Comparison of Doppler waveform and mean velocity of hepatic vein in cirrhotic patients with healthy subjects and their correlation with severity of cirrhosis.

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Abstract

This descriptive study was carried out in the Department of Radiology and Imaging, BIRDEM (Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorder) Dhaka during the period of 1st June 2008 to 30th May 2009, to compare the pattern of the Doppler waveform and mean velocity of hepatic vein between healthy subjects and that in cirrhotic patients and to detect possible differences and also to assess the accuracy of the detection of changes in hepatic vein waveform and mean velocity for the diagnosis of liver cirrhosis. A total of 40 cirrhotic patients and 40 healthy subjects were enrolled in this study. Doppler waveform was done in all the patients and the healthy subjects. The mean hepatic vein velocity (MHVV) was 12.22±4.22 cm/sec and 5.17±1.19 cm/sec in case and healthy group respectively. The mean MHVV difference was significantly (p<0.001) higher in case group. 37.5% patient had wave form HV-0 and HV-1 and 25.0% had wave form HV-2 in case group, however, in healthy group all subjects had wave form HV-0 and the difference was statistically significant (p<0.05) between case and healthy. In Child's class A wave form HV-0 was found in 75.0%, HV-1 was 25.0% and HV-2 was not found in case group. In Child's class B wave form HV-0 was found in 21.4%, HV-1 was 71.5% and HV-2 was 7.1%. In Child's class C wave form HV-0 was not found, HV-1 was 10.0% and HV-2 was 90.0%. The and the difference was statistically significant (p<0.05) among the different grading level with wave form. In Child's class A the mean velocity was 9.18±1.81 cm/sec and velocity ranged from 7.5 to 14.2 cm/sec. In Child's class B the mean velocity was 11.26 ±1.81 cm/sec and velocity ranged from 7.5 to 14.2 cm/sec. In Child's class C the mean velocity was 18.44±1.91 cm/sec and velocity ranged from 15.5 to 20.9 cm/sec. The mean velocity was statistically significant (p<0.05) among Child's class A, Child's class B and Child's class C. From the above summary and previous study it is observed that there is a significant difference between Doppler waveform and mean velocity of right hepatic vein in cirrhotic patients and in normal subjects. It can be used as a new parameter in the assessment of liver cirrhosis.

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Introduction

The diagnosis of liver cirrhosis is important in the evaluation and management of patients. Liver biopsy is the gold standard but it is invasive. Ultrasonography is a non-invasive and useful modality in assessing the liver for certain conditions but low frequency ultrasonography is not a sensitive test for the diagnosis of liver cirrhosis in daily clinical practice¹.

In liver cirrhosis there are changes in liver parenchyma as well as alteration of hepatic vasculature, including morphologic changes of hepatic veins (HVs)². It is accepted that abnormal circulation caused by hyper dynamic circulation and intrahepatic shunt persists in cirrhotic liver². Although above alterations of these vessels are already known, normal and

pathologic aspects of Doppler waveform³ and mean velocity of HVs have been less studied².

Doppler waveform of the hepatic veins in healthy human is a triphasic waveform,

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*Address of correspondence Email: akashovan@yahoo.co.uk Mobile: 01711269017 containing two negative waves and one positive wave⁴. As for abnormal hemodynamics of the hepatic veins in cirrhotic liver reported and suggested^{5,6} that the Doppler waveform becomes flat and mean velocity changes when hepatocellular function is impaired². Some studies even proposed that flattening of the hepatic wave form and altered mean velocity of HVs could be used as a diagnostic tool for liver cirrhosis ^{2,3,7}.

study compared the This Doppler ultrasonographic wave pattern and mean velocity of hepatic veins in a group of patients affected by liver cirrhosis with a group of healthy subjects comparable for sex and age. This was done to detect possible differences in hepatic vein waveform and mean velocity in these two groups and investigate the relationship of these differences with the severity of disease according to Child-Pugh scoring8 and to assess the accuracy of the detection of changes in hepatic vein waveform and mean velocity for the diagnosis of liver cirrhosis.

