

Platelet Indices and their role in Detecting the Degree of Liver Fibrosis in Patients with Chronic Hepatitis B Infection

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Receive date:13/6/2025

Revise date:10/8/2025

Accept date:24/9/2025

Publish date:23/10/2025

Keywords: Platelet
Indices, Liver Fibrosis,
Chronic Hepatitis B,
APRI, FIB-4

Background and study aim: Chronic hepatitis B (CHB) is a long term liver infection caused by the Hepatitis B Virus (HBV) that lasts for more than six months. Which is a critical worldwide health issue, often resulting in hepatic cirrhosis, fibrosis, and hepatocellular carcinoma. Early recognition of hepatic fibrosis is critical for preventing illness progression. The aim of this research is to evaluate the role of platelet indices (Platelet Count, Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), and Plateletcrit (PCT)) in detecting the extent of liver fibrosis in CHB cases and to compare their diagnostic value with FIB-4 and APRI scores,

Patients and Methods: This descriptive cross-sectional study was conducted at the Internal Medicine outpatient clinic of Assiut University Hospital from October 2022 to January 2024, involving 73 patients aged 18–70 years with chronic

hepatitis B (HBsAg positive for over six months),

Results: Platelet count and PCT significantly decreased as fibrosis progressed, while MPV showed an increasing trend. APRI and FIB-4 scores increased with advanced fibrosis stages. At a platelet count cut-off $\leq 209 \times 10^9/L$, the sensitivity and specificity for expecting fibrosis were 88.2% and 90.9%, correspondingly. APRI and FIB-4 demonstrated excellent diagnostic accuracy, with areas under the curve (AUC) of 0.990 and 0.983, correspondingly.

Conclusion: Platelet indices, particularly platelet count and MPV, are valuable non-invasive indicators for identifying hepatic fibrosis in CHB cases. In combination with APRI and FIB-4, they offer a good non invasive alternatives to liver biopsy for fibrosis assessment, particularly in resource-limited settings.

INTRODUCTION

Chronic hepatitis B affects an estimated 240 million individuals worldwide, posing a significant health burden because of its possible progression to hepatic cirrhosis, fibrosis, and hepatocellular carcinoma (HCC) [1]. Liver fibrosis, characterized by the accumulation of scar tissue, is a pivotal step toward more severe liver damage and functional loss. Early detection of hepatic fibrosis is critical for guiding clinical decisions and preventing further progression [2].

Liver biopsy, despite being the gold standard for evaluating fibrosis, is invasive, costly, and associated with complications [3]. Non-invasive techniques, like the Fibrosis-4 (FIB-4) and the Aspartate Aminotransferase-to-Platelet Ratio Index (APRI) index, have emerged as alternatives. Both have been

confirmed in chronic hepatitis C (CHC) and CHB cases for their utility in assessing liver fibrosis [4]. Moreover, FIB-4 and APRI are biochemical indicators for HBV that consider alanine aminotransferase (ALT), platelet count, AST, and age of patient [5]. Platelets can act as indicators for hepatic inflammation, since diminished platelet activation is related to progression of chronic hepatitis and tumors. Hepatocyte growth factor produced through platelets mitigated the fibrotic process, and platelet transfusion enhanced residual hepatic function in cases having cirrhosis [6].

Therefore, platelets may exert dual effects during liver fibrosis: they have the potential to suppress fibrogenesis and stimulate hepatic mitogenesis. However, under specific conditions, platelets can also inhibit hepatocyte regeneration and worsen fibrosis [7]. Monitoring platelet quantity and function is crucial in assessing bleeding risks, especially in hospitalized patients. Normally, platelets are abundant, ranging from 150 to $350 \times 10^9/L$ in healthy individuals. A decrease in platelet count can indicate platelet consumption due to conditions like autoimmune destruction or disseminated intravascular coagulation seen in immune thrombocytopenia. This monitoring helps healthcare providers manage and treat patients effectively to prevent complications related to bleeding disorders [8]. This study investigates the diagnostic value of platelet indices in detecting hepatic fibrosis in CHB cases and compares them with APRI and FIB-4 indices to determine their efficacy as non-invasive substitutes to liver biopsy.

PATIENTS AND METHODS

This descriptive cross-sectional study was conducted at the Internal Medicine outpatient clinic of Assiut University Hospital from October 2022 to January 2024, involving 72 patients aged 18–70 years with chronic hepatitis B (HBsAg positive for over six months) and no history of critical illness.

Exclusion criteria: We excluded cases with other hepatitis virus infection. Also, we excluded patients with: Any illness correlated with fibrosis (like chronic obstructive pulmonary disease, connective tissue diseases, tumors, renal failure, and so on), alcoholic liver disease, Pregnancy and have received any anti-fibrosis treatment.

Methods

We took the history from the cases and registered patients' vital signs, general examination, chest, abdominal and cardiac examinations.

Investigations

Initial investigations: Complete blood count liver function, HBV-DNA, HBV markers, & coagulation function. The platelet count has been demonstrated in the blood

Routine examination.

Non-invasive serological markers for hepatic fibrosis:

APRI has been evaluated depend on the ratio of aspartate aminotransferase and platelet, and the formulae have been presented as $(AST (U/L)/ULN) \times 100 / \text{platelet } (10^9/L)$.

The FIB-4 score has been determined depending on AST, ALT, age, and platelet count, with the formula expressed as $(\text{age (years)} \times AST (U/L)) / (\text{platelets } (10^9/L) \times ALT (10^9/L)^{(1/2)}) \times 10$

Imaging: Liver elastography through Fibroscan

Measured outcome

Primary outcome: value of platelet counts and indices in assessing the extent of hepatic fibrosis in cases having CHB.

