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Portal vein pulsatility pattern in cirrhotic patients with portal hypertension: A cross-sectional study to determine the severity of liver disease in early stage in a low-setting tertiary hospital of Bangladesh

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Abstract

Introduction: Liver cirrhosis is associated with significant morbidity and mortality. Simple parameters such as portal vein pulsatility index (PI) and complete spectral widening (CSW) have been observed in some studies to reflect early alterations in portal hemodynamics associated with the severity of liver disease.

Methods: It was a cross-sectional comparative study, and a purposive non-probability sampling technique was used for selecting cases. The sample size was thirty-three in each group; cirrhotic and healthy.

Results: Among 33 patients with liver disease, 5 (15.2%) of them were in Child–Pugh (CP) class A, 10 (30.3%) in Class B, and 18 (54.5%) in Class C. In the healthy group, 97.0% (32 of 33) had PI between 0.2 and 0.5 and 3.0% (1 of 33) had pronounced pulsatility >0.5, whereas, in the cirrhotic patients, 63.6% (21 of 33) had PI between <0.2 and 36.4% (12 of 33) had a PI between 0.2 and 0.5. The mean PI in CP Class A was 0.28 ± 0.11, in CP Class B 0.20 ± 0.03, and in CP Class C, it was 0.14 ± 0.05, indicating that the PI becomes lower with increasing severity of cirrhosis. CSW was present in 60.6 % of patients with cirrhosis (20 of 33) and none of the healthy subjects in the control group (0 of 33).

Conclusion: A decrease in the PI and the presence of CSW are valuable predictors of cirrhotic patients with portal hypertension, with alterations become significantly more pronounced as disease severity increases. However, this study could emphasize the role of duplex Doppler in recognizing disease in its early stages and determining disease severity in low low-setting tertiary hospital.

Keywords: Complete spectral widening, Diagnostic radiology, Doppler ultrasound, Liver cirrhosis, Pulsatility index.

Introduction

Cirrhosis is a prevalent problem globally, with high mortality and morbidity. It is the fourteenth leading cause of death worldwide and one of the most significant causes of death in Bangladesh.[1,2] According to the World Health Organization (WHO), cirrhosis is a diffuse

condition marked by fibrosis and the transformation of normal liver architecture into nodules with aberrant structural characteristics.[3] Ascites, fluid-electrolyte redistribution, hepatorenal syndrome, and hepatic encephalopathy are all symptoms of portal hypertension, which are severe sequelae of cirrhosis.[4] The modified Child–Pugh (CP) score has been shown to be a reliable prognostic indicator and independent predictor of survival. Poorer survival is highly linked with the CP class C. As a result, it is the most commonly used approach and, therefore, should be considered for an accurate diagnosis and staging of cirrhosis.[5] Early diagnosis can play a crucial role in preventing the complications associated with liver cirrhosis.[1]

The CP scoring method, also known as the CP-Turcotte score, was developed to anticipate mortality in cirrhotic patients. To facilitate the selection of patients who could really benefit from elective portal decompression surgery, it was first proposed by Child and Turcotte in 1964.[6] It classifies patients into three clusters: A, which stands for good liver function; B, which stands for moderately impaired hepatic function; and C, which stands for advanced hepatic dysfunction. Serum bilirubin, serum albumin, ascites, neurological disease, and clinical nutrition status were the five clinical and laboratory criteria used in the initial scoring technique to categorize patients. Later, Pugh *et al*. revised the scoring method, substituting clinical nutrition status for prothrombin time.[7] In addition, different points were applied for each requirement based on increasing severity.

Ultrasonography is the most frequently used imaging modality for diagnosing and monitoring patients with cirrhosis. The diagnosis is typically based on late findings of volume redistribution, liver surface irregularity, and secondary results of portal hypertension. However, in the absence of these late effects, B-mode sonography cannot diagnose cirrhotic patients in the early stages.[8] Doppler sonography is a noninvasive diagnostic procedure that monitors hemodynamic parameters; hemodynamic changes may have developed in cases with normal B-mode sonography findings.[9] Evaluation of these alterations is therefore essential for early diagnosis and close monitoring of previously diagnosed patients.[10]

Despite the wide range, there are typically two pulsatility patterns in normal conditions: the more prevalent one is a slight fluctuation pattern with a PI value between 0.2 and 0.5, and another pattern is a PI value <0.2 (almost non-pulsatile or flat wave envelope), which is highly suggestive of chronic liver disease.[11] The spectral width varies, particularly complete spectral widening (CSW), which is another radiological sign of chronic liver disease.

