

ORIGINAL ARTICLE

Diagnostic Accuracy of Doppler Scan of Portal Vein to Determine Early Cirrhosis of Hepatitis-C Patients in Gujranwala PopulationMIAN WAHEED AHMAD¹, NAWAZ RASHID², IQBAL HUSSAIN DOGAR³, MUHAMMAD UMER⁴, HAFIZA SAMEEYA SHEHZADI⁵, RAMEEZ AHMAD⁶¹Department of Diagnostic Radiology, DHQ Hospital Gujranwala²Assistant Professor of Radiology, Mayo Hospital, Lahore³Professor of Pediatric Radiology, Faisalabad Medical University, Faisalabad⁴Master Medical Center Gujranwala⁵PGR Radiology, DHQ Hospital Gujranwala⁶PSO to Principal, Gujranwala Medical College/DHQ Teaching Hospital GujranwalaCorrespondence to: Mian Waheed Ahmad, Email: drmianwaheedahmad@gmail.com, Cell: 0333-4383045**ABSTRACT****Objective:** The purpose of study is to establish accuracy of doppler sonography in diagnosis of early cirrhosis in hepatitis C positive patients, which is based on portal vein velocity and resistive index considering Histopathology as a gold level standard**Student Design:** It was a cross sectional comparative study (validation study).**Place & Duration of Study:** The student was held in Radiology department of District Headquarter Teaching Hospital Gujranwala from 1st July 2019 to 30th June 2020.**Materials and Methods:** The calculated sample size was 50 cases of anti-HCV anti bodies positive on their blood test fulfilling the inclusion criteria were examined for color Doppler ultrasound to see direction and average blood flow in the portal vein. All these cases were undergone core biopsy of liver and histopathology carried out. The results of histopathology were taken as superior quality / gold standard.**Results:** Mean age of the patients was found to be 42.5 years. The frequency of the hepatitis C in the different age group varied. Out of the 50 about 37 patients (74%) show decrease in the portal vein velocity towards lower limits regardless no ultrasonic appearance of the cirrhosis and remaining 13 patients (26%), show normal velocities towards upper limits. According to this study portal vein velocity in early cirrhosis is between 10-16 cm/sec and these initial cirrhotic changes confirmed on core liver biopsy (gold standard). Sensitivity was found to be 94.4%, specificity 78.5%, diagnostic accuracy 90.0%, both the NPV (negative predictive value) and PPV (positive predictive value) are high (NPV: 78.5%).**Practical Implication:** To best of our knowledge, there is very little information on this research topic in our area. The design of improved medical strategies to handle such situations and the improvement of their management will be made possible by the availability of such evidence.**Conclusion:** In our study, the maximum patients (38%) were suffering with this disease for more than 7 years but less than 9 years. 74% patients showed a decrease in the portal vein velocity towards the lower limit, and 26% patients showed normal velocity towards the upper limit.**Keyword:** Portal Vein, Doppler Ultrasound, Anti HCV, Core Liver Biopsy, Histopathology, Hepatitis C**INTRODUCTION**

Chronic liver disease (CLD) is brought on by a prolonged inflammatory response in the liver as a result of several factors, such as viral infection (HCV/HBV), alcohol use (ALD), and obesity brought on by nutrition (Non-alcoholic steatohepatitis-NASH). But in the end, CLD causes fibrosis, cirrhosis, and a decline in liver function¹. So, people with CLD have an increased chance of having hepatocellular carcinoma². The pervasiveness of hepatitis shifts nation to nation, and now and then similarly, fluctuate in various areas with similar nation. According to the WHO's epidemiology study, Hepatitis C is uncommon (less than 1% prevalence) in Australia, Canada, and northern Europe, and about 1% in countries with a medium incidence, such the USA and a significant chunk of Europe. Numerous countries in South-East Asia, Latin America, Central America, and Africa have high rates (>2%). Figures between 5% and 10% are frequently reported in these nations.³ According to the "Burden of Disease Study" conducted by Hyder and Morrow in 2001, chronic liver disorders are the 11th most prevalent cause of impairments and the fifth most common cause of premature death in Pakistan⁴. Portal hypertension and liver cirrhosis influence the flow state of the vessels of liver. In these conditions, Doppler ultrasound can be an important data on the flow statistics of the whole venous framework, the hepatic course and the hepatic veins.⁵ Spectral Doppler imaging is essential to quantify the flow velocity and assess the hemodynamics in cirrhosis and portal hypertension. It's crucial to compensate for the angle to 60° or less between the beam and the vessel's long axis^{6,7}. In cirrhosis patients with evolving portal hypertension, the spectral waveform may represent changing flow in a starting transitional phase, with the both hepatofugal and hepatopetal flows in the similar waveform⁸. The patients who develop severe portal hypertension flow eventually

