The Role of Mean Platelet Volume in the Diagnosis of Spontaneous Bacterial Peritonitis: A Cross Sectional Study

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Background and study aim: Spontaneous bacterial peritonitis is a serious condition that needs rapid diagnosis and rapid management due to its serious sequelae. SBP is diagnosed when the polymorpho-nuclear cells count in the ascetic fluid exceeds 250 cell/µL. Mean platelet volume (MPV) was found to be significantly larger in the cirrhotic patients with ascetic fluid infection than cirrhotic patients without ascetic fluid infection. In our study we aimed to assess the role and clinical performance of MPV as a diagnostic marker of SBP.

Patients and Methods: This cross sectional study was performed on 124 cirrhotic patients with ascites. They were classified into two groups according to ascetic fluid PMN count into two groups. Group I: 38 patients with ascetic fluid infection, PMN >250 cell/µL and group II: 86 patients without ascetic fluid infection, PMN count <250 cells/µL.

Results: The MPV was significantly higher among patients with ascetic fluid infection (11.1±1.2 vs 9.4±1.1 p<0.001). Blotting the ROC curve, MPV was proved to diagnose SBP at a cut off value of 10.45 fL with sensitivity and specificity of 74.4% and 78.9% respectively.

Conclusion: MPV is a useful diagnostic marker that can predict the presence of SBP in cirrhotic patients with ascites.

INTRODUCTION

Spontaneous bacterial peritonitis (SBP) is acute monomicrobial bacterial infection of the ascetic fluid without any identifiable source of infection. It is a common complication of cirrhosis and ascites. It is the most frequent and serious infection in patients with liver cirrhosis, with a frequency of 10-30% out of all reported bacterial infections in cirrhotic patients **[1,2]**. It is diagnosed when the polymorophonuclear cells count in the ascetic fluid rises above 250 cell/µL **[2]**. SBP has a serious impact on the patient's condition and survival **[3]**.

Circulating platelets are a source of prothrombotic and hemostatic agents which also play a role in the initiation and generation of vascular and inflammatory disease. Platelets size mostly depends on the degree of fragmentation of mega-karyocytes. IL6, an inflammatory mediator, plays a role in the fragmentation of platelets and thrombopoiesis. Platelets with increased size have a greater content of granules and can therefore exert their hemostatic and pro-inflammatory actions with greater efficiency. For this reason mean platelet volume (MPV) is proposed to be an indicator of platelet function and activation **[4,5]**.

MPV, which is measured by full blood count analyzers as part of the complete blood count, has been studied as a simple inflammatory marker in several diseases. Some studies have reported that MPV increases in myocardial infarction, congestive heart failure and cerebrovascular diseas and decreases in active rheumatologic diseases including rheumatoid arthritis (RA), ankylosing spondylitis and ulcerative colitis. These studies suggest that the size of platelets is affected by systemic inflammatory response **[6,7]**.

The previous studies of the platelet size in patients with cirrhosis suggest that the MPV increases in patients with cirrhosis. The studies also suggest that the MPV increases more in cirrhotic patients with infections especially SBP and that it is affected by the severity of the systemic inflammatory response syndrome (SIRS) associated with these infections. MPV can be the earliest laboratory tests that can provide a rapid

diagnostic tool for AFI even before you perform ascetic fluid sampling and examination **[8]**.

Aim of the work:
This study aims at investigating the role and clinical performance of MPV as a predictor of spontaneous bacterial peritonitis.

PATIENTS AND METHODS

This cross-sectional study was carried out in Tropical Medicine Department, Zagazig University hospitals. In the period between march 2015 And december 2017. The study included; Patients with liver cirrhosis diagnosed by combination of clinical, sonographic and laboratory data admitted to hospital with ascites with or without evidence of ascitic fluid infection. One hundred and twenty four patients were included in this study.

The exclusion of patients from the study was done according to the following criteria; patients <18 years of age, patients who did not give informed consent to participate in the study, evidence of other ongoing bacterial infection such as chest and urinary tract infections, patients received antibiotics within the last 2 weeks, evidence of secondary peritonitis, patients received anti-platelet and/or anticoagulant therapy for cardiovascular diseases, evidence of intra or extrahepatic malignancy and evidence of other non-infectious inflammatory conditions like rheumatoid artheritis, ankylosing spondylitis and or auto immune diseases.