Statistical Analysis

Data analysis has been carried out applying SPSS version 26.0. Categorical data have been presented as percentages and frequencies, while continuous data have been expressed as means $\pm$ SD or medians (range) based on their normality. The Shapiro-Wilk test has been applied to check for normality. Comparisons between different fibrosis stages (F0 to F4) were made utilizing the Chi-square test for categorical variables, while the independent sample T-test or Mann-Whitney U test has been utilized for continuous variables. Kruskal-Wallis or One-Way ANOVA tests have been applied to compare platelet indices, APRI, and FIB-4 between fibrosis stages. Associations between platelet indices, FIB-4, APRI, and other parameters have been assessed utilizing Pearson's or Spearman's correlation coefficients. The analysis of the receiver operating characteristic (ROC) curve has been carried out to evaluate the diagnostic accuracy of platelet indices, FIB-4, and APRI in expecting fibrosis of the liver. The sensitivity, AUC, positive predictive value (PPV), specificity, and negative predictive value (NPV) have been determined for each indicator. A p-value less than 0.05 has been considered statistically significant.

RESULTS

The current research is cross-sectional research aimed to examine the value of platelet indices in assessing the extent of hepatic fibrosis in cases having CHB virus who was admitted to the Internal Medicine Department, at Assiut

University Hospital. The study included 73 cases with chronic hepatitis B virus (HBV) (Table 1).

Table (2) shows median WBCs was 5.4 and ranged from 2.7 to 15.0, mean hemoglobin count was 13.83 ± 1.68 , median platelets count was 190.0 and ranged from 98.0 to 387.0, median APRI was 0.64 and ranged from 0.05 to 2.36, median FIB-4 was 1.80 and ranged from 0.14 to 3.95, median AST was 52.0 and ranged from 12.0 to 199.0, median ALT was 46.0 and ranged from 4.0 to 257.0.

Table (3) shows 100% were positive for HBs AG, 90.4% were positive for HBV DNA, 60.3% were positive for HBe Ab, 0% were positive for HBs AB, and 39.7% positive for HBe Ag and 100% were positive to HBcAb.

Table (4) shows pathological stages of fibrosis and steatosis among studied cases, 30.1%, 16.4%, 17.8%, 19.2% and 16.4% were on F0, F1, F2, F3 and F4 stages of fibrosis correspondingly. Moreover, 37.0%, 9.6%, 35.6% and 17.8% were on S0, S1, S2, and S3 stage of steatosis respectively.

Table (5) shows variances of platelet indices, FIB-4, and APRI depending on dissimilar pathological stages of liver fibrosis: Regarding platelets indices, Regarding platelets count, there was statistically significant median reduction in trend of platelets counts from stage F0 to stage F4 (250.0, 196.50, 185.0, 114.50, 111.0). Regarding platelets PCT, there was statistically significant mean reduction in trend of platelets PCT from stage F0 to stage F4 (0.20 ± 0.03 , 0.16 ± 0.02 , 0.15 ± 0.04 , 0.12 ± 0.02 and 0.10 ± 0.02). Regarding platelets MPV, there was statistically significant mean increase in trend of platelets MPV from stage F0 to stage F4 (7.26 ± 0.58 , 8.10 ± 0.70 , 8.20 ± 1.112 , 8.64 ± 0.54 and 8.93 ± 1.10). Regarding platelets PDW, there was no statistically significant mean difference from stage F0 to stage F4 (14.39 ± 1.35 , 14.06 ± 2.05 , 13.51 ± 1.80 , 13.87 ± 2.03 and 14.20 ± 2.95). Regarding APRI, there was statistically significant median increase in trend of APRI from stage F0 to stage F4 (0.15, 0.45, 0.91, 1.44, 1.90). Regarding FIB-4, there was a statistically significant median rise in trend of FIB-4 from stage F0 to stage F4.

Table (6) shows statistically significant lower median platelets count among fibrosis compared to no fibrosis group (145.0 vs 250.50 respectively), lower mean platelets PCT among

fibrosis compared to no fibrosis group (0.13 ± 0.03 vs 0.20 ± 0.03 respectively), higher mean platelets MPV among fibrosis compared to no fibrosis group (8.47 ± 0.93 vs 7.26 ± 0.58 respectively), higher median APRI among fibrosis compared to no fibrosis group (0.97 vs 0.15 respectively), higher median FIB-4 among fibrosis compared to no fibrosis group (2.36 vs 0.60 respectively), higher median AST among fibrosis compared to no fibrosis group (70.0 vs 16.50 respectively), higher median ALT among fibrosis compared to no fibrosis group (60.0 vs 16.0 respectively). Nevertheless, there was a statistically insignificant variance among fibrosis and non-fibrosis groups with regard to age, gender, duration of illness, WBCs count and hemoglobin level.

Table (7) shows that: Regarding platelets count, a strong positive association has been observed between Platelets counts with platelets PCT, strong negative correlation with Platelets MPV, APRI, FIB-4. Regarding platelets PCT, a strong positive correlation has been observed between Platelets PCT with platelets count, strong negative correlation with Platelets MPV, APRI, FIB-4. Regarding platelets MPV, a strong negative association has been observed between Platelets MPV with platelets count and platelets PCT, strong positive correlation with APRI, moderate positive correlation with FIB-4. Regarding APRI, a strong negative association has been observed between APRI with platelets count and platelets PCT, strong positive correlation with platelets MPV, FIB-4. Regarding FIB-4, a strong negative correlation has been observed between FIB-4 with platelets count and platelets PCT, strong moderate correlation with platelets MPV strong positive correlation with platelets APRI.

