

The role of mean platelet volume in predicting severity and prognosis of liver cirrhosis in Egyptian patients

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Background and aims

Liver cirrhosis is a major public health problem in Egypt due to widespread infection of hepatitis C virus. Mean platelet volume (MPV) is a noninvasive, inexpensive parameter of complete blood count. In this study we aimed at evaluating the association between MPV and clinical features, complications, and severity of cirrhosis in Egyptian patients.

Patients and methods

One hundred and fourteen patients with cirrhosis of various grades of severity and various presentations were enrolled in our study. The patients were evaluated to assess the association between MPV values and cirrhosis parameters, model for end-stage liver disease score, and fibrosis (FIB4) score.

Results

The study demonstrates the positive correlation between MPV values and international normalized ratio, serum bilirubin, lower serum albumin in cirrhotic patients. Also, the MPV values were significantly higher in patients with more severe liver disease according to the model for end-stage liver disease ($r=+0.424$, $P=0.008$) and FIB4 scores ($r=+0.353$, $P=0.03$).

Conclusion

MPV can be used as an important inexpensive biomarker in cirrhotic patients for the degree of severity and prognosis of the disease.

Keywords:

cirrhosis, liver function parameters, mean platelet volume, model for end-stage liver disease score

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Introduction

Chronic liver disease secondary to liver cirrhosis from chronic hepatitis C virus infection is a leading cause of morbidity and mortality and a major public health problem in Egypt. Although thrombocytopenia is one of the most common hematological disorders in patients with liver cirrhosis, both quantitative and qualitative platelets defects are frequently noted in patients with chronic liver disease [1].

In patients with end-stage liver disease thrombocytopenia can be used as a part of noninvasive tests for the assessment of portal hypertension, and as a prognostic parameter for liver status. Also, those patients have alterations in platelet morphology which may have clinical value in the diagnostic assessment of their disease severity [2].

Mean platelet volume (MPV) is a marker that reflects platelet activation and function. MPV values were increased in patients with nonalcoholic fatty liver disease, intrahepatic cholestasis of pregnancy, chronic hepatitis, and liver cirrhosis [3].

Recently, MPV and MPV/platelet count ratio were proposed as markers for the diagnosis of HCC in patients with chronic liver disease [4].

MPV was associated with greater fibrosis histological scores and necro-inflammatory activity, especially in patients with chronic hepatitis B virus infection and primary biliary cirrhosis. Moreover, MPV was an independent, very short-term (i.e. 4 weeks) prognostic indicator in patients with hepatitis B virus-related acute-on-chronic liver failure [5].

In cirrhotic patients, increased MPV was noted in patients with spontaneous bacterial peritonitis, emphasizing the role of MPV as a possible marker of inflammation. However, there are not enough data on the possible association between either clinical features or prognosis of cirrhotic patients and MPV [6].

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In this study, we aimed at evaluating the association between MPV and clinical features, complications, and severity of cirrhosis in Egyptian patients.

Patients and methods

This study was carried out in the Internal Medicine Department and the outpatient clinic of Zagazig University Hospitals. One hundred and fourteen patients with cirrhosis of various grades of severity and various presentations were enrolled in the study. Written informed consent was obtained from each patient or first-degree relative. Liver cirrhosis was diagnosed on the basis of instrumental findings (ultrasonographic, endoscopic) and clinical findings (shrunken liver, splenomegaly, variceal bleeding, presence of ascites, and/or hepatic encephalopathy). The patients were grouped according to the Child–Pugh score with Child-A patients have compensated cirrhosis while Child-B and Child-C patients had decompensated cirrhosis. All patients were evaluated according to the age, sex, smoking status, history of encephalopathy, history of bleeding varices, ultrasonographic findings, presence of diabetes mellitus, hypertension, ascites, splenomegaly, international normalized ratio (INR), MPV, platelet count, serum total bilirubin, albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, FIB4, model for end-stage liver disease (MELD) and Child scores. We evaluated the association of MPV values with the disease clinical features, complications, and severity according to Child, the MELD score, and FIB4 scores. Blood samples were taken by venipuncture and platelet counts and MPV were measured using EDTA blood in Advia 2120 (Siemens Healthcare Diagnostics Inc., Tarrytown, New York, USA) within 2 h of blood withdrawal. Normal values for MPV were 7.1–11.5 femtoliter.

