

Plateletcrit and Mean Platelet Volume in the Evaluation of Liver Cirrhosis and Nonalcoholic Fatty Liver Disease in Egyptian Patients

Abdel-Naser Abdel-Atty Gadallah^{1*}, Elsayed Ibrahim Elshayeb¹, Belal Abd El-Mohsen Montaser², Ghada Ahmed Abdel-Fattah Shaheen³, Ahmed Ezz El-Arab Abd El-Alim Mostafa¹

¹Department of Internal Medicine, Gastroenterology and Hepatology Unit, Menoufia University, Shebin Elkom, Menoufia Egypt

²Department of Clinical Pathology, Menoufia University, Shebin Elkom, Menoufia Egypt

³Department of Internal Medicine, Ahmed Maher Teaching Hospital, Ministry of Health, Cairo, Egypt

*Corresponding author:

Abdel-Naser Abdel-Atty Gadallah, M.D.
Menoufia, 32511, Egypt
E-mail: ahmed_naser2004@yahoo.com

ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) and cirrhosis represent significant global health concerns, often diagnosed through invasive methods like liver biopsy. Identifying non-invasive biomarkers for these conditions could greatly enhance early detection and management. **Objective:** To evaluate the relationship between Procalcitonin (PCT) and Mean Platelet Volume (MPV) levels and hepatic steatosis in patients with NAFLD and cirrhosis.

Methods: a case-control study included 133 participants divided into NAFLD patients, cirrhotic patients, and a healthy control group, recruited from Menoufia University hospital between April 2022 and May 2023. Demographic data, clinical parameters, and laboratory findings, including PCT and MPV levels, were collected and analyzed.

Results: Both NAFLD and cirrhotic patients exhibited significantly higher PCT levels compared to the control group, with PCT levels increasing in accordance with the degree of hepatic steatosis. MPV levels were also marginally elevated in patient groups versus controls. However, Platelet Distribution Width (PDW) levels did not correlate with hepatic steatosis severity. Additional findings indicated a higher prevalence of obesity, diabetes, and hypertension in the NAFLD and cirrhotic groups. Multivariate logistic regression analysis identified body mass index (BMI), waist circumference (WC), and several other factors as significant predictors of NAFLD and cirrhosis.

Conclusion: PCT and MPV levels are significantly associated with NAFLD and cirrhosis, suggesting their potential utility as non-invasive markers for detecting these liver conditions. However, further research is warranted to explore their diagnostic accuracy and clinical applicability.

Key words: non-alcoholic fatty liver disease, cirrhosis, procalcitonin, mean platelet volume, hepatic steatosis, biomarkers

Abbreviations:

MPV: mean platelet volume;
LC: Liver cirrhosis;
CLDs: chronic liver diseases;
NAFLD: Nonalcoholic fatty liver disease;
NASH: nonalcoholic steatohepatitis;
HCC: hepatocellular carcinoma;
HBV: hepatitis B virus;
HCV: hepatitis C virus;
PLT: platelet; PCT: platelet crit;
BMI: Body mass index;
AH: Arterial hypertension;
PDW: Platelet distribution width;
AST: Aspartate aminotransferase;
ALT: Alanine transaminase;
PT: Prothrombin time;
INR: International normalized ratio;
ALP: alkaline phosphatase;
GGT: Gamma-glutamyl transferase;
TAG: Triglycerides;
HDL: High-density lipoprotein;
LDL: low-density lipoprotein;
APRI: AST TO PLT Ratio Index;
FIB-4: Fibrosis 4;
ALC: Liver cirrhosis patients;
RBCs: red blood cells;
HGB: hemoglobin;
WBCs: white blood cells;
MELD: Model for End-Stage Liver Disease.

INTRODUCTION

Liver cirrhosis (LC) represents the advanced stage of various chronic liver diseases (CLDs) and poses a significant systemic health burden due to its wide array of potentially life-threatening complications. Often asymptomatic until disease decompensation occurs, LC is characterized by an irreversible fibrotic cascade within hepatocytes (1).