Despite being the most frequently used imaging modality for diagnosing liver cirrhosis, it cannot identify cirrhosis in its early stages. In Portal Hypertension, the inclusion of color and spectral Doppler of the Portal vein reveals important hemodynamic information and assists in the accurate evaluation of the vascular anatomy. However, this study may highlight the importance of duplex Doppler in detecting disease at an early stage and determining the severity of the condition to improve prognosis and prevent the potentially life-threatening consequences of cirrhosis in a minimal healthcare setup in developing countries.

Methods

Patients and setting

This cross-sectional comparative study was conducted in the Department of Radiology and Imaging of a tertiary medical college hospital from April 2019 to September 2020. The study includes people of either sex who had liver cirrhosis and portal hypertension and were sent for ultrasonography from the medicine and hepatology outpatient department (OPD) and indoor of the same hospital to the department of radiology and imaging. Thirty-three patients with liver cirrhosis were selected as the case group, while healthy visitors who came with patients to the OPD were chosen as the control group. A purposive type of non-probability sampling was done. All cases of

clinically diagnosed liver cirrhosis with portal hypertension (Presentations, lab findings, and imaging studies) were included in the study, except the patients with known encephalopathy, a previous history of sclerotherapy or band ligation, or patients with portal vein thrombosis or portal vein flow reversal, or bidirectional portal flow.

Study measurements

At first, Socio-Demographic variables age, sex, history of current illness, and treatment history were taken. A general examination was done to see the clinical picture of liver cirrhosis such as jaundice, ascites, hematemesis, and encephalopathy. Then, a blood sample was taken for investigations to evaluate total bilirubin, serum Albumin, and prothrombin time (prolongation) from well-recognized laboratory. USG of the abdomen and duplex color Doppler was carried out to measure the pulsatility index (PI) and CSW. Portal vein Pulsed Doppler examination was performed with machine MEDISON SONOACHE X8 and SAMSUNG SONOACHE X8 with a curvilinear transducer 3.5–5 MHz frequency probe with Doppler facility by the hand of expert radiologists. All measurements were taken while the patients were fasting and breathing quietly.

Data collection and statistical analysis

Data were collected using a semi-structured case record form containing all the variables of interest. The case record form was finalized following pretesting. Data were processed using the software IBM SPSS v25.0. Data were presented in tables and diagrams based on nature. This study's significance was tested statistically using the independent "*t*" test and Chi-square test.

Quality assurance strategy

Interviews were conducted, and the principal investigator filled out the case record form. In addition, at the end of each interview and after filling up each case record form, these were checked for incompleteness. Data were cross-checked for consistency, correctness, and any discrepancy. The appropriate measure was taken in case of inconsistency, incorrectness, and difference.

Ethical implications

The study subjects were informed verbally about the study design, the purpose of the study, and their right to withdraw from the project at any time for any reason whatsoever. Subjects who will give informed written consent to participate in the study were included as the study sample. Ethical clearance from the Institutional Review Board (IRB) was obtained to conduct the study. The aims and objectives of the study, along with its procedures, alternative diagnostic methods, risks, and benefits, were explained to the patient's guardian in an easily understandable local language.

Results

Patients in the cirrhotic group had a mean age of 47.9 ± 11.5, with a minimum age of 22 and a maximum age of 75. In contrast, subjects in the healthy group had a mean age of 41.6 ± 10.1, with minimum and maximum ages of 21 years and 60 years, respectively. Twelve (36.4%) women and twenty-one (63.6%) men comprised the cirrhotic group. In comparison, 14 patients (42.4%) were male, and 19 (57.6%) were female in the healthy group. In the cirrhotic group, jaundice was always present in every case (100%). Hematemesis and ascites were reported in 21.2% and 78.8% of cases, respectively. The cirrhotic group had mean serum bilirubin, serum albumin, and prothrombin time prolongation of 3.3 ± 2.1 mg/dL, 3.2 ± 0.5 mg/dL, and 7.0 ± 3.2 s, among other laboratory values. Thirty-three patients were diagnosed with liver disease, of which 5 (15.2%) were classified into CP class A, 10 (30.3%) into class B, and 18 (54.5%) into class C.

Three percent (1 of 33) of the healthy group had pronounced pulsatility >0.5 on Doppler imaging, while 97.0% (32 of 33) had PI between 0.2 and 0.5. None of the participants, however, had PI 0.2.