Model for end-stage liver disease score

The MELD score was calculated using an online calculator (<https://www.mayoclinic.org/medical-professionals/model-end-stage-liver-disease/meld-model>).

FIB4 index was calculated using the following formula [7]:

$$\text{FIB} - 4 \text{ index} = \frac{\text{age}(\text{years}) \times \text{AST}(\text{IU/L}) / \text{Platelet count}(\times 10^9/\text{L})}{(\text{ALT}[\text{IU/L}])^{1/2}}$$

Statistical analysis

The collected data were computerized and statistically analyzed using the Statistical Package for the Social

Sciences program, version 20 (SPSS; SPSS Inc., Chicago, Illinois, USA). Qualitative data were represented as frequencies and relative percentages. χ^2 and Fisher's exact was used to calculate the difference between qualitative variables as indicated. Quantitative data were expressed as mean \pm SD for parametric and median and range for nonparametric data. One-way analysis of variance *F* test and Kruskal–Wallis test were used to calculate the difference between quantitative variables in more than two groups in normally normal and nonparametric variables, respectively. Pearson's and Spearman's correlation tests were used for correlating normal and nonparametric variables, respectively. The + sign was considered an indication for direct correlation, that is increased frequency of independent leads to increased frequency of dependent and – sign as indication for inverse correlation, that is increased frequency of independent leads to decreased frequency of dependent. Also we consider values close to 1 as strong correlation and values near 0 as weak correlation. The significance level for all the above-mentioned statistical tests was done with the threshold of significance fixed at 5% level (*P* value). A *P* value of more than 0.05 indicates nonsignificant results. A *P* value of less than or equal to 0.05 indicates significant results.

Results

One hundred fourteen patients with cirrhosis of various grades of severity and various presentations were recruited in the study, with a mean age of 55.3 \pm 12.9 years. The majority of them were men ($n=60$, 52.6%). Twenty-seven (22%) were compensated Child A, while Child B and Child C were 54 (47.3%) and 33 (28.9%), respectively. Of the patients 24% were smokers, while 76% were nonsmokers. Thirty-four percent of the patients were diabetics. Focal lesions were found as ultrasonographic finding in 8% of patients only. The other main demographic characteristics and clinical data of the study population are reported in Table 1.

Table 2 shows the positive correlation between MPV values and INR, serum bilirubin, lower serum albumin, and advanced age in cirrhotic patients. The study also demonstrated that MPV values were significantly higher in patients with more severe liver disease according to MELD ($r=0.424$, $P=0.008$) and FIB4 scores ($r=0.353$, $P=0.03$). No significant correlation could be established between MPVs and age, platelet count, ALT, AST, and creatinine level.