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Nonalcoholic fatty liver disease (NAFLD), encompassing a spectrum of liver conditions in individuals with minimal to no alcohol consumption, is typified by excessive fat accumulation within hepatocytes (1). Estimated to afflict approximately 25% of the general population, the true prevalence remains elusive due to the absence of highly specific and sensitive diagnostic modalities (2). NAFLD encompasses a spectrum of disorders ranging from simple steatosis to nonalcoholic steatohepatitis (NASH), the latter characterized by hepatic necro-inflammation and a propensity for rapid fibrotic progression, culminating in cirrhosis and hepatocellular carcinoma (HCC) (2). Often referred to as a "silent" liver disease, NAFLD can progress asymptotically in many cases, with only a minority developing NASH and subsequent liver damage (1). Symptoms of NASH may manifest after years of disease progression and can include profound fatigue, weakness, weight loss, jaundice, spider-like blood vessels on the skin, pruritus, and, in advanced cases, complications such as fluid retention, hemorrhage, muscle wasting, and cognitive impairment (3).

Ultimately, individuals with cirrhosis may progress to liver failure necessitating liver transplantation (3). The current gold standard for diagnosing NAFLD and liver cirrhosis is liver biopsy, despite its limitations including sampling variability, pathologist-dependent interpretation, and associated procedural risks such as bleeding and biliary tract injury (4). Advances in imaging modalities, including ultrasound and magnetic resonance elastography, have enhanced the non-invasive assessment of liver fibrosis, particularly in patients with LC secondary to hepatitis B and C viruses (HBV and HCV) (5).

Nevertheless, the quest for noninvasive biomarkers derived from blood samples remains paramount in hepatology. Platelet parameters, such as mean platelet volume (MPV) and platelet crit (PCT), have emerged as promising indicators of liver fibrosis (6). Our study endeavors to identify noninvasive, cost-effective markers for diagnosing and staging NAFLD and cirrhotic patients, obviating the need for liver biopsy, with a particular focus on platelet indices, namely plateletcrit and mean platelet volume.

MATERIAL AND METHODS

Study design and setting

This case-control study was conducted at the hepatology outpatient clinics, inpatient ward, and intensive care unit of Menoufia University Hospital over a period from April 2022 to May 2023. The study received

approval from the local ethical scientific committee of the Menoufia Faculty of Medicine (IRB protocol approval number: 11/2022INTM7), and all participants provided signed informed consent in accordance with the principles outlined in the Declaration of Helsinki and its subsequent amendments.

Patients

Participants were categorized into three groups: Group I comprised patients with various stages of non-alcoholic fatty liver disease (NAFLD), including steatosis, steatohepatitis, and fibrosis; Group II consisted of cirrhotic patients diagnosed based on clinical history, physical examination, and imaging studies such as ultrasound or upper endoscopy if available; and Group III served as apparently healthy controls recruited during routine check-ups.

Sample size

The sample size was determined using a statistical power analysis based on previous literature findings, indicating a minimum sample size of 126 participants to achieve 80% power and a 95% confidence level (7). Inclusion criteria encompassed individuals aged 18 to 65 years, both sexes, with BMI, weight, height, and waist circumference recorded. Exclusion criteria included significant alcohol consumption (>30 g/day for males, >20 g/day for females), hepatic encephalopathy, spontaneous bacterial peritonitis, gastrointestinal bleeding, viral hepatitis, and patient refusal.

Data collection

Demographic and clinical data, including age, sex, and complaints, were collected from medical records, along with family history of similar conditions. Anthropometric measurements, such as weight, height, BMI, and waist circumference, were obtained using standardized techniques. Blood samples were collected from each participant for complete blood count (CBC) analysis, including platelet indices (PLT, PCT, MPV, PDW), and serum was stored at -80°C for subsequent renal and liver function tests.

Statistical analysis

Statistical analyses were performed using Microsoft Excel 2019 and SPSS V.25 software. Descriptive statistics presented data as mean $\pm$ SD for quantitative variables and frequency with proportions for qualitative variables.

