International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Impact Factor (2012): 3.358

Comparative Study of Various Sonographic Doppler Parameters of Chronic Hepatitis C Patients with Healthy Individuals of South India

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Abstract: ***Aim:*** ***The aim of this prospective study was to determine and compare the various parameters and indices of portal vein, hepatic artery and splenic artery by sonographic Doppler imaging in chronic hepatitis C patients and healthy individuals.*** ***Methods:*** ***45 Chronic Hepatitis C patients and 90 Healthy adults formed two groups. All participants underwent color Doppler imaging of the portal vein, hepatic artery and splenic artery by a single radiologist and sonographic Doppler measurements were obtained. The examination protocol included measurements of portal vein and hepatic artery diameter (D), Time averaged velocity (TAV), blood flow (BF) , Doppler Perfusion Index (DPI) of liver, liver vascularity index (LVI), congestive index of portal vein(CI), venous pulsatility index of portal vein (VPI) and splenic artery pulsatility index (SAPI).*** ***Results:*** ***Chronic Hepatitis C (CHC) patients show statistically significant increase in portal vein diameter, blood flow, SAPI value and Significant decrease in portal vein TAV, hepatic artery diameter, TAV & blood flow, DPI, LVI, CI and VPI comparision to normal healthy individuals.*** ***Conclusion:*** ***Sonographic Doppler parameters of portal vein, hepatic artery and splenic artery can detect significant hemodynamic changes in Chronic Hepatitis C patients. Applying these simple Doppler indices can decrease the need for staging liver biopsy.***

Keywords: Chronic Hepatitis C, Doppler, CI, DPI, LVI, SAPI

1. Introduction

Hepatitis C is a liver disease caused by the hepatitis C virus. The virus estimated to infect about 3% of the world population, is primarily transmitted via the parenteral route which includes blood transfusion, unsafe injection practices, and other healthcare related procedures. HCV causes acute hepatitis which is mostly subclinical, but which gradually evolves into chronic hepatitis in about 80% of those infected [1]. HCV infected people are at risk for developing chronic liver disease, cirrhosis and primary hepatocellular carcinoma. It has been estimated that HCV accounts for 27% of cirrhosis and 25% of HCC worldwide [2].

HCV is considered an emerging infection in India. There is a lack of existing literature on the true prevalence in general population due to paucity of well-designed population-based studies from the country. The estimated HCV prevalence in India at present is 1-1.9% [3].

Noninvasive methods to evaluate the hepatic histology in hepatitis C virus–infected patients include symptoms and signs, routine laboratory tests, serum markers of fibrosis and inflammation, quantitative tests of liver function, and radiologic imaging (4). At present, liver biopsy remains the definite test for staging and grading HCV-related liver disease although it is an interventional procedure and carries a small risk of various complications. Therefore, the use of a non-invasive method for monitoring patients with chronic hepatitis C is of major clinical concern.

Color Doppler imaging may further provide hemodynamic indices that may be correlated with the status of liver disease [5-7]. A number of positive correlation studies along with negative ones have investigated the role of Doppler sonography of liver disease in adults and healthy population [7-12]. There are very limited studies on these hemodynamic indices in the Indian population that are useful in avoiding liver biopsy.

Our study included evaluation of various hemodynamic Doppler indices in chronic hepatitis C patients and comparision with healthy individuals in south India. The aim of the study is to record diameter, TAV, Blood Flow of hepatic artery and portal vein, Doppler Perfusion Index (DPI), Congestive Index (CI), Liver Vascularity Index (LVI), Venous Pulsatility Index of Portal Vein (VPI), Splenic Artery Pulsatility Index (SAPI) in the Chronic Hepatitis C patients and compare with the healthy individuals.

2. Materials and Methods

A sample of 45 patients with chronic hepatitis C patients and 90 healthy individuals was studied prospectively, during Oct 2012– April 2014 attending the Suguna Multispecialty hospital, Bangalore. The population for the study was divided into two groups. Group 1 consisted of 90 healthy individuals (50 Male, 40 Female, Mean Age 53.03 years, range 30 to 75 years) and Group 2 consisted of 45 Chronic Hepatitis C patients (31 male, 14 female, mean age 56.17 years, range 36 to 73years).

