ORIGINAL ARTICLE

Mean Platelet Volume as a Non-Invasive Marker of Liver Fibrosis in Patients with Chronic Hepatitis B: A Multicenter Study from Rawalpindi and Quetta

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ABSTRACT

Objective: To determine the mean platelet volume as a noninvasive marker of liver fibrosis in patients with chronic hepatitis B.

Study Design: Prospective observational study.

Place and Duration of Study: This study was conducted at the Department of Gastroenterology, Combined Military Hospital (CMH), Quetta and Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan from August 2023 to April 2024.

Methods: A total of 132 hepatitis B patients reported to the Department of Gastroenterology were included in the study. Convenience sampling was performed. The platelet count, Mean platelet volume, and haemoglobin level were assessed. After a Transient Elastography (Fibroscan), fibrosis and chronicity indices were compared to the patient haematological parameter, Mean Platelet Volume, and the accuracy and consistency of haematological values in predicting hepatic fibrosis were investigated. Version 26.0 of the Statistical Package for the Social Sciences was used for data entry and analysis. An independent t-test was applied between groups.

Results: Among the total of 132 patients, 86 were male and 46 were female. Subjects were separated into two cohorts, each consisting of 66 patients matched in age and gender. Group A with fibrosis grades F0, F1, and F2 and group B with F3 and F4. The mean platelet volume was determined in each group. Group A had a Mean Platelet Volume (10.456 $\pm$ 0.922 femtolitre). Group B had a Mean Platelet Volume of (12.745$\pm$ 1.049 femtolitre). There were statistically significant variations in Mean Platelet Volume across the groups, as shown by an independent sample t-test (P<0.01).

Conclusion: MPV is a noninvasive indicator of liver fibrosis in chronic hepatitis B patients. We suggest that MPV could be helpful in evaluating fibrosis in these patients. Because a stand-alone test is nonspecific concerning other illnesses, it should not be considered for this purpose.

Keywords: *Chronic Hepatitis B, Liver Fibrosis, Mean Platelet Volume.*

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Introduction

Hepatitis B virus (HBV) is a global issue today as the primary cause of cirrhosis and chronic hepatitis. HBV had an approximate count of 820,000 fatalities, with complications like cirrhosis and hepatocellular carcinoma being the primary causes.[1,2] In Pakistan, 7-9 million individuals are of HBV, with an emergence ranging from 3% to 5%.[3] Approximately 20% to 30% of individuals with chronic hepatitis B virus (HBV) infection develop progressive liver disease, which can ultimately result in cirrhosis and chronic liver

failure.[4] A liver biopsy is The gold standard for evaluating liver damage, providing crucial insights into the disease histological activity and fibrosis level. This procedure can offer advanced insights into the disease progression and treatment efficacy. However, biopsy of the liver is sometimes challenging, expensive, and time-consuming, requiring input from a specialized pathologist, given these constraints, there is a pressing need for noninvasive histological predictors.[5] For patients who cannot have a liver biopsy, the concept of routinely using biochemical assays in clinical practice may be helpful. The mean platelet volume (MPV) determines the platelet function, which indicates higher activity. The average size of platelets is indicated by the metric known as MPV, which is frequently measured by complete blood count analyzers. It also reflects the stimulation and production rate of platelets.[6] calculating the NLR and MPV yields readily available markers and full blood counts at a low cost.[7] Research findings indicate that MPV is prognostic for the risk of stroke, myocardial infarction (MI), and cardiovascular mortality. MPV has been extensively studied as a surrogate marker of platelet function and inflammation in various conditions.[8] MPV has been associated with the disease in chronic hepatitis B.[9] Furthermore, MPV has been investigated in HBV-DeCi, where higher MPV levels found in patients, indicating its potential as a predictive marker for mortality.[10] Additionally, MPV has shown promise in diagnosing the severity of fibrosis in CHB patients, with higher MPV values correlating with severe fibrosis.[11] These findings suggest that MPV could serve as a valuable indicator for inflammation in CHB and predicting fibrosis severity, highlighting its potential clinical utility in assessing liver health in patients with chronic hepatitis B. The present study aims to determine MPV as a noninvasive marker of liver fibrosis in patients with chronic hepatitis B.

Methods

This prospective research was conducted at the Combined Military Hospital (CMH), Quetta and the Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan from August 2023 to April 2024 after taking the approval of the hospitals' Ethical Review Committees vide ERC letter No. A/29/ERC/602/23, dated: 23rd August 2023, and IERB letter No. CMH Qta-IERB/20/2024, dated: 1st December 2023. The investigation comprised 132 patients, all of whom were 18 years of age or older and had been diagnosed with chronic hepatitis B. The WHO sample size calculator was employed to determine the sample size based on the 3% prevalence rate of hepatitis in Pakistan. The initial sample size was 45 with a 95% confidence level and a 5% margin of error. However, it was increased to improve the generalizability of the results. Convenience sampling was implemented to accumulate the sample.