Methods

This descriptive study was carried out on total of 83 subjects (both cirrhotic patients and healthy adults, cirrhotic and healthy subjects being 43 and 40 respectively. The case group was admitted to the Gastro hepatic and pancreatic department (GHPD) of BIRDEM and diagnosed as cirrhotics. All of them were referred in the department of Radiology and Imaging of BIRDEM and Doppler examination was done from 1st June, 2008 to 30th May, 2009. They were routinely investigated using appropriate haematological and biochemical parameters to come to the clinical diagnosis. The patients were then referred for sonographic evaluation for the diagnosis of cirrhosis and Doppler examination was done. Consecutively 43 cirrhotic patients were taken in case group. Among the 43 cirrhotic patients 3 patients were excluded from the case group due to presence of nodule of HCC. Finally 40 patients were included in the case group. There were 32 male and 8 female patients in case group and 27 male and 13 female in

normal healthy subjects. Normal healthy subjects were those people who came to the Radiology & Imaging department of BIRDEM for other complaints and sonographically no abnormality was detected. Relevant data for the scoring of the severity of the cirrhosis were collected from the patients' record.

Doppler ultrasonographic examination was performed by means of duplex ultrasonographic equipment with a convex probe of 3.5 MHz provided by a pulsed Doppler device operating at frequency of 2.5 MHz. The system was equipped with software to compute the time-averaged velocity from the spectral display after placement of the calipers. Each subject was examined while in a supine position after overnight fasting to avoid any influence of meal and posture on splanchnic hemodynamics. The morphological appearance of the hepatic veins was evaluated by assessing caliber and course. Doppler study was then performed by positioning the same volume, as large as at least one-third of the vessel diameter, within the right hepatic vein and was approached from right intercostals space. The reason behind choosing the right hepatic vein over other was that the middle and left hepatic vein often join each other before draining to the inferior vena cava. In each case the angle of incidence of the Doppler ultrasound beam was maintained between 20° and 50°, and the spectral analysis was always recorded for at least 4-6 seconds with a filter of 100 Hz. During examination each subject was asked to breathe normally or to just simple holdup of breathing to avoid modification by deep inspiration. Mean flow velocity was calculated automatically by the instrument after tracing of the spectral display.

The Doppler ultrasound wave pattern was then arbitrarily classified into one of three groups according to the Doppler signal characteristics:

- 1. HV0, triphasic waveform (i.e., presence of a short phase of reverse flow)
- HV1, decreased amplitude of the phasic oscillations without the short phase of reverse flow.

3. HV2, completely flat waveform without any phasic oscillation, similar to the Doppler trace of a portal branch.

Finally the severity of liver cirrhosis was assessed by Child-Pugh scoring system.
Choice of ultrasound machine and transducer:
Ultrasound machine:

Siemens Antares Sonoline Medisone Sono Ace 8000 Live

Transducer:

3.5 Megahertz curvilinear transducer provided by a pulse Doppler device operating at frequently of 2.5 MHz

All the relevant collected data were compiled on a master chart first, then organized by using scientific calculator and standard statistical formula. Percentages were calculated to find out the proportion of the findings. Further statistical analyses of the results were done by computer software devised as the statistical package for social scientist (SPSS). The results were presented in Tables, Figures, and Diagrams etc. For significant of differences unpaired't' test and Chi square tests and ANOVA test were applied. A 'p' value <0.05 was considered as significant.

Results

Mean hepatic vein velocity (MHVV) (cm/sec) of the study subjects in case and healthy (n=80)

In case group the mean hepatic vein velocity (MHVV) was 12.22 cm/sec with standard deviation of mean (SD) ±4.22 cm/sec and their MHVV ranged from 6.2 to 20.9 cm/sec. However, in healthy group, the mean MHVV was 5.17 cm/sec with standard deviation of mean (SD) ±1.19 cm/sec and their MHVV ranged from 3.0 to 7.2 cm/sec. The mean MHVV difference was statistically highly significant (p<0.001) between case and healthy in unpaired t-test. The results are shown in the table I.

Table I: Mean hepatic vein velocity (MHVV) (cm/sec) of the study subjects in case and control (n=80).

MHVV (cm/sec)		ase =40)	Control (n=40)		P value	
Mean ±SD	12.22	±4.22	5.17	±1.19	0.001 ^S	
Range (Min-max)	(6.2	-20.9)	(3.0	-7.2)	54.342	

unpaired t test, t value= 10.19, df= 78, p=0.001, s= significant, significant (p< 0.05) with unpaired t test.

Right hepatic vein wave form of the study subjects in case and healthy (n=80)

The Doppler ultrasound wave pattern in right hepatic vein was classified in three groups according to the Doppler signal. HV-0 was the normal triphasic waveform, HV-1 was biphasic waveform and HV-2 was completely flat waveform. The highest percentage of patients (37.5%) had wave form HV-0 and HV-1 and 10 (25.0%) had wave form HV-2 in case group, however, in healthy group all subjects had wave form HV-0 and the difference was statistically significant (p<0.05) between case and control in chi square test. The results are shown in the figure I.

