

Platelet Volume Indices as Non - Invasive Physiological Marker of Liver Fibrosis in Chronic Hepatitis C Patients

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ABSTRACT

BACKGROUND: Mean platelet volume (MPV), platelet distribution width (PDW) and P-LCR (platelet large cell ratio) are known platelet volume indices (PVI). Currently, the platelet volume indices (PVI) have emerged to determine its value as biomarker of liver fibrosis.

OBJECTIVES: The present study determined the Platelet volume indices (PVI) as non invasive physiological marker of liver fibrosis in chronic hepatitis C patients.

STUDY DESIGN: Case control study

STUDY SETTINGS: Department of Gastroenterology, ISRA University Hospital and Asian Institute of Medical Sciences (AIMS) Hyderabad from May- December 2014.

SUBJECTS AND METHODS: A sample of 64 patients; 32 controls and 32 chronic hepatitis C cases were studied. Subjects were selected by non-probability (purposive) sampling as per inclusion and exclusion criteria. Roche Hitachi Hematolyzer was used for platelet count and platelet volume indices. Liver fibrosis was determined from liver biopsies by METAVIR Score. Data was analysed on Statistix 10.0 (USA) at 95% confidence interval (P<0.05).

RESULTS: The PVI (MPV, PDW and P-LCR) and platelet count were raised in cases compared to controls (p<0.05). PVI showed major differences for METAVIR SCORE F₀ -F₄ of liver fibrosis (p<0.05). MPV, PDW and P-LCR showed positive correlation (r= 0.93, r= 0.80 and r= 0.75) with METAVIR (p <0.0001) respectively.

CONCLUSION: The Platelet volume indices may be used as non-invasive physiological markers for liver fibrosis in chronic hepatitis C patients instead of invasive technique of liver biopsy.

KEY WORDS: PVI, Chronic hepatitis C, Liver fibrosis, Metavir score.

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INTRODUCTION

Hepatitis C virus (HCV) has become a major cause of chronic viral hepatitis (CHC), liver fibrosis, liver cirrhosis and liver malignancy throughout the World.^{1,2} World prevalence of 3% which accounts 170 million people has been reported by WHO^{1,2}. Infectivity rate is estimated at 3-4 million people, of whom 65-80% are in chronic intermediate phase. Prevalence of liver cirrhosis and liver malignancy are estimated at 20% and 25% respectively. This accounts for high mortality and morbidity caused by HCV^{1,2}.

Transmission of HCV occurs by sexual practices, blood transfusions, injections, tourists, barbers and shaving blades in the developed and developing countries. Unsafe injection practice and blood transfusion is the major mode of HCV transmission in Pakistan^{3,4}. Natural course of chronic hepatic C (CHC) culminates into hepatic fibrosis, and liver cirrhosis is its end stage. Grading of liver fibrosis is essential for the clinical staging of liver damage for the clinical management, for example for initiating the

interferon therapy to cure the patient⁵⁻⁸. Currently, liver biopsy is used for histological scoring and is a gold standard, but it is highly invasive method. Various fibrosis scoring systems are available but Metavir is an ideal one. Recently, many non-invasive methods of liver fibrosis estimation for example elastography are under practice, but they need instruments and expert hands. Hence alternate methods of non-invasive nature are being searched for staging the liver fibrosis⁹.

PVI include; the mean platelet volume (MPV), platelet distribution width (PDW) and P-LCR (platelet large cell ratio) which are the determinants of platelet physiology¹⁰. A measure of platelet shape and size is known as the mean platelet volume (MPV). The platelet large cell ratio (P-LCR) is defined as the % of large size platelets while platelet distribution width (PDW) shows the platelet distribution. Currently, the platelet volume indices (PVI) have emerged as highly researched topic as marker of liver fibrosis. Because PVI is non-expensive easy to perform and valuable tool for the clinical diagnosis of liver fibrosis in CHC patients¹¹⁻¹⁴.

