

# TO DETERMINE THE DIAGNOSTIC ACCURACY OF DOPPLER WAVEFORM PATTERN OF HEPATIC VEINS IN DETECTION OF CHRONIC LIVER DISEASE IN HEPATITIS C PATIENTS KEEPING HISTOPATHOLOGY AS GOLD STANDARD

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## ABSTRACT

**INTRODUCTION:** Hepatitis B virus (HBV) and hepatitis C virus (HCV) are the most important cause of chronic liver disease in Pakistan. The diagnosis of cirrhosis is of great prognostic value and requires liver biopsy for further management. The structural changes in cirrhosis lead to abnormal wave form in hepatic veins. **OBJECTIVES:** To determine the diagnostic accuracy of the Doppler waveform pattern of hepatic veins in detection of cirrhosis in HCV positive patients based upon histopathology as gold standard. **STUDY DESIGN:** Descriptive Cross-sectional. **DURATION AND SETTING:** Conducted at P.N.S Shifa, naval hospital Karachi from 27-01-2014 to 26-07-2014. **SUBJECTS AND METHODS:** 152 patients were included in the study. Doppler examination of hepatic veins was performed followed by liver biopsy. Hepatic wave form patterns were divided into normal triphasic pattern and abnormal biphasic/monophasic patterns and were analyzed by comparing with histopathology reports. **RESULTS:** Doppler waveform pattern of hepatic veins showed sensitivity (75.61%), specificity (92.79%), diagnostic accuracy (88.15%), positive predictive value (79.49%) and negative predictive value (91.15%) for detection of cirrhosis. **CONCLUSION:** It was concluded from the results of this study that non invasive Doppler waveform pattern of hepatic veins have high diagnostic accuracy and, negative predictive value in the detection of cirrhosis in hepatitis C patients.

**Keywords:** Viral Hepatitis; Cirrhosis; positive predictive value, waveform pattern of hepatic veins, histopathology

## Introduction

Global prevalence of Hepatitis C infection is around 2.8% equating to 185 million infections worldwide<sup>1</sup> while in Pakistan average estimated prevalence rate is 4.95% in general adult population.<sup>2</sup> A significant number of chronically infected HCV patients develop cirrhosis or liver cancer. In Pakistan one of the studies shows 13.5% prevalence of cirrhosis in HCV positive patients.<sup>3</sup> Another local study shows that amongst cirrhosis patients, 61.05% were HCV posi-

tive, 18.95% were HBsAg positive and 4.2% were positive for both HBsAg and anti-HDV antibodies and 3.2% patients had alcoholic liver.<sup>4</sup> Doppler ultrasonography is a non-invasive and inexpensive modality without radiation hazard which can be used for diagnosis and follow up of patients with chronic liver disease. Hepatic venous waveform pattern in normal individuals is triphasic while it changes to a biphasic or monophasic patterns in cirrhotic patients<sup>5</sup> because hepatic fibrosis leads to loss of hepatic veins compliance. We aimed to study diagnostic ac-

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curacy of loss of normal hepatic venous waveforms in predicting cirrhosis in a cross-sectional analysis.

## Material & Methods

The study was conducted in PNS Shifa Naval Hospital Karachi. This study was a prospective descriptive cross sectional analysis of 6 months duration from 27 Jan 2014 to 26 July 2014. Adults between 20 - 50 years who were HCV positive for more than 6 months with serum ALT levels more than two times the upper limit of normal within last six months and who consented for liver biopsy were included. Patients who had de-compensated liver disease or ascites or hepatocellular carcinoma or history of hypertensive/ ischemic heart disease or previous liver biopsy were excluded.

The selected 152 patients were subjected to the Doppler ultrasonographic examination of hepatic veins at the radiology department of PNS Shifa Karachi. Duplex sonographic examination was performed on TOSHIBA Nemio 20 with a convex 3.5-MHz probe using color, pulse wave and duplex doppler. Every patient was examined while supine after overnight fasting. Duplex sonographic examination of the hepatic veins was performed. For this purpose flow in right, middle and left hepatic veins was observed at a distance of 3-6 cm away from IVC with an angle of 60 degree both with intercostal and subcostal approaches. Measurements were done during mid inspiration and normal breathing in supine or 30 degree left lateral position. At least 4-6 sec of the trace was recorded at the end of a non forced expiration.

Liver biopsies were performed under ultrasound guidance using local anesthesia and aseptic measures. Sample were fixed in formalin and sent for histopathology analysis. Those biopsy samples which showed established cirrhosis in the form of diffuse fibrosis with architecturally abnormal regenerating nodules (METAVIR score F4) were labeled positive for cirrhosis while those without fibrosis or with fibrosis in absence of regenerating nodules (METAVIR score F0, F1,F2,F3) were labeled as negative for cirrhosis.