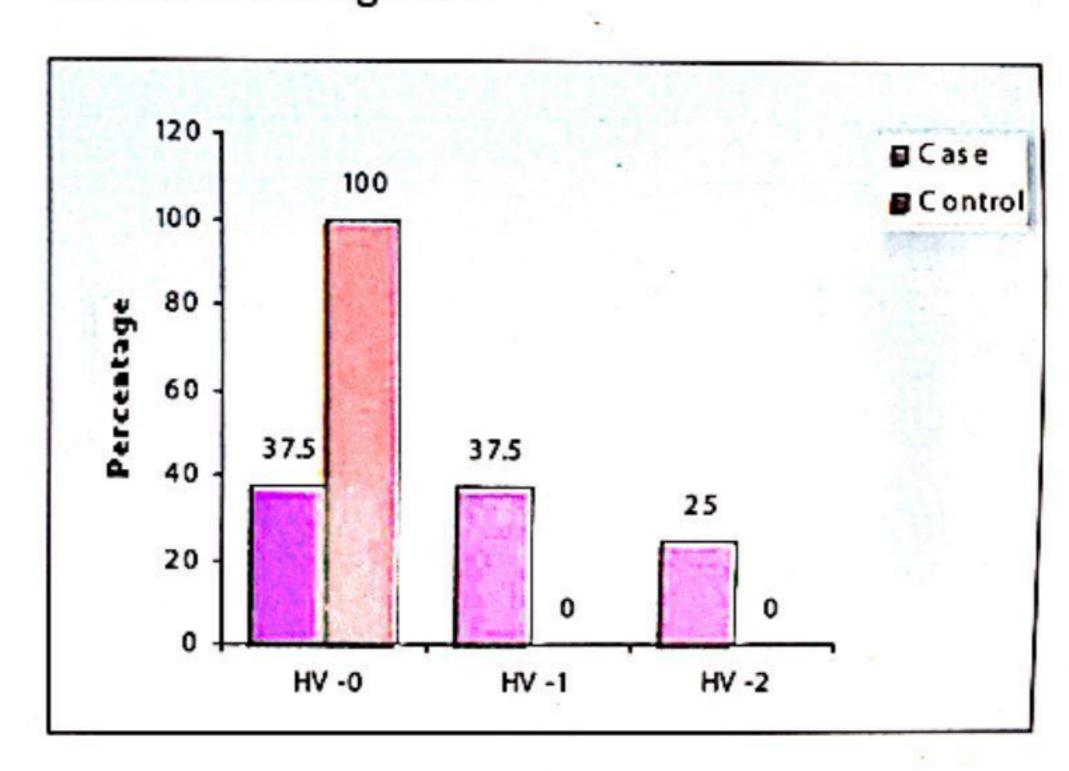


Figure I: Bar diagram showing right hepatic vein wave form of the study subjects in case and healthy (n=80).

Association between Wave form and severity of the liver cirrhosis according to Child-Pugh scoring of the study subjects in case (n=40)

The severity of the liver cirrhosis was assessed by Child-Pugh scoring system with the parameters of encephalopathy, serum

bilirubin, serum albumin, prothombin time and ascites. Adding the individual score < 7 was Child's class A, 7-9 was Child's class B and > 9 was Child's class C. In Child's class A wave form HV-0 was found in 12 (75.0%), HV-1 was 4 (25.0%) and HV-2 was not found in case group. In Child's class B wave form HV-0 was found in 3 (21.4%), HV-1 was 10 (71.5%) and HV-2 was 1 (7.1%). In Child's class C wave form HV-0 was not found, HV-1 was 1 (10.0%) and HV-2 was 9 (90.0%). The difference was statistically significant (p<0.05) among the different grading level with wave form in chi square test. The results are shown in the table II and figure II.

Table II: Association between Wave form and severity of the liver cirrhosis according to Child-Pugh scoring of the study subjects in case (n=40).

Wave form	Child's A		Child's B		Child's C		
	n	%	n	%	n	%	P value
HV-0	12	75.0	3	21.4	0	0.0	
HV-1	4	25.0	10	71.5	1	10.0	0.001 ^s
HV-2	0	0.0	1	7.1	9	90.0	

Chi square test, chi value= 40.38, df= 4, p= 0.001, s= significant, significant (p< 0.001) with chi square test.

