ORIGINAL ARTICLE

Association of Portal Vein Doppler Parameters with Chronic Liver Disease Child Pugh Classes: A Single Center Experience at Rawalpindi, Pakistan

Abdul Ahad Farooq[1], Ahsen Farooq[2], Muhammad Rashid[3], Junaid Haris Farooq[4], Salma Umbreen[5], Rabia Waseem[6]

ABSTRACT

Objective: To determine the association between Doppler Parameters of average peak portal vein velocity and flow direction and Child Pugh classes of patients suffering from the chronic liver disease.

Study Design: It was a descriptive study.

Place and Duration of Study: The study was conducted from December 2013 to January 2015 at the Radiology Department of Holy Family Hospital, Rawalpindi, Pakistan.

Materials and Methods: Selected chronic liver disease (CLD) patients were examined with gray scale and Doppler USG for assessment of portal vein (PV). Average peak portal venous velocity (PVV) and direction of flow in the main portal vein were recorded. Doppler findings were correlated with clinical features and laboratory findings in three classes (A,B & C) of patients using Child Pugh criteria to establish any probable association between them (appendix: I).

Results: Out of total 115 CLD patients studied, 47.8% were in Child Pugh class C. The main portal vein average PVV (cm/sec) in 24.34% patients with Child Pugh class A was 18.75 + 1.88, in 27.82% patients with Child Pugh class B was 14.25 + 0.98 and in 47.82% patients with Child Pugh class C was 8.15 + 1.84. This showed significant fall in portal vein average PVV with advancing Child Pugh class of cirrhosis. Only 10.4% patients showed continuous hepatofugal flow and 4.3% showed bidirectional flow. It was recorded only in Child Pugh class C patients.

Conclusion: Doppler findings of average peak velocity in the main portal vein fall progressively with worsening of the Child Pugh class. In addition, the direction of flow is also reversed in cases of the Child Pugh class C cirrhosis.

Key Words: *Child, Cirrhosis, CLD, Doppler, Direction, Flow, Hypertension, Hepatic, Liver, Portal, Pugh, Transplant, Ultrasound, Vein, Velocity.*

[1]*Department of Radiology*
Rawalpindi Institute of Cardiology, Rawalpindi
Quaid-e-Azam International Hospital, Islamabad
[2]*Department of Radiology*
Islamic International Medical College, Rawalpindi
Riphah International University, Islamabad
[3]*Department of Medicine / Nephrology*
KRL Hospital, Islamabad
[4]*Department of Internal Medicine*
Charleston Area Medical Center
Charleston, West Virginia, USA
[5]*Department of Radiology*
Wah Medical College, Wah
[6]*Department of Radiology*
HITEC Institute of Medical Sciences, Taxila

Correspondence:
Dr. Abdul Ahad Farooq
Senior Registrar
Rawalpindi Institute of Cardiology, Rawalpindi
Associate Consultant Radiologist
Quaid-e-Azam International Hospital, Islamabad
E-mail: docahad@gmail.com

Funding Source: NIL; Conflict of Interest: NIL
Received: October 24, 2018; Revised: February 13, 2019
Accepted: March 06, 2019

Introduction

Pakistan has been positioned in intermediate prevalence zone for viral hepatitis B and C that is responsible for >75% of cirrhosis and hepatocellular carcinoma (HCC) in WHO EMRO region.[1] The burden of the disease and its end-stage complications are a huge challenge for the healthcare providers because a majority of patients remain asymptomatic and unaware, leading to a silent epidemic and therefore resulting in significant morbidity and mortality in our country.[2,3] The chronic liver disease leads to many complications such as portal hypertension (ascites, hypersplenism, varices), systemic dysfunction (hypoalbuminemia, coagulopathy), hepatopulmonary and hepatorenal syndromes, encephalopathy, hepatocellular carcinoma, and the notorious cirrhosis which is the common endpoint of a wide variety of CLD processes causing hepatocellular necrosis.[4,5] The World Health Organization (WHO) has defined Cirrhosis as "a

diffuse process characterized by fibrosis and conversion of normal liver architecture into structurally abnormal nodules."[6] The Child Pugh classification system is the most commonly used tool for clinically predicting the prognosis in cirrhosis. Child and Turcotte first presented their criteria in 1964 that was later revised by Pugh in 1973.[7]

Chronic liver disease, especially in asymptomatic patients has been diagnosed mainly by the liver biopsy which helps in its staging and grading.[8] However, the risks and limitations associated with this invasive method have led to the development of safer methods of investigation.