Analytical statistics included Chi-Squared (χ^2) test for qualitative variables, Mann-Whitney U test for non-normally distributed quantitative variables, one-way ANOVA (F) for normally distributed quantitative variables, and Kruskal-Wallis test (K) for non-normally distributed quantitative variables. Receiver operating characteristic (ROC) curves were constructed to evaluate diagnostic performance, with significance set at $p < 0.05$, $p < 0.01$, and $p < 0.001$ for various levels of statistical significance.

RESULTS

Demographic characteristics

There were no significant differences in age or sex distribution among the groups ($p > 0.05$). However, significant differences were observed in weight, height, BMI, waist circumference, and prevalence of comorbidities such as diabetes mellitus and hypertension

($p < 0.05$). Cirrhotic patients exhibited lower weight (68.27 ± 5.42 kg vs. 80.61 ± 7.29 kg), BMI (24.63 ± 2.88 kg/m² vs. 30.27 ± 3.40 kg/m²), and waist circumference (82.33 ± 9.61 cm vs. 89.78 ± 9.22 cm) compared to NAFLD patients. NAFLD patients had the highest BMI and waist circumference compared to both cirrhotic patients and controls (table 1).

Hematological parameters and platelet indices

Significant differences were noted in red blood cell count (RBC), hemoglobin (HGB), platelet count, plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW) among the groups ($p < 0.05$). Specifically, NAFLD patients exhibited higher RBC count (4.58 ± 0.70 vs. 3.93 ± 0.68 vs. $4.95 \pm 0.56 \times 10^6/\mu\text{L}$), HGB levels (11.11 ± 1.94 vs. 9.51 ± 1.12 vs. 11.97 ± 1.56 g/dL), platelet count (263.79 ± 92.14 vs.

Personal and clinical	NAFLD (n=76) No (%)	Cirrhosis (n=15) No (%)	Control (n=42) No (%)	Test of significance	p-value
Age (years) Mean $\pm$ SD	51.97 $\pm$ 9.18	54.20 $\pm$ 8.13	52.57 $\pm$ 9.23	F=0.34	0.735
Sex:				$\chi^2=0.98$	0.613
Male	40 (46.4)	8 (53.3)	26 (61.9)		
Female	36 (47.4)	7 (46.7)	16 (38.1)		
Weight (kg): Mean $\pm$ SD	80.61 $\pm$ 7.29	68.27 $\pm$ 5.42	70.86 $\pm$ 6.68	F=37.78	<0.001 P1=0.082 P2<0.001 P3<0.001
Height (cm): Mean $\pm$ SD	163.39 $\pm$ 6.92	165.93 $\pm$ 5.85	166.19 $\pm$ 9.37	F=2.06	0.131 P1=0.244 P2=0.061 P3=0.912
BMI (kg/m ²): Mean $\pm$ SD	30.27 $\pm$ 3.40	24.63 $\pm$ 2.88	25.62 $\pm$ 2.64	F=40.60	<0.001 P1<0.001 P2<0.001 P3=0.216
Waist circumference (cm): Mean $\pm$ SD	89.78 $\pm$ 9.22	82.33 $\pm$ 9.61	71.38 $\pm$ 16.69	F=31.0	<0.001 P1<0.001 P2<0.001 P3=0.294
Diabetes mellitus:				$\chi^2=10.07$	0.006
present	28 (36.8)	8 (53.3)	6 (14.3)		
absent	48 (63.2)	7 (46.7)	36 (85.7)		
Hypertension:				$\chi^2=15.77$	<0.001
present	18 (23.7)	9 (60.0)	0		
absent	58 (76.3)	6 (40.0)	42 (100.0)		
Examination:				$\chi^2=195.02$	<0.001
hepatomegaly	46 (60.5)	0	0		
ascites	0	1 (6.7)	0		
bilateral II edema	4 (7.8)	6 (40.0)	0		
combined	4 (7.8)	8 (53.3)	0		
NAD	22 (28.9)	0	42 (100.0)		

F: ANOVA test; P1: NAFLD group vs cirrhotic group; P2: NAFLD group vs control group; P3: Cirrhotic group vs control group
BMI: body mass index; NAD: no abnormality detected

Table 1 - Personal and anthropometric data clinical examination of the studied groups

163.87±43.06 vs. 282.71±85.10 $\times 10^3/\mu\text{L}$), and MPV (10.75±2.18 vs. 12.14±1.36 vs. 9.46±1.72 fL) compared to cirrhotic patients and controls. Conversely, cirrhotic patients demonstrated lower RBC count, HGB levels, platelet count, and MPV compared to NAFLD patients and controls. Notably, PCT levels were elevated in cirrhotic patients compared to both NAFLD patients and controls (0.26±0.06 vs. 0.23±0.12 vs. 0.14±0.06) (table 2).