Inclusion Criteria: Patients aged 18 years or older diagnosed with chronic hepatitis B through clinical evaluation and laboratory testing.

Exclusion Criteria: Pregnant females, individuals diagnosed with cancer (particularly hepatocellular carcinoma), patients with heart diseases or heart failure, and those with autoimmune liver disease or concurrent infections such as HCV, hepatitis D virus, or HIV.

Patients meeting the criteria above were recruited, with consent obtained voluntarily and documented in writing. The diagnostic criteria for Chronic Hepatitis B include liver cirrhosis, a blood total bilirubin level greater than 10 times normal (171 µmol/L), and a history of HBsAg positivity for longer than six months.[12]

Following an overnight fast, every patient had blood drawn within 24 hours of admission. Platelet count, Mean Platelet Volume (MPV), and hemoglobin levels were assessed. MPV levels falling between 7.0 and 11.0 fl were considered normal, with 10.0 fl chosen as the predetermined cutoff threshold. The modified METAVIR scoring system was employed for calculating liver fibrosis scores. This system, commonly used for histopathological evaluation in patients with hepatitis C, assesses both inflammation and fibrosis levels in liver biopsies. The grade reflects the degree of inflammation (activity), while the stage indicates the extent of fibrosis or scarring. Fibrosis scores was performed by consultant having 10 years of experience categorized as follows F0 (no fibrosis), F1 (portal fibrosis with the expansion of portal zones, Transient Elastography (TE) equivalent score <7.2kpa), F2 (portal fibrosis with the expansion of most portal zones and

occasional bridging, TE equivalent score 7.2Kpa-9.5Kpa), F3 (portal fibrosis with the expansion of most portal zones and marked bridging and occasional nodules. TE equivalent score 9.5kpa-12.5kpa), and F4 (cirrhosis, TE equivalent score >12.5kpa). Fibrosis and chronicity indices were compared to patient hematological parameters, specifically MPV, to investigate the accuracy and consistency of these values in predicting hepatic fibrosis. SPSS version 26.0 was used for recording, entering, and analyzing data samples. While frequency and percentage were used to communicate qualitative data, mean ± standard deviation (SD) was used to present quantitative data. A separate t-test was conducted between the groups, and a p-value less than 0.05 is significant.

Results

Patients were allocated into two groups based on METAVIR classification: one comprising patients without notable fibrosis (classified as F0, F1, or F2) designated as Group A, and the other with significant fibrosis (classified as F3 or F4) labeled as Group B. An equal one-to-one ratio was maintained to conduct comparative analysis in the current study, so each group had 66 patients.

Both groups were characterized by an equal distribution of age and gender, as matching was done based on gender and age groups. For each group, gender distribution is males, comprising 65.2%, and females, 34.8%. In terms of age distribution, both groups also exhibit similar patterns, with the majority falling within the 18-30 years and 31-45 years' age categories, accounting for 34.8% and 30.3% respectively in each group. The age distribution gradually decreases in frequency as age increases, with 21.2% in the 45-60 years category and 13.6% in the >60 years category in both Group A and Group B. (Table-1).

Table-1: Gender and age distribution of respondents (n=132)

Variable	n (%)
Gender	
Male	86 (65.29%)
Female	46 (34.8%)
Age	
18-30 years	46 (34.8%)
31-45years	40 (30.3%)
45-60 years	28 (21.2%)
>60 years	18 (13.6%)

The comparison between patients in Group A, diagnosed with F0, F1, or F2 fibrosis, and those in Group B, diagnosed with chronic HB, uncovered numerous noteworthy discoveries. Group A and Group B did not exhibit significant differences in hemoglobin levels (12.17 ± 1.21 g/dl and 12.09 ± 1.30 g/dl, respectively; *P* = 0.08). Nevertheless, there were substantial disparities in AST (*P* = 0.00), ALT levels (*P* = 0.00), platelet counts (*P* = 0.00), and MPV levels (*P* = 0.00).

The mean MPV level in Group A was 10.456 + 0.922 fl, while it was significantly higher in Group B at 12.745 + 1.049 fl. The *P*-value of less than and equal to 0.01 for this comparison indicated a statistically significant difference in MPV levels between the two groups. (Table-2). Additionally, the negative predictive value is approximately 86.76%, while the positive predictive value is approximately 89.06%.

