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Original Article

Internal Medicine Section

Abdominal Ultrasonography and Splenoportal Doppler Study for Predicting Oesophageal Varices in Patients Admitted with Chronic Liver Disease at a Tertiary Medical Hospital in Kolkata, India: A Cross-sectional Study

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ABSTRACT

Introduction: Upper Gastrointestinal Endoscopy is considered the best screening tool for varices among patients with chronic liver disease. However, it is an expensive and invasive procedure that is not routinely available in rural India. Abdominal ultrasonography along with colour Doppler study is an inexpensive test commonly ordered for patients with chronic liver disease. Recent literature suggests that ultrasonographic parameters can be used to predict varices.

Aim: To determine if ultrasonography of the entire abdomen and spleno-portal Doppler study findings can predict oesophageal varices in patients with chronic liver disease.

Materials and Methods: The present hospital-based observational, cross-sectional study was conducted in the indoor ward of the Department of General Medicine at Medical College and Hospital, Kolkata, India, over a duration of one year from February 2021 to February 2022.

Total 100 patients with chronic liver disease, admitted to the hospital ward, were included in the study. Child-Turcotte-Pugh (CTP) scores were obtained for all patients. Ultrasonographic and spleno-portal Doppler indices, such as liver size, spleen size, portal vein diameter, splenic vein diameter, peak systolic velocity of the portal vein, and portal vein/splenic vein diameter ratio, were measured alongside upper gastrointestinal endoscopy to detect varices. The data were analysed using Statistical Package for Social Sciences (SPSS) version 28.0. The Chi-square test was used to test for significant differences in proportions (categorical data), and the independent t-test and Analysis of Variance (ANOVA) with Tukey's Post-hoc test were employed to test for significant differences in means (continuous data). Additionally, Receiver Operating Characteristic (ROC) curves were obtained for statistically significant parameters to predict the presence of varices.

Results: The study enrolled 100 patients (63% males, 37% females) with a mean age of 49.19±14.965 years, ranging from 14 to 91 years. (median age of 52, range 14-91 years). Of these, 68 patients (68%) had oesophageal varices, while 32 (32%) did not. The study found that a mean spleen size of 13.55 cm, a mean portal vein diameter of 12.5 mm, and a mean splenic vein diameter of ≥9.05 mm were predictive of varices. Additionally, a mean portal vein/splenic vein diameter ratio of 1.6150 was also predictive of varices. However, there was no significant difference in mean liver size and peak systolic velocity between those with and without varices.

Conclusion: The present study suggests that a spleen size, portal vein diameter, splenic vein diameter, and portal vein/splenic vein diameter ratio can be reliably used to predict oesophageal varices among patients with chronic liver disease.

Keywords: Child-Turcotte-Pugh score, Endoscopy, Peak systolic velocity, Portal vein diameter, Splenic vein diameter

INTRODUCTION

Chronic liver disease refers to any clinical, biochemical, radiological, or histological evidence of liver disease lasting for more than six months. It encompasses a wide range of liver pathologies, including inflammation (chronic hepatitis) and liver cirrhosis [1].

Morbidity in cirrhosis primarily arises from portal hypertension, which leads to the formation of venous collaterals and significant circulatory as well as vascular abnormalities. Portal hypertension occurs due to an increase in resistance to portal blood flow caused by structural and dynamic changes within a fibrotic liver [2]. Most individuals with cirrhosis have an elevated portal pressure gradient, and more than one-third of them develop oesophageal varices. The rate of variceal formation in patients with cirrhosis has been estimated to be around 8% per year [3]. The mortality rate of variceal bleeding approaches 30%, with an additional one-third of patients dying within a year [4].

Previous literature has shown that approximately one-third of patients with histologically confirmed cirrhosis have varices. Furthermore, it is anticipated that one-third of patients with varices will develop bleeding [5]. Variceal haemorrhage is an immediate life-threatening problem with a mortality rate of 20-30% associated with each episode of bleeding [6]. An elevated hepatic-portal vein pressure gradient of >10 mmHg is the most accurate predictor for the development of varices. However, its measurement is often impeded by a lack of technical expertise and complications, such as intraperitoneal bleeding [7]. Upper GI endoscopy remains the gold standard procedure for diagnosing oesophageal varices but is associated with risks inherent to invasive procedures, such as infection, bleeding, and perforation [8].

Abdominal ultrasonography is one of the first tests ordered in patients suspected of having chronic liver disease. Combined with Doppler imaging, it can detect the patency of the portal vein, hepatic artery, and hepatic veins, and determine the direction of blood flow [9].

Recent literature suggests that portal vein diameter, spleen size, splenic vein diameter, and portal vein/splenic vein diameter ratio

can be used to predict oesophageal varices [10-13]. Non invasive prediction of varices can facilitate the early initiation of non selective beta blockers in patients with chronic liver disease. Especially in countries like India, where there are fewer endoscopy set-ups in rural areas and poor patient compliance due to financial constraints or other reasons, the detection and treatment of oesophageal varices are often inadequate [10].

The study aimed to determine if ultrasonography of the entire abdomen and spleno-portal Doppler study findings can predict oesophageal varices in patients with chronic liver disease.

MATERIALS AND METHODS

The present observational, cross-sectional, hospital-based study was conducted in the Department of General Medicine at Medical College and Hospital, Kolkata, India, from February 2021 to February 2022. Clearance from the Institutional Ethics Committee (IEC clearance number: MC/KOL/IEC/NON-SPON/970/01/2021 dated 20/01/2021) and informed consent from the patients were obtained.