Correlation between Plateletcrit (PCT) and Mean Platelet Volume (MPV) with Hematological and Serological Parameters in NAFLD and Cirrhotic Patients

In NAFLD patients, PCT levels showed a significant positive correlation with platelet count ($\rho = 0.36$, $p = 0.001$) and MPV ($\rho = 0.36$, $p = 0.001$). However, there were no significant correlations observed between PCT levels and red blood cell count, hemoglobin, white blood cell count, or platelet distribution width in NAFLD patients ($p > 0.05$). Similarly, in cirrhotic

patients, PCT levels did not correlate significantly with any of the hematological or serological parameters analyzed ($p > 0.05$) (table 3).

MPV showed a significant positive correlation with platelet distribution width ($\rho = 0.35$, $p = 0.002$). Conversely, in cirrhotic patients, MPV exhibited a significant positive correlation with platelet distribution width ($\rho = 0.72$, $p = 0.002$). No significant correlations were observed between MPV and red blood cell count, hemoglobin, white blood cell count, or platelet count in either NAFLD or cirrhotic patients ($p > 0.05$) (table 4).

Receiver Operator Characteristic (ROC) Curve Analysis for Prediction of NAFLD and Cirrhotic Patients

For PCT, the optimal cutoff point was 0.135%, with a sensitivity of 84% and a specificity of 52%, yielding an AUC of 0.748 (95% CI: 0.661-0.835, $p < 0.001$). Similarly, for MPV, the optimal cutoff point was 8.75 fL, with a sensitivity of 79% and a specificity of 33%, resulting in an AUC of 0.671 (95%

Hematological parameters	NAFLD (n=76) Mean±SD	Cirrhosis (n=15) Mean±SD	Control (n=42) Mean±SD	Test of significance	p-value
RBCs ($10^6/\mu\text{L}$)	4.58±0.70	3.93±0.68	4.95±0.56	F=13.82	<0.001 P1=0.001 P2=0.004 P3<0.001
HGB (g/dl)	11.11±1.94	9.51±1.12	11.97±1.56	F=11.12	<0.001 P1=0.002 P2=0.012 P3<0.001
WBCs ($10^9/\mu\text{L}$)	8.44±5.19	7.31±1.87	7.84±2.47	K=0.59	0.558 P1=0.345 P2=0.462 P3=0.676
Platelets ($10^3/\mu\text{L}$)	263.79±92.14	163.87±43.06	282.71±85.10	K=10.91	<0.001 P1<0.001 P2=0.254 P3<0.001
PCT (%)	0.23±0.12	0.26±0.06	0.14±0.06	K=12.62	<0.001 P1=0.371 P2<0.001 P3<0.001
MPV (fL)	10.75±2.18	12.14±1.36	9.46±1.72	F=11.63	<0.001 P1=0.013 P2=0.001 P3<0.001
PDW (fL)	13.22±4.03	14.27±2.13	12.39±2.57	F=1.78	0.172 P1=0.288 P2=0.212 P3=0.074

Table 2 - Hematological parameters and platelet indices in the studied groups

F: ANOVA test, K: Kruskal-Wallis test, RBCs: Red blood cells, HGB: Hemoglobin
WBCs: White blood cells, PCT: Platelet crit, MPV: Mean platelet volume, PDW: Platelet distribution width
P1: NAFLD group vs cirrhotic group P2: NAFLD group vs control group P3: Cirrhotic group vs control group

Table 3 - Correlation between PCT levels with hematological, serological parameters and liver size in NAFLD and cirrhotic patients

Indices of liver fibrosis	PCT levels (%)			
	NAFLD (n=76)		Cirrhosis (n=15)	
	rho	p-value	rho	p-value
RBCs (106/ μ L)	0.19	0.101	0.06	0.834
HGB (g/dl)	0.08	0.486	-0.10	0.724
WBCs (103/ μ L)	-0.05	0.682	0.03	0.914
Platelets (103/ μ L)	0.36	0.001	-0.10	0.735
MPV (fL)	0.36	0.001	-0.11	0.694
PDW (fL)	-0.18	0.130	-0.18	0.531

rho: Spearman' correlation coefficient; MPV: Mean platelet volume; PDW: Platelet distribution width.