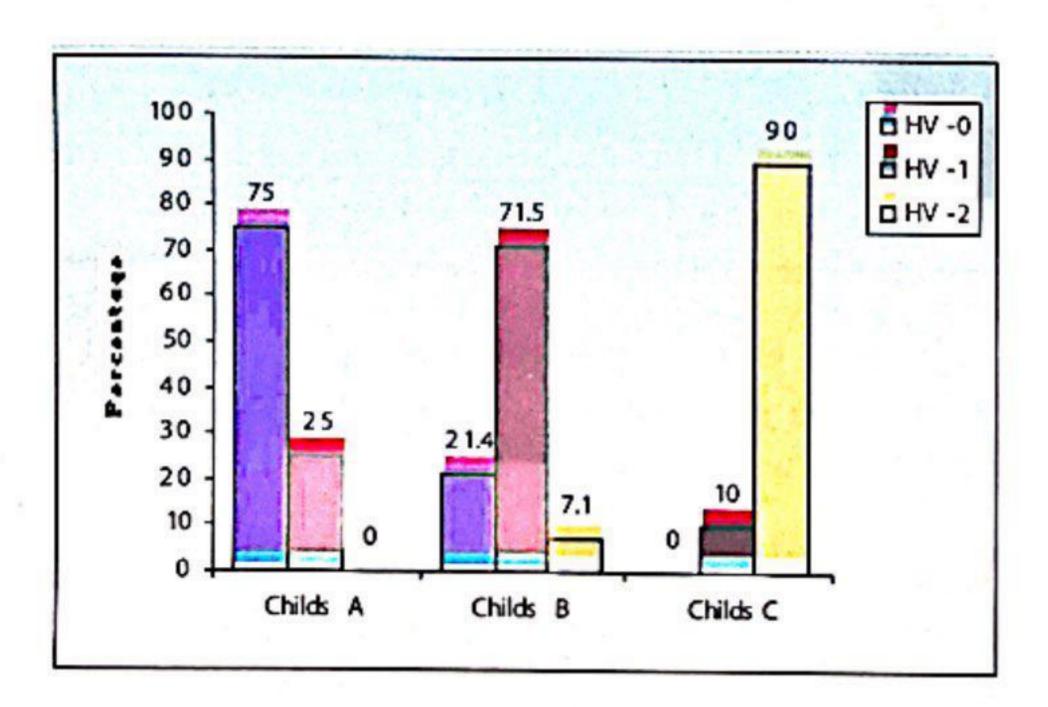


Figure II: Bar diagram showing association between wave form and severity of the liver cirrhosis according to Child-Pugh scoring of the study subjects in case (n=40).

