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Correlation between Hepatic Vein Wave form Changes on Doppler Ultrasound and the Severity of Diseases in Cirrhotic Patients

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Abstracts:

Background: *Cirrhosis is a common problem and is a leading cause of chronic liver disease. Early diagnosis with assessment of severity of diseases may help prevent the associated complications and patients' sufferings. Now a days Hepatic venous Doppler can be a tool for diagnosis of cirrhosis and to assess correlation between waveform changes and severity of diseases.*

Objective: *The purposes of this study was to determine the significance of hepatic vein waveform changes on doppler ultrasound in cirrhotic patients and to correlate with liver dysfunction.*

Materials and methods: *This study was carried out in the department of Radiology and Imaging of Enam Medical College and Hospital during January 2017 to May 2018. Doppler waveforms were obtained from right hepatic vein in all the cases and classified as triphasic, biphasic and monophasic. Waveform comparisons were made among patients with differing grades of cirrhosis. Child- Pugh class was used to assess severity of cirrhosis. Doppler sonography was done in 80 patients suspecting of having liver cirrhosis. Data on clinical findings, B mode sonographic findings and hepatic vein doppler ultrasound findings were collected and documented in structured forms. Analysis was done using SPSS - 20.*

Results: *Total of 80 patients who met the inclusion criteria are included in the study with mean age of 45.37±7.64 (range 25-75) years. Among these 57 (71%) were males while 23(29%) were females. On the basis of hepatic function 25 (31%) patients presented in Child-Pugh Class A, 31(39%) with Class B and 24(30%) patients had Class C. Hepatic venous waveform was triphasic in 22 (27.5%), biphasic in 28(35%), and monophasic in 30 (37.5%) cases. Our study revealed 88% (21) of Child- Pugh Class C, 23% (7) of Class B and 8% (2) of class A patients had monophasic HV waveform. The hepatic venous waveform progressively changed from triphasic to biphasic to monophasic with advancing grade of cirrhosis. The relationship of these waveforms change had significant relation with hepatic dysfunction ($p < 0.022$).*

Conclusion: *Hepatic vein wave form changes reflects the change in hepatic circulation associated with progression of liver cirrhosis. It can be used as a new parameter in the assessment of severity of liver cirrhosis. Thus, alteration in hepatic venous blood flow pattern on doppler ultrasound can be a useful noninvasive tool for evaluating diseases severity in patients with cirrhosis.*

Key words: *Hepatic vein waveforms, Doppler, Cirrhosis, Child-Pugh Class.*

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Introduction:

Liver cirrhosis is a major cause of morbidity and mortality[1] and is currently the 14th leading cause of death worldwide[2]. With the help of grading of liver cirrhosis, we can get prognostic information and directs appropriate therapy. The scoring system used for predicting the cirrhosis was first introduced by Child and Turcotte in 1964 and later revised by Pugh in 1974[3,4,5,6]. Every patient is divided as grade – A, B and C. Grade A is prognostically better and grade C is worst[7].

Knowledge of vascular flow patterns in cirrhotic patients provides information about severity of diseases. Doppler ultrasonography of the hepatic vasculature can be used for evaluating precirrhotic and cirrhotic patients. The normal

and abnormal spectral Doppler waveforms from the hepatic veins and knowledge of their respective physiology and pathophysiology provide valuable information. Accurate interpretation of the spectral Doppler tracing from the hepatic veins reflects important hepatic physiology. Various Doppler indices have been used for assessing severity of diseases with cirrhosis[8-14]. Hepatic venous waveform changes are one of them. Normal hepatic venous waveform is triphasic. In hepatic disease, these normal waves may be absent. In cirrhosis this changes to biphasic and then monophasic mainly due to the loss of compliance of liver[15,16,17].