Table (8) shows: Regarding platelets indices: there was statistically significant moderate negative association among Platelets count and AST ($r = -0.682$, P value under 0.001), moderate negative correlation among Platelets counts and ALT ($r = -0.699$, P value under 0.001), significant moderate negative association between Platelets PCT and AST ($r = -0.667$, P value under 0.001), moderate negative association between Platelets PCT and ALT ($r = -0.682$, P value under 0.001), significant moderate positive association among Platelets MPV and AST ($r = 0.503$, P value under 0.001), moderate positive correlation among Platelets MPV and ALT ($r = 0.509$, P value under 0.001). Moreover, a statistically significant

strong negative association has been observed between APRI and AST ($r = -0.950$, P value under 0.001), strong negative correlation among APRI and ALT ($r = -0.913$, P value under 0.001). However, there was statistically significant strong positive association among FIB-4 and AST ($r = 0.852$, P value under 0.001), strong positive correlation among FIB-4 and ALT ($r = 0.799$, P value under 0.001), moderate positive association between FIB-4 and age ($r = 0.417$, P value under 0.001), and mild positive association between FIB-4 and WBCs ($r = 0.258$, P value equal 0.027).

Figure (1) shows diagnostic ability of platelet indices, APRI, and FIB-4 in prediction of fibrosis in cases having chronic hepatitis B infection: Regarding platelets indices, Regarding platelet count, at cut of point ≤ 209 , it has accuracy 89.5%, sensitivity 88.2%, specificity 90.9%, PPV 95.7% and NPV of 76.9% in prediction of fibrosis, AUC=0.934 and P Value <0.001. Regarding platelet PCT, at cut of point ≤ 0.16 , it has accuracy 86.0%, sensitivity 80.4%, specificity 90.9%, PPV 95.3% and NPV of 66.7% in prediction of fibrosis, AUC=0.914 and P Value <0.001. Regarding platelet MPV, at cut of point > 7.9 , it has accuracy 80.5%, sensitivity 70.0%, specificity 90.9%, PPV 94.6% and NPV of 57.1% in prediction of fibrosis, AUC=0.854 and P Value <0.001. Regarding APRI, at cut of point > 0.27 , it has accuracy 96.0%, sensitivity 96.1%, specificity 95.5%, PPV 98.0% and NPV of 91.3% in prediction of fibrosis, AUC=0.990

and P Value <0.001. Regarding FIB-4, at cut of point > 0.91 , it has accuracy 98.0%, sensitivity 96.1%, specificity 100.0%, PPV 100.0% and NPV of 91.7% in prediction of fibrosis, AUC=0.983 and P Value under 0.001.

Figure (2) shows diagnostic ability of platelet indices, APRI, and FIB-4 for predicating of high-risk fibrosis ($F > 2$) in cases with chronic hepatitis B infection: Regarding platelets indices: Regarding platelet count, at cut of point ≤ 123 , it has accuracy 82.5%, sensitivity 69.2%, specificity 96.0%, PPV 94.7% and NPV of 75.0% in prediction of high-risk fibrosis, AUC=0.871 and P Value <0.001. Regarding platelet PCT, at cut of point ≤ 0.113 , it has accuracy 81.0%, sensitivity 65.4%, specificity 96.0%, PPV 94.4% and NPV of 72.7% in prediction of high-risk fibrosis, AUC=0.865 and P Value <0.001. Regarding platelet MPV, at cut of point > 7.7 , it has accuracy 71.0%, sensitivity 96.2%, specificity 45.8%, PPV 65.8% and NPV of 91.7% in prediction of high-risk fibrosis, AUC=0.700 and P Value =0.009. Regarding APRI, at cut of point > 1.02 , it has accuracy 84.5%, sensitivity 80.8%, specificity 88.0%, PPV 87.5% and NPV of 81.5% in expecting of high-risk fibrosis, AUC=0.905 and P Value <0.001. Regarding FIB-4, at cut of point > 2.38 , it has accuracy 96.0%, sensitivity 92.3%, specificity 100.0%, PPV 100.0% and NPV of 92.6% in prediction of high-risk fibrosis, AUC=0.983 and P Value under 0.001.

Table (1) characteristics of studied cases with chronic hepatitis B infection

	n=73	%
Age (years)		
Mean $\pm$ SD (range)	40.58 $\pm$ 9.61 (19-65)	
Gender		
▪ Male	44	60.3%
▪ Female	29	39.7%
Duration of disease (Years)		
▪ Median (range)	3 years (0.58-20.0)	

Data have been represented as mean $\pm$ SD/median (range) or frequency and %

Table (2): laboratory investigation of studied cases with chronic hepatitis B infection

Variables	n=73
WBCs: Median (range)	5.40 (2.7-15.0)
Hemoglobin: Mean $\pm$ SD (range)	13.83 $\pm$ 1.68 (10.7-17.6)
Platelets indices	
▪ Platelets count($10^9/L$): Median (range)	190.00 (98.0-387.0)
▪ Platelets PCT: Mean $\pm$ SD (range)	0.15 $\pm$ 0.05 (0.05-0.28)
▪ Platelets MPV: Mean $\pm$ SD (range)	8.03 $\pm$ 1.00 (6.50-11.00)
▪ Platelets PDW: Mean $\pm$ SD (range)	14.05 $\pm$ 1.97 (9.20-18.10)
APRI: Median (range)	0.64 (0.05-2.36)
FIB-4: Median (range)	1.80 (0.14-3.95)
AST: Median (range)	52.00 (12.0-199.0)
ALT: Median (range)	46.00 (4.0-257.0)

MPV: Mean Platelet Volume, PCT: Plateletcrit, ALT: alanine aminotransferase; PDW: Platelet Distribution Width, AST: aspartate aminotransferase; FIB-4: fibrosis index depending on four factors; APRI: aspartate aminotransferase-to-platelet ratio index

Table (3): Hepatitis B markers among studied cases with chronic hepatitis B infection

Variables	n=73	%
Positive HBs AG	73	100%
Positive HBV DNA	66	90.4%
Positive HBe Ab	44	60.3%
Positive HBe Ag	29	39.7%
Positive HBs AB	0	0%
Positive HBc AB	73	100%

Data were expressed as frequency and %

Table (4): liver fibrosis and steatosis among studied cases with chronic hepatitis B infection

Variables	n=73	%
Pathological stages of fibrosis		
▪ F0	22	30.1%
▪ F1	12	16.4%
▪ F2	13	17.8%
▪ F3	14	19.2%
▪ F4	12	16.4%
Steatosis		
▪ S0	27	37.0%
▪ S1	7	9.6%
▪ S2	26	35.6%
▪ S3	13	17.8%

Data were expressed as frequency and %

Table (5): The variances of platelet indices, APRI, and FIB-4 depend on numerous pathological stages of hepatic fibrosis.