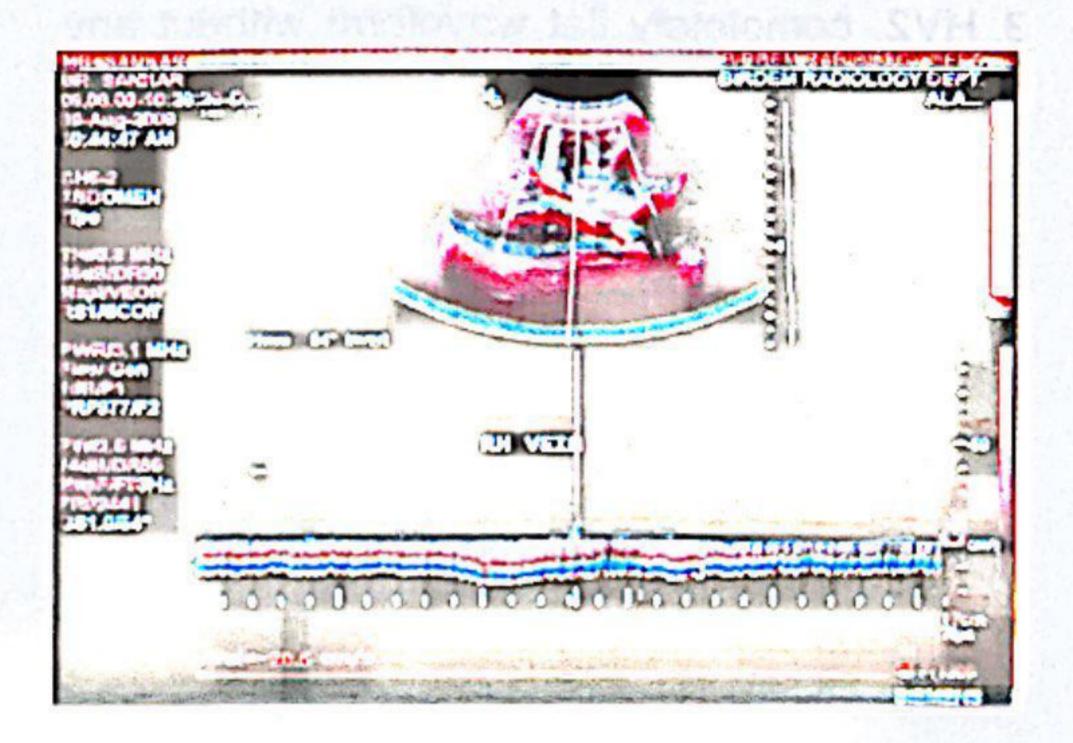


Figure III: Flat Doppler flow patterns of right hepatic vein of a 61 years male patient with liver cirrhosis. Mean velocity was 20.5 cm/sec (case no. 11).

Association between mean hepatic vein velocity and severity of liver cirrhosis according to Child-Pugh scoring of the study subjects in case (n=40)

According to Child's class A the mean velocity was 9.18 cm/sec with standard deviation of mean (SD) ±2.17 cm/sec and their velocity ranged from 6.2 to 15.0 cm/sec. In Child's class B the mean velocity was 11.26 cm/sec with standard deviation of mean (SD) ±1.81 cm/sec and their velocity ranged from 7.5 to 14.2 cm/sec. In Child's class C the mean velocity was 18.44 cm/sec with standard deviation of mean (SD) ±1.91 cm/sec and their velocity ranged from 15.5 to 20.9 cm/sec. The mean velocity was statistically significant (p<0.05) among Child's class A, Child's class B and Child's class C in ANOVA test. The results are shown in the table III.

Table III: Association between mean hepatic vein velocity and severity of liver cirrhosis according to Child-Pugh scoring of the study subjects in case (n=40).

Child-Pugh Scoring	Mean	±SD	Range	P value
Child's class A	9.18	±2.17	(6.2-15.0)	
Child's class B	11.26	±1.81	(7.5-14.2)	0.001 ^S
Child's class C			(15.5-20.9)	

ANOVA test, F value= 69.43, df=2,37, p= 0.001, s= significant, significant (p< 0.05) with ANOVA test.

Discussion

Vulnerable to wide variety of metabolic, circulatory, toxic, microbial and neoplastic insults, the liver is the most frequently injured organs in the body and there are various diseases of the liver. Among the diseases of the liver cirrhosis is most common.

The exact prevalence of cirrhosis in world wide is unknown. It is the 9th leading cause of death in USA and etiology is mainly alcohol abuse. Almost same picture is reported in Europe and numbers are even higher in most Asian and African countries where chronic hepatitis B & C infection is common⁹.

Definitive diagnosis of liver cirrhosis remains a challenging problem for both physician and radiologist, especially in early cases, as many remain symptom less. Often a poor correlation exists between histologic findings and the clinical picture. Cirrhosis can lead to many complications, among them hepato cellular carcinoma (HCC) is the dangerous one. Early diagnosis, staging and regular follow up of the cirrhosis are important for the proper treatment to prevent or minimize complications of cirrhosis.

A rational selection and combination of diagnostic imaging modalities such as ultrasonography and pulsed Doppler examination of hepatic vein are essential for the detection and evaluation of cirrhosis at an early stage to prevent different complications, progression of the disease and regular follow up.

This case healthy study was carried out with an objective to compare the pattern of the Doppler waveform and mean velocity of hepatic vein between healthy subjects and that in cirrhotic patients and also to detect possible differences and to assess the accuracy of the detection of changes in hepatic vein waveform and mean velocity for the diagnosis and severity of liver cirrhosis.

Sudhamshu et al² found in their study that the mean hepatic vein velocity was 12.7±6.4 cm/sec and 6.2±3.2 cm/sec in cirrhotics and non cirrhotics group respectively, which is significantly higher in cirrhotic patients.

Similarly, Herbay et al.⁶ observed identical mean hepatic vein velocity between patient with liver disease and healthy group. It closely resemble with the present study where the mean hepatic vein velocity (MHVV) was 12.22±4.22 cm/sec with the range from 6.2 to 20.9 cm/sec. In control group, the mean MHVV was 5.17±1.19 cm/sec with the range from 3.0 to 7.2 cm/sec. The mean MHVV difference was significantly (p<0.001) higher in case group in this study.