All study patients underwent: Complete history taking, through clinical examination and the following laboratory investigations; complete blood count, MPV determination was performed using the Coulter Counter (Coulter Electronics, Hialeah, FL). Normal level of MPV is 7.5 to 9.5 fl. **[9]** kidney function tests (creatinine, blood urea nitrogen), liver function tests (Serum Albumin - Serum Bilirubin - Alanine Transaminase - Aspartate Aminotransferase), coagulation profile (prothrombin time and INR), complete ascetic fluid analysis to diagnose asetic fluid infection and exclude other causes of ascites including the following: cytological; different types of cells, exclusion of malignant aascites, total and differential leucocytic count, biochemical: total protien, albumin, SAAG, glucose, LDH and bacteriological: gram stained smear, ascitic fluid cultures. Abdominal ultrasound was performed to all patients in the study.

According to the ascetic fluid analysis patients were divided according to the polymorphnuclear cells count in the ascetic fluid into two groups patients with PMN count >250 cells/µL without any source of infection are diagnosed with spontaneous bacterial peritonitis according to what was stated by international ascites club **[1, 10]**: Group I: eighty six patients with spontaneous bacterial peritonitis (PMN>250 cells/µL) and Group II: thirty eight patients with uncomplicated ascites (PMN<250 cells/µL)

The rate of spontaneous ascetic fluid infection (spontaneous bacterial peritonitis) among patients admitted to the hospital with cirrhosis and ascites was claculted.

The diagnostic accuracy of mean platelet count and its clinical performance as dignostic marker for ascitic fluid infection was tested against complete ascitic fluid analysis as gold standred for diagnosis of ascitic fluid infection.

Statistical analysis:
Statistical analysis was performed using SPSS version 20. According to the type of data, qualitative data were represented as number and percentage, quantitative data were represented as mean ± SD, the following tests were used to test differences for significance; difference and association of qualitative variable by Chi square test (X2) and quantitative variables in two independent groups by t test, analysis of ROC curve was done to detect AUROC, the cut off value sensitivity and specificity.

RESULTS

The rate of spontaneous ascetic fluid infection (spontaneous bacterial peritonitis) among patients with ascites admitted to the hospital in this study is 69.3%. The demographic clinical and sonographic data were summerized in table 1. Among all clinical data only fever and abdominal pain were significantly more evident among patients with SBP (65.1% and 90.7% vs 10.5 and 36.8% successively P<0.001). The laboratory data are summerized in table 2. The WBC's in blood were significantly higher among patients with SBP (6.9±3.9 vs 4.7±2.3 P=0.02). The creatinine level was significantly higher among patients with SBP (1.1±0.34 vs 1.0±0.28 P=0.027). In ascetic fluid analysis, TLC and PMN count in ascetic fluid which are the key for diagnosis were significantly higher in group I (827.2±892.3 and 495.11±135 vs 288.8±93.8 and 205.78±70.21 P<0.001). It was also worth noticing that total protein was

significantly lower in group I (1.3±0.3 vs 1.7±0.7 P=0.005). The LDH which is a marker for tissue destruction was also significantly higher in group I (146.6±80.2 vs 103.6±30.5 P=0.009) this is represented in table 2. Table 3 represents the clinical performance of the MPV as diagnostic marker of SBP. On plotting the ROC curve seen in Figure (1) it shows that at the cut off value of 10.45 fL MPV can predict the presence of SBP with sensitivity of 74.4% and 78.9%.

Table (1): Comparison between the studied groups as regards demographic, clinical and sonographic data

		Group I N=86	Group II N=38	X^2	P
Age (years)		58.8±8.1	58.3±8.3	T=0.3	0.7(NS)
Gender	**Male**	42(48.8%)	16(42.1%)	0.48	0.4(NS)
	Female	44(52.2%)	22(57.9%)		
Chronic illness	**Diabetes**	36(41.9%)	20(2.6%)	1.23	0.26(NS)
	Hypertension	9(10.4%)	3(7.8%)	0.52	0.46 NS
Viral markers	**HCV**	84(97.7%)	38(100%)	0.89	0.34(NS)
	HBV	4(4.7%)	0(0%)	1.82	0.17(NS)
Bilharziaisis		40(46.5%)	16(42.1%)	0.18	0.66(NS)
Fever		56(65.1%)	4(10.5%)	31.44	0.001(HS)
Abdominal pain		78(90.7%)	14(36.8%)	39.92	0.001(HS)
Grade of ascites	**Moderate**	56(65.1%)	26**(68.4%)**	0.12	0.72(NS)
	Tense	30(34.9%)	12(31.6%)		
Gastroenteritis		20(23.3%)	8 (21.1%)	0.11	0.69(NS)
Encephalopathy		20(23.3%)	4 (10.5%)	2.07	0.09(NS)
PV diameter (cm)		1.4±0.17	1.5±0.13	**T=-1.6**	**0.08(NS)**
Spleen diameter (cm)		15.6±1.67	16.1±1.7	**T=-1.8**	**0.06(NS)**

