MPV was significantly higher in cirrhotic patients with SBP than in those without SBP, and MPV values above 8.3 fL could predict this condition with a diagnostic accuracy of > 60%, a finding consistent with the results of previous studies (12-17). This observation was consistent with the results of previous studies. However, some studies have argued that

although the incidence of these comorbidities may be similar in patients with and without SBP, their presence confers a significantly poorer prognosis for these patients compared with cirrhotic patients without this complication. Therefore, it is prudent to screen at-risk cirrhotic patients for other possible comorbidities in addition to SBP to initiate appropriate treatment and resolve these complications as soon as possible to help patients survive longer (23, 24).

Among the limitations of the present study are being conducted as a single-center retrospective experiment, not examining patients during their hospitalization, the lack of following-up with the patients, and not assessing the prognostic value of MPV in terms of response to treatment. Mean platelet volume provides an inexpensive, easily accessible biomarker with clinically plausible diagnostic accuracy for identifying spontaneous bacterial peritonitis (SBP) in patients with cirrhosis. This parameter shows potential as a predictor of SBP and an alternative complementary test for prompt diagnosis of SBP in liver cirrhosis patients.

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**Authors' contribution:** Study concept, design and supervision: N.NB, M.T, A.F, M.M; acquisition of data: A.F; analysis and interpretation of data: M.M, MT; drafting of the manuscript, technical and material support: N.NB, M.T., M.M.

**Availability of data and materials:** The anonymous data which form the basis for this study are available from the authors on reasonable request.

**Informed consent:** The requirement for individual patient consent was waived by the Clinical Research Ethics Committee due to the retrospective and anonymous nature of the study.

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