become hepatofugal.^{9,10} Different positive and negative correlating studies have investigated the role of Doppler sonography of liver disease in adults, and healthy population.¹¹ Histological findings remain the gold standard for about a decade.¹²

Despite the fact that it involves intervention and bears a slight risk of potential problems. Therefore, a significant clinical concern is use of a noninvasive technique for monitoring of patients with hepatitis B and C.¹³

To the best of author's knowledge there is a lack of local data on doppler ultrasonography for early cirrhosis prognosis in hepatitis-C patients. So, this research would provide a non-invasive option for identifying complications of a condition that is rather widespread in this region.

MATERIALS AND METHODS**Study Design:** It was a cross sectional comparative study (validation study).**Study Setting & Duration:** The student was held in Radiology department of District Headquarter Teaching Hospital Gujranwala from 1st July 2019 to 30th June 2020.**Inclusion Criteria:** Patients having range from 15 to 70 years old and gender from both sexes. Subjects were selected for the study using a non-probability consecutive sampling method.**Exclusion Criteria:** Patients with esophageal varices, portal vein thrombosis, and hepatocellular cancer were not included.**Methodology:** Every patient having no symptom and healthy adults were asked not to eat or drink 6 hours before the examination. Every ultrasound was done the supine position of the patient by using the similar ultrasound machine (Xario 200 DOPPLER) by a well-trained radiologist utilising a 2.5–5 MHz transducer that is curved. Xario 200 was sustained with the right

arrangement for fast and arranged count of the haemodynamic boundaries dependent on the spectral Doppler waveform.

Gray-scale scanning was used to measure the size of the liver and examine the liver parenchyma. Following the cirrhosis's onset, 13 of the remaining patients (26%) exhibit normal velocities approaching the upper limits (Table No. 1)

This study determined that the portal vein velocity in early cirrhosis is between 10 and 16 cm per second, and the core liver biopsy validated these early cirrhotic alterations (gold standard). Table No. 2's positive predictive value (PPV) was found to be 94.4%, Negative predictive value (NPV) was found to be 78.5%, specificity was found to be 78.5%, and diagnostic accuracy was found to be 90.0%.

At the porta hepatis, the angle of isonation or sonic interference from the nearby vessels was used to evaluate the hepatic artery as close to its origin as feasible. At right angles to the vessel's long axis, callipers were used to assess the size from a longitudinal view. Since no abnormal anatomy was discovered in the research participants, The right hepatic artery is crossed by the portal vein, which was examined and had its diameter and time-averaged velocity measured. Less than 60-degree isolation angles between the longitudinal axis and the sound wave were used for evaluation. One issue of difficulty in measurement by bowel gas was adjusted with one or the other changing of filtering time or by asking the patient to come on another day. Doppler Ultrasonography (CDU) in assessment of Chronic viral liver disease has been made on the conjecture that changing of the liver hemodynamics because of persistent developing changes may in a way show histological adjustments.

Data Analysis: SPSS 20.0 was used to conduct statistical analyses on the collected data. Quantitative variables like age have been analyzed by determining their means and standard deviations. Quantitative characteristics, such as gender and the presence or absence of Early Cirrhosis on ultrasonography were analyzed using frequency and percentage. Doppler ultrasonography's sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in predicting the presence of Early Cirrhosis, using endoscopy as the gold standard, were calculated using a 2x2 frequency table.