PV, portal vein ; X^2 chi-square; T, student test; NS, non-significant

Table (2): Comparison between the studied groups as regards laboratory parameters and ascetic fluid analysis

	Group I N=86	Group II N=38	Test	P
Hemoglobin (g/dl)	10.5±1.6	9.9±1.2	**T= 1.021**	0.21 (NS)
WBC's (x10^{3}cells/µL)	6.9±3.9	4.7±2.3	Z= 2.2	0.02 (S)
Platelet (x10^{3}cells/µL)	118.4±55.3	111.9±72.1	Z= 0.9	0.33 (NS)
Mean platelet volume(fL)	11.1±1.2	9.4±1.1	7.214	0.001(HS)
Total bilirubin (mg/dl)	2±1.4	2.2±2	Z= 0.12	0.9 (NS)
Direct bilirubin (mg/dl)	1.2±1	1.3±1.2	Z= 0.3	0.9 (NS)
Serum albumin (g/dl)	2.3±0.5	2.4±0.3	T= -1.603	0.112 (NS)
ALT (IU/L)	29.4±14.7	28.8±12.9	Z=-1.9	0.8(NS)
AST(IU/L)	58.1±71.8	55.3±50.1	Z=0.4	0.7(NS)
INR	1.3±0.33	1.2±0.3	T=1.913	0.058(NS)
Creatinine (mg/dl)	1.1±0.34	1.0±0.28	T=2.2	0.027(S)
Ascetic fluid analysis				
Total leucocytic count (cell/µL)	827.2±892.3	288.8±93.8	Z=5.85	<0.001(HS)
PMN count (cell/µL)	495.11±135	205.78±70.21	Z=6.13	<0.001(HS)
Total protein (gm/dl)	1.3±0.3	1.7±0.7	T= -2.860	0.005(S)
Glucose (mg/dl)	125.6±36.1	131.7±35.8	T= -0.867	0.388(NS)
LDH (IU/L)	146.6±80.2	103.6±30.5	Z=2.6	0.009(S)
SAAG(g/dl)	2.3±1.7	1.4±0.18	Z=1.6	0.09(NS)

WBC's: white blood cells, ALT: alanine transaminase, AST: aspartate transaminase, INR: international normalizing ratio, PMN: polymorphonuclear count, LDH: lactate dehydrogenase, SAAG: serum-asites albumin gradient. NS: non-significant, S: significant, HS: highly significant.

Table (3): The clinical performance of MPV as a predictor to ascetic fluid infection

AUROC	0.838
Cut off value	10.45 fL
Sensitivity	74.4%
Specificity	78.9%
PPV	88.8%
NPV	57.6%
Accuracy	75.8%
P value	<0.001

PPV: positive predictive value, NPP: negative predictive value

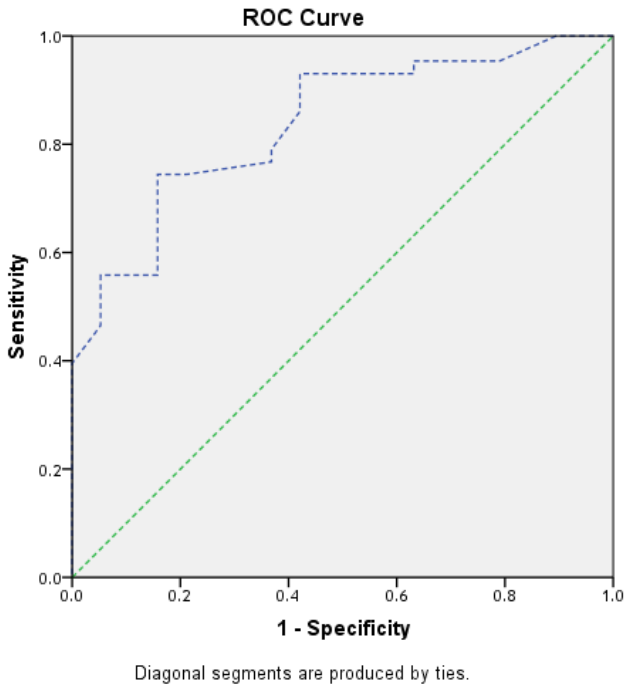

Figure1: ROC curve representing the clinical performance of MPV as predictor of SBP.