Inclusion criteria: Patients who were either previously diagnosed or newly diagnosed and admitted to the indoor ward with clinical features, laboratory and sonological findings suggestive of chronic liver disease, and with ultrasonographic/endoscopic evidence of portal hypertension were enrolled in the study.

Exclusion criteria: The study excluded patients who were already on beta blocker therapy, those who had undergone endoscopic treatments (sclerotherapy/band ligation), those with severe cardiopulmonary disease, Grade III or IV hepatic encephalopathy, critical illness, patients with end-stage renal failure, or other conditions that would preclude upper GI endoscopy, those who had undergone splenectomy/liver transplantation, those with previous surgeries for portal hypertension or transjugular intrahepatic portosystemic shunting, those with portal or splenic vein thrombosis, and those with current or past history of hepatocellular carcinoma.

Study Procedure

A total of 100 cases of chronic liver disease were enrolled in the study. The study was conducted in a hospital designated as a dedicated Coronavirus Disease (COVID) facility in the city during the pandemic, which unfortunately resulted in limited non Coronavirus Disease (COVID) patient admissions. Therefore, only 100 cases that met the inclusion criteria for the study could be enrolled during the designated one-year study period. The parameters obtained for the study included patient demographics (age, sex), Child-Turcotte-Pugh (CTP) score, liver size, spleen size, portal vein diameter, splenic vein diameter, peak systolic velocity of the portal vein, portal vein/splenic vein ratio, and upper GI endoscopic findings.

The CTP score was calculated based on five parameters: serum total bilirubin levels, serum albumin, severity of ascites (none/mild or moderate/severe), and severity of encephalopathy (none/Grade-I or 2/Grade-III or 4) [14]. Each parameter was assigned a score ranging from one (lowest) to three (highest). The total CTP score was obtained by summing the scores for each parameter. The patients were then assigned to CTP classes based on their scores: CTP Class A for scores of 5 or 6, CTP Class B for scores of 7-9, and CTP Class C for scores of 10-15.

All subjects underwent ultrasonography of the whole abdomen with spleno-portal Doppler study after an overnight fast. A comprehensive evaluation of liver size, spleen size, portal vein diameter, peak systolic velocity of the portal vein, and splenic vein diameter was performed. The measurements were obtained using doppler ultrasonography capable of B-mode imaging with a 3.5 MHz curved array transducer. The measurements were taken with the patients in the supine position and during full inspiration.

Each patient also underwent upper gastrointestinal endoscopy to assess the presence and grade of varices. Varices were graded according to the Baveno classification of oesophageal varices as follows [15]:

- **Grade-I:** Small, straight varices.
- **Grade-II:** Enlarged, tortuous varices, occupying less than one-third of the lumen.
- **Grade-III:** Large, coil-shaped varices, occupying more than one-third of the lumen.

Varices with a diameter of ≤5 mm were considered small, while those with a diameter ≥5 mm were considered large [15].

Objectives of the study:

1. To document the parameters of abdominal ultrasonography and spleno-portal Doppler study in patients with chronic liver disease, including liver size, spleen size, portal vein diameter, peak systolic velocity of the portal vein, and portal vein/splenic vein diameter ratio.
2. To determine the presence of oesophageal varices in patients using upper gastrointestinal endoscopy.
3. To assess whether each individual ultrasonographic parameter can independently predict the presence and grade of varices.
4. To establish cut-off values for each parameter, above or below which the presence of varices is more likely.

STATISTICAL ANALYSIS

All categorical data were expressed as percentages and frequencies, while numerical continuous data were expressed as mean and standard deviation. Data analysis was performed using Statistical Package for Social Sciences (SPSS) version 28.0. The Chi-square test was used to determine significant differences in proportions for categorical data, and independent t-tests and Analysis of Variance (ANOVA) with Tukey's Post-hoc test were employed to assess significant differences in means for continuous data. Additionally, Receiver Operating Characteristic (ROC) curves were constructed for statistically significant parameters to predict the presence of varices. Further analyses were conducted to estimate the optimal cut-off points for parameters that showed a significant association with varices. All statistical tests were performed with a 95% confidence interval, and a p-value of less than 0.05 was considered significant.

RESULTS

A total of 100 patients with cirrhosis of the liver participated in the study, of whom 63 were male and 37 were female. The mean age of the study population was 49.19±14.965 years, ranging from 14 to 91 years.

Alcoholic liver disease accounted for 33 (33%) of the total cases. Non Alcoholic Steatohepatitis (NASH)-related chronic liver disease accounted for 29 (29%) cases. Chronic Hepatitis B accounted for 19 (19%) cases. Eight cases were diagnosed with chronic hepatitis C. There were three cases of haemochromatosis secondary to thalassaemia major, four cases of Wilson's disease, and one case of Chronic Budd-Chiari syndrome. The remaining three cases were diagnosed as cryptogenic chronic liver disease [Table/Fig-1].

Oesophageal varices were observed in 68 (68%) of the cases. Among the 68 patients with varices, 34 (50%) had Grade-II varices, 18 (26%) had Grade-III varices, and the remaining 16 (24%) had Grade-I varices.

All subjects were classified according to the CTP score. The mean CTP score obtained from the data was 9.55±1.85, ranging from 7 to 14.