Table 1 Demographic data among Child classes of the studied patients

	Child class			Total (N=114)
	A (N=27)	B (N=54)	C (N=33)	
Age (years)	47.8±14.9	55.8±12.2	60.7±10.2	55.3±12.9
Sex				
Male	15 (55.60)	30 (55.60)	15 (45.50)	60 (52.60)
Female	12 (44.40)	24 (44.40)	18 (54.50)	54 (47.40)
Smoking				
Yes	6 (22.20)	12 (22.20)	9 (27.30)	27 (23.70)
No	21 (77.80)	42 (77.80)	24 (72.70)	87 (76.30)
History of HE				
Yes	0 (0.00)	15 (27.80)	30 (90.90)	45 (39.50)
No	27 (100.00)	39 (72.20)	3 (9.10)	69 (60.50)
History of bleeding OV				
Yes	0 (0.00)	30 (55.60)	27 (81.80)	57 (50.00)
No	27 (100.00)	24 (44.40)	6 (18.20)	57 (50.00)
DM				
Yes	9 (33.30)	15 (27.80)	15 (45.50)	39 (34.20)
No	18 (66.70)	39 (72.20)	18 (54.50)	75 (65.80)
HTN				
Yes	3 (11.10)	9 (16.70)	0 (0.00)	12 (10.50)
No	24 (88.90)	45 (83.30)	33 (100.00)	102 (89.50)
Ascites				
No	27 (100.00)	30 (55.60)	6 (18.20)	63 (55.30)
Ascites	0 (0.00)	24 (44.40)	27 (81.80)	51 (44.70)
Spleen				
Splenomegaly	3 (11.10)	24 (44.40)	21 (63.60)	48 (42.10)
Splenectomy	0 (0.00)	3 (5.60)	3 (9.10)	6 (5.30)
No	24 (88.90)	27 (50.00)	9 (27.30)	60 (52.60)
Focal lesion				
Single	0 (0.00)	3 (5.60)	3 (9.10)	6 (5.30)
Multiple	0 (0.00)	0 (0.00)	3 (9.10)	3 (2.60)
No	27 (100.00)	51 (94.40)	27 (81.80)	105 (92.10)

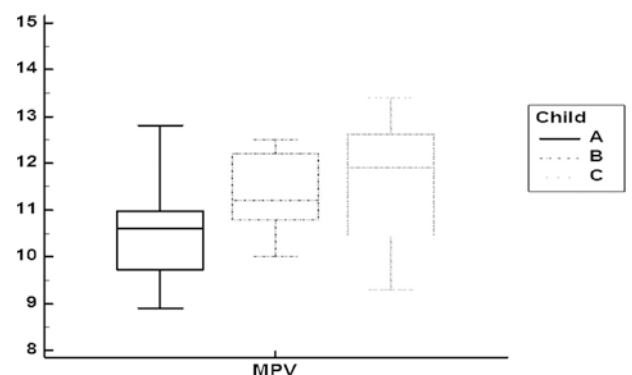
Data are expressed in mean and SD or absolute value and percentage. DM, diabetes mellitus; HE, hepatic encephalopathy; HTN, hypertension; OV, esophageal varices.

Table 2 Correlation between mean platelet volume and other variables

	MPV	
	<i>r</i>	<i>P</i>
Age (years)	+0.062	0.712
INR	+0.462	0.003
Platelet count	-0.319	0.051
Total Bilirubin	+0.433	0.007
Albumin	-0.449	0.005
ALT	+0.260	0.115
AST	+0.297	0.071
Creatinine	+0.189	0.256
FIB4	+0.353	0.030
MELD	+0.424	0.008
Child score	+0.361	0.026

ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; MELD, model for end-stage liver disease; MPV, mean platelet volume; *r*, correlation coefficient.

The study showed significant positive correlation between the MPVs and Child–Pugh scores (Figs 1 and 2), with the highest MPV values being observed in patients with Child C score.

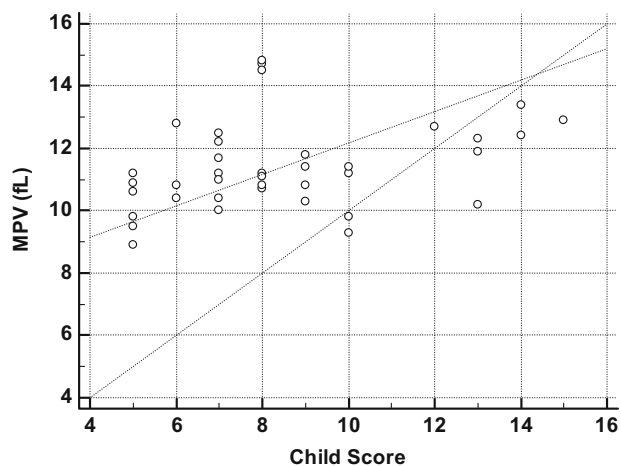
Figure 1

Box-plot diagram of MPV values of the patients in each child class, $p=0.026$.

