FREQUENCY OF ABNORMAL HEPATIC VENOUS WAVEFORMS IN CIRRHOTIC PATIENTS

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ABSTRACT

Objective: To determine the frequency of abnormal hepatic venous waveforms in patients suffering from hepatic cirrhosis.

Study Design: Cross sectional.

Place and of Study Duration: Shafique Medical Centre Quetta & Radiology Department Combined Military Hospital, Quetta from December 15th 2009 to July 15th 2010.

Material and Methods: The instrument used in this study was Toshiba Eccocee SSA-340A and ALOKA SSD-5000 doppler ultrasound machines with linear and convex probes. Hepatic venous Doppler was performed with convex 3-5 MHz probe. Hepatic venous Doppler examination was performed by two radiologists (operators) on all the 135 patients with positive HCV, HBV, chronically raised amino transferase level and clinical & radiological features of cirrhosis, who independently and blindly recorded their findings. Non-probability, purposive sampling was done. After Doppler ultrasonographic examination liver biopsy & histopathology of all the patients was performed. Data from each patient was collected on designed form for age, gender, types of hepatic vein waveforms and grades / severity of liver cirrhosis on histopathology.

Results: 135 patients with maximum 50 years and minimum 41 years of age have mean age of 46.79 ± 2.37. Out of 135 patients in 103 (76.3%) Type 1 (Triphasic) flow was observed in 3%, Type II (Biphasic without reduced oscillation) flow was observed in 29.6%, type III (Biphasic with reduced oscillation) flow was observed in 34.1% and type IV (Monophasic) flow noted in 33.33 %. There was significant correlation between hepatic venous waveform and severity of cirrhosis on histopathology ($r=0.887$, $p< 0.001$)

Conclusion: Hepatic venous Doppler is noninvasive tool which can be employed to assess the types of abnormal hepatic venous waveforms in patients with hepatic cirrhosis. There is significant correlation between hepatic venous waveform and severity of cirrhosis on histopathology.

Keywords: Hepatic vein waveform, Liver cirrhosis, Doppler ultrasound.

INTRODUCTION

Hepatic veins are thin walled structures that drain into the inferior vena cava, running deeply and within enclosed by hepatic parenchyma. Flow in the hepatic veins is antegrade but at least in healthy subjects it is phasic (triphasic), reflecting the variations in central venous pressure due to cardiac cycle. The Doppler spectrum obtained from normal subjects, therefore is multiphasic, two large antegrade diastolic and systolic waves and a small retrograde wave corresponding to atrial systole. Liver parenchymal disease can impair the compliance of the walls of the hepatic veins, decreasing and flattening the phasic oscillation. Change in the Doppler waveform (smaller oscillation without reverse phase or completely flat waveform) are seen in at least 50% of patients with cirrhosis[1] These changes might correlate with the severity of the disease. Hepatic veins show normal triphasic waveform (type I) with two hepatofugal and one hepatopetal (retrograde) velocity peaks and abnormal biphasic waveform (Type II) without retrograde flow phase and without reduced oscillation, biphasic with reduced oscillation (type III) & flat (monophasic) waveform (type IV). (Fig-1). The abnormal hepatic venous waveforms are due to decreased compliance of the hepatic veins caused by liver parenchymal disease like cirrhosis.

Liver cirrhosis is one of the major health problems in Asia, the major etiological factors such as chronic hepatitis B and C are common in south East Asian countries[2] The World Health Organization (WHO) has compared hepatitis C to a "viral time bomb" and estimates

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that about 180 million people (some 3% of the world's population) are infected with hepatitis C virus (HCV), 130 million of whom are chronic carriers at risk of developing liver cirrhosis and/or liver cancer. Three to four million persons are newly infected each year, 70% of whom will develop chronic hepatitis[3]. Certain hemodynamic disruptions in liver vessels accompany the chronic hepatic disease. These alterations are generally the result rather than the cause of hepatic dysfunction. Waveform in hepatic veins is a parameter susceptible to pathologic changes[4]. Many international studies showed significant relationship of waveform abnormalities of hepatic veins and histological finding of fibrosis (p<0.001). Liver biopsy is considered to be the gold standard for diagnosing the liver damage. Although relatively safe it is still associated with a risk of complications like hematoma, intra-peritoneal hemorrhage, biliary leak and pneumothorax. Therefore, there is a need to develop a simple, reliable and non-invasive technique in order to assess the extent of liver damage[5].