Aetiology	Varices		Total
	No	Yes	
Alcoholic liver disease	14	19	33
Budd-Chiari syndrome	0	1	1
Cryptogenic	0	3	3
Hepatitis B	3	16	19
Hepatitis C	2	6	8
NASH	11	18	29
Secondary haemochromatosis	1	2	3
Wilson's disease	1	3	4

[Table/Fig-1]: Aetiological distribution of the cases obtained.

In the study population, 48 patients (48%) were classified as Class B, and 52% were classified as Class C.

Among the 48 subjects in CTP Class B, 21 (44%) had oesophageal varices, while the remaining 27 (56%) did not. Among the 52 subjects in Class C, 47 (90%) showed varices, and the remaining 5 (10%) did not. Among the 68 patients with oesophageal varices, 47 (69%) were from CTP Class C, and 21 (31%) were from Class B. Among the 32 patients who did not show any varices, 27 (84%) were from CTP Class B, and the remaining 5 (16%) were from Class C [Table/Fig-2].

There was a statistically significant association between CTP Class and the distribution (grade) of varices (p<0.001**) [Table/Fig-2].

Among the patient population, there appeared to be no association between gender and the distribution of varices (p=0.108) [Table/Fig-3].

There seemed to be no significant difference between the mean age and the grade of varices (t=1.178, df=98, p=0.70) [Table/Fig-4].

Grade of varices [15]	CTP class [14]		Total
	B	C	
No varices	27	5	32
I	4	12	16
II	13	21	34
III	4	14	18
Total	48	52	100

[Table/Fig-2]: CTP classes and distribution of varices.
*Chi-square test; Chi-sq. Test statistic=26.445, df=3, p<0.001**

Gender (M/F) with grade of varices distribution			
Grade of varices [15]	Gender		Total
	F	M	
No varices	11	21	32
I	9	7	16
II	14	20	34
III	3	15	18
Total	37[a]	63	100

[Table/Fig-3]: Distribution of varices according to gender.
*Chi-square test
Chi-sq. Test statistic=6.085, df=3, p=0.108

In the study population, the mean liver size of patients with oesophageal varices was 13.02 cm±3.39 cm, while those who did not have varices had a mean liver size of 14.08 cm±3.17 cm. An independent sample t-test did not show a significant difference in means between liver size and the presence/grade of varices (t=-1.491, df=98, p-value=0.70) The mean spleen size among patients with oesophageal varices was 15.310±1.6385 cm, while those who did not have varices had a mean size of 12.619±2.21 cm. An independent samples t-test showed a significant difference in means between spleen size and the presence of varices (t=6.830, df=98, p=0.01). The mean portal vein diameter among patients with oesophageal varices was 13.737±0.9534 mm, while those who did not have varices had a mean size of 11.469±1.172 mm. An independent samples t-test showed a significant difference in means between portal vein diameter and the presence of varices (t=10.293, df=98, p<0.001) [Table/Fig-5].

The mean peak systolic velocity of patients with oesophageal varices was 11.228±2.9627 cm/s, while those who did not have varices had a mean velocity of 10.287±2.4546 cm/s. An independent samples t-test did not show any significant difference in means between peak systolic velocity and the presence/grade of varices (t=-1.560, df=98, p-value=0.122). The mean splenic vein diameter among patients with oesophageal varices was 10.082±0.6390 mm, while those who did not have varices had a mean diameter of 5.475±0.7687 mm. An independent samples t-test showed a significant difference in means between splenic vein diameter and the presence of varices (t=31.48, df=98, p<0.001). The mean portal vein/splenic vein diameter ratio among patients with oesophageal varices was 1.3646±0.116, while those who did not have varices had a mean ratio of 2.11±0.223. An independent samples t-test showed a significant difference in means between portal vein/splenic vein diameter and the presence of varices (t=22.02, df=98, p<0.001) [Table/Fig-5].

Liver size: There was no significant difference in group means between liver size and the distribution of varices [Table/Fig-6], p=0.355.

Spleen size: Analysis of variance results showed that the mean spleen size differed significantly among the four groups, as shown above in [Table/Fig-7]. Patients with Grade-1 varices had a mean size of 15.606±1.643 cm, those with Grade-2 varices had a mean size of 15.062±1.53 cm, and those with Grade-3 varices had a mean size of 15.517 cm±1.84 cm.

Spleen size: Post-hoc (Tukey) analysis showed that the mean spleen size of individuals with varices differed significantly from those who did not show varices [Table/Fig-8].

Among the patients with varices, there was no significant difference in mean spleen size across the various grades of varices [Table/Fig-8].

There appeared to be no statistically significant difference in means between those who had small varices and those who had large varices (t=0.620, df=66, p=0.537) [Table/Fig-9].

Portal vein diameter: Analysis of Variance results showed that the mean portal vein diameter differed significantly (p<0.001**) among the four groups, as shown above in [Table/Fig-10]. Patients with Grade-1 varices had a mean diameter of 11.469±1.172 mm,

Grades of varices	No. of patients (N)	Mean age (in years)			95% confidence interval for mean		f-value	p-value
		Mean	Standard deviation	Std. Error	Lower bound	Upper bound		
No varices	32	46.63	17.741	3.136	40.23	53.02	0.475	0.701
I	16	49.69	11.464	2.866	43.58	55.80		
II	34	50.41	13.643	2.340	45.65	55.17		
III	18	51.00	15.297	3.606	43.39	58.61		
Total	100	49.19	14.966	1.497	46.22	52.16		