	Platelet indices				APRI	FIB-4
	Platelets count	Platelets PCT	Platelets MPV	Platelets PDW		
F0	250.50 (184-387)	0.20±0.03 (0.14-0.28)	7.26±0.58 (6.50-8.70)	14.39±1.35 (11.20-16.80)	0.15 (0.05-0.41)	0.60 (0.14-0.91)
F1	196.50 (135-282)	0.16±0.02 (0.12-0.23)	8.10±0.70 (7.20-9.30)	14.06±2.05 (10.30-18.10)	0.45 (0.24-0.91)	1.41 (0.61-1.9)
F2	185.00 (103-317)	0.15±0.04 (0.08-0.25)	8.20±1.112 (6.90-10.20)	13.51±1.80 (10.00-15.30)	0.91 (0.26-1.39)	2.17 (0.98-2.38)
F3	114.50 (103-202)	0.12±0.02 (0.09-0.18)	8.64±0.54 (8.0-9.90)	13.87±2.03 (9.70-16.10)	1.44 (0.49-1.90)	2.89 (1.89-3.29)
F4	111.00 (98-218)	0.10±0.02 (0.05-0.16)	8.93±1.10 (7.50-11.00)	14.20±2.95 (9.20-16.50)	1.90 (0.69-2.36)	3.76 (3.22-3.95)
P Value*	<0.001	<0.001	<0.001	0.784	<0.001	<0.001

Data were expressed as mean ± SD/median (range) *One Way ANOVA/Kruskal Wallis test compares mean/median difference between groups. PCT: Plateletcrit, MPV: Mean Platelet Volume, ALT: alanine aminotransferase; PDW: Platelet Distribution Width, AST: aspartate aminotransferase; APRI: aspartate aminotransferase-to-platelet ratio index; FIB-4: fibrosis index depending on four factors

Table (6): comparison between demographic and clinical data of cases with chronic hepatitis B infection and hepatic fibrosis classifications.

	No fibrosis (n=22)	Fibrosis (n=51)	P-Value
Age (years): mean $\pm$ SD	37.18$\pm$7.90	42.04$\pm$9.98	0.031*
Gender			
▪ Male	11 (50.0%)	33 (64.7%)	0.239**
▪ Female	11 (50.0%)	18 (35.3%)	
Duration of disease	3.50 (0.66-14.00)	3.00 (0.58-20.00)	0.899***
Laboratory investigations: Median (range)			
WBCS	5.55 (3.6-11.2)	5.30 (2.7-15.0)	0.630***
HB	13.65 (10.9-17.0)	14.00 (10.7-17.6)	0.159***
Platelets indices			
▪ Platelets count	250.50 (184-387)	145.00 (98-317)	<0.001***
▪ Platelets PCT	0.20$\pm$0.03	0.13$\pm$0.03	<0.001*
▪ Platelets MPV	7.26$\pm$0.58	8.47$\pm$0.93	<0.001*
▪ Platelets PDW	14.39$\pm$1.35	13.90$\pm$2.18	<0.001*
APRI	0.15 (0.05-0.41)	0.97 (0.24-2.36)	<0.001***
FIB-4	0.60 (0.14-0.91)	2.36 (0.61-3.95)	<0.001***
AST	16.50 (12-41)	70.00 (17-199)	<0.001***
ALT	16.00 (4.0-52.0)	60.00 (10.0-257.0)	<0.001***

* Mann Whitney U test compares median difference among groups. **Chi square test compares proportions among groups. * Independent Sample T test compares mean variance among groups.

MPV: Mean Platelet Volume, PCT: Plateletcrit, APRI: aspartate aminotransferase-to-platelet ratio index; ALT: alanine aminotransferase; PDW: Platelet Distribution Width, AST: aspartate aminotransferase; FIB-4: fibrosis index depending on four factors

Table (7): inter correlation between platelet indices, APRI, and FIB-4 among studied cases with chronic hepatitis B infection.

Variables	platelet indices								APRI		FIB-4	
	Platelets count		Platelets PCT		Platelets MPV		Platelets PDW					
	r	P	r	P	r	P	r	P	r	P	r	P
Platelets count			0.970	<0.001	-0.786	<0.001	-0.048	0.687	-0.847	<0.001	-0.825	<0.001
Platelets PCT	0.970	<0.001			0.789	<0.001	-0.069	0.565	-0.827	<0.001	-0.818	<0.001
Platelets MPV	-0.786	<0.001	-0.789	<0.001			0.088	0.461	0.728	<0.001	0.594	<0.001
Platelets PDW	-0.048	0.687	-0.069	0.565	0.088	0.461			0.069	0.562	0.054	0.649
APRI	-0.847	<0.001	-0.827	<0.001	0.728	<0.001	0.069	0.562			0.923	<0.001
FIB-4	-0.825	<0.001	-0.818	<0.001	0.594	<0.001	0.054	0.649	0.923	<0.001		

r (correlation coefficient), spearman correlation. PCT: Plateletcrit, AST: aspartate aminotransferase; PDW: Platelet Distribution Width, MPV Mean Platelet Volume; APRI: aspartate aminotransferase-to-platelet ratio index; ALT: alanine aminotransferase; FIB-4: fibrosis index based on four factors **NB: Degrees of correlation:** Negligible correlation $r < 0.2$, Mild correlation $r = 0.2$ to < 0.4 , Moderate correlation $r = 0.4$ to < 0.7 , Strong correlation $r = 0.7$ to < 1 , Perfect correlation $r = 1$ and No correlation $r = 0$

Table (8): Correlation between platelet indices, APRI, and FIB-4 and other variables of cases with chronic hepatitis B infection.