In liver cirrhosis, there are changes in liver parenchyma characterized by diffuse parenchymal destruction, fibrosis with alteration of hepatic architecture, formation of multiple regenerative nodules as well as alteration of hepatic vasculature, including morphological changes of the hepatic vein[18]. Furthermore, it is accepted that abnormal circulation caused by hyperdynamic circulation and intrahepatic shunt persists in cirrhotic liver and this lead to an alteration in hepatic venous hemodynamics in cirrhotic liver. The aim of our study was to assess the hepatic venous hemodynamics changes according to diseases severity in liver cirrhosis using non-invasive Doppler ultrasonography.

Materials and Methods:

This study was carried out in the department of Radiology and Imaging of Enam Medical College and Hospital from January 2017 to May 2018. A total number of 80 cirrhotic patients were enrolled in the study.

We analyzed theses patient by recording age, sex, associated symptoms for clinical evaluation. In our study, doppler study of right hepatic vein was performed in cirrhotic patients during the study period. B mode, color Doppler and spectral doppler ultrasound were used for the examination.

In cirrhosis, Child-Pugh grade was used to assess the hepato-cellular function. The determining five factors were: serum bilirubin, serum albumin, ascites, encephalopathy, and prothrombin time. Every patient was categorized as grade – A, B and C where grade A had better prognosis and that of grade C was worst and grade B was in between.

Doppler ultrasound was conducted after 8 hours fasting on patients by using Doppler ultrasound machine with a 3.5 MHz convex probe. The right hepatic vein was identified at a distance of 3-5 cm from the junction of hepatic vein with inferior vena cava and waveforms were recorded. These waveforms were classified as triphasic (reversed flow in at least one phase), biphasic (no reversed flow) and monophasic (flat - without flutter).

Ultrasound of whole abdomen, liver function test, HBsAg, anti HCV, serum albumin, total protein, A/G ratio, prothrombin time, complete blood count were done. Upper GI endoscopy report was also collected for oesophageal varices which were classified into small and large varices. Thus, hepatic function was assessed and grouped by Child-Pugh classification.

Then correlation of hepatic vein waveforms changes with Child-Pugh class were evaluated. Thereafter statistical analysis was done using SPSS-20 and statistical significance was defined as $P < 0.05$.

Result:

Total of 80 patients who met the inclusion criteria are included in the study with mean age of 45.37±7.64 (range 25-75) years. Among them 57 (71%) patients were males while 23(29%) were female patients.

Sonographically – Atrophied hepatic size were found in 35(44%) cases, 5(6%) cases shown hepatomegaly and 40(50%) cases shown normal hepatic size. 60(75%) cases were coarse in echotexture. Hepatic surface were lobulated in 52(65%) cases. Macronodules were present in 45(56%) cases and absent in 35(44%) cases. Splenomegaly were seen in 42(53%) cases. Portal vein was dilated in 48(60%) cases whereas splenic vein was dilated in 42(53%) cases. Ascites was seen in 70 (88%) cases. (Table I)

Table-I. *Distribution of respondents according to morphological sonographic features in cirrhotic patients. (n- 80)*

Morphological sonographic criteria	No of respondents	Percentage
Hepatic size		
Atrophied	35	44
Enlarged	5	6
Normal	40	50
Hepatic Surface		
Smooth	28	35
Lobulated	52	65
Hepatic parenchymal echotexture		
Coarse	60	75
Mildly coarse	15	19
Normal	5	6
Macronodules		
Present	45	56
Absent	35	44
Splenic Size		
Enlarged	70	88
Normal	10	12
Portal vein		
Dilated (>14cm)	48	60
Normal	32	40
Splenic vein		
Dilated	42	53
Normal	38	47
Ascites		
Present	70	88
Absent	10	12

cases shown serum bilirubin level within 3mg/dl whereas 25(31%) cases in above this level. HbsAg was detected in 35(44%) cases and Anti-HCVin 15(19%) cases. Serum albumin level was <2.8 gm/dl in 20(25%) cases and prothrombin time was >6 seconds in 27(34%) cases. Large oesophageal varices were seen in 26(32%) cases and small oesophageal varices were in 30(38%) cases. Encephalopathy was mild in 10(12%) cases, moderate in 25 (31%) cases and severe in 15 (19%) cases. (Table II)