[Table/Fig-4]: Mean age (in years) and distribution of varices.
*ANOVA

Parameters	Varices	Mean	Standard deviation	Std. Error mean	t-value, p-value, df
Liver size (cm)	Present	13.0209	3.39975	0.41228	t=-1.491, df=98, p=0.70
	Absent	14.0859	3.17905	0.56198	
Spleen size (cm)	Present	15.310	1.6385	0.1987	t=6.830, df=98, p=0.01*
	Absent	12.619	2.2094	0.3906	
Portal vein diameter (mm)	Present	13.737	0.9534	0.1156	t=10.293, df=98, p<0.001**
	Absent	11.469	1.1727	0.2073	
Splenic vein diameter (mm)	Present	10.082	0.6390	0.0775	t=31.48, df=98, p<0.001**
	Absent	5.475	0.7687	0.1359	
Peak systolic velocity (cm/s)	Present	11.228	2.9627	0.3593	t=1.560, df=98, p=0.122
	Absent	10.287	2.4546	0.4339	
Portal vein diameter/splenic vein diameter ratio	Present	1.3646	0.11619	0.01409	t=-22.02, df=98, p<0.001**
	Absent	2.11	0.22358	0.03952	

[Table/Fig-5]: Table showing statistical difference in means among patients with and without varices using USG parameters.
*Independent samples t-test

Grade of varices (No. of patients)	Mean liver size (in cm)	Standard deviation	Std. Error	95% Confidence interval for mean		f-value	p-value
				Lower bound	Upper bound		
No varices (32)	14.0859	3.17905	0.56198	12.9398	15.2321	1.145	0.335
Grade-I (16)	12.5000	2.89390	0.72348	10.9579	14.0421		
Grade-II (34)	12.8944	3.58870	0.61546	11.6423	14.1466		
Grade-III (18)	13.7228	3.51497	0.82849	11.9748	15.4707		

[Table/Fig-6]: Statistical difference in group means between liver size and distribution of varices.
*ANOVA

Grades of varices (No. of patients)	Spleen size (in cm) Mean	Standard deviation	Std. Error	95% confidence interval for mean		f-value	p-value
				Lower bound	Upper bound		
No varices (32)	12.619	2.2094	0.3906	11.822	13.415	15.848	<0.001**
Grade-I (16)	15.606	1.6434	0.4108	14.731	16.482		
Grade-II (34)	15.062	1.5327	0.2629	14.527	15.597		
Grade-III 18)	15.517	1.8402	0.4337	14.602	16.432		

[Table/Fig-7]: Statistical difference in means between spleen size and distribution of varices.
*ANOVA

(I) Grade of varices	(J) Grade of varices	Mean difference (I-J)	Std. Error	Significant	95% Confidence interval	
					Lower bound	Upper bound
No varices	I	-2.9875*	0.5650	<0.001**	-4.465	-1.510
	II	-2.4430*	0.4545	<0.001**	-3.631	-1.255
	III	-2.8979*	0.5437	<0.001**	-4.319	-1.476
I	No varices	2.9875*	0.5650	<0.001**	1.510	4.465
	II	0.5445	0.5595	0.765	-0.918	2.007
	III	0.0896	0.6341	0.999	-1.568	1.747
II	No varices	2.4430*	0.4545	<0.001**	1.255	3.631
	I	-0.5445	0.5595	0.765	-2.007	0.918
	III	-0.4549	0.5379	0.832	-1.861	0.952
III	No varices	2.8979*	0.5437	<0.001**	1.476	4.319
	I	-0.0896	0.6341	0.999	-1.747	1.568
	II		0.5379	0.832	-0.952	1.861

[Table/Fig-8]: Post-hoc (Tukey) analysis between spleen size and grade of varices.

	Size of varices	No. of patients	Mean spleen size (in cm)	Standard deviation	Std. Error mean	T-value	p-value
Spleen size (cm)	Small varices	50	15.236	1.5731	0.2225	0.620	0.537
	Large varices	18	15.517	1.8402	0.4337		

[Table/Fig-9]: Statistical difference in means between spleen size and size of varices.
*t-test

those with Grade-2 varices had a mean diameter of 13.494±0.596 mm, and those with Grade-3 varices had a mean diameter of 14.089±1.179 mm.

Portal vein diameter: Post-hoc (Tukey) analysis showed that the mean portal vein diameter of individuals with varices differed significantly from those who did not show varices [Table/Fig-11].

Grades of varices (No. of patients)	Mean diameter (in mm)	Standard deviation	Std. Error	95% Confidence interval for mean		f-value	p-value
				Lower bound	Upper bound		
No varices (32)	11.469	1.1727	0.2073	11.046	11.892	36.827	<0.001**
Grade-I (16)	13.494	0.5961	0.1490	13.176	13.811		
Grade-II (34)	13.665	0.9303	0.1595	13.340	13.989		
Grade-III (16)	14.089	1.1797	0.2781	13.502	14.676		

[Table/Fig-10]: Statistical difference in means between portal vein diameter and distribution of varices.
*ANOVA

(I) Grade of varices	(J) Grade of varices	Mean difference (I-J)	Std. Error	Significant	95% Confidence interval	
					Lower bound	Upper bound
No varices	I	-2.0250*	0.3128	<0.001	-2.843	-1.207
	II	-2.1960*	0.2516	<0.001	-2.854	-1.538
	III	-2.6201*	0.3010	<0.001	-3.407	-1.833
Grade-I	No varices	2.0250*	0.3128	<0.001	1.207	2.843
	II	-0.1710	0.3097	0.946	-0.981	0.639
	III	-0.5951	0.3510	0.332	-1.513	0.323
Grade-II	No varices	2.1960*	0.2516	<0.001	1.538	2.854
	I	0.1710	0.3097	0.946	-0.639	0.981
	III	-0.4242	0.2978	0.487	-1.203	0.354
Grade-III	No varices	2.6201*	0.3010	<0.001	1.833	3.407
	I	0.5951	0.3510	0.332	-0.323	1.513
	II	0.4242	0.2978	0.487	-0.354	1.203

[Table/Fig-11]: Post-Hoc (Tukey) analysis between portal vein diameter and grade of varices.