Variables	platelet indices								APRI		FIB-4	
	Platelets count		Platelets PCT		Platelets MPV		Platelets PDW					
	r	P	r	P	r	P	r	P	r	P	r	P
Age	-0.098	0.410	-0.106	0.372	-0.043	0.720	0.068	0.570	0.183	0.121	0.417	<0.001
Duration of disease	0.110	0.352	0.080	0.501	-0.158	0.186	-0.001	0.992	-0.055	0.644	-0.009	0.943
WBCS	-0.119	0.317	-0.099	0.407	-0.038	0.753	-0.215	0.068	0.172	0.145	0.258	0.027
HB	-0.075	0.530	-0.077	0.518	0.016	0.897	-0.076	0.525	0.152	0.199	0.044	0.712
AST	-0.682	<0.001	-0.667**	<0.001	0.503**	<0.001	0.090	0.448	0.950	<0.001	0.852	<0.001
ALT	-0.699	<0.001	-0.682**	<0.001	0.509**	<0.001	0.096	0.418	0.913	<0.001	0.799	<0.001

r (correlation coefficient), spearman correlation. PCT: Plateletcrit, APRI: aspartate aminotransferase-to-platelet ratio index; MPV: Mean Platelet Volume, ALT: alanine aminotransferase; PDW: Platelet Distribution Width, AST: aspartate aminotransferase; FIB-4: fibrosis index depending on four factors

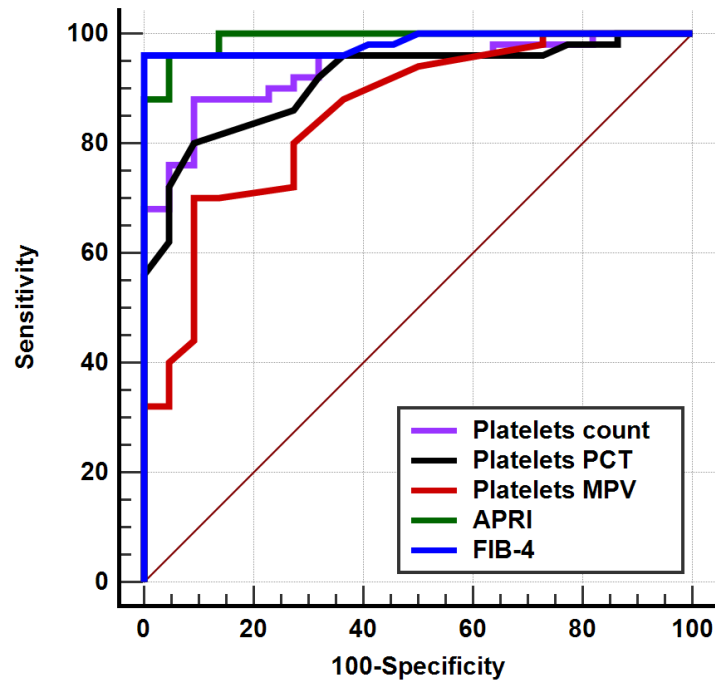


Figure (1): ROC curve for ability of PLT, APRI, FIB-4 in expecting of fibrosis.

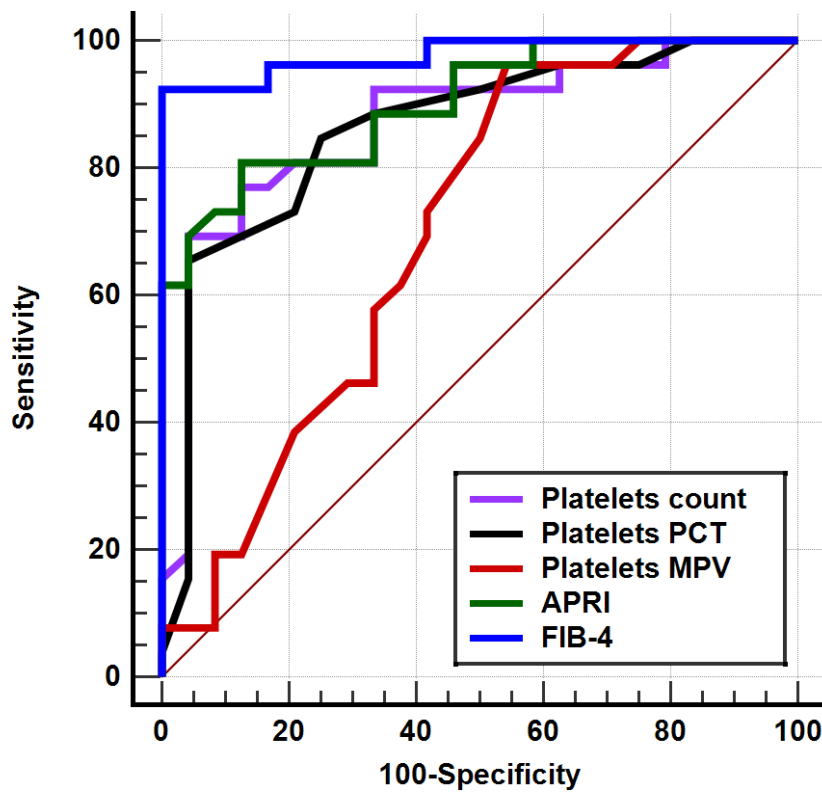


Figure (2): Roc curve for ability of PLT, APRI, FIB-4 in prediction of high-risk fibrosis (F>2).

DISCUSSION

Globally, around 65,000 individuals die each year due to hepatic cirrhosis, failure, and HCC resulting from infection with hepatitis B virus [9]. In Egypt, the occurrence of HBV infection has reached 3.67% [10]. While liver biopsy is still the most reliable technique for evaluating the extent of hepatic damage, its use is limited due to the significant risk of its complications [11]. Elastography has emerged as a promising non-invasive imaging technique, but its availability is restricted due to its high cost [12].