Keeping in view, the present study was conducted to determine Platelet volume indices in chronic hepatitis C patients and their diagnostic utility for liver fibrosis in comparison to Metavir score at our tertiary care hospital.

SUBJECTS AND METHODS

The present case control study was conducted at the Department of Gastroenterology, ISRA University Hospital and Asian Institute of Medical Sciences (AIMS) Hyderabad, Sindh from May 2014 to December 2014. Prior permission was taken from the ethical review committee. Volunteer subjects were asked for written informed consent. A sample of 64 patients; 32 controls and 32 of chronic hepatitis C cases were studied. Subjects were selected by non-probability (purposive) sampling as per inclusion and exclusion criteria. Male subjects of chronic hepatitis C without any associated co-morbid condition were the inclusion criteria. CHC with chronic hepatitis B (CHB), decompensated liver cirrhosis, esophageal varices, Variceal hemorrhage and bleeding disorders were the exclusion criteria.

Five ml of venous blood was collected by Venepuncture and processed on Roche Hitachi Hematolyzer platelet count and platelet volume indices. Percutaneous Liver biopsy of liver fibrosis patients was performed only. Procedure was carried out by a Gastroenterologist under Sonography guidance. Liver biopsy was stained with Hematoxylin and eosin. Liver fibrosis was graded by METAVIR score five categories as F0, F1, F2, F3 and F4.

Data was collected on a pre-designed pre-structured proforma. The confidentiality of study population was strictly maintained. The Data was analyzed using *Statistix 10.0* (USA). One way analysis of variance (ANOVA) and student t-test were used for continuous variable data. Metavir intra- and inter- group comparisons was calculated by post-hoc Tukey-Cramer test. Pearson's correlation was used for the correlation estimation. Data was analyzed at 95% confidence interval (P<0.05) taken statistically significant.

RESULTS

The PVI (MPV, PDW and P-LCR) and platelet count showed were raised in cases compared to controls (p<0.05) (Table I). PVI showed major differences for METAVIR SCORE F₀-F₄ of liver fibrosis (p<0.05). MPV, PDW and P-LCR showed positive correlation (r= 0.93, r= 0.80 and r= 0.75) with METAVIR (p <0.0001) respectively. MPV, PDW, and P-LCR among Metavir groups- F₀ through F₄ of liver fibrosis score showed highly significant differences (p=0.0001) (Table II). A positive association was found between liver fibrosis score and MPV, PDW and P-LCR

(r= 0.93, r= 0.80 and r= 0.75) (p <0.0001) respectively. Platelet counts showed non-significant correlation with Metavir score (Table III).

TABLE I: PLATELET VOLUME INDICES (PVI) IN CONTROLS AND CASES

	Cases (n=30)	Controls (n=30)	P-value
MPV (fl)	11.28 ± 1.19	9.23 ± 0.55	0.0001
PDW (%)	16.21 ± 4.27	10.37 ± 0.43	0.0001
P-LCR (%)	36.4 ± 2.93	27.5 ± 6.20	0.0001
PC (10 ⁶ /μ L)	290.1 ± 76.1	302.5 ± 67.1	0.04

MPV- mean platelet volume, PDW- platelet distribution width, P-LCR- platelet large cell ratio, PC- Platelet count. Student t-test

TABLE II: PLATELET VOLUME INDICES (PVI) ACCORDING TO METAVIR SCORE IN CASES (n=30)

METAVIR score	MPV (fl)	PDW (fl)	P – LCR (%)	PC (x10 ⁶ /μL)
Score F0	9.90 ± 0.17	12.43 ± 1.21	33.49 ± 2.15	269.62 ± 70.38
Score F1	10.25 ± 0.12	13.68 ± 2.15	34.01 ± 0.83	269.81 ± 65.53
Score F2	10.81 ± 0.19	15.11 ± 2.01	37.15 ± 2.90	292.23 ± 113.04
Score F3	11.78 ± 0.30	17.45 ± 1.15	38.13 ± 2.10	319.56 ± 118.09
Score F4	13.19 ± 0.60	20.80 ± 3.62	39.27 ± 1.45	287.75 ± 38.12
P-value	0.0001	0.0001	0.0001	0.081