Little work has been done in this field in our country. Most of the literature available is from the west and there is a need to explore this issue in our own setup. Aim of this study was to determine the frequency of abnormal hepatic venous waveforms in patients suffering from hepatic cirrhosis. By interpreting the types of hepatic venous waveforms one can assess the extent of liver damage by non- invasive method.

MATERIAL AND METHODS

This cross sectional study was conducted at two different places i.e. Naveed ultrasound at Shafique Medical Centre Quetta & Radiology Department, Combined Military Hospital, Quetta. The study was of six months duration from December 15th 2009 to July 15th2010. The patients tested positive for antibodies to HCV and positive for antigen to HBV, all the patients having chronically increased aminotransferase level and clinical & radiological features of cirrhosis were included in the study. The patients with liver pathology other than cirrhosis such as fatty liver, liver abscess or a space occupying lesion within the liver were excluded. 135 patients with above mentioned criteria were included in the study through non-probability, purposive sampling. Two different ultrasound machines with Doppler facility were used. Naveed ultrasound at Shafique Medical Centre, Toshiba Eccocee SSA-340A doppler ultrasound machine with linear and convex probes was used. Hepatic venous Doppler was performed with convex 3-5 MHz probe. At Radiology Department,

Table-1: Description of different types of hepatic venous waveforms (n=135).

Type of hepatic vein waveform	Frequency	Percent%
Type 1(Triphasic)	04	3
Type II(Biphasic without reduced oscillation)	40	29.6
Type III (Biphasic with reduced oscillation)	46	34.1
Type IV(Monophasic)	45	33.3

Table-2: Showing correlation of different types of hepatic venous waveforms with severity of hepatic cirrhosis on histopathology (n=135).

Hepatic venous waveform Types	Severity of cirrhosis on Histopathology		
	Mild disease-fibrous portal expansion	Moderate disease--bridging fibrosis	Severe disease-cirrhosis
Triphasic(Normal) --Type-I	4 (100%)	0 (0%)	0 (0%)
Biphasic without reduced oscillation --Type-II	0 (0%)	40 (100%)	0 (0%)
Biphasic with reduced oscillation--Type-III	0 (0%)	46 (100%)	0 (0%)
Monophasic--Type-IV	0 (0%)	0 (0%)	45 (100%)

Combined Military Hospital, Quetta ALOKA SSD-5000 doppler ultrasound machine with linear and convex probes was used. Hepatic venous Doppler was performed with convex 3-5 MHz probe. Sonographic examination was performed by two radiologists (operators) on all the patients who independently and blindly recorded their findings. One operator with twelve years & second with eight years experience performed the hepatic venous doppler study. The doppler sample volume was set as large as at least one third of the vessel's diameter. It was positioned within the middle hepatic vein at a distance of 3-5 cm from the outlet into the inferior vena cava, keeping the angle of incidence of the doppler ultrasound beam at less than 600. After Doppler ultrasonographic examination liver biopsy & histopathology of all the patients was performed and correlation of abnormal hepatic venous waveform with histopathology findings was done. Data from each patient was collected on designed form for age, gender, types of hepatic vein waveforms and histopathology of liver biopsy. Data was analyzed with SPSS version 14. Mean and standard deviation (SD) of age were calculated while frequency & percentages were calculated for venous waveforms. Spearman's rank correlation of abnormal hepatic venous waveform was done with histopathogical findings by calculating correlation coefficient(r).A *p*-value <0.05 was considered as significant.

RESULTS

135 patients with maximum 50 years and minimum 41 years of age have mean age of 46.79 + 2.37 years. Out of 135 patients 103 (76.3%) were male and 32(23.7%) were female. Type 1(Triphasic) flow was observed in 04 (3%), type II (Biphasic without reduced oscillation) flow was observed in 40(29.6%), Type III (Biphasic with reduced oscillation) flow was observed in 46 (34.1%) and type IV (Monophasic) flow noted in 45 (33%) patients (table-1) In patients with type I hepatic venous flow histopathology showed fibrous portal expansion i.e mild disease, in patients with type II &type III hepatic venous flow histopathology showed bridging fibrosis i.e moderate disease and in patients with type IV hepatic venous flow histopathology showed cirrhosis i.e. severe disease. Only 04 patients with normal (triphasic venous flow) showed mild disease on histopathology rest of the patients with abnormal hepatic venous flow showed moderate and severe disease. (table-2) There was significant correlation between hepatic venous waveform and severity of cirrhosis on histopathology.(r=0.887,*p*<0.001)

Fig-1 Hepatic vein Doppler waveforms. Type I: normal triphasic waveform, type II : Biphasic without reduced oscillations, type III: Biphasic with reduced oscillation and type IV : Monophasic hepatic venous waveform.