It is known that in chronic liver illnesses, platelets play a crucial role in hepatic injury via T cell-mediated immune responses and in repair of tissue by secreting growth factors [13]. An increase in platelet count has been linked to the improvement of hepatic fibrosis in cases with significant liver scarring who are receiving anti-HBV therapy [14].

The aim of this study is to detect the value of different platelet measurements in assessing the extent of hepatic fibrosis in 73 cases having chronic hepatitis B infection. The average age of the participants was 40.58 ± 9.61 years, varying from 19 to 65 years. Most of (60.3%) were male. The median period of the disease was 3 years, ranging from about 6 months to 20 years. The higher prevalence of CHB in men aligns with the well-documented male predominance in acute infection with hepatitis B, where males are more probable to become chronic carriers and develop HCC, and women carriers typically have reduced concentration of HBsAg and viral DNA [15]

All patients at this study were positive for HBsAg, 90.4% were positive for HBV DNA, 60.3% were positive for HBeAb, and 39.7% were positive for HBeAg. These results are comparable to those stated by Morsy et al. [16], who found that all patients had positive HBsAg, most were negative for HBeAg (91.7%), and 65.9% were positive for HBV DNA by PCR.

Based on this study, the stages of fibrosis among the patients were: F0 (30.1%), F1 (16.4%), F2 (17.8%), F3 (19.2%), and F4 (16.4%). Steatosis stages were S0 (37.0%), S1 (9.6%), S2 (35.6%), and S3 (17.8%). These findings are somewhat different from a previous report that found F0 (3.2%), F1 (23.4%), F2 (34.8%), F3 (24.7%), and F4 (13.9%) [13].

A key finding of these investigations were significant decrease in platelet count with

increasing stages of fibrosis. Conversely, APRI and FIB-4 scores increased with advancing fibrosis. A prior Egyptian study reported similar results regarding FIB-4 and APRI [17]. While some studies link low platelet counts to advanced liver fibrosis, others have reported the opposite [18, 19].

Multiple previous researches have indicated that increasing platelets could decrease liver fibrosis via administering thrombopoietin. Some researchers proposed a fibrosis index depend on platelet count and protein levels to reflect fibrosis stages in hepatitis C patients [20]. Additionally, PCT was observed to be significantly reduced in advanced fibrosis. Cases with F0 and F1 had significantly higher PCT in comparison with those with advanced fibrosis, consistent with research by Wang Jian et al. [21].

In contrast to platelet count and PCT, this study observed that MPV was significantly lower in cases with F0/F1 than those with advanced fibrosis. Similarly, Gouda Asmaa Moustafa et al. found lower MPV in cases with Child A/B cirrhosis compared to those with Child C LC and HCC [22].

Another finding was a significant variance in PDW across different fibrosis stages. It is expected that increased platelet entry into the bloodstream would not only rise MPV but also PDW due to the presence of platelets of variable sizes. These results align with Yang et al.'s study [23]. Comparing patients with and without fibrosis in this research illustrated that those with fibrosis had significantly higher age, ALT, AST, APRI, and FIB-4, along with reduced platelets. This was consistent with Yang et al.'s findings [23]. The present research additionally found that there's a strong negative association between platelet count and APRI/FIB-4, and a strong positive correlation between FIB-4 and APRI. Furthermore, APRI and FIB-4 showed negative correlations with PCT and positive correlations with MPV, with no correlation with PDW.

These outcomes were in line with the research by Yang et al. [24], which additionally observed a negative correlation between platelet count and FIB-4 and APRI.

The main findings of this study indicate that for predicting fibrosis in CHB cases, a platelet count cutoff ≤ 209 ($10^6/\text{ul}$) has 89.5% accuracy; APRI >0.27 has 96% accuracy; and FIB-4 >0.91 has 98% accuracy. Platelet PCT ≤ 0.16 has 86.0%

accuracy, and platelet MPV >7.9 has 80.5% accuracy.

For expecting advanced fibrosis in CHB cases, platelet count ≤ 123 ($10^6/\text{ul}$) has 82.5% accuracy; APRI > 1.02 has 84.5% accuracy; and FIB-4 > 2.38 has 96% accuracy. For high-risk fibrosis, platelet count ≤ 123 has 82.5% accuracy, platelet PCT ≤ 0.113 has 81.0% accuracy, and platelet MPV >7.7 has 71.0% accuracy.

This finding indicates that platelet count and Indices could act as an assessment standard in primary hospitals for evaluating significant fibrosis and early hepatic cirrhosis.

A previous study reported that platelet count was significantly reduced in cases having chronic infection with HBV and advanced fibrosis and was inversely related to the CTP score. Specifically, platelet count was independently related to F4 and could distinguish F4 with an AUC of 0.791, an optimum cutoff of $73 \times 10^9/\text{l}$, a sensitivity of 70.73%, and a specificity of 75.18% [24].

PCT was found to be an independent predictor of significant fibrosis ($\geq \text{S2}$), advanced fibrosis ($\geq \text{S3}$), and cirrhosis (S4). The AUC ROC of PCT in predicting these stages was 0.645, 0.709, and 0.714, respectively. With an optimal cutoff of 0.16, it had 63% sensitivity and 62% specificity for predicting advanced fibrosis [21].

Another study found that an MPV value above 7.3 femtoliter determined advanced fibrosis with seventy-six percent sensitivity and fifty-nine percent specificity [19]. Furthermore, another study noted that the AUC of platelet count, FIB-4, and APRI for diagnosing significant fibrosis were 0.70, 0.68, and 0.73, correspondingly, with cutoff points of < 191 , > 0.511 , and > 1.256 , and no statistical difference among them, suggesting similar diagnostic effectiveness for platelet count in identifying significant fibrosis compared to FIB-4 and APRI [13].

There was significant diversity in the proposed cutoff values for detecting significant fibrosis and hepatic cirrhosis across various investigations. Possible causes for this heterogeneity including the time periods between liver biopsy and blood tests, inadequate descriptions of hepatic biopsy evaluation, and blinding [25].