Table-2: Laboratory findings in Group A and Group B (n=132)

Variables	Group A (F0, F1 or F2)	Group B (F3 or F4)	*t test*	*P*-value
Hemoglobin (gr/dl)	12.17 ±1.21	12.09 ±1.30	0.08	0.08
AST (IU/ml)	21.67± 2.43	35.52 ± 8.38	0.02*	0.00*
ALT (IU/ml)	21.57± 2.24	46.29±4.39	0.01*	0.00*
Platelet count (10^3 /ml)	214.61 ±10.64	82.19± 27.22	0.00*	0.00*
MPV (fl)	10.456 ± 0.922	12.745± 1.049	0.00*	0.00*

*Group A= Group B, Independent t-test, *=P< 0.05*

Discussion

The present investigation revealed that patients with chronic hepatitis B exhibit significantly elevated MPV values. A range of clinical symptoms are associated with chronic HBV infection, from normal liver tissue and carrier status without symptoms, such as cirrhosis and hepatocellular carcinoma.[13] Asia, in particular, faces a significant burden of chronic HBV, with approximately 10% of the population identified as chronic HBV carriers. Studies estimate that 25-40% of these individuals eventually develop liver-related complications, including cirrhosis and HCC.[14] Over the past decade, researchers have prioritized non-invasive methods to evaluate liver fibrosis to reduce reliance on liver biopsies, which carry risks and limitations. Previous studies have developed predictive models incorporating serum biomarkers to assess fibrosis. For example, research on non-obese NAFLD patients established a scoring system using parameters like age, AST, platelet count, and RBC levels to predict fibrosis progression accurately.[15] Similarly, studies on systemic sclerosis and chronic hepatitis B have demonstrated the potential of inflammatory and demographic markers in fibrosis staging. While these approaches show promise, high costs and limited accessibility often hinder their clinical utility.[16-18]

The present prospective observational study, which included 132 patients, highlights the utility of MPV as a cost-effective and accessible marker. Patients were stratified into two groups: Group A, with an MPV of 10.456 ± 0.922, and Group B, with an MPV of 12.745 ± 1.049. The initial division of the patient collection was made into two groups based on the available criteria. MPV, reflecting platelet size and activation, was significantly associated with liver fibrosis and cirrhosis, corroborating findings by Bath et al. and studies by Ekmen et al., which also identified a positive association between MPV, fibrosis, and inflammatory markers like the neutrophil–lymphocyte ratio.[19-21] In line with prior research, our findings emphasize the importance of ALT and AST levels as initial markers for assessing HBV infection and liver fibrosis. This supports the recommendations for combining viral load assessments and liver enzyme levels to guide treatment initiation and ongoing monitoring.[22,23] Qi et al. further substantiated MPV's role by demonstrating its elevation in higher METAVIR fibrosis grades (F4 and F5), indicating its utility in differentiating advanced liver disease stages.[24]

However, our study revealed a lower prevalence of cirrhosis fibrosis among females, which contradicts Atay's findings of a predisposition towards extensive fibrosis in female patients.[25,26] This discrepancy underscores the importance of gender-specific investigations in liver disease research. Additionally, elevated platelet levels observed in our study align with earlier research showing increased young platelet proportions in chronic liver disease, reflecting heightened bone marrow activity in response to liver pathology.[27]

Despite these insights, our study has certain limitations. The relatively small sample size may limit the generalizability of the findings. Moreover, external factors influencing MPV, such as coexisting metabolic or cardiovascular conditions, were not fully accounted for. Future research should explore larger, multicenter cohorts to validate MPV's utility as a fibrosis marker. Comparative studies examining MPV alongside other established fibrosis indices, such as the Fibrosis-4 (FIB-4) index or the AST-to-platelet ratio index (APRI), could provide a clearer picture of its relative efficacy.[28]

In conclusion, this study reinforces MPV as a valuable, non-invasive marker for liver fibrosis and cirrhosis in chronic hepatitis B patients. The gender-specific trends observed warrant further investigation to elucidate underlying mechanisms. Comprehensive management strategies, incorporating MPV and other predictive models, could improve the assessment and treatment of chronic HBV-related liver disease.

Limitations include, small sample size, observational nature of study, lack of training, exclusion of patients with normal results, no control group, and no correlation with risk factors were studied.

Conclusion

This study identifies the mean platelet volume (MPV) as a potential non-invasive marker for assessing hepatic fibrosis in patients with chronic hepatitis B. While MPV shows promise in fibrosis evaluation, it should not be relied upon as a stand-alone diagnostic tool due to its lack of specificity and potential overlap with other conditions.

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MIA: Conception and design of the work, writing original draft (methodology, investigation), data acquisition, curation, and statistical analysis, validation of data, interpretation, and write-up of results
IA: Conception and design of the work, writing original draft (methodology, investigation)
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