RESULTS

This study showed that most in the patients 25 (50%) in the younger age group, i.e., 5 years between 32-40 years. Minimum number i.e., only 5 cases (10%) in the age group less than 30 years and greater than 50 years. Mean age of the patients was found to be 42.5 ±4.0 years. Distribution of cases by duration of the hepatitis showed 6 patients (12 %) had hepatitis C for 3 years. 11 patients (22%) had this disease for more than 3 years but less than 5 years. In our study 14 (28%) patients had this disease for 5 to 7 years. But our maximum patients 19(38%) had this disease for more than 7 years but less than 9 years. In this study, there were 20 patients who were women and 30 patients (60%) who were men. Out of fifty (n=50), 37 patients (74%) showed a decrease in the portal vein velocity towards lower limits regardless no ultrasonic appearance of the cirrhosis and remaining 13 patients (26%) show normal velocities towards upper limits (Table No. 1)

Table 1: Comparison of Liver core biopsy vs portal vein n = 50

Portal vein velocity (PPV)	Liver core biopsy (Gold Standard)		Total
	Positive	Negative	
Positive	34 (TP)	3 (FP)	37
Negative	2 (FN)	11 (TN)	13
Total	36	14	50

According to this study, portal vein velocity in early cirrhosis is between 10-16 cm per/sec and these initial cirrhotic changes were confirmed on core liver biopsy (gold standard). Sensitivity was found to the 94.4%, specificity 78.5%, diagnostic accuracy

90.0% (Table No. 2) positive predictive value (PPV) 91.2 and negative predictive value (NPV) 78.5%.

Table 2: Sensitivity, Specificity and Accuracy of portal vein velocity in Hepatitis-C

Variable	Sensitivity	Specificity	Accuracy
Portal Vein Velocity	94.44%	78.5%	90.0%

Sensitivity Rate = 34/36*100=94.44%
 Specificity Rate= 11/14*100 = 78.5%
 Diagnostic Accuracy = 45/50* 100=90.0%

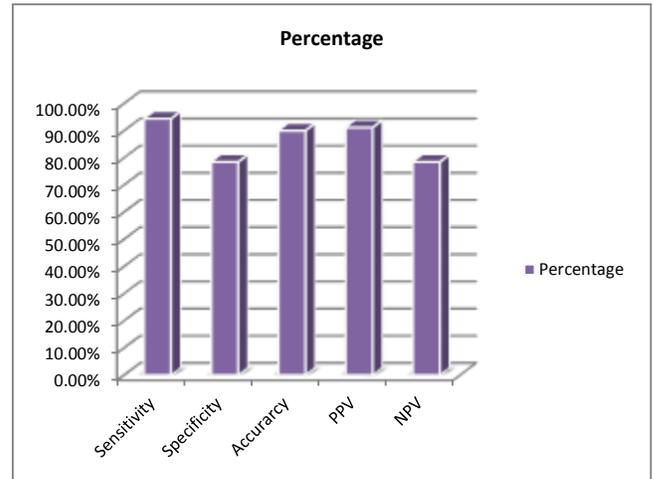


Figure 1: Sensitivity, Specificity and Accuracy of portal vein velocity in Hepatitis-C

DISCUSSION

HCV is one of the most known disease, which is present worldwide and is causing morbidity and mortality and resulting in burden on country's budget yearly^{14,15}. Patients with chronic hepatitis C (CHC), the end result is liver fibrosis due to continuous inflammation induced by continuous viral load. There is increased risk of developing cirrhosis, hepatic carcinoma and number of complications due to portal hypertension¹⁶.

The left portal vein branch (LPV) and the right portal vein branch (RPV), which enter the left and right lobes of the liver, respectively, make up the portal vein system. The portal vein system is made up of the superior mesenteric vein (SMV) and superior vena cava (SV), which join to form the portal vein (PV). The portal vein, which supplies 70%–80% of the blood that goes through the liver, is the organ's principal blood channel (17).¹⁸ Cirrhosis of the liver causes a condition called portal hypertension, which is a blood flow resistance.¹⁹ The bulk of cirrhosis-related issues, including ascites, spontaneous bacterial peritonitis, hepatic encephalopathy, hepatorenal syndrome, gastroesophageal varices, and variceal bleeding, are caused by portal hypertension.²⁰ It is advised that patients with CLD undergo screening with ultrasonography because it can reveal details about the liver's texture, portal hypertension, the presence of focal liver lesions, and the effects of cirrhosis.²¹ By examining the portal vein and its collaterals with power and spectral Doppler, it is possible to diagnose clinically significant portal hypertension with a high degree of specificity.^{22,23}