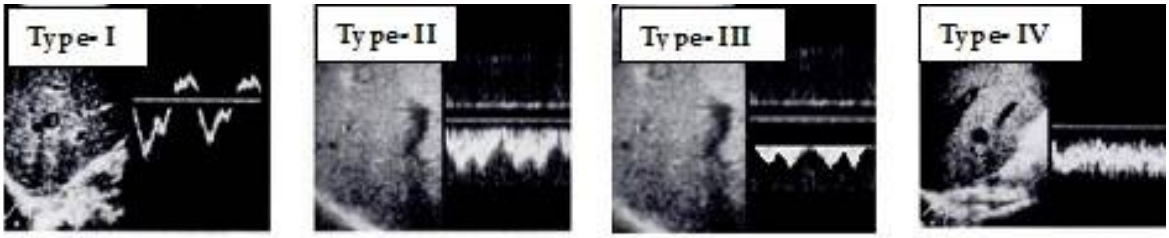

Figure-1: Hepatic vein doppler waveforms. Type-I: normal triphasic waveform, Type-II Biphasic without reduced oscillations, Type-III: Biphasic with reduced Oscillation and Type-I : Monophasic hepatic venous waveform.

DISCUSSION

The World Health Organization (WHO) has compared hepatitis C to a "viral time bomb" and estimates that about 180 million people (some 3% of the world's population) are infected with hepatitis C virus (HCV), 130 million of whom are chronic carriers at risk of developing liver cirrhosis and/or liver cancer. Three to four million persons are newly infected each year, 70% of whom will develop chronic hepatitis. HCV is responsible for 50-76% of all liver cancer cases, and two thirds of all liver transplants in the developed world[3]. Cirrhosis

is mostly due to the untreated Hepatitis B or C infections. Progression to chronic disease occurs in majority of HCV infected patients. The diagnosis of cirrhosis is of great prognostic value and requires histological proof of diffuse fibrosis associated with architecturally abnormal regenerative nodules along with the typical clinical features. Certain hemodynamic disruptions in liver vessels accompany these chronic hepatic diseases.

A study conducted in Pakistan by Javed et al[5] showed significant relationship of waveform abnormalities of hepatic veins and histological finding of fibrosis (p<0.001). Liver biopsy is considered to be the gold standard for diagnosing the liver damage. Although relatively safe it is still associated with a risk of complications like patient discomfort and high cost. Therefore, there is a need to develop a simple, reliable and non-invasive technique in order to assess the extent of liver damage.

In a study conducted by Kawanaka et al[6] about 103 consecutive patients were selected and hepatic venous waveforms were classified into four groups : type I, triphasic waveform; type II, biphasic waveform; type III, biphasic waveform with reduced phasic oscillations; and type IV, a flat waveform. The results of this international study and our study are comparable. The above mentioned study by Kawanaka et al also determined the prognostic value of hepatic venous waveforms and concluded that analyzing the HV waveforms was found to be a simple and non invasive method for assessing the prognosis in cirrhotic patients with portal hypertension.

The mean age in our study is 42 ± 10 years which corresponds well to a similar study carried out by Barakat M[7] in which the mean age was found to be 44 ± 11 years suggesting that cirrhosis is most commonly found in third and fourth decades. In the same study the hepatic venous waveform was recorded from the middle hepatic vein at a point 2–3 cm away from the inferior vena cava; this is the same method that we employed in our study as well.

Scheinfeld et al[8] suggest that accurate interpretation of the spectral Doppler tracing from the hepatic veins reflects important cardiac and hepatic physiology. Normally, there are four phases: A, S, V, and D; the S and D waves indicate flow in the ante grade direction toward the heart. In hepatic and cardiac disease, these normal waves may be absent, a finding indicative of flow in a non physiologic manner. In addition, transient patient factors such as phase of the respiratory cycle may influence the appearance of the spectral tracing. Familiarity with the normal and abnormal spectral doppler waveforms from the hepatic veins and knowledge of their respective physiology and pathophysiology provide valuable insights. Systematic analysis of the direction, regularity, and phasicity of the spectral tracing and the ratio of the amplitudes of the S and D waves allows one to arrive at the correct differential diagnosis in most situations[9].