Grayscale USG is now an integral part of the routine liver examination and Doppler studies have been considered as the gold standard tool for evaluating the velocity and direction of blood flow in the portal venous system.[4,9] It is a non-invasive, rapid and cost-effective investigation and well accepted by the patients.[4,10]

In Pakistan, now there are centers offering liver transplant as prospective management of CLD, therefore, use of Child Pugh classification and Doppler studies have become a vital assessment tool. Only a few studies have been conducted evaluating the role of Doppler ultrasound in the assessment of chronic liver disease patients in Pakistan.[2] The aim of this study was to explore the value of Doppler ultrasonography in the assessment of PV hemodynamics in CLD patients and to determine the association between Doppler Parameters of PPV and flow direction and Child Pugh classes of the Pakistani patients suffering from the chronic liver disease.

Materials and Methods

This descriptive cross-sectional study was conducted in the Department of Radiology in collaboration with the Department of Medicine at Holy Family Hospital Rawalpindi. Approval was taken from the hospital ethical committee. Nonprobability convenience consecutive sampling technique was used. Using WHO sample size calculator, the sample size of 115 was calculated by taking a confidence level of 95 % and population mean of 18.33. All the patients of either gender and of age more than 20-year, having clinical, biochemical and radiological evidence of chronic liver disease, presenting to the departments of medicine and radiology from December 2013 onwards was included in the study. Child Pugh classification (A, B and C) was done as per standard criteria by the medical and radiological department.[7] (Appendix 1). Patients having portal vein thrombosis (PVT) were excluded from the study. Informed consent was obtained from all the patients fulfilling the inclusion criteria. Patients were subjected to conventional grayscale and Doppler ultrasound using Toshiba Nemio ultrasound machine equipped with multi-frequency linear and curvilinear transducer probes. The examination was performed or supervised at least by a registrar level radiologist. All the patients were examined preferably in the supine position. During the examination, every patient was required to hold breath in deep inspiration, to avoid motion artifacts. The scanning of the portal vein was carried out longitudinally throughout its entire length from an anterior abdominal subcostal and/or right intercostal approach. It was analyzed for the presence or absence of intra-luminal thrombus, blood flow velocity in cm/s and direction of blood flow within the portal vein. All the findings were reconfirmed by another consultant radiologist.

Data were collected by the principal investigator on the study proforma. Data were entered and analyzed by Statistical Package for the Social Sciences (SPSS) version 22. Descriptive statistics were calculated. The quantitative variable of the study included; average peak venous velocity in the main portal vein compared with different Child Pugh classes A, B & C and expressed as Mean ± SD. The qualitative variable of the study included; the direction of portal vein blood flow compared with different Child Pugh classes A, B & C and expressed as frequency.

Results

A total of 125 CLD patients presented from December 2013 till January 2015. Ten patients were excluded from the study because of either incompletely available medical record or loss to follow up and portal vein thrombosis in 2 cases. Therefore, a total number of 115 CLD patients without PVT were included in this study. The age ranged from 21-77 years with a mean age of 40.6$\pm$11.54 years. Most of them (43, 37.4%) ranged between 31-40 year age group. Males were 70 (60.87%) and females 45 (39.13%) with M:F of 1.6:1 approximately. Majority of patients (47.8%) were in

Child Pugh class C (Table-I). Doppler findings of the average peak venous velocity (PVV) and the direction of blood flow in the main portal vein were evaluated in all the subjects and were compared with Child Pugh classes A, B, and C. The main portal vein average PVV (cm/sec) in 28 (24.34%) patients with Child Pugh A was 18.75 $\pm$ 1.88, in 32 (27.82%) patients with Child Pugh B was 14.25 $\pm$ 0.98 and in 55 (47.82%) patients with Child Pugh C was 8.15 $\pm$ 1.84 (Table-II). Only 17 (14.7%) patients demonstrated non hepatopetal flow (hepatofugal / bidirectional), 12 (10.4%) showed continuous hepatofugal flow and 5 (4.3%) showed bidirectional flow (Table-III). It was recorded only in Child Pugh class C patients.