DISCUSSION

This study aims at evaluating the role of MPV as an inflammatory marker in the diagnosis of SBP, being an easy readily available marker and faster to obtain than ascetic fluid PMN count. This cross sectional study was performed on 124 patients admitted to the in patients ward with portal hypertension associated ascites, with exclusion of other infections and malignancy and patients admitted to ICU. This is done to exclude all other conditions, other than AFI, that can change the MPV.

Among the patients in our study, SBP patients were 86 that represents about 70% of all cases. This is a higher percentage than expected, this percentage is not a representation of the incidence of SPB among those patients but it can be considered the frequency of SPB being a cause of hospital admission in those patients. In other words, after exclusion of other infections, inflammations and malignancy, ascetic fluid infection is the cause of about 70% of hepatic patient admissions to the hospital ward. This disagress with Rimola et al. **[10]** who said that ascetic fluid infection represent almost 30% of infections encountered in hepatic patients, in our study we excluded other infections and this can explain why the percentage of SBP in the sample was doubled. From this finding we can say that

in any patient admitted to the hospital with liver cirrhosis and ascites the exclusion of ascetic fluid infection is a priority in management.

Among all clinical presenting signs fever and abdominal pain were most intimately related to AFI than others. This finding agrees with Riggio and Angeloni **[11]** who said that fever is present in 80% of patients with SBP and abdominal pain is present in 70% of them. WBCs count in peripheral blood showed to be significantly higher among patients with SBP than cirrhotic patients without SBP, this agrees with Gálvez-Martinez et al. **[8]** who said that WBC's count can be a good predictor of the presence of AFI in cirrhotic patients (AUROC >0.80). This also agrees with Lashin et al. **[12]** and Suvak et al. **[13]**. Our finding doesn't agree with Abdelmoez et al. **[14]** and Abdel-Razik et al. **[15]** who reported that WBC's count may not increase significantly in the cases of AFI. It is also worth saying that the platelet count was not significantly different between the two groups of patients and this is also agreed with by most of the previous literature. The protein content of ascetic fluid was significantly lower in SBP group, this indicates that the opsonic capacity of ascetic fluid is low which is considered a risk factor of ascetic fluid infection **[3]**.

This study shows that MPV is significantly higher in patients with liver cirrhosis with SBP compared to cirrhotic patients without SBP and these results were in agreement with Suvak et al. **[13]** who stated that MPV is significantly elevated in cirrhotic patients with SBP. Abdel-Razik et al. **[15]** also recorded a significant increase in MPV levels in cirrhotic patients with AFI. Abdelmoez et al. **[14]** also said that a significant elevation was noted in MPV in the SBP group as compared to the non-SBP group. This finding agrees also with Lashin et al. **[12]** and Gálvez-Martínez et al. **[8]**.

It was also worth noticing that creatinine serum level appears to be significantly higher among patients with SBP. This finding is very important, because it gives us an idea about the serious nature of the condition and that these patients are at risk of renal impairment and hepatorenal syndrome and justifies the need for use of volume expanders like human salt free albumin during the period of treatment, hand in hand with antibiotic therapy. This finding agrees with Abdel-Razik et al. **[15]** and Lashin et al. **[12]**. This finding also agrees with Riggio and Angeloni **[11]** who said that the new onset renal failure can often be the presenting manifestation of SBP.

In our study receiver operator characteristic (ROC) curve analysis suggested that the optimum MPV level cut-off points for cirrhotic patients with SBP was 10.45 fL, with a sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) of 74.4%, 78.9%, 88.8% and 57.6%, respectively (area under curve: 0.83). In the previous studies, the cutoff values of MPV ranged from 8.3fl to 8.7fl. The sensitivity ranged from 68 to 95% and specificity ranged from 67 to 91%. Also, negative predictive value (NPV) range was (75-97%) And positive predictive value ranges was (54-83%). Also acuracy ranges between (68-79%). The results of our studies fall in the ranges of the previous studies. The only disagreement was in the cut off value in our study it is significantly higher than that stated by most of the previous studies this difference may be attributed to the type of liver disease in our study as the majority of patients with chronic hepatitis were due to viral hepatitis C in contrast to alcoholic liver cirrhosis in their study. The exclusion criteria in our study were meant to get more focused approach to SBP and excluded other infection and this may have also manipulated our results **[8,12-15]**.

CONCLUSION

MPV is significantly elevated in cirrhotic patients with SBP. The estimation of MPV in cirrhotic patients with ascites can be a useful diagnostic marker that can predict the presence of SBP in cirrhotic patients with ascites.

Ethical consideration: the study design was approved by the IRB of Faculty of Medicine, Zagazig University.

Fund: none

Conflict of interset: none

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