CHC was defined as the presence of hepatitis C virus RNA by polymerase chain reaction (PCR) test and biopsy proven as chronic hepatitis. Patients who were co-infected with human immunodeficiency virus or hepatitis B virus, history of heavy alcohol use or other causes of liver diseases, declined percutaneous liver biopsy, or who were contraindicated for percutaneous liver biopsy were excluded from the study. Patients with abnormal imaging findings in

previous US scan such as Ascites, nodules, focal liver lesions, and abnormal liver echotexture were also excluded from the study.

The control group was chosen from healthy volunteers with normal blood profile, No history of alcohol consumption, No cardiac or liver disease, risk factors for viral hepatitis or were receiving therapy with medications known to alter liver blood flow. Oral informed consent was obtained from each subject in order to perform the sonographic examination.

2.1 Color Doppler Ultrasonography

All scans were performed with the patients lying supine using the same sonography system (GE Voluson PRO 730) by a single experienced observer using a low frequency curvilinear transducer. The machine was supported with the proper software for direct and automatic calculation of the hemodynamic parameters based on the spectral Doppler waveform. The examination started with the observation of liver size and parenchyma in gray-scale scanning. Subsequently, the examination proceeded with spectral Doppler US.

The portal vein Doppler was performed during apnea, at the beginning of inspiration to avoid changes caused by deep inspiration. Spectral analysis of the portal vein flow velocity waveform (FVW) was recorded for at least 5 seconds of suspended inspiration [13]. The measurement point for the portal vein FVW was in the extra hepatic portion, adjacent to the hepatic hilum (Figure 1) and measurements of diameter in centimeters (cms) and time-averaged velocity (TAV) in cms/sec, blood flow (BF) in ml/min were recorded. All measurements were performed with insonation angles between longitudinal axis and sound wave being less than 60° [14, 15].

The hepatic artery was measured as near to its origin as was allowed by the angle of insonation or acoustic Interference from adjacent vessels at the porta hepatis (figure 2). At longitudinal view, the diameter (D) in centimeters (cms) was measured with calipers placed at right angles to the long axis of the vessel along with time-averaged velocity TAV in cms/sec and Blood flow (BF) in ml/min.

The Doppler Perfusion Index (DPI) was calculated by using the following formula [16-17]. Doppler Perfusion Index = Blood flow of hepatic artery/(Blood flow of hepatic artery + blood flow of portal vein)

DPI= BFHA / (BFHA+BFPV)

The liver vascular index (LVI) is calculated from the ratio between the maximum portal vein velocity and the hepatic artery PI (5)

The congestion index (CI) described by Moriyasu and others [18] has been used to diagnose cirrhosis and portal hypertension. The index is calculated from the ratio of the cross-sectional area of the portal vein (cm^2) and the average flow velocity (cm/sec).

The venous pulsatility index (VPI) was calculated by the formula after obtaining maximum and minimum portal vein velocities **[6]**. The formula is by subtracting V_{min} from V_{max} and dividing the remainder of V_{max} in a single wave for each patient.

$VPI = (V_{max} - V_{min}) / V_{max}$

The SAPI were measured according to the formula as Follows by placing the sampling cursor in the main branches of the intrasplenic artery near the splenic hilum at the left intercostal space [19, 20] (figure 3)