Table II. *Distribution of respondents according to other variables for diagnosis of cirrhosis. (n= 80)*

Variables	No of respondents	Percentage
Ascites		
Absent	10	12
Mild	20	25
Moderate	26	33
Severe	24	30
Bilirubin mg/dl		
<2	20	25
3	35	44
>3	25	31
HBsAg		
Present	35	44
Absent	45	56
Anti- HCV		
Present	15	19
Absent	65	81
DNA markers		
Detected	32	40
Non-Detected	48	60
SGPT level		
Increased	25	31
Normal	55	69
Albumin gm/dl		
>3.5	25	31
2.8-3.5	35	44
<2.8	20	25
Prothrombin time (seconds over control)		
<4	25	31
4-6	28	35
>6	27	34
Oesophageal varices		
No varices	24	30
Small varices	30	38
Large varices	26	32
Encephalopathy		
None	30	38
Mild	10	12
Moderate	25	31
Severe	15	19

Child-Pugh classification was used to assess the hepato-cellular function. The determining five factors were: serum bilirubin, serum albumin, ascites, encephalopathy, and prothrombin time. Every patient was assigned as grade – A, B and C. (Table III)

Table III. *Child-Pugh classification of the severity of cirrhosis*

Score	1	2	3
Ascites	None	Mild/Moderate (diuretic-responsive	Severe (diuretic refractory)
Bilirubin (mg/dl)	<2	2-3	>3
Albumin (g/dl)	>3.5	2.8-3.5	<2.8
Prothrombin time (Seconds over control)		<4	4-6>6
Encephalopathy	None	Grade 1-2	Grade 3-4

Child-Pugh score is obtained by adding the score for each parameter:

Total score of 5-6 = Grade A (Well compensated disease)

Total score of 7-9 = Grade B (Disease with significant functional compromise)

Total score of 10-15 = Grade C (Decompensated liver disease)

On the basis of hepatic function 25 (31%) patients presented in Child-Pugh Class A, 31(39%) with Class B and 24(30%) patients had Class C. Hepatic venous waveform was triphasic in 22 (27.5%), biphasic in 28(35%), and monophasic in 30 (37.5%) cases. Our study revealed 88% (21) of Child-Pugh Class C, 23% (7) of Class B and 8% (2) of class A patients had monophasic HV waveform. So the hepatic venous waveform progressively changed from triphasic to biphasic to monophasic with advancing grade of cirrhosis. The relationship of these waveforms had significant relation with hepatic dysfunction ($p < 0.022$). (Table IV) & (Figure 1 to 3)

Table IV. *Pattern of hepatic vein waveforms in Cirrhotic patient with Child's grading*

Pattern of	Cirrhotic group (N=80)			
Wave form	Total	Child's A (n= 25)	Child's B (n= 31)	Child's C (n= 24)
Triphasic	22(27.5%)	17(68%)	5(16%)	0(0%)
Biphasic	28 (35%)	6(24%)	19(61%)	3(12%)
Monophasic	30 (37.5%)	2(8%)	7(23%)	21(88%)