In this study the Doppler ultrasound wave pattern in right hepatic vein was classified in three groups according to the Doppler signal. HV-0 was the normal triphagic waveform, HV-1 was biphasic waveform and HV-2 is completely flat waveform. It was observed that more than one third (37.5%) of patients had wave form HV-0 (normal triphagic waveform) & HV-1 (biphasic waveform) and 25.0% had wave form HV-2 (completely flat waveform) in case group. In control group all subjects had wave form HV-0 (normal triphagic waveform) and the HV-0 was significantly (p<0.05) higher in control group. Sudhamshu et al.2 reported all non-cirrhotic control showed triplphasic waveforms of HV. In cirrhotic patients triphasic pattern, biphasic and flat were observed 49.0%, 48.0% and 3.0% of the patients respectively. Similarly, Bolondi et al.3 showed in their study that triphasic pattern was 50.0%, biphasic 31.7% and flat 18.3% of the cirrhotic patients. On the other hand Arda et al. 10 has observed in cirrhotic patients that triphasic pattern was 26.7%, biphasic 60.0% and flat 13.3%. The result obtained in the present study is a little less than the above mentioned study. This may be due to lack of awareness and delayed health seeking practices in our country.

Herbay et al⁶ observed that the patients with live cirrhosis had regular triphasic (type 1) waveforms occurred significantly less frequently in those with Child B and child C cirrhosis than in those with Child A cirrhosis, which were 60.0% in Child A, 34.0% in Child B and 17.0% in child C. Type 2 waveforms occurred in decreasing order of incidence in

patients with cirrhosis. Type 3 waveforms occurred in decreasing order of incidence in patients with Child C (66.0%), child B (49.0%) and Child A (24.0%). Similarly, Bolondi et al.3 and Sudhamshu et al.2 reported the pattern of continuous turbulent HV flow had been more frequent in cirrhotic patients with relatively severer disease as shown by the significant correlation with the Child-Pugh score. In the present series the severity of the liver cirrhosis was assessed by Child-Pugh scoring system with the parameters of encephalopathy, serum bilirubin, serum albumin, prothombin time and ascites. Adding the individual score <7 was Child's class A, 7-9 was Child's class B and > 9 was Child's class C. It was observed in Child's class A wave form HV-0 was found in 75.0%, HV-1 25.0% and HV-2 was not found in case group. In Child's class B wave form HV-0 was found in 21.4%, HV-1 was 71.5% and HV-2 was 7.1%. In Child's class C wave form HV-0 was not found, HV-1 was 10.0% and HV-2 was 90.0% and the difference was statistically significant (p<0.05) among the different grading level with wave form. The results obtained in the present study are comparable with the above studies.

It was found in the present study according to Child's class A the mean (±SD) velocity was 9.18±2.17 cm/sec and their velocity ranged from 6.2 to 15.0 cm/sec. In Child's class B the mean (±SD) velocity was 11.26±1.81 cm/sec and their velocity ranged from 7.5 to 14.2 cm/sec. In Child's class C the mean (±SD) velocity was 18.44±191 cm/sec and their velocity was 18.44±191 cm/sec and their velocity ranged from 15.5 to 20.9 cm/sec. The mean velocity was statistically significant (p<0.05) among Child's class A, Child's class B and Child's class C.

Sudhamshu et al.² had also made identical observation. According to them the mean(±SD) hepatic vein velocity were 9.7±4.1 cm/sec in grade A, 11.6±5.4 cm/sec in grade B, and 19.2±10.3 cm/sec in grade C. This result is closely consistent with the present study.

Conclusion

In this study it was found that Doppler waveform and mean velocity in right hepatic

vein is relatively accurate and reproducible. This current study applied to study the right hepatic vein and an attempt has been made to correlate the findings with severity in cirrhotic patients and observed that the cirrhotic patients had increased velocity of the hepatic vein and those cases with very high velocity were having poorer liver function as graded by Child-Pugh classification. On the other hand, the Doppler ultrasound abnormality in hepatic vein waveform could be reasonably considered as an adjunctive sign of liver cirrhosis and are somewhat related to the severity of cirrhosis. Hence, the study advocates that Doppler waveform and measurement of mean hepatic vein velocity, which is non-invasive, can be used as new parameter in the investigation of liver cirrhosis.

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