SAPI: Peak systolic velocity –End diastolic Velocity / Mean velocity

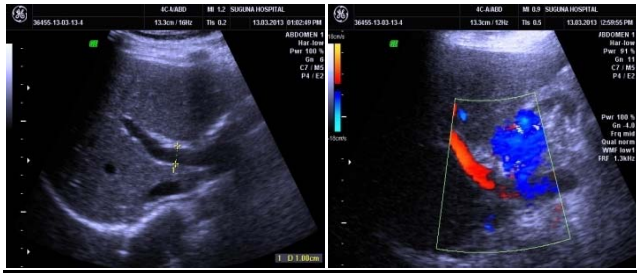


Figure 1: Measurement of Portal vein diameter and color Doppler delineation

Figure 2: Measurement of Hepatic artery diameter and color Doppler

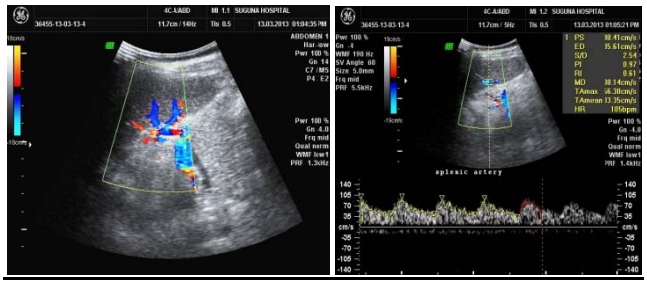


Figure 3: Splenic artery color doppler

2.2 Statistical Analysis

The collected data was analyzed using SPSS 16. The quantitative data was analyzed using mean, standard deviation and confidence interval. The significance of the difference between means was analyzed using independent Student‘t’ test. The P value <0.05 was considered as statistically significant.

3. Results

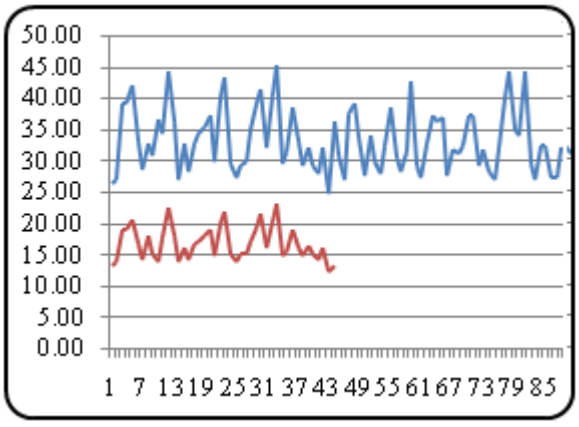
Measurements of portal vein, hepatic artery and splenic artery parameters were performed in all chronic hepatitis C patients and healthy adults (Table 1). The distribution pattern of the various Doppler indices was depicted in the graph

accordingly (Graph 1). There was no statistically significant difference between the mean ages of healthy adults and CHC patients.

