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Original Article

By-pass Marker for detecting Esophageal Varices in Patients with Chronic Liver Disease

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Abstract

This study was designed to make a relation between gall bladder wall thickening (GBWT) measured by ultrasonography and esophageal varices (EV) measured byupper gastrointestinal endoscopy in chronic liver disease patients. Itwas cross- sectional descriptive study. 50 cases ofChronic Liver Disease were recruited. GBWT was measured by ultrasonography and upper gastrointestinal endoscopy was done for assessment of the presence and grade of EV in all cases. Among 50 cases, 34 (68%) were male and 16(32%) were female. Mean age (±SD) of the study population was 46.7 (±13.28) years of age. Esophageal varices were found in 42(84%) cases and 8(16%) cases had no varix. Among 42 cases of esophageal varices 9 cases had grade-I, 17 cases had grade-II and 16 cases had Grade-III esophageal varices. Gall bladder wall thickness up to 3mm was considered as normal. In this study GBWT value between (1-3) mm8 cases had no EV GBWT value between (3.1-5.9) mm ,10 cases had EV(9 cases had grade 1 and 1 case had grade 11 EV); GBWT value between (6-8.9) mm, 16 cases had grade 11 EV and GBWT value between (9-12) mm 16 cases had grade 111 EV. A significant statistical correlation was found between the level of GBWT and EV (P<0.001) and also between mean GBWT and EV (P<0.001). This study shows that the presence of EV is directly related to the level of GBWT and there is also association with the grade of EV and level of GBWT. This finding will permit the use of GBWT as a preliminary indirect parameter that will predict the presence EV. It can help clinicians in determining the urgency of care, especially where endoscopy facilities are not available.

Keywords: Gall bladder wall thickening (GBWT), Esophageal varices (EV)

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Introduction

Liver cirrhosis may be defined as a diffuse process characterized by fibrosis and conversion of normal liver architecture into abnormal nodules[1]. Liver cirrhosis is the end stage of many liver diseases and considered to be irreversible. The triad of parenchymal necrosis, regeneration and scarring is always present regardless of individuals' manifestation[2].

Liver cirrhosis is an emerging health problem in our country. The prevalence of chronic liver disease/cirrhosis worldwide is estimated to be 100 (range, 25 to 400) per 100,000 subjects, but it varies widely by country and by region[3]. A study done in Bangladesh at BSMMU Hospital and Sir Salimullah Medical College Hospital, Dhaka, showed that prevalence of cirrhosis is 2.6%[4].

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Liver cirrhosis results in liver damage and development of portal hypertension. Portal hypertension is defined as an increase in the portal venous pressure greater than 7mmHg[6]. One of the main features of portal hypertension is the development of Gastro-esophageal varices. At least 90% of portal hypertension is due to liver cirrhosis[6]. At the diagnosis of liver cirrhosis, varices are present in about 45% of compensated patients and 80% of those who present with ascites[7].

The gold standard for diagnosis of Portal hypertension (PHTN) is direct measurement of portal pressure or hepatic venous pressure gradient[8]. These parameters being obtained by invasive methods which are not feasible in most centers in the world. The indirect way to assess PTHN by detection of esophageal varices (EV).Currently endoscopy of upper GIT is the best method to detect EV. Varices are graded according to Japanese classification. Japanese Classification of esophageal Varices

Grade-I	The varices can be depressed by the endoscope.
Grade-II	The varices cannot be depressed by the endoscope and are separated by normal mucosa.
Grade-III	The varices are confluent around the circumference of the esophagus and cannot be depressed by the endoscope.

As bleeding from esophageal varices is a life-threatening condition, an early prediction and detection of esophageal varices is important. Endoscopic examination is an invasive as well as expensive procedure for the detection of esophageal varices. Therefore, alternative non-invasive procedure is