Among the patients with varices, there appeared to be no significant difference in mean portal vein diameter across the grades of varices.

There appeared to be no statistically significant difference in means between those who had small varices and those who had large varices (t=1.861, df=66, p=0.67) [Table/Fig-12].

Peak systolic velocity: There was no significant difference in means between peak systolic velocity and the grade of varices [Table/Fig-13].

	Size of varices	N	Mean	Standard deviation	Std. Error mean	t-value	p-value
Portal vein diameter (in mm)	Small varices	50	13.610	0.8355	0.1182	1.861	0.67
	Large varices	18	14.089	1.1797	0.2781		

[Table/Fig-12]: Statistical difference in means between portal vein diameter and size of varices.
*t-test

Splenic vein diameter: Analysis of variance results showed that the mean splenic vein diameter differed significantly among the four groups, as shown below in [Table/Fig-14].

Post-hoc (Tukey) analysis showed that the mean splenic vein diameter of individuals with varices differed significantly from those who did not show varices. Patients with Grade-1 varices had a mean diameter of 10.006±0.7197 mm, those with Grade-2 varices had a mean diameter of 10.079±0.5233 mm, and those with Grade-3 varices had a mean diameter of 10.156±0.7808 mm. Post-hoc (Tukey) analysis showed that the mean portal vein diameter of individuals with varices differed significantly from those who did not show varices [Table/Fig-15].

Among the patients with varices, there appeared to be no significant difference in mean portal vein diameter across the grades of varices.

There appeared to be no statistically significant difference in means between those who had small varices and those who had large varices (t=0.564, df=66, p=0.575) [Table/Fig-16].

Analysis of Variance results showed that the mean portal vein/splenic vein diameter ratio differed significantly among the four groups, as shown above in [Table/Fig-17].

Patients with Grade-I varices had a mean ratio of 1.325±0.118, those with Grade-II varices had a mean ratio of 1.3571±0.107, and those with Grade-III varices had a mean ratio of 1.3894±0.132.

Post-hoc (Tukey) analysis showed that the mean portal vein/splenic vein diameter ratio of individuals with varices differed significantly from those who did not show varices. Among the patients with varices, there appeared to be no significant difference in mean portal vein/splenic vein diameter ratio across the grades of varices [Table/Fig-18].

There appeared to be no statistically significant difference in means between those who had small varices and those who had large varices (t=1.061, df=66, p=0.293) [Table/Fig-19].

An independent samples t-test showed a significant difference in means between spleen size and the presence of varices (t=6.830, df=98, p=0.001**) [Table/Fig-5].

Grade of varices (no.of patients)	Mean peak systolic velocity (cm/s)	Standard deviation	Std. Error	95% confidence interval for mean		f-value	p-value
				Lower bound	Upper bound		
No varices (32)	10.287	2.4546	0.4339	9.403	11.172	2.644	0.064
Grade-I (16)	9.825	2.5598	0.6400	8.461	11.189		
Grade-II (34)	11.618	3.3892	0.5812	10.435	12.800		
Grade-III (18)	11.739	2.0208	0.4763	10.734	12.744		

[Table/Fig-13]: Statistical difference in means between peak systolic velocity and distribution of varices.
*ANOVA

Grades of varices (no. of patients)	Mean	Standard deviation	Std. Error	95% Confidence interval for mean		f-value	p-value
				Lower bound	Upper bound		
No varices (32)	5.475	0.7687	0.1359	5.198	5.752	325.072	<0.001**
Grade-I (16)	10.006	0.7197	0.1799	9.623	10.390		
Grade-II (34)	10.079	0.5233	0.0897	9.897	10.262		
Grade-III (18)	10.156	0.7808	0.1840	9.767	10.544		

[Table/Fig-14]: Statistical difference in means between splenic vein diameter and distribution of varices.
*ANOVA

(I) Grade of varices	(J) Grade of varices	Mean difference (I-J)	Std. Error	Significant	95% Confidence interval	
					Lower bound	Upper bound
No varices	I	-4.5313*	0.2108	<0.001	-5.082	-3.980
	II	-4.6044*	0.1695	<0.001	-5.048	-4.161
	III	-4.6806*	0.2028	<0.001	-5.211	-4.150
Grade-I	No varices	4.5313*	0.2108	<0.001	3.980	5.082
	II	-0.0732	0.2087	0.985	-0.619	0.472
	III	- 0.1493	0.2365	0.922	-0.768	0.469
Grade-II	No varices	4.6044*	0.1695	<0.001	4.161	5.048
	II	0.0732	0.2087	0.985	-0.472	0.619
	III	- 0.0761	0.2007	0.981	-0.601	0.448
Grade-III	No varices	4.6806*	0.2028	<0.001	4.150	5.211
	I	0.1493	0.2365	0.922	-0.469	0.768
	II	0.0761	0.2007	0.981	-0.448	0.601

[Table/Fig-15]: Post-Hoc (Tukey) analysis between portal vein diameter and grade of varices.