Again, none of the patients with cirrhosis had a PI >0.5, while 63.6% (21 of 33) had a PI between 0.2% and 36.4% (12 of 33) had pulsatility between 0.2 and 0.5. However, the PI values in cirrhotic patients ranged from 0.04 to 0.4, with a mean PI value of 0.18 ± 0.08. In the control group, PI values ranged from 0.20 to 0.55, with a mean value of 0.32 ± 0.09. With a $P = 0.001$, an independent t-test for equality of means found the difference highly significant [Table 1]. CP class A had a mean PI of 0.28 ± 0.11, class B had a mean PI of 0.20 ± 0.03, and class C had a mean PI of 0.14 ± 0.05. This demonstrates that as cirrhosis severity increases, the PI decreases, indicating that the variations in mean PI values among the Child classes were noteworthy. Child A and B, B and C, and A and C all had $P \leq 0.05$ between them.

CSW was observed in 20 of 33 cirrhotic patients or 60.6% but not in any healthy people (0 of 33). With a Chi-square test $P \leq 0.001$, the difference between the distribution of CSW in the healthy and cirrhotic groups was highly statistically significant [Table 2]. In contrast to patients with CP class A and 2 of 10 patients (20%) with CP class B, all patients in CP class C exhibited CSW. There was a significant ($P \leq 0.001$) correlation between the presence of CSW and the severity of CP classes [Table 3].

Discussion

Due to high morbidity and mortality, liver cirrhosis has emerged as a serious global health concern in developing and developed countries.

Table 1: Distribution of the portal vein pulsatility index value in the study group with healthy control

Portal vein pulsatility index value	Cirrhotic group (*n*=33)	Healthy group (*n*=33)	*P*-value
<0.2	21 (63.6%)	0 (0%)	
0.2–0.5	12 (36.4%)	32 (97.0%)	
>0.5	0 (0%)	1 (3.0%)	
Mean value (SD)	0.18±0.08	0.32±0.09	<0.001
Range (min, max)	0.04–0.4	0.20–0.55	

The prevalence of liver cirrhosis is typically underreported since individuals in the early stages of the disease are frequently asymptomatic, and the majority of patients with the condition are admitted due to the consequences it may induce. The 1-year mortality rate related to liver cirrhosis varies from 1% to 57% based on the intensity of comorbidities.[1,12,13] Early diagnosis may help prevent the associated detrimental effects, including variceal bleeding, hepatic encephalopathy, and portal vein thrombosis. However, Spectral and color Doppler ultrasonography can demonstrate many characteristic flow patterns from hepatic vasculature in patients with liver cirrhosis with or without portal hypertension.[1,14]

The typical waveform of the portal vein demonstrates gentle undulations [Figure 1]. In cirrhotic patients, arterio-portal shunting is a primary determinant of pulsatility. The PI, the ratio of the difference between the peak systolic velocity and the end-diastolic velocity divided by the mean velocity, could also be used to quantify increased pulsatility. After diastole, pressure is transmitted through the hepatic sinusoids, increasing pulsatility as indicated by a rise in the PI.[15,16] Alternatively, increasing right atrial pressure may coexist with a higher PI (>0.5), which is seen in right heart failure and tricuspid regurgitation. Arterio-portal shunting depends on anatomical distortion, seen in patients with cirrhosis, as well as a reversal of portal venous flow and higher hepatic venular resistance. Furthermore, peri-lesional shunting through drainage veins may be driven by hepatocellular carcinoma, frequently seen in cirrhotic individuals.[1] Increased portal vein pulsatility in cirrhotic individuals may provoke an evaluation for the presence of an arterio-portal fistula or vascular lesion, depending on the clinical history. Arterio-portal shunts can be identified by pulsatility that is synchronized with the waveforms of the adjoining hepatic arteries.[17]

The usual portal vein presents an undulating hepatopetal flow. Between 15 and 18 centimeters per second is the spectrum for the mean portal venous velocity. Within the same person, normal

Table 2: Spectral widening in cirrhotic and healthy groups

Complete spectral widening	Cirrhotic group (*n*=33) (%)	Healthy group (*n*=33) (%)	Total (*n*=66) (%)	*P*-value
Present	20 (60.6)	0 (0)	20 (30.3)	<0.001
Absent	13 (39.4)	33 (100)	46 (69.6)	
Total	33 (100)	33 (100)	66 (100)	