Table 4 - Correlation between MPV with hematological, serological parameters and liver size in NAFLD and cirrhotic patients

Indices of liver fibrosis	MPV (fL)			
	NAFLD (n=76)		Cirrhosis (n=15)	
	rho	p-value	rho	p-value
RBCs (106/ μ L)	-0.16	0.165	-0.06	0.843
HGB (g/dl)	-0.01	0.970	0.01	0.990
WBCs (103/ μ L)	0.08	0.470	-0.18	0.510
Platelets (103/ μ L)	0.14	0.241	-0.32	0.243
PDW (fL)	0.35	0.002	0.72	0.002

MPV: mean platelet volume; PDW: platelet distribution width; TAG: triglycerides; INR: international normalized ratio; ALP: alkaline phosphatase.

CI: 0.573-0.769, $p = 0.002$). These results indicate moderate predictive ability for both PCT and MPV in identifying NAFLD patients (*table 5, fig. 1*).

For PCT, the optimal cutoff point was 0.185%, achieving a sensitivity of 100% and a specificity of 67%, with an excellent AUC of 0.905 (95% CI: 0.822-0.988, p

< 0.001). Similarly, for MPV, the optimal cutoff point was 10.60 fL, demonstrating a sensitivity of 87% and a specificity of 76%, resulting in an excellent AUC of 0.889 (95% CI: 0.807-0.971, $p < 0.001$). These findings suggest that both PCT and MPV exhibit excellent predictive ability for identifying cirrhotic patients (*table 6*).

Table 5 - Sensitivity, specificity, cutoff points and area under the curve of PCT and MPV for prediction of NAFLD patients

Variable	Cutoff point	Sensitivity	Specificity	AUC	P -value	95%CI (lower limit-upper limit)
PCT (%)	0.135	84%	52%	0.748	<0.001	0.661-0.835
MPV (fL)	8.75	79%	33%	0.671	0.002	0.573-0.769

AUC: Area under the curve

CI: Confidence interval

Table 6 - Sensitivity, specificity, cutoff points and area under the curve of PCT and MPV for prediction of cirrhotic patients

Variable	Cutoff point	Sensitivity	Specificity	AUC	P -value	95%CI (lower limit-upper limit)
PCT (%)	0.185	100%	67%	0.905	<0.001	0.822-0.988
MPV (fL)	10.60	87%	76%	0.889	<0.001	0.807-0.971

AUC: Area under the curve

CI: Confidence interval

AUC:-
0.90-1 = excellent (A) 0.80-0.90 = good (B) 0.70-0.80 = fair (C) 0.60-0.70 = poor (D)

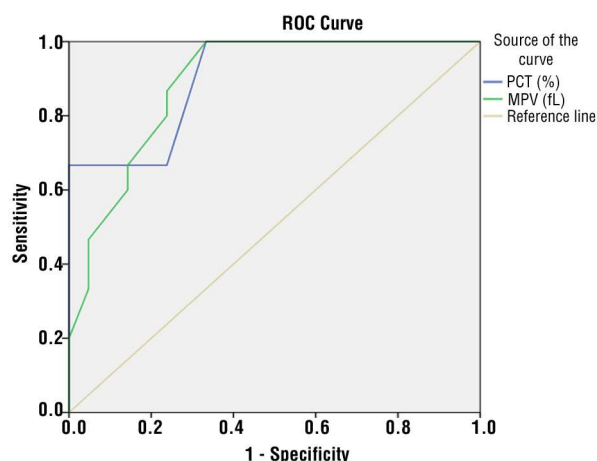


Figure 1 - Receiver Operator characteristic (ROC) curve of PCT and MPV for prediction of cirrhotic patients