Discussion

MPV as an index to platelet size and a parameter measured in routine blood counts demonstrates the average size of platelets and reflects the platelet

Figure 2



Correlation analysis indicates significant correlation between (MPV) & Child score, $r=+.361$, $p=.026$.

generation rate and stimulation [8]. MPV is also a sign of inflammation and its severity. Because of splenic sequestration, the patients with chronic liver disease have a shorter lifespan of their platelets with an increase in bone marrow platelet production, increasing the number of young platelets in circulation [9].

The assessment of the degree of liver damage by noninvasive parameters as an alternative to liver biopsy, which is not preferred for both patients and doctors is an important area of research nowadays. Several indirect markers for the assessment of liver state exist today such as serum albumin, bilirubin ALT, AST, and platelet count [10].

In chronic liver disease patients, thrombocytopenia is used as a noninvasive diagnostic tool for the presence of portal hypertension, and as a prognostic parameter in patients with cirrhosis. Actually not only the change in platelets count can be observed in those patients, but also qualitative platelet defects with alteration in platelet morphology, which could be of clinical value in the assessment of those patients [11].

High MPV values have been associated with worse histological fibrosis stage in patients with chronic viral hepatitis and nonalcoholic fatty liver disease compared with controls due to the potential role of activated large platelets in microthrombi formation causing obliteration of both the portal vascular bed and intrahepatic vessels leading to parenchymal extinction and progression of liver disease [9]. On the basis of these findings, we deemed it of interest to assess whether elevated MPV values may be correlated with clinical features,

complications, and severity of cirrhosis in Egyptian patients.

The study demonstrated the positive correlation between MPV and the degree of hepatic decompensation with an increase in MPV values with the increase in values of Child–Pugh. Also, there was a significant positive correlation between Child score values in Child–C patients and MPV. These results support the potential role played by larger platelets in the liver harming conditions in cirrhotic patients and the role of MPV as a valuable indicator of systemic inflammation in those patients [5,6].

Even when we assessed the correlation between different features of decompensation and MPV values, we found that MPV values had positive correlation with the presence of high serum bilirubin, high INR, and low serum albumin. This is consistent with previous studies which reported that the increase in MPV is considered to be an independent predictor of degree of liver cirrhosis in patients with chronic hepatitis and that MPV could be a useful biomarker for both thrombosis and inflammation. Also the increased MPV could be a consequence of chronic portal microthrombosis with hepatoportal sclerosis that might be the implicit mechanism for the progression of fibrotic damage of the liver [9,12,13].

The FIB4 index was established initially for patients coinfecting with hepatitis C virus (HIV). It is stated to have a specificity of 97% and sensitivity of 70% for the differentiation of mild from advanced fibrosis according to the Ishak scoring system [5]. The study has clearly revealed that patients with higher FIB4 as a marker for advanced fibrosis have higher MPV values compared with those with lower FIB4. This result supports the possible role of interleukin-6 production secondary to the inflammatory process that may increase the circulating young platelets which are responsible for the increased MPV cirrhotic patients [14,15].

In the present study, significant positive correlations between MPV values and MELD scores were noted. MELD score is the most widely used score to determine organ allocation in liver transplantation, estimate relative disease severity, and predicts survival in patients (age 12+) with liver cirrhosis.

Although our study is the only one which investigated the possible relationship between MPV and liver cirrhosis in Egyptian patients to the best of our knowledge, the limitations of the study were that the study was conducted at a single center. Further

multicenter studies with a larger sample size should be carried out.