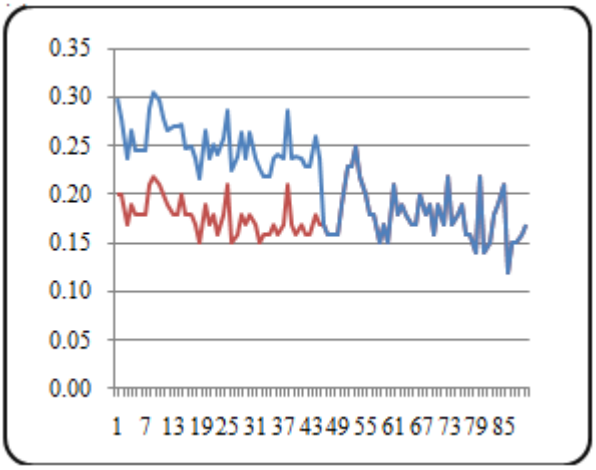
Table 1

Parameters	*group*	*N*	*Mean*	*Std. Deviation*	*Std. Error Mean*	*P value*
PV Dia	1	90	0.9073	0.04266	0.0045	<0.001
	2	45	1.0453	0.03667	0.00547	
PV.TAV	1	90	16.92	1.828108	0.1927	<0.001
	2	45	11.84	1.216272	0.181311	
PV BF	1	90	656.6	81.7248	8.614551	<0.001
	2	45	923.2	103.8671	15.48359	
HA.TAV	1	90	19.2896	1.82754	0.19264	<0.001
	2	45	14.1771	1.28674	0.19182	
HA. BF	1	90	135.1	17.71987	1.86784	<0.001
	2	45	77.8	12.56418	1.87296	
HA. Dia	1	90	0.3852	0.01737	0.00183	<0.001
	2	45	0.3294	0.01468	0.00219	
DPI	1	90	0.1786	0.02286	0.00241	<0.001
	2	45	0.0749	0.0085	0.00127	
LVI	1	90	33.2733	4.96933	0.52381	<0.001
	2	45	16.7728	2.68399	0.40011	
VPI PV	1	90	0.3072	0.01406	0.00148	<0.001
	2	45	0.1724	0.0083	0.00124	
SAPI	1	90	0.8809	0.05166	0.00545	<0.001
	2	45	1.3218	0.0685	0.01021	
CI	1	90	0.0696	0.00947	0.001	<0.000
	2	45	0.0343	0.00283	0.00042	

Portal vein diameter was greater in CHC than in healthy adults with statistical significance ($p<0.001$). Portal vein TAV is significantly reduced in CHC than healthy adults. Portal vein blood flow is significantly increased in CHC patients than healthy adults ($p<0.001$). Hepatic artery diameter, TAV and blood flow was reduced in CHC patients in comparision to healthy adults with statistical significance ($p<0.001$). Doppler perfusion index (DPI) value, liver vascularity index (LVI), Venous pulsatility index of portal Vein (VPI PV) and congestive index (CI) of the chronic hepatitis patients shows lower values in comparision to the healthy individuals with statistical difference of $p <0.0001$. SAPI showed significant elevation in the chronic hepatitis C patients.



(a)



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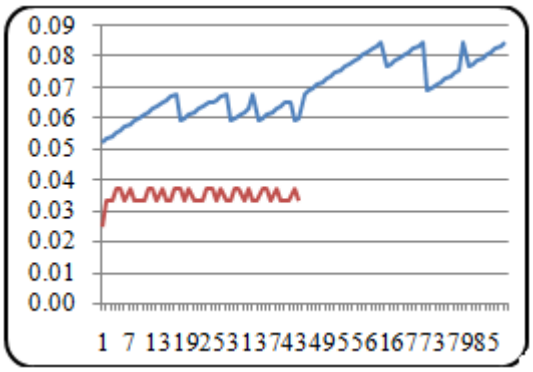
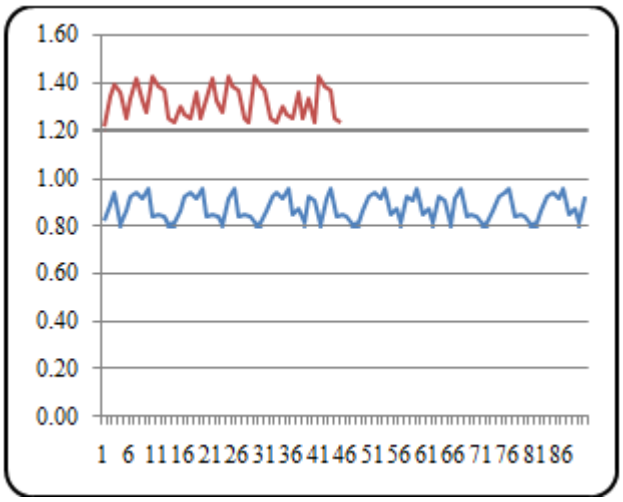
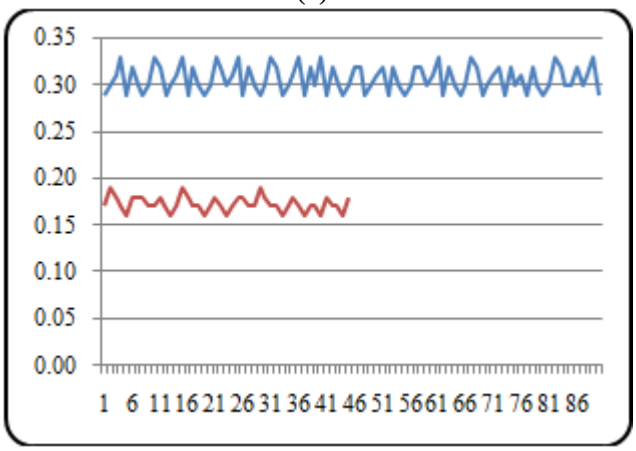