MPV- mean platelet volume, PDW- platelet distribution width, P-LCR- platelet large cell ratio, PC- Platelet count. ANOVA testing

TABLE III: CORRELATION CO-EFFICIENT OF PLATELET VOLUME INDICES AND LIVER FIBROSIS (METAVIR SCORE) IN CASES

	MPV (fl)	PDW (fl)	P-LCR (%)	PC (x10 ⁶ /dl)
r-value	0.921**	0.812**	0.735**	0.104
p-value	0.0001	0.0001	0.0001	0.426

** Correlation co-efficient (r-value) is significant at the 0.01 level (2-tailed)

MPV- mean platelet volume, PDW- platelet distribution width, P-LCR- platelet large cell ratio, PC- Platelet count

DISCUSSION

The present research is being reported for the first time on an ever increasing health problem of CHC. Non- invasive techniques are preferred over the invasive techniques like liver biopsy. The cases for this study were taken from the Department of Gastroenterology, ISRA University and Asian Institute of Medical Sciences (AIMS), Hyderabad. The Department of Gastroenterology of Isra University caters thousands CHC patients yearly. The present study

was conducted to determine the Platelet volume indices (PVI) in comparison to Metavir score of liver fibrosis. As the CHC infection runs a stealthily natural course, hence there is need of some non-invasive technique for screening and predicting the onset of liver fibrosis¹³⁻¹⁵. Platelet volume indices (PVI) are negative correlates of platelet size and physiology. Physiologically, the circulating platelets are closely regulated within limits by the bone marrow feedback mechanisms. In cases of increased platelet consumption, megakaryocyte proliferate, newly released platelets are large in number and more aggressive physiologically. Megakaryocyte proliferation is influenced by the thrombopoietin^{13,15}. As the liver fibrosis is associated with clotting and hemostasis abnormalities, hence there is a change in the circulating platelets, majority of who are newly released from bone marrow with different PVI. This concept was exploited for the present study.

The present study reports raised PVI in CHC patients compared to the controls. The PVI were compared with Metavir score and a positive correlation was found. This finding is of clinical importance as it may be used as a non-invasive physiological marker of liver fibrosis. PVI shows positive correlation with the METAVIR scores F₀ - F₄ and is found statistically significant ($p < 0.05$) in the present study reports (table III). The findings of raised MPV of present study is a worth finding as it is consistent with a previously reported study¹⁶. A previous study¹⁷ reported the MPV and PDW were found increased in CHC fibrosis compared to non-fibrosis patients. These findings of present study are in agreement with previous study¹⁷. Above previous study reported the PDW was found highly indicative of advanced liver fibrosis, hence our present study supported by above study. Chen B, et al¹⁸ reported the raised PVI values in the liver fibrosis of chronic hepatitis B. They reported positive correlation with Metavir scoring, which is consistent finding with the present study. Many previous studies^{6,19-21} have reported PVI results which support our present study and previous studies^{17,18}. The finding of positive correlation of severity of liver fibrosis (Metavir score) of present study is supported by previous studies^{21,22} as they reported positive association of severity of liver fibrosis with PVI. The findings of raised MPV, PDW, P-LCR and reduced PC of present study are supported by previous medical research studies as mentioned above. The present study reports the PVI indices may prove helpful as non-invasive physiological marker of liver fibrosis in chronic hepatic C patients. The present study concludes sufficient information has been achieved on the topic which needs further large sample nationwide studies to make cut off values and guidelines on the PVI as marker of liver

fibrosis. The major limitation of present study is a small sample size, however, PVI were compared with gold standard test; the liver biopsy which is a strong evidence of the association.

CONCLUSION

The Platelet volume indice (PVI) were elevated in chronic hepatitis C patients. The PVI are easy, inexpensive, and non-invasive markers which may be exploited for predicting liver fibrosis at earlier stage even in remote rural areas of country, but this needs further large scale nationwide studies.

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