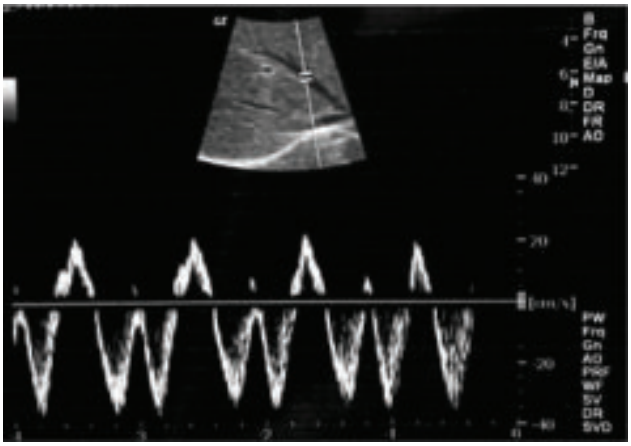

Figure-1: *Triphasic Hepatic vein waveform*

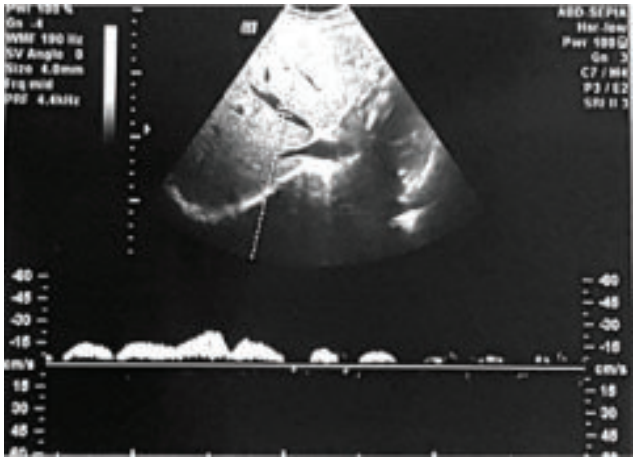

Figure-2: *Biphasic Hepatic vein waveform*

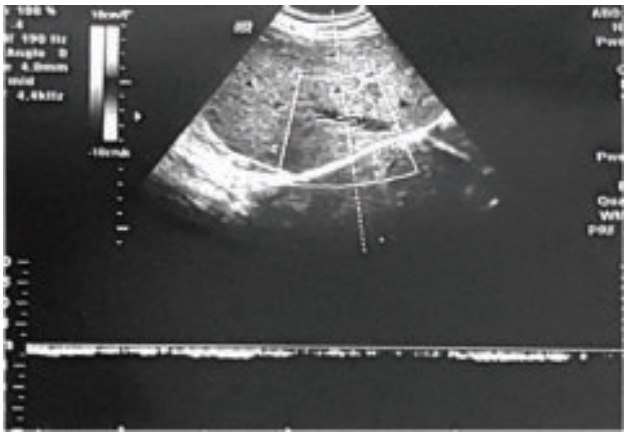

Figure-3: *Monophasic Hepatic waveform*

Discussion:

Cirrhosis is defined as an abnormal liver pathology in which there is diffuse irreversible scarring of the liver parenchyma and replacement by structurally abnormal nodules[19]. Liver biopsy is considered gold standard for diagnosis of cirrhosis, but it has several potential complications including death[7].Thus if we can predict cirrhosis and its grade noninvasively with ultrasound then biopsy may not be necessary and complications would be avoided. Alteration in hepatic venous waveform pattern in doppler ultrasound can be a useful noninvasive tool to distinguish patients in different grades of cirrhosis.

Because the walls of the hepatic veins are thin, diseases of the hepatic parenchyma may alter their compliance. In many patients with compensated cirrhosis, the doppler waveform is abnormal. The compression of the hepatic veins in cirrhosis by regenerative nodules may explain changes in phasic oscillation. The abnormal wave pattern of hepatic veins is correlated with parenchymal fibrosis around the hepatic veins. Doppler waveform of the hepatic vein (HV) in healthy humans is a triphasic waveform, consisting of two negative waves and one positive wave[20]. With increased stiffness in the liver parenchyma (especially around the HVs), the hepatic waveform becomes less pulsatile with no retrograde flow, and can eventually lead to a flat waveform[21,22,23]. As for abnormal hemodynamics of the hepatic vein in cirrhotic liver, there are reports of doppler studies suggesting that the waveform becomes flat when hepatocellular function is impaired, and some studies even proposed that flattening of the hepatic waveform could be used as a diagnostic tool for chronic parenchymal liver disease[10,12,15,16,24].