	Size of varices	N	Mean	Std. Deviation	Std. Error mean	t-value	p-value
Portal vein diameter (in mm)	Small varices	50	13.610	0.8355	0.1182	0.564	0.575
	Large varices	18	14.089	1.1797	0.2781		

[Table/Fig-16]: Statistical difference in means between splenic vein diameter and size of varices.
*t-test

Grades of varices	Mean	Standard deviation	Std. Error	95% Confidence interval for mean		f-value	p-value
				Lower bound	Upper bound		
No varices (32)	2.1116	0.22358	0.03952	2.0310	2.1922	159.53	<0.001**
Grade-I (16)	1.3525	0.11818	0.02955	1.2895	1.4155		
Grade-II (34)	1.3571	0.10752	0.01844	1.3195	1.3946		
Grade-III (18)	1.3894	0.13242	0.03121	1.3236	1.4553		

[Table/Fig-17]: Statistical difference in means between portal vein/splenic vein diameter ratio and distribution of varices.
*ANOVA

(I) Grade of varices	(J) Grade of varices	Mean difference (I-J)	Std. Error	Significant	95% Confidence interval	
					Lower bound	Upper bound
No varices	I	0.75906*	0.04880	<0.001	0.6315	0.8867
	II	0.75450*	0.03926	<0.001	0.6519	0.8571
	III	0.72212*	0.04696	<0.001	0.5993	0.8449
Grade-I	No varices	-0.75906*	0.04880	<0.001	-0.8867	-0.6315
	II	-0.00456	0.04832	1.000	-0.1309	0.1218
	III	-0.03694	0.05476	0.906	-0.1801	0.1062
Grade-II	No varices	-0.75450*	0.03926	<0.001	-0.8571	-0.6519
	I	0.00456	0.04832	1.000	-0.1218	0.1309
	III	-0.03239	0.04646	0.898	-0.1539	0.0891
Grade-III	No varices	-0.72212*	0.04696	<0.001	-0.8449	-0.5993
	I	0.03694	0.05476	0.906	-0.1062	0.1801
	II	0.03239	0.04646	0.898	-0.0891	0.1539

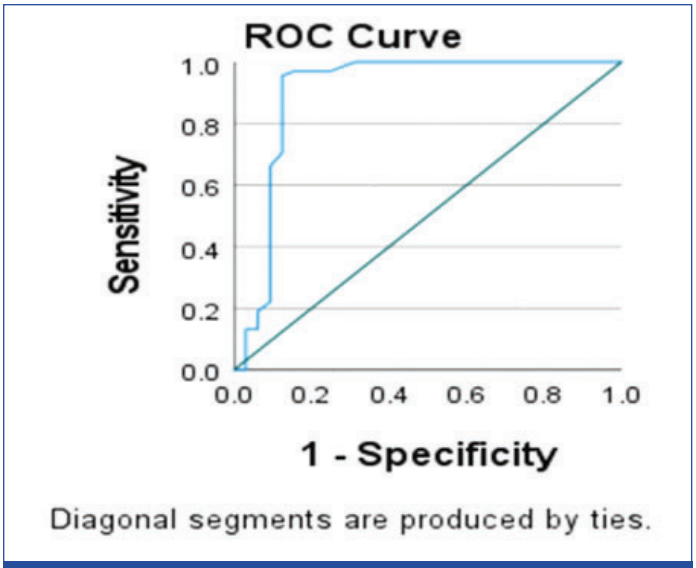
[Table/Fig-18]: Post-hoc (Tukey) analysis between portal vein/splenic vein diameter ratio and grade of varices.

	Size of varices	N	Mean	Standard deviation	Std. Error mean	t-value	p-value
Portal vein diameter/splenic vein diameter ratio	Small varices	50	1.3556	0.10985	0.01553	1.061	0.293**
	Large varices	18	1.3894	0.13242	0.03121		

[Table/Fig-19]: Statistical difference in means between portal vein/splenic vein diameter ratio and size of varices.
*t-test

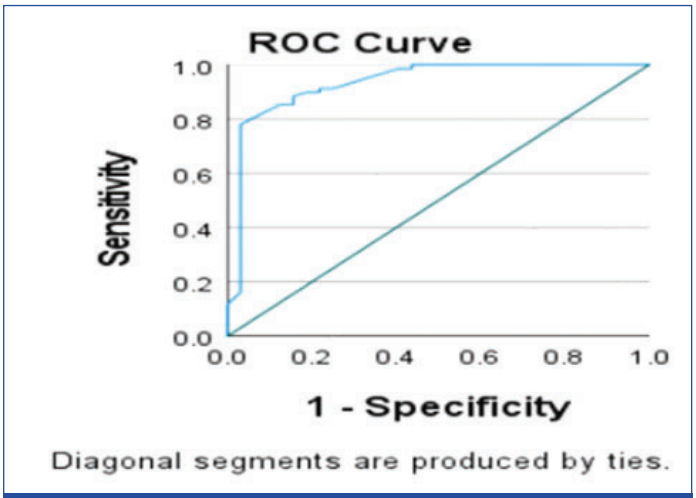
Thus, an increment in spleen size is indicative of the presence of varices, but it does not correlate with the grade of varices [Table/Fig-8]. Receiver Operator Curve (ROC) analysis (given below) showed that spleen size could be predictive of varices. The cut-off value for spleen size for the presence of varices was found to be 13.55 cm (sensitivity of 95.6%, specificity of 87.5%) {AUC=0.902, p<0.001 (95% CI: 0.811-0.993)} [Table/Fig-20].