Conclusion

There is a significant positive correlation between MPV and the degree of hepatic decompensation and prognosis in cirrhotic patients. As MPV is inexpensive, noninvasive, and rapid, it may be used as an important predictor of the degree of severity of liver cirrhosis.

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Conflicts of interest

There are no conflicts of interest.

References

- Giannini EG, Marengo S, Fazio V, Pieri G, Savarino V, Picciotto A. Peripheral blood cytopaenia limiting initiation of treatment in chronic hepatitis C patients otherwise eligible for antiviral therapy. *Liver Int* 2012; 32:1113–1119.
- Witters P, Freson K, Verslype C, Peerlinck K, Hoylaerts M, Nevens F, *et al.* Blood platelet number and function in chronic liver disease and cirrhosis. *Aliment Pharmacol Ther* 2008; 27:1017–1029.
- Karagöz E, Tanoglu A. Prognostic role of mean platelet volume in patients with chronic hepatitis C. *Clin Res Hepatol Gastroenterol* 2014; 38:e113.
- Cho SY, Yang JJ, You E, Kim BH, Shim J, Lee HJ, *et al.* Mean platelet volume/platelet count ratio in hepatocellular carcinoma. *Platelets* 2013; 24:375–377.
- Han L, Han T, Nie C, Zhang Q, Cai J. Elevated mean platelet volume is associated with poor short-term outcomes in hepatitis B virus-related acute-on-chronic liver failure patients. *Clin Res Hepatol Gastroenterol* 2015; 39:331–339.
- Abdel-Razik A, Eldars W, Rizk E. Platelet indices and inflammatory markers as diagnostic predictors for ascitic fluid infection. *Eur J Gastroenterol Hepatol* 2014; 26:1342–1347.
- Vallet-Pichard A, Mallet V, Nalpas B, Verkarre V, Nalpas A, Dhalluin-Venier V, *et al.* FIB-4: an inexpensive and accurate marker of fibrosis in HCV infection. comparison with liver biopsy and fibrotest. *Hepatology* 2007; 46:32–36.
- Ceylan B, Mete B, Fincanci M, Aslan T, Akkoyunlu Y, Ozgunes N, *et al.* A new model using platelet indices to predict liver fibrosis in patients with chronic hepatitis B infection. *Wien Klin Wochenschr* 2013; 125:453–460.
- Gasparyan AY, Ayzazyan L, Mikhailidis DP, Kitis GD. Mean platelet volume: a link between thrombosis and inflammation. *Curr Pharm Des* 2011; 17:47–58.
- Purnak T, Olmez S, Torun S, Efe C, Sayilir A, Ozaslan E, *et al.* Mean platelet volume is increased in chronic hepatitis C patients with advanced fibrosis. *Clin Res Hepatol Gastroenterol* 2013; 37:41–46.
- Giannini EG, Moscatelli A, Brunacci M, Zentilin P, Savarino V. Prognostic role of mean platelet volume in patients with cirrhosis. *Dig Liver Dis* 2016; 48:409–413.
- Köksal AŞ, Köklü S, İbiş M, Balci M, Çiçek B, Saşmaz N, *et al.* Clinical features, serum interleukin-6, and interferon- γ levels of 34 turkish patients with hepatoportal sclerosis. *Dig Dis Sci* 2007; 52:3493–3498.
- Hessel G, Escanhoela CA, de Oliveira AD, De-Maria HK, Onishi E, Yamada RM, *et al.* Hepatoportal sclerosis associated with portal vein thrombosis in children: report of 3 cases. *Arq Gastroenterol* 1997; 34:121–125.
- Sterling RK, Lissen E, Clumeck N, Sola R, Correa MC, Montaner J, *et al.* Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. *Hepatology* 2006; 43:1317–1325.
- Ekiz F, Yüksel O, Koçak E, Yılmaz B, Altınbaş A, Çoban S, *et al.* Mean platelet volume as a fibrosis marker in patients with chronic hepatitis B. *J Clin Lab Anal* 2011; 25:162–165.