A study conducted by Nuoman Khan et al. found that there were total 188 individuals half (94) were cirrhotic and half (94) were normal .The mean ages of patents were 46.15±15.88 years(9-83 years).The mean velocity of portal vein in cirrhosis patients was 10.72±1.91cm/sec and 23.36 ± 6.06 cm/sec in normal individuals.²⁴ Whereas in our study, there were total 50 patients out of 37 patients (74%) show decrease in the portal vein velocity towards lower limits regardless no ultrasonic appearance of the cirrhosis and remaining 13 patients (26%) show normal

velocities towards upper limits. According to this study portal vein velocity in early cirrhosis is between 10-16 cm/sec and these early cirrhotic changes confirmed on core liver biopsy (gold standard). Another study conducted by Mukhopadhyay and Saha et al in which there were 180 individuals out of 100 were normal and 80 were cirrhosis patients. In a healthy person, the mean portal vein velocity was 15.5 x 4.0 cm/sec, but in a person with liver cirrhosis, it was 9.8 x 2.8 cm/sec.²⁵ Another study was done in 2016 by Maryam Riahinezhad et al. Iranian research compared children with liver cirrhosis and portal hypertension to a healthy control group using Doppler imaging. The portal vein mean velocities in the group of 33 children with cirrhosis were 15.03 7.3 cm/s, 16.47 6.4 cm/s in the group of 19 controls (P = 0.51), and 11.6 4.7 cm/s in.²⁶

CONCLUSION

Mean age of hepatitis C patient was 42.5 years. Liver blood flow changes were proportional to the duration of the disease process i.e., the changes in portal vein velocity increased with duration of the disease. In our study, the maximum patients (38%) were suffering with this disease for more than 7 years but less than 9 years. 74% patients showed a decrease in the portal vein velocity towards the lower limit, and 26% patients showed normal velocity towards the upper limit.

Acknowledgement: Special thanks to Dr. Iqbal Hussain Dogar, Dr Muhammad Umer for their kind cooperation during the research conducted for the publishing of this article and to Dr. Hafiza Sameeya Shehzadi and Rameez Ahmed for proof reading.