An independent samples t-test showed a significant difference in means between portal vein diameter and the presence of varices (t=10.293, df=98, p<0.001) [Table/Fig-5].



[Table/Fig-20]: ROC curve analysis to predict sensitivity and specificity of spleen size for predicting varices.

Thus, an increment in portal vein diameter is indicative of the presence of varices, but it does not correlate with the grade of varices [Table/Fig-11]. ROC analysis (given below) showed that portal vein diameter could be predictive of varices. The cut-off value for portal vein diameter of 12.5 mm predicted varices with a sensitivity of 89.7% and a specificity of 81.2%. AUC={0.933, p<0.001 (95% CI: 0.874-0.992)} [Table/Fig-21].



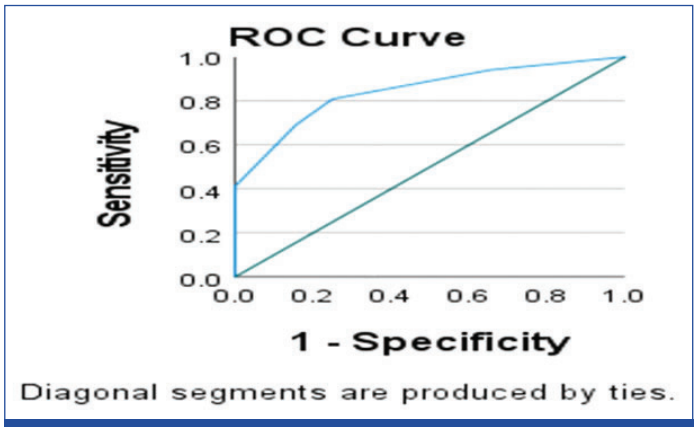
[Table/Fig-21]: ROC analysis showing sensitivity and specificity of portal vein diameter for predicting oesophageal varices.

An independent samples t-test showed a significant difference in means between splenic vein diameter and the presence of varices (t=31.48, df=98, p<0.001) [Table/Fig-5].

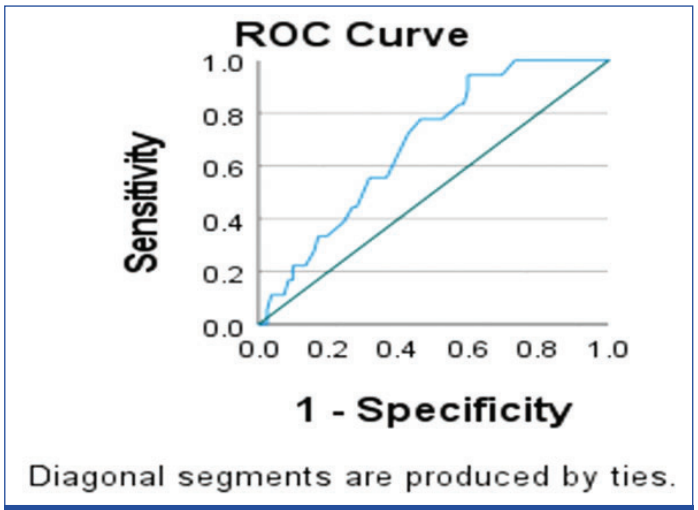
Thus, an increment in splenic vein diameter is indicative of the presence of varices, but it does not correlate with the grade of varices [Table/Fig-15]. ROC analysis (given below) showed that splenic vein diameter could be predictive of varices. The cut-off value for splenic vein diameter of 9.05 mm predicted varices with a sensitivity of 80.9% and a specificity of 75%. AUC={0.846, p<0.001 (95% CI=0.770-0.921)} [Table/Fig-22].

An independent samples t-test showed a significant association between portal vein/splenic vein diameter ratio and the presence of varices (t=22.02, df=98, p<0.001) [Table/Fig-5].

Thus, a decrement in portal vein/splenic vein diameter ratio is indicative of the presence of varices, but it does not correlate with the grade of varices [Table/Fig-18]. ROC analysis (given below) showed that the portal vein/splenic vein diameter ratio shows a good prediction (negative predictive value) of varices. The cut-off value for a ratio of 1.6150 predicted the absence of varices with a sensitivity of 77.8% and a specificity of 53.7%. AUC={0.683, p<0.001 (95% CI=0.566-0.800)} [Table/Fig-23].



[Table/Fig-22]: ROC analysis showing sensitivity and specificity of splenic vein diameter for predicting oesophageal varices.



[Table/Fig-23]: ROC analysis showing sensitivity and specificity of portal vein/splenic vein diameter ratio for predicting oesophageal varices.

DISCUSSION

A total of 100 patients (63% male, 37% female) with a mean age of 49.19 (median age of 52, range 14-91 years) were enrolled in the present study.

In an Indian study by Mandal L et al., a total of 82 patients were selected, out of which 56 were males, and the median age of the study population was 40 years, with a range of 19 to 64 years [10]. In another Indian study on chronic liver disease conducted by Sharma SK and Aggarwal R [11], the median age was 45, and there were 87 males.