(c)



(d)



(e)

Graph 1: Distribution pattern of Doppler parameters of (a) Liver vascularity index, (b) Doppler perfusion index, (c) Congestive index, (d) Splenic artery pulsatility index and (e) Venous pulsatility index of portal vein in healthy Individuals (Blue color) & chronic hepatitis C (red line)

4. Discussion

Ultrasound is the imaging examination of choice for the follow-up of patients infected with HCV due to increased risk of developing cirrhosis and hepatocellular carcinoma (HCC). Grey scale and color Doppler ultrasound not only provides data on liver hemodynamics by flow imaging but also valuable information about the morphological changes occurring in the liver [21]. A few reports have demonstrated no consistent correlation between the gray scale ultrasound findings and histological findings, thus claiming that grey scale ultrasound is unreliable for grading and staging of liver damage [22]. On the other hand, it has been suggested that hepatic hemodynamic changes may have developed even in cases with normal findings on B-mode sonography [23]. A number of reports have analyzed chronic liver diseases in relation to portal and splenic haemodynamics as assessed by Doppler ultrasonography [24-27, 19].

This study with comparison of Doppler parameters between the CHC and normal individuals showed some interesting results that are of clinical significance.

Portal vein diameter shows significantly increased diameter in chronic hepatitis patients compared to healthy individuals which showed no significant elevation in the previous study [17].

Portal vein TAV showed a significant decrease among CHC that may be attributed to the underlying progression of fibrosis with distortion of parenchymal architecture. This hypothesis has also been suggested by previous studies [28, 29] although it remains controversial due to conflicting results reported by other authors [16, 30].

Portal vein BF showed a significant increase according to our study in chronic hepatic C patients. Hyperemia of the liver parenchyma due to inflammation may explain the elevation of the above parameter [28]. Nevertheless, there is documented evidence from other studies that reject the significance of this finding [16, 31].

Hepatic artery diameter, TAV and blood flow is significantly decreased in CHC compared to normal adults which is in disagreement with previous study suggesting increased blood flow [16]. However one of the study shows decreasing trend in the hepatic artery flow in chronic hepatitis [17].

LVI in our study in chronic hepatitis patients was significantly decreased than the healthy individual due to increased flow resistance which is supported by earlier study [29].

Congestive index in our study is consistently and significantly decreased in chronic hepatitis patients as referred in the earlier study [18] even though one of the studies shows no significant changes [32].

Regarding VPI, the portal vein velocity wave form was more pulsatile in the healthy adults than the CHC. The mean value of VPI is significantly reduced in the CHC patients when compared with healthy individuals as mentioned in the previous study [6].

SAPI value is undisputedly high in chronic hepatitis C patients in our study compared to the healthy individuals. Previous study shows that SAPI was accurate in predicting significant fibrosis in chronic hepatitis [20].

There is limited number of previous reports especially in India that shows significant changes in the various Doppler parameters changes in chronic hepatitis C patients irrespective of histological staging or severity of fibrosis. There is significant number of studies which accept that there are detectable changes related to sonographic Doppler measurements in portal vein and hepatic artery in patients with chronic liver disease [33-36] compared with the control group.

The use of color Doppler ultrasonography in investigating chronic viral liver pathologic changes was a major advance, not only because it enabled morphologic analysis of patients with this disease, but also because it provided a non-invasive method of plotting hemodynamic changes contributing to the early detection of signs indicating status of the disease. Thus our findings could potentially be used as the method of non-invasive diagnosis of chronic hepatitis infected with hepatitis C virus and prevent the Liver biopsy in general.

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