Gorka et al[10] observed the relationship of esophageal varices, grades and waveform characteristics of the hepatic vein, and they found monophasic flow in 92% of cases with advanced varices Baik et al[11] also concluded that Doppler US hepatic vein waveform assessment is useful in the noninvasive evaluation of the severity of portal hypertension and the response to vasoactive drugs in patients with portal hypertension and variceal bleeding.

Oshima et al[12] suggested that the usefulness of the analysis of the doppler waveform of hepatic veins is an easy, non-invasive and reliable method for determining hepatic functional reserve O'Donohue et al[13] observed that splenic size and abnormal HVP as useful predictors of chronic liver disease and cirrhosis, and both can be measured reliably and reproducibly.

There are certain limitations to this study like patient co-operation as the hepatic venous waveform analysis was done in quite respiration. The results of our study are comparable to international studies which assessed the abnormal hepatic venous waveform and its correlation with liver biopsy& histopathology in the diagnosis of severity of liver cirrhosis.

CONCLUSION

Hepatic venous doppler is non invasive tool which can be employed to assess the types of abnormal hepatic venous waveforms in patients with hepatic cirrhosis. There is significant correlation between hepatic venous waveform and severity of cirrhosis on histopathology hence hepatic venous doppler is helpful in the assessment of severity of hepatic cirrhosis.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

REFERENCES

1. Blondi L, Li Bassi S, Gaiani S. Liver Cirrhosis: change of Doppler waveform of hepatic veins. Radiology 1991; 178:513-516.
2. Wai D. Fatty liver. [Internet] 2008. Available from; http:/ / www.asianlivercentre.com.sg/ images/ pdf/ drwaichuntao/ 1Fatty Liver_mod.htm
3. World Health Organization. Hepatitis C. [Internet] Available at: www.who.int/ vaccine_research/ viral_cancers. Retrieved on 16.4.2009.
4. Vyas K, Gala B, Sawant P, Das HS, Kulhalli PM, Mahajan SS. Assessment of portal hemodynamics by ultrasound color doppler and laser dopplervelocimetry in liver cirrhosis.Indian J Gastroentrol. 2002; 21:176-8
5. Javed K, Azam MN, Akram MH. Correlation of doppler waveform abnormalities of hepatic veins with histological findings in chronic liver disease (Hcv Infection). Pak Armed Forces Med J. 2008; 58:414-17.
6. Kawanaka H, Kinjo N, Anegawa G, Yoshida D, Migoh S, Konishi K. Abnormality of the hepatic vein waveforms in cirrhotic patients with portal hypertension and its prognostic implications. J Gastroenterol Hepatol. 2008; 23: 129-36.
7. Barakat M . Non-pulsatile hepatic and portal vein waveforms in patients with liver cirrhosis: concordant and discordant relationships. Br J Radiol. 2004; 77: 547-50.
8. Scheinfeld M H. Bilali A, Koenigsberg M. Understanding the spectral doppler waveform of the hepatic veins in health and disease. Radio Graphics. 2009; 29: 2081-98.
9. Annet L, Materne R, Danse E, Jamart J, Horsmans Y, Van Beers BE. Hepatic flow parameters measured with MR imaging and doppler us: correlations with degree of cirrhosis and portal hypertension. Radiology. 2003; 229: 409–14.
10. Gorka W, Kagalwalla A, McParland BJ, Kagalwalla Y, al Zaben A. Diagnostic value of doppler ultrasound in the assessment of liver cirrhosis in children: histopathological correlation. J Clin Ultrasound 1996; 24:287–95.
11. Baik SK, Kim JW, Kim HS. Recent variceal bleeding: doppler US hepatic vein waveform in assessment of severity of portal hypertension and vasoactive drug response. Radiology 2006; 240: 574–80.
12. Oshima K, Kaneko T, Kawase Y, Nakao A. Quantitative analysis of doppler waveform of hepatic veins for assessment of hepatic functional reserve. Hepatogastroenterology. 2007; 54:180-5.
13. O'donohue J, Ng C, Catnach S, Farrant P, Williams R. Diagnostic value of doppler assessment of the hepatic and portal vessels and ultrasound of the spleen in liver disease. Eur J Gastroenterol Hepatol. 2004; 16:147–155.