Table I: Distribution of Child Pugh Classes A, B, and C among the Patients

Child Pugh Class	Frequency	Percent	Valid percent
Child Pugh A	28	24.3	24.3
Child Pugh B	32	27.8	27.8
Child Pugh C	55	47.8	47.8
TOTAL	115	100.0	100.0

Table II: Comparison of Average Peak Venous Velocity in the Main Portal Vein in Child Pugh Classes A, B, and C

Child Pugh Class	Average Pvv	No. Of Patients	Std. Deviation
Child Pugh A	18.75	28	1.878
Child Pugh B	14.25	32	0.984
Child Pugh C	8.15	55	1.840
TOTAL	12.43	115	4.722

Table III: Patterns of Flow in the Main Portal Vein among Child Pugh's Classes A, B, and C.

Child Pugh Class	Hepatopetal	Hepatofugal	Bidirectional	Total
Child Pugh A	28	0	0	28
Child Pugh B	32	0	0	32
Child Pugh C	38	12	5	55
TOTAL	98	12	5	115

Discussion

Accurate evaluation of liver parenchymal damage and altered vascular hemodynamics is crucial for therapeutic decisions, surveillance, and assessment of the prognosis in chronic liver diseases of various aetiologies. Since long, liver biopsy has been considered as the gold standard for diagnosing, staging and grading the liver damage in CLD, especially in asymptomatic patients.[8] This invasive method has several risks and limitations, including morbidity and mortality, sampling error, diagnostic inaccuracy, interobserver and intraobserver variability, and difficulties in follow-up.[11] Therefore, it led to the development of safer methods for evaluation of CLD and its complications. The non-invasive Grayscale and Doppler USG studies have now been considered as an essential part of the investigation battery for assessing the CLD patients.[9,10.] With increasing accessibility of liver transplant facility for the management of end stage CLD world over, the use of Child Pugh classification as a valuable indicator of the prognosis in CLD patients have become vital as well.[9] Combined together imaging, pathological and clinical assessment methods help explore new therapeutic avenues.

The role of ultrasound imaging in the evaluation of CLD / cirrhosis is well known.[4,12,13,14,15] Doppler USG is an important diagnostic modality for the analysis of the hepatic vasculature and blood flow.[9,10,16,17] The standard dynamics of blood flow in the hepatic artery, hepatic veins, and the portal vein, have been well defined in the literature.[4,9,10,15,17] Changes in hepatic blood flow dynamics might be alternate markers for significant parenchymal changes in chronic liver diseases and their complications.[9.10,11]

The Child Pugh classification is mostly used to stage chronic liver disease based on clinical and laboratory parameters that is ascites, encephalopathy, bilirubin and albumin levels, and prothrombin time. There are three stages of the Child Pugh classification system, A, B and C depicting increasing severity of CLD.[7] (Appendix-I)

On Doppler US, the characteristic portal vein hemodynamic features of liver cirrhosis include reducing blood-flow velocity, absent pulsatility, and change in flow direction from hepatopetal to hepatofugal in more advanced cases.[9,10,11,15,16,17] The normal portal vein velocity ranges from 16 to 40 cm/sec with variations caused by respiration.[15,16] Portal venous flow velocities progressively fall with rising portal venous pressure because back pressure limits forward velocity that is characteristic for portal hypertension and also due to collaterals formation,

Appendix I: Child Pugh Classification for Liver Cirrhosis

Parameter	Points assigned		
	1	2	3
Ascites	None	Suppressed with meds	Refractory
Bilirubin	<34 uM	34-50 uM	>50 uM
Albumin	>35 g/L	28-35 g/L	<28 g/L
INR	<1.7	1.7-2.2	>2.2
Encephalopathy	Grade 0	Grade 1-2 or suppressed with meds	Grade 3-4 or refractory
Grade 0: Normal Cognition Grade 1: Euphoria, Fluctuation in level of Consciousness, slurred/disoriented speech Grade 2: Drowsiness, Inappropriate behavior, loss of sphinteric control Grade 3: Marked Confusion, Stupor, incoherent Speech Grade 4: Coma			
Class A	5-6 Points	"Well- Compensated"	
Class B	7-9 Points	"Significant functional impairment"	
Class C	10-15 Points	"decompensated liver function"	

which is caused by cirrhosis in most of the cases.[4,16]