Table 3: Distribution of spectral widening in cirrhosis according to severity (*n*=33)

Complete spectral widening	Modified Child-Pugh grading (%)			Total (%)	*P*-value
	A	B	C		
Present	0 (0)	2 (20)	18 (100)	20 (60.6)	<0.001
Absent	5 (100)	8 (80)	0 (0)	13 (39.4)	
Total	5 (100)	10 (100)	18 (100)	33 (100)	

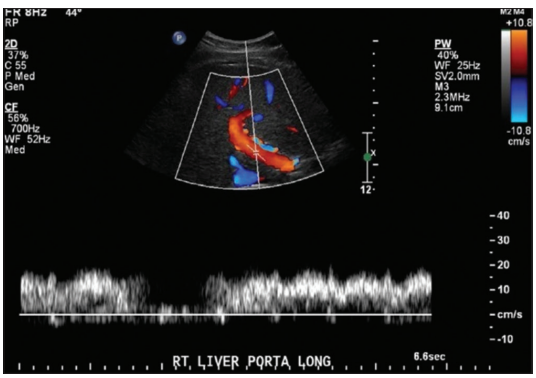

Figure 1: Normal portal vein waves were found in a healthy individual during the study period

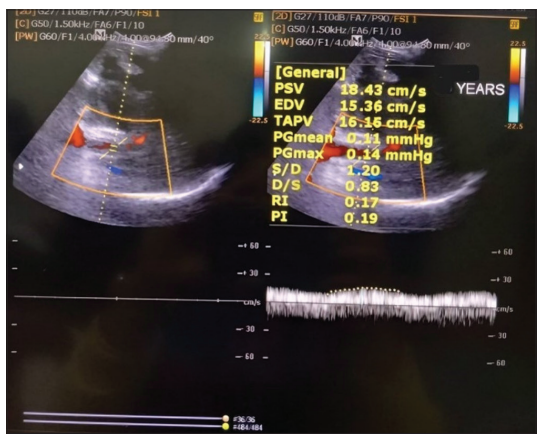

Figure 2: Doppler study of the portal vein in a liver cirrhosis patient with portal hypertension during our research

portal venous flow rates may fluctuate, rising after a meal and falling after exercise or when the patient is standing. In addition, it changes with respiration.[18,19] The undulating pattern of the portal vein's flow eventually disappears as portal hypertension advances and gradually becomes more uniform [Figure 2]. As the severity of portal hypertension rises, the flow first becomes biphasic and finally hepatofugal.[11] Different authors have adopted portal flow and pulsatility pattern measures to evaluate portal hemodynamics and as indicators of liver morphological alterations.[20] The congestion index, modified hepatic index, hepatic vascular index, and portal blood flow are a few indicators of portal blood flow, but they are challenging to calculate, which limits their widespread use, and their accuracy has not yet been proven. According to a 2005 study by Haktanir *et al*., measurements of portal vein flow are also questionable.[9,21]

Our research aims to identify a valuable technique for detecting early liver cirrhosis using Doppler ultrasound. In healthy participants in our study, the mean PI value was 0.320 ± 0.09, which is pretty comparable to other studies that found values of 0.377 ± 0.108, 0.39 ± 0.1, and 0.48 ± 0.31 by Subedee *et al*., Barakat, and Gallix *et al*., accordingly.[11,20,22] In studies by Duerinkx *et al*. and Wachsberg *et al*., healthy subjects' PI values were <0.61 and <0.54, respectively.[19,23] According

to Subedee *et al*., 8.33% (3 of 36) of healthy individuals exhibited pronounced pulsatility >0.5, and 91.66% (33 of 36) had PI between 0.2 and 0.5, which was consistent with the current study.[20] However, in our investigation, none of the participants had PI 0.2. In accordance with the present study, Barakat observed that 77.6% of healthy people had PI between 0.2 and 0.5; 22.4% had pronounced PI >0.5, and none had PI <0.2.[11] These results are also in line with the common assumption that healthy adults' portal vein PI values range between 0.2 and 0.5.