Chronic alcohol consumption accounted for 33% of the total cases of liver cirrhosis, followed by NASH and chronic hepatitis B. In a study by Bhattarai et al., on 150 patients with chronic liver disease, they found that 120 (80%) of them were due to alcoholic liver disease [16].

In the present study, 68% of the patients had varices, while the remaining 32% did not. Bhattarai et al., [16] noted that 73.4% of their study population had varices. Mandal L et al., [10] noted that 75.6% of cirrhotic patients had varices.

In present study, the majority of the cases with varices were in CTP class C. The mean liver size did not differ significantly with the presence/distribution of varices (p=0.70).

Alempijevic et al., [17] found in their study that the mean value of the right liver lobe diameter/albumin ratio for the presence of varices was 5.51±1.82 (ranging from 2.76 to 11.44). The findings were significant.

According to present study, there was a statistically significant difference in means between spleen size and the presence of varices

(p=0.01). There appeared to be no statistically significant difference in means between those who had small varices and those who had large varices (p=0.537). Thus, an increment in spleen size was indicative of the presence of varices, but it did not correlate with the grade of varices.

Sudhindra D Lakshman Kumar et al., found in their study that a spleen size >14 cm indicates the presence of varices [12].

Sudha Rani KVL et al., noted that an ultrasonographic measurement of spleen size >15 cm can be considered as a non invasive predictor of the presence of varices [13].

The present study showed that a spleen size of ≥13.55 cm indicates the presence of varices. In this study, there was a statistically significant difference in means between the mean portal vein diameter and the presence of varices (p<0.001**). There appeared to be no statistically significant difference in means between those who had small varices and those who had large varices (p=0.67). Thus, an increment in portal vein diameter was indicative of the presence of varices, but it did not correlate with the grade of varices.

Sudhindra et al., Sudha Rani KVL et al., and Bintintan A et al., all noted that a portal vein diameter of >13 mm was predictive of oesophageal varices [12,13,18]. Sarwar S et al., had previously noted that a portal vein diameter of >11 mm was predictive of varices [8]. Bhattarai S et al., noted that there was a high likelihood for the presence of varices at a portal vein diameter >12.25 mm [16]. In present study, a portal vein diameter of ≥12.5 mm indicated the presence of varices.

Riahinezhad M et al., in their study, noted a peak systolic velocity of 11.6±4.7 cm/s in patients with varices and 17.9±7.3 cm/s in patients without varices (p=0.015). The difference was statistically significant [19]. In present study, there was no significant difference in means between peak systolic velocity and the presence/distribution of varices (p-value=0.122).

In present study population, there was a significant difference in means between splenic vein diameter and the presence of varices (p<0.001). There appeared to be no statistically significant difference in means between those who had small varices and those who had large varices (p=0.575). Thus, an increment in splenic vein diameter was indicative of the presence of varices, but it did not correlate with the grade of varices.

Zhou HY et al., had noted that a splenic vein diameter of 8.5 mm had a sensitivity of 83.3% and specificity of 58.1% for predicting oesophageal varices [20].

The present study showed that a splenic vein diameter of ≥9.05 mm indicated the presence of varices. In present study, the mean portal vein/splenic vein diameter ratio differed significantly with the presence of varices (p<0.001**). There appeared to be no statistically significant difference in means between those who had small varices and those who had large varices (p=0.293). Thus, a decrement in the portal vein/splenic vein diameter ratio was indicative of the presence of varices, but it did not correlate with the grade of varices.

Giannini E et al., found that the platelet count/spleen diameter ratio was the only independent variable associated with the presence of oesophageal varices on multivariate analysis [21]. Gadupati V et al., noted that the mean ratio of portal vein to splenic vein diameters in patients with varices was 1.27 (±0.2), whereas it was 1.5 (±0.23) in those without varices (p<0.001**) [1]. The present study showed that a portal vein/splenic vein diameter ratio of 1.6150 and above predicted the absence of varices.

From the study, a portal vein diameter of ≥12.5 mm (AUC for ROC Curve=0.933) appeared to be the best predictor of oesophageal varices among all the parameters that were studied.

Most of the findings in present study seemed to be consistent with the results previously published by Gaduputi V et al., Sarwar S et al., Bhattarai S et al., Mandal L et al., Sudha Rani KVL et al., and Zhou HY et al., [1,8,13,16,20].

Limitation(s)

Despite the acceptable and satisfactory results obtained in present study and the absence of apparent constraints, authors acknowledge certain limitations. Firstly, we could not rule out the possibility of hospital bias since present study was conducted in a metropolitan tertiary care center, and the data may not uniformly reflect the disease pattern in the entire population. Additionally, present study was carried out during the Coronavirus Disease-2019 (COVID-19) pandemic, and the hospital served as a dedicated COVID referral centre. This may have limited the usual patient attendance to the hospital. Furthermore, it is important to note that the entirety of our study population consisted of patients with decompensated chronic liver disease (CTP class B and C), and therefore, the study results may not be applicable to those with compensated chronic liver disease CTP class A.

CONCLUSION(S)

Thus, based on present study, it can be concluded that the measurement of spleen size, portal vein diameter, splenic vein diameter, and the portal vein/splenic vein diameter ratio using ultrasonography and spleno-portal Doppler study can be recommended as non invasive predictors of oesophageal varices. Ultrasonographic assessment of patients with chronic liver disease is an inexpensive and widely available tool that can be utilised to improve the delivery of care for chronic liver disease patients, particularly in developing countries like India, where advanced diagnostic tools such as endoscopic studies are often not accessible to the majority of the population.

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