In retrospective research by Ma et al. [26] involving 1,168 Chinese HBV cases, FIB-4

illustrated a sensitivity of ninety-four percent, specificity of forty-six percent, and an AUC of 0.79 to differentiate Metavir fibrosis stages F1 & F2 from F3 and F4 at a cutoff value of 1.433–1.858.

A systematic review and meta-analysis published in 2015, encompassing sixteen articles, indicated that APRI thresholds of 0.5, 1.0, and 1.5 produced sensitivity and specificity values of seventy percent and sixty percent, fifty percent and eighty-three percent, and 36.9 percent and 92.5 percent for significant fibrosis, severe fibrosis, and cirrhosis, correspondingly. The summary AUROC values utilizing APRI for these stages were 0.74, 0.74, and This study possesses various restrictions, including a limited sample size and its execution at a single center. In addition, the cutoffs among fibrosis stages aren't highly significant. This research is the 1st in this region to demonstrate that platelet count might serve as a possible indicator for evaluating hepatic fibrosis and cirrhosis, regardless to its limitations.

These findings highlight the potential utility of platelet indices as noninvasive markers in liver fibrosis assessment. However, further research is warranted to validate these observations. Future studies should include larger cohorts across multiple centers to ensure the generalizability of results. Additionally, comparative analyses between platelet indices and established direct fibrosis markers such as hyaluronic acid and metalloproteinases may provide deeper insights. It would also be valuable to investigate the role of platelet indices in the early detection of fibrosis among patients with chronic hepatitis B receiving antiviral therapy, as this could enhance clinical decision-making and disease monitoring.

CONCLUSION

According to the present research, platelet indices serve as a practical, cost-effective, straightforward, and non-invasive measure for assessing the extent of hepatic fibrosis in cases having chronic hepatitis B. The correct assessment may help attaining delaying the frequency of cirrhosis or hepatic tumor, timely treatment, and eventually enhancing life quality of case. Platelet count might be an auxiliary diagnostic indicator for liver fibrosis in the absence of pathological examination.

Ethical considerations: Ethical consideration: All cases provided a written informed consent prior to being involved in the research. Ethical approval has been certified by the institutional review board of Faculty of Medicine, Assuit University, Egypt. (IRB Code: 04-2023-200171)

Contribution:

Ahmed Abdelfadeel Maghraby, Osama Ibrahim, Reem Ezzat Mahdy are responsible for the idea of the manuscript.

Wafaa adel abdelghany and Ahmed Abdelfadeel Maghraby are responsible for data collection.

Ahmed Abdelfadeel Maghraby, Osama Ibrahim, Wafaa Adel, Reem Ezzat Mahdy performed the statistical analysis and wrote the manuscript.

Fibroscan was performed to all patients by Reem Ezzat Mahdy.

All authors revised the manuscript.

Acknowledgement:

First of all, thanks GOD, the merciful, the beneficent for helping me during this work.

I would like to thank all the staff members of the internal medicine department.

I would like to express my indebtedness and deepest gratitude to prof.

Osama Ibrahim, Professor of Internal medicine, Faculty of Medicine, Assiut University for his valuable advice, guidance and constructive criticism, also for the invaluable assistance and efforts she devoted in the supervision of this study.

I would also like to thank Professor Dr, Reem Ezzat Mahdy, Fellow of Internal Medicine of Gastroenterology and Hepatology, Faculty of Medicine, Assiut University for her constant advice and guidance in the supervision of this study.

I'll never forget, how co-operative was Ahmed Abdelfadeel Maghraby. Lecture of Internal Medicine of Gastroenterology and Hepatology, Faculty of Medicine, Assiut University, also she was encouraging all the time. It is honorable to be supervised by her.

Conflict of interest: No conflict of interest

Funding declaration: No funding was provided to this work.

HIGHLIGHTS

- Based on the current study, platelet indices are a convenient, cheap, simple, and non-invasive indicators to evaluate the degree of hepatic fibrosis in patients with chronic hepatitis B. The correct evaluation could assist achieving timely treatment, delaying the incidence of cirrhosis or liver cancer, and eventually improving patients' quality of life. Platelet count could be an auxiliary diagnosis marker of hepatic fibrosis in the absence of pathological examination.
- Platelet indices, particularly platelet count and MPV, are valuable non-invasive indicators for identifying hepatic fibrosis in CHB cases. In combination with APRI and FIB-4, they offer a reliable substitute to liver biopsy for fibrosis assessment, particularly in resource-limited settings.

REFERENCES

1. WHO Guidelines Approved by the Guidelines Review Committee. Guidelines for the Prevention, Care and Treatment of Persons with Chronic Hepatitis B Infection. Geneva: World Health Organization Copyright © World Health Organization 2015.; 2015.
2. Kim KH, Shin HJ, Kim K. Hepatitis B virus X protein induces hepatic steatosis via transcriptional activation of SREBP1 and PPARgamma. *Gastroenterology*. 2007;132(5):1955-1967. doi:10.1053/j.gastro.2007.03.039
3. Kim WR, Berg T, Asselah T. Evaluation of APRI and FIB-4 scoring systems for non-invasive assessment of hepatic fibrosis in chronic hepatitis B patients. *J Hepatol*. 2016;64(4):773-780. doi:10.1016/j.jhep.2015.11.012
4. Holmberg SD, Lu M, Rupp LB. Noninvasive serum fibrosis markers for screening and staging chronic hepatitis C virus patients in a large US cohort. *Clin Infect Dis*. 2013;57(2):240-246.
5. Richard K Sterling, Eduardo Lissen, Nathan Clumeck, Ricard Sola, Mendes Cassia Correa, Julio Montaner, et al. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. *Hepatology*. 2006;43(6):1317-1325. doi:10.1002/hep.21178