Spectral and color Doppler ultrasonography can demonstrate many characteristic flow patterns from hepatic vasculature in patients with liver cirrhosis with or without portal hypertension. Knowledge of these different flow patterns provides additional information that may reinforce the diagnosis of cirrhosis, help in staging, and offer prognostic information for determining the direction of therapy. Doppler ultrasonography is invaluable when liver transplantation is being considered and aids in the diagnosis of cirrhosis and portal hypertension. This article discussed the different characteristic flow patterns observed from the hepatic vein in patients with liver cirrhosis.

Many studies[23,25,26] having good sensitivity and positive predictive value described sonographic features of liver cirrhosis by changes in liver volume distribution, surface nodularity, accentuation of the fissure, heterogeneity, bright and coarsening of the hepatic architecture, cirrhotic nodules including regenerative and dysplastic nodules, and signs of portal hypertension which were comparable to our study findings regarding sonographic features of liver cirrhosis.

In this study we used the Doppler parameter to identify the correlation of hepatic venous waveforms changes with Child-

Pugh classification in cirrhotic patients.

In our study, on the basis of hepatic function 25 (31%) patients presented in Child-Pugh Class A, 31(39%) with Class B and 24(30%) patients had Class C. Hepatic venous waveform was triphasic in 22 (27.5%), biphasic in 28(35%), and monophasic in 30 (37.5%) cases. Our study revealed 88% (21) of Child- Pugh Class C, 23% (7) of Class B and 8% (2) of class A patients had monophasic HV waveform. So, the hepatic venous waveform progressively changed from triphasic to biphasic to monophasic with advancing grade of cirrhosis. The relationship of these waveforms had significant relation with hepatic dysfunction ($p < 0.022$). This could be because of the increasing severity of architectural distortion of liver parenchyma with increasing grade of cirrhosis. However statistical analysis showed this to be significant.

Recent studies suggest that the flattening of the phasic oscillations of the hepatic veins pulse is significantly associated with liver cirrhosis had high sensitivity and specificity in the diagnosis of cirrhosis[16,27]. Many studies[18,28,29] found significant correlation between waveform changes and liver dysfunction in their studies. Some Other studies[30,31] also revealed same results supporting our study findings. Bolondi et al[10] have reported that the underlying mechanism of the change in the hepatic vein waveform may be related to liver fibrosis, which progressively reduces phasic oscillation in hepatic veins. Changes in the Doppler waveform (smaller oscillations without the reversed phase or a completely flat waveform) are seen in at least 50% of patients with cirrhosis[10]. Three grades of hepatic waveforms have been described to indicate changes from the normal triphasic pattern to the flat pattern widely used in many studies of chronic liver disease[10,15,16]. Several studies suggest that abnormal curves in hepatic vein may indicate some degree of abnormality in liver[22,24,32-35].Various studies have been designed for evaluating the severity of liver abnormalities by Doppler ultrasound in patients with chronic liver disease [36,37,38].

We undertook this study to evaluate the correlation of hepatic vein wave form changes on doppler ultrasound in cirrhotic patients with Child's status. According to our study hepatic venous waveform changes have significant relation with severity of hepatic dysfunction and our study was also comparable to many other similar studies. So, Hepatic venous waveform changes is useful in the noninvasive evaluation of severity of liver cirrhosis and doppler ultrasound of hepatic vein can be used as a noninvasive technique that can be performed on outpatient basis. Sharma S & et al[18] also described doppler ultrasound of hepatic vein as a noninvasive tool to assess liver cirrhosis in their study. However, the findings of few studies using Doppler waveform parameter were not consistent with our results[39,40]. So, further studies using a combination of various Doppler parameters are required to create indices with a better predictive value.

Conclusion:

Duplex sonography a simple and reproducible tool for studying liver disease. Examination of the Doppler waveform of the hepatic vein was easy, possible in all patients, and less time consuming. As the changes in hepatic vein wave form correlated significantly with the severity of the disease so change in the Doppler waveforms of hepatic veins might be a valuable adjunctive sign of this disease. Hence, we advocate that Doppler ultrasound of hepatic vein, which is non-invasive, can be used as a new parameter in the investigation of liver cirrhosis.

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