With this background, not many studies have been conducted evaluating the role of Doppler ultrasound in the assessment of chronic liver disease patients in Pakistan.[2] Likewise, few regional studies have examined the association of Doppler parameters of direction and velocity of flow in the main portal vein with the Child Pugh class.[9,18]

Our study has determined that Doppler ultrasonography is a valuable modality for the assessment of portal vein hemodynamics in the Pakistani patients suffering from the chronic liver disease. It has established an association between Doppler findings of average peak velocity and flow direction in the main portal vein and Child Pugh classes of cirrhosis. Doppler findings of average peak velocity in the main portal vein fell progressively with worsening of the Child Pugh class. In addition, the direction of flow was also reversed in cases of the Child Pugh class C cirrhosis.

A study by Mittal, et al published in 2011, have examined the association of Doppler findings of flow velocity and direction in the main portal vein with the Child Pugh class in the Iranian population. This study shows average peak portal venous velocity of 18.33 $\pm$ 2.22,14.59 $\pm$ 3.57 and 10.96 $\pm$ 2.33 cm/s in the Child Pugh class A, B and C respectively and non-hepatopetal flow (hepatofugal or bidirectional) in 12 % of patients which all corresponds to the Child Pugh class C.[9] Afif, et al in 2017, studied the maximum velocities in portal vein, hepatic vein and hepatic artery and hepatic artery resistive index in liver cirrhosis patients of the Singapore population. They found that flattening of the hepatic vein waveforms was related to the degree of liver cirrhosis. The cirrhotic patients showed higher maximum hepatic vein velocity. However, they had lower maximum portal vein velocity and there was a further decrease in average maximum portal vein velocity as the severity of liver cirrhosis worsened.

In our study of 115 Pakistani CLD patients, the main portal vein average PVV was 18.75 $\pm$ 1.88, 14.25 $\pm$ 0.98 and 8.15 $\pm$ 1.84 cm/sec in the Child Pugh classes A, B and C respectively (Table-II). This showed a significant fall in portal vein average PVV with the increasing severity grade of cirrhosis based on the Child Pugh class. The results are consistent with results of Chawla et al, Shi et al and by Vyaset al studies.[19,20,21]

Normal individuals display a hepatopetal portal venous blood flow.[15,16,17] In deteriorating CLD, portal venous flow progressively slows down with rising portal venous resistance and pressure, first nearing the level of stagnation demonstrated by the phenomenon of a to-and-fro (bidirectional) flow.[16,17] Later with advancing cirrhosis, obstruction of the hepatic venules and sinusoids due to fibrosis and architectural distortion, and further by arterioportal and porto-systemic shunting, eventually leading to hepatofugal (reversed) portal venous flow and fall in velocity.[4,16,17]

In our study, only 4.3% patients showed bidirectional flow and 10.4% showed continuous hepatofugal flow (Table-III). It was recorded only in the Child Pugh class C. None of the patient in the Child Pugh class A and B demonstrated hepatofugal flow. Gaiani et al have reported the similar patterns.[22] It implies that with more reversal of the portal venous flow, there is increased deterioration of liver function and hence poorer the Child Pugh score.

Despite the single center's small study and some limitations of the final diagnoses and follow up, the results of our study are by and large supported by the various international studies. This study imparts a deeper insight into the non-invasive and cost-effective mode for the assessment of progression

and subsequent management of the patients suffering from the deadly disease of chronic liver disease in Pakistan.

Conclusion

Doppler ultrasonography is a valuable modality for assessing the complex hemodynamics of hepatic vasculature (portal vein in our study), in patients with chronic liver disease and its progression as well. Doppler findings of average peak velocity in the main portal vein fall progressively with worsening of the Child Pugh class. In addition, the direction of flow is also reversed in cases of the Child Pugh class C cirrhosis. The findings of our study are in line with other published studies.

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