6. Balaphas A, Meyer J, Sadoul K, Fontana P , Morel P , Robson S , et al. Platelets and Platelet-Derived Extracellular Vesicles in Liver Physiology and Disease. *Hepatol Commun.* 2019;3(7):855-866. Published 2019 Apr 22.
7. Chauhan A, Adams DH, Watson SP, Lalor PF. Platelets: No longer bystanders in liver disease. *Hepatology.* 2016;64(5):1774-1784.
8. Tsai HM. Thrombotic Thrombocytopenic Purpura: Beyond Empiricism and Plasma Exchange. *Am J Med.* 2019;132(9):1032-1037.
9. Iannacone M, Guidotti LG. Immunobiology and pathogenesis of hepatitis B virus infection. *Nat Rev Immunol.* 2022;22(1):19-32.
10. Azzam A, Khaled H, Elbohy OA. Seroprevalence of hepatitis B virus surface antigen (HBsAg) in Egypt (2000-2022): a systematic review with meta-analysis. *BMC Infect Dis.* 2023;23(1):151. Published 2023 Mar 10.
11. Lin MH, Li HQ, Zhu L. Liver Fibrosis in the Natural Course of Chronic Hepatitis B Viral Infection: A Systematic Review with Meta-Analysis. *Dig Dis Sci.* 2022;67(6):2608-2626.
12. Luca Rinaldi1 , Chiara Giorgione, Andrea Mormone, Francesca Esposito, Michele Rinaldi , Massimiliano Berretta, et al. Non-Invasive Measurement of Hepatic Fibrosis by Transient Elastography: A Narrative Review. *Viruses.* 2023;15(8):1730. Published 2023 Aug 13.
13. Zhong LK, Zhang G, Luo SY, Yin W, Song HY. The value of platelet count in evaluating the degree of liver fibrosis in patients with chronic hepatitis B. *J Clin Lab Anal.* 2020;34(7):e23270.
14. Tsuji Yuki, Namisaki Tadashi, Kaji Kosuke, Takaya Hiroaki, Nakanishi Keisuke, Sato Shinya, et al. Comparison of serum fibrosis biomarkers for diagnosing significant liver fibrosis in patients with chronic hepatitis B. *Experimental and Therapeutic Medicine* 2020; 20, 985-995.
15. Gwang Hyeon Choi , Eun Sun Jang , Jin-Wook Kim , Sook-Hyang Jeong. Epidemiological and Clinical Characteristics of Hepatitis C Virus Infection in South Korea from 2007 to 2017: A Prospective Multicenter Cohort Study. *Gut Liver.* 2020;14(2):207-217.
16. Morsy KH, Ghaliony MA, ElMel egy TT. Clinical, laboratory, and virological characteristics of patients with positive hepatitis B surface antigen in Upper Egypt. *The Egyptian Journal of Internal Medicine.* 2015 Mar;27(1):32-7.
17. Metwally K, Elsabaawy M, Abdel-Samiee M, Morad W, Ehsan N, Abdelsameea E. FIB-5 versus FIB-4 index for assessment of hepatic fibrosis in chronic hepatitis B affected patients. *Clin Exp Hepatol.* 2020;6(4):335-338.
18. Kekilli M, Tanoglu A, Sakin YS, Kurt M, Ocal S, Bagci S. Is the neutrophil to lymphocyte ratio associated with liver fibrosis in patients with chronic hepatitis B?. *World J Gastroenterol.* 2015;21(18):5575-5581.
19. Kosekli MA. Mean platelet volume and platelet to lymphocyte count ratio are associated with hepatitis B-related liver fibrosis. *Eur J Gastroenterol Hepatol.* 2022;34(3):324-327.
20. Kurokawa T, Ohkohchi N. Platelets in liver disease, cancer and regeneration. *World J Gastroenterol.* 2017;23(18):3228-3239.
21. Wang J, Xia J, Yan X. Plateletcrit as a potential index for predicting liver fibrosis in chronic hepatitis B. *J Viral Hepat.* 2020;27(6):602-609.
22. Gouda AM, Abd Elaziz MA, Mousa MA, Saad HM, Helaly NA. Evaluation of platelet indices in Egyptian cirrhotic patients. *African Journal of Gastroenterology and Hepatology.* 2024 May 17;7(1):163-84.
23. Yang K, Sun B, Zhang S, Pan Y, Fang J. RDW-SD is Superior to RDW-CV in Reflecting Liver Fibrosis Stage in Patients with Chronic Hepatitis B. *Infect Drug Resist.* 2023;16:6881-6891. Published 2023 Oct 27.
24. Yang YT, Wang LL, Yan LT . Platelet count is closely associated with the severity of liver injury in patients with chronic hepatitis B virus infection: A cross-sectional study. *Exp Ther Med.* 2020;20(1):243-250.
25. El Serafy MA, Kassem AM, Omar H, Mahfouz MS, El Said El Raziky M. APRI test and hyaluronic acid as non-invasive diagnostic tools for post HCV liver fibrosis: Systematic review and meta-analysis. *Arab J Gastroenterol.* 2017;18(2):51-57.
26. Ma J, Jiang Y, Gong G. Evaluation of seven noninvasive models in staging liver fibrosis in patients with chronic hepatitis B virus infection. *Eur J Gastroenterol Hepatol.* 2013;25(4):428-434.
27. Xiao G, Yang J, Yan L. Comparison of diagnostic accuracy of aspartate aminotransferase to platelet ratio index and fibrosis-4 index for detecting liver fibrosis in adult patients with chronic hepatitis B virus infection: a systemic review and meta-analysis. *Hepatology.* 2015;61(1):292-302.

Cite as: Maghraby, A., Ibrahiem, O., Abdelghany, W., Mahdy, R. Platelet Indices and their role in Detecting the Degree of Liver Fibrosis in Patients with Chronic Hepatitis B Infection. *Afro-Egyptian Journal of Infectious and Endemic Diseases*, 2025; (); -. doi: 10.21608/aeji.2025.461588