In the current study, patients with cirrhosis and portal hypertension had a mean PI value of 0.18 ± 0.08. A survey by Subedee *et al*. (2013) reported a statistically significant difference in PI value between the healthy and cirrhosis groups, similar to the current research. In that study, the mean PI value in patients with cirrhosis and portal hypertension was 0.17 ± 0.03.[20] In a survey including 157 patients, Barakat (2002) reported that patients with cirrhosis had a PI of 0.23 ± 0.08. Because there were fewer patients in CP class A (15.2% in the current study vs. 38.2% in the Barakat study), the PI value was lower.[11] The relatively low number of Child-A patients in the present study was attributed to the absence of liver biopsy as a diagnostic precondition for cirrhosis. Liver biopsy is crucial for detecting cirrhosis in the early stages of the disease with minimal clinical, laboratory, and morphological changes consistent with Subedee *et al*. (2013).[20] This is one of the limitations of our study due to the lack of logistical support.

In the present study, the mean PI value was 0.28 ± 0.11 in CP class A and 0.20±0.03 in CP class B. CP class C was 0.14 ± 0.05, and differences in mean PI values within the Child classes were statistically significant. ($P \leq 0.05$ between Child A and B, B and C, and A and C). As per the study of Subedee *et al*. (2013), child A had a mean PI value of 0.21, child B had a mean PI value of 0.18, and child C had a mean PI value of 0.14, with differences being statistically significant and consistent with the present study.[20] The research revealed that the PI value declines with increasing severity of liver disease, which was in line with Barakat's findings from 2002, who reported that the mean PI value in Child A, B, and C was 0.25, 0.23, and 0.21, respectively. While most of the patients in this study had alcoholic cirrhosis, Barakat (2002) did not include individuals with the condition in his analysis. There are no studies investigating the relationship between portal vein PI and the pathophysiology of cirrhosis in the literature.[11]

CSW was detected in the present study in 20 of 33 cirrhotic patients, 60.6%, but not in any healthy people (0 of 33). Similar findings were made by Subedee *et al*., who reported that 76.92 percent of patients with cirrhosis and PH in their study exhibited CSW compared to none of the patients in the control group.[20] This was in line with Barakat's survey of 157 individuals with liver cirrhosis, where 71.9% of such patients had total spectral widening.[11] CSW was observed to occur in 28.5% of Child A patients, 66.6% of Child B patients, and 100% of Child C patients in Subedee *et al*. study. This finding was consistent with the current investigation.[20] When comparing the presence of CSW between various Child groups, Barakat (2002) did not find any statistical significance.[11]

Limitations

The main aim of the study is to diagnose cirrhosis in the early stage using Doppler USG in low setting centers. As mentioned earlier, we were not able to perform liver biopsy, though it was the gold standard to diagnose cirrhosis. Liver biopsy was not available in our center. Moreover, the sample size was small because the study was done during COVID-19 pandemic, and we excluded COVID-19 positive patients due to a lack of scientific data regarding any correlation between COVID-19 and liver cirrhosis in that period.

Conclusion

Understanding the vascular flow patterns in patients with liver cirrhosis and portal hypertension is essential for generating important insights

regarding their disease condition. A decline in the PI is a significant indicator of cirrhotic individuals with portal hypertension in the presence of cirrhosis, with alterations becoming markedly more pronounced with increasing disease severity. CSW is another significant predictor of increased disease severity. As a result, these two indicators can be employed in clinical settings to diagnose liver cirrhosis in its early stages, evaluate the seriousness for a better prognosis, and avoid the life-threatening consequences related to the condition.

Declarations

Provenance and peer review

Not commissioned, externally peer-reviewed.

Conflicts of interest

None to declare.

Source of funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit organizations.

Ethics approval and consent to participate

The institutional review board of Mymensingh Medical College approved the study protocol (Memo no: MMC/IRB/2019/166). Informed written consent was taken from the study participants. The study was conducted according to Good Clinical Practice and the Helsinki accords. Participants' identities were kept confidential at all times. Subjects were neither placed at any health risk by the study nor by treatment decisions based on it. In addition, no financial compensation was offered for participation. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Consent for publication

Not applicable.

Author contribution

TS conceived, designed, and took entire responsibility for publishing this study under the supervision of MR. TS was the chief investigator and was responsible for data collection. TS and AS worked with data curation, data analysis, data visualization, and writing the original manuscript. SKK, SPS, MB, and AF reviewed the draft and made valuable corrections. All the authors provided intellectual input to the study and approved the final version of the manuscript.

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Research registration

Not applicable.

Guarantor

Dr. Tithi Saha accepts full responsibility for the work and/or the conduct of the study, had access to data, and controlled the decision to publish.

Data availability

The dataset is available on request to the corresponding author.(tithisaha.ssmc@gmail.com).

Additional information

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