DISCUSSION

This study aimed to investigate the relationship between platelet indices, specifically plateletcrit (PCT) and mean platelet volume (MPV), and hepatic steatosis in patients with nonalcoholic fatty liver disease (NAFLD) and cirrhosis. Our findings revealed that both NAFLD and cirrhotic patients exhibited significantly higher PCT levels compared to the healthy control group. Additionally, PCT levels were significantly associated with the degree of hepatic steatosis. However, while MPV levels were also elevated in NAFLD and cirrhotic patients compared to the control group, they did not correlate with the degree of hepatic steatosis. These results underscore the potential of PCT as a diagnostic marker for liver disease severity, particularly in NAFLD and cirrhotic patients.

Nonalcoholic fatty liver disease (NAFLD) represents a prevalent chronic liver condition globally and is a major contributor to chronic liver disease and cirrhosis. The reliance on liver biopsy for NAFLD staging poses several limitations, necessitating the exploration of alternative diagnostic tools. Our study reinforces the need for noninvasive diagnostic markers to accurately assess NAFLD severity and progression (8).

Consistent with previous literature, our study observed higher body mass index (BMI) and waist circumference (WC) in NAFLD patients compared to healthy controls. Obesity plays a significant role in the pathogenesis and severity of NAFLD, with increased BMI correlating with a higher prevalence of the disease (9, 10). Moreover, central obesity, as indicated by higher WC levels, has been linked to a greater risk of

NAFLD development compared to general obesity (11).

The association between NAFLD and comorbidities such as diabetes mellitus and hypertension was evident in our study, aligning with previous research demonstrating a higher prevalence of these conditions in NAFLD patients (10,12). These findings emphasize the importance of managing metabolic risk factors in NAFLD patients to mitigate disease progression and complications.

Regarding platelet indices, our study found significantly elevated PCT levels in both NAFLD and cirrhotic patients compared to controls. However, PCT levels were higher in cirrhotic patients than in NAFLD patients. Similarly, MPV levels were significantly higher in NAFLD and cirrhotic patients compared to controls. Previous studies have reported conflicting findings regarding the association between platelet indices and NAFLD severity. While some studies support the elevation of PCT and MPV in NAFLD patients (13-15) others have found no significant differences (16). The variations in study findings may stem from differences in patient populations, study designs, and laboratory methodologies.

In our study, PCT demonstrated fair diagnostic accuracy in predicting NAFLD, with a sensitivity of 84% and specificity of 52%, while MPV exhibited poor predictive value. These results are consistent with previous studies suggesting PCT as a potential marker for NAFLD diagnosis (17,18). In contrast, MPV showed limited utility as a predictive marker for NAFLD in our study, corroborating findings from previous research (16,13).

In the case of cirrhotic patients, PCT exhibited excellent diagnostic accuracy, with a sensitivity of 100% and specificity of 67%. However, MPV showed poor predictive value for cirrhosis. These findings highlight the potential of PCT as a robust diagnostic marker for cirrhosis, aligning with previous research suggesting its utility in detecting liver fibrosis (17). Conversely, MPV demonstrated limited diagnostic value for cirrhosis, emphasizing the need for further research to explore alternative markers.

CONCLUSION

This study underscores the potential of platelet indices, particularly PCT, as noninvasive markers for assessing liver disease severity in NAFLD and cirrhotic patients. The observed associations between PCT levels and hepatic steatosis warrant further investigation into its utility as a diagnostic tool in clinical practice. Future studies should aim to validate these

findings in larger cohorts and explore additional biomarkers to enhance diagnostic accuracy in liver disease.

Author's contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare no competing interests in this work.

Conflicts of interest and source of funding

No conflicts of Interest or funding source to declare.

Ethics approval and consent to participate

Our local Ethics Committee approved our study and a written consent for participation was obtained from all patients.

Human and animal rights

No animals were used for studies that are the basis of this research. All the humans were used in accordance with the Helsinki Declaration of 1975.

Data sharing statement

All data and materials included in this work are available.

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