REFERENCES

- Schuppan D, Surabattula R, Wang XY. Determinants of fibrosis progression and regression in NASH. *Journal of hepatology*. 2018 Feb 1;68(2):238-50.
- Roche B, Coilly A, Duclos-Vallée JC, Samuel D. The impact of treatment of hepatitis C with DAA s on the occurrence of HCC. *Liver international*. 2018 Feb;38:139-45.
- World Health Organization. Hepatitis C. Available at: www.who.int/vaccine_research/viral_cancers. Retrieved on 16.4.2009
- Asghar MS, Ahsan MN, Rasheed U, Hassan M, Jawed R, Abbas MB, Yaseen R, Ali Naqvi SA, Rizvi H, Syed M . Severity of Non-B and Non-C Hepatitis Versus Hepatitis B and C Associated Chronic Liver Disease: A Retrospective, Observational, Comparative Study. *Cureus*. 2020 Dec 26;12(12)
- Baz, A.A.M., Mohamed, R.M. & El-kaffas, K.H. Doppler ultrasound in liver cirrhosis: correlation of hepatic artery and portal vein measurements with model for end-stage liver disease score in Egypt. *Egypt J Radiol Nucl Med* 51, 228 (2020).
- Park HS, Desser TS, Jeffrey RB et al (2016) Doppler ultrasound in liver cirrhosis: Correlation of hepatic artery and portal vein measurements with model for end-stage liver disease score. *J Ultrasound Med* 36:725–730
- Topal NB, Sarkut P, Dündar HZ et al (2016) The correlation between Doppler US measurement of hepatic arterial flow and the MELD score in patients with chronic liver disease. *Eur Rev Med Pharmacol Sci* 20(2):291
- Elzawawy MS, Hassanein SA, El Nomrosy RM (2018) The role of fibroscan in the assessment of liver cirrhosis in patients with chronic liver disease. *Menoufia Med J* 31:520–524
- Iranpour P, Lall C, Houshyar R et al (2016) Altered Doppler flow patterns in cirrhosis patients: an overview. *Ultrasonography*. 35(1):3–12
- Maruyama H, Kobayashi K, Kiyono S, et al. Left gastric vein–based noninvasive test for esophageal varices: a same-day comparison of portal hemodynamic assessment with endoscopic appearance. *Clin Transl Gastroenterol* 2018; 9: 154.
- Meringer H, Shibolet O, Deutsch L. *World J Gastroenterol*. 2019 Aug 7; 25(29):3929-3940.
- Khalifa A, Rockey DC. The utility of liver biopsy in 2020. *Current Opinion in Gastroenterology*. 2020 May 1;36(3):184-91.
- van der Meer AJ, Feld JJ, Hofer H, Almasio PL, Calvaruso V, Fernández-Rodríguez CM, Aleman S, Ganne-Carrié N, D'Ambrosio R, Pol S, et al. *J Hepatol*. 2017 Mar; 66(3):485-493. Epub 2016 Oct 22.
- Akhtar S, Nasir JA, Usman M, Sarwar A, Majeed R, Billah B. The prevalence of hepatitis C virus in hemodialysis patients in Pakistan: A systematic review and meta-analysis. *PLoS one*. 2020 May 14;15(5):e0232931.
- Kanwal F, Kramer J, Asch SM, Chayanupatkul M, Cao Y, El-Serag HB. Risk of hepatocellular cancer in HCV patients treated with direct-acting antiviral agents. *Gastroenterology*. 2017;153:996–1005
- Romeo R, Petruzzello A, Pecheur EI, Facchetti F, Perbellini R, Galmozzi E, Khan NU, Di Capua L, Sabatino R, Botti G, Loquercio G. Hepatitis delta virus and hepatocellular carcinoma: an update. *Epidemiol Infect*. 2018;146(13):1612–8.
- Li X, Wang XK, Chen B, Pu YS, Li ZF, Nie P, Su K. Computational hemodynamics of portal vein hypertension in hepatic cirrhosis patients. *Bio-medical materials and engineering*. 2015 Jan 1;26(s1):S233-43.
- Bruno S, Di Marco V, Iavarone M, Roffi L, Crosignani A, Calvaruso V, Aghemo A, Cabibbo G, Viganò M, Boccaccio V, Craxi A. Survival of patients with HCV cirrhosis and sustained virologic response is similar to the general population. *J Hepatol*. 2016;64(6):1217–23.
- Toubia N, Sanyal AJ. Portal hypertension and variceal hemorrhage. *Medical Clinics of North America*. 2008 May 1;92(3):551-74.
- Mauro E, Gadano A. What's new in portal hypertension?. *Liver International*. 2020 Feb;40:122-7.
- Heimbach JK, Kulik LM, Finn RS, Sirlin CB, Abecassis MM, Roberts LR, Zhu AX, Murad MH, Marrero JA. AASLD guidelines for the treatment of hepatocellular carcinoma. *Hepatology*. 2018;67(1):358–80.
- Galle PR, Forner A, Llovet JM, Mazzaferro V, Piscaglia F, Raoul JL, Schirmacher P, Vilgrain V. EASL clinical practice guidelines: management of hepatocellular carcinoma. *J Hepatol*. 2018;69(1):182–236.
- Kudo M, Izumi N, Sakamoto M, Matsuyama Y, Ichida T, Nakashima O, Matsui O, Ku Y, Kokudo N, Makuuchi M. Liver Cancer study Group of Japan. Survival analysis over 28 years of 173,378 patients with hepatocellular carcinoma in Japan. *Liver Cancer*. 2016;5(3):190–7.
- Khan N, Hussain I, Alam I, Bacha R, Rehman A, Mikrani MM, Fatima M, Farooq SM, Malik SS, Gilani10 SA. Sonographic Comparison of Mean Velocity of Portal Vein in Liver Cirrhosis and Normal Individuals. *Journal of Health and Medical Sciences*. 2018;1(1):101-7
- Khan N, Hussain I, Alam I, Bacha R, Rehman A, Mikrani MM, Fatima M, Farooq SM, Malik SS, Gilani10 SA. Sonographic Comparison of Mean Velocity of Portal Vein in Liver Cirrhosis and Normal Individuals. *Journal of Health and Medical Sciences*. 2018;1(1):101-7.
- Riahinezhad M, Rezaei M, Saneian H, Famouri F, Farghadani M. Doppler assessment of children with liver cirrhosis and portal hypertension in comparison with a healthy control group: An analytical cross-sectional study. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences*. 2018;23.