Data was analyzed using 2 x 2 table and SPSS (Statistical program for social sciences) version 10.0. Age was presented by Mean  $\pm$  Standard deviation. Frequencies and percentages were calculated for gender, waveform pattern of hepatic veins and cirrhosis on histopathology. Sensitivity, specificity, positive and negative predictive values and diagnostic accuracy were calculated. Stratification with respect to age and gender were done. Post stratification chi-square test was applied and  $P \leq 0.05$  was taken as significant.

## Results

Mean age of 152 adult patients included in study was  $33.32 \pm 10.699$  years and out of these 98(64.5%) were males and 54 (35.5%) were females. Normal triphasic wave pattern was found in 113 (73.68%) while it was abnormal in 39 (27%). Out of these 39 abnormal waveforms 28 (71.79%) had biphasic while 11 (28.21%) had monophasic pattern. Biopsy revealed established cirrhosis in 41 (26.97%) while 111 (73.03%) were negative for established cirrhosis. Out of 28 biphasic forms 22 (78.57%) had cirrhosis while 6 (21.43%) were seen in non cirrhotic cases. Amongst 11 monophasic cases 9 (81.81%) had cirrhosis while 2 (18.19%) were non cirrhotic. Among 113 triphasic cases, 103 (91.15%) were in non cirrhotic and 10 (8.85%) in cirrhosis. The data was entered in 2 x 2 table and sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were calculated using formulae given below

Results of Dopler wave form	Histopathology		Total
	Positive	Negative	
Dopler waveform (Positive)	True positive(a) 31	False positive (b) 8	a + b 39
Dopler waveform (Negative)	False negative(c) 10	True negative (d) 103	c + d 113
<b>Total</b>	<b>a + c 41</b>	<b>b + d 111</b>	<b>n 152</b>

Sensitivity =  $a / (a + c) \times 100 = 75.61\%$

Specificity =  $d / (d + b) \times 100 = 92.79\%$

Positive PV =  $a / (a + b) \times 100 = 79.49\%$

Negative PV =  $d / (d + c) \times 100 = 91.15\%$

Diagnostic Accuracy =  $TP + TN \times 100 / TP+TN+FP+FN$

Diagnostic Accuracy = 88.15%

## Discussion

Hepatitis C is leading cause of chronic liver disease in Pakistan and accounts for almost 70% cases. Detection of hepatic fibrosis and cirrhosis in hepatitis C patients has prognostic value and liver biopsy has remained gold standard till now. However since liver biopsy is invasive with small but considerable risk of complications, now a day's non invasive tests including hepatic Doppler are being evaluated to assess hepatic fibrosis.<sup>6</sup>

It is hypothesized that hepatic fibrosis in cirrhosis leads to loss of compliance in walls of the hepatic veins and thus the wave form pattern is changed. In normal individuals a triphasic flow pattern is seen, while in cirrhosis the pattern either becomes biphasic or monophasic due to stiffness of the liver parenchyma.

Statistical analysis of the current study revealed that overall diagnostic accuracy of Doppler waveform is reasonably good 88.15% and was comparable to 77%<sup>5</sup>, 83.57 and 88.1%<sup>8</sup> international studies. A negative predictive value of 91.15% for exclusion of cirrhosis also seems quite promising.

In our study 64.5% males and 35.5% females with mean age of  $33.32 \pm 10.69$  years is almost similar to another international study<sup>9</sup> which had 57.7% male and 42.3% females and mean age of  $35.89 \pm 8.9$  years. Chronic liver diseases due to viral infection manifest varying degrees of hepatic fibrosis ranging from no fibrosis to cirrhosis. Determination of fibrosis stage is key factor in prognosis and management. A rise in annual incidence of hepatocellular carcinoma from 0.5% among patients with the stage F0 or F1 fibrosis to 7.9% among the patients with stage F4 fibrosis is reported.<sup>10</sup> The relationship between fibrosis and abnormalities in the Doppler waveform of the hepatic veins in our study was similar to Colli A et al.<sup>5</sup>


One limitation of our study is that relationship of Doppler waveforms with grades of fibrosis or scores of histopathology reports were not analyzed like in other studies<sup>8</sup> however since we aimed to target relationship with established cirrhosis only hence histopathology reports were divided into only two categories i.e cirrhosis (METAVIR F4) and non cirrhosis (METAVIR F0,F1,F2,F3).

## Conclusion

It is concluded from this study that hepatic veins Doppler has reasonably high diagnostic accuracy for detecting cirrhosis in chronic hepatitis C patients hence due to its easy availability and non invasive nature it can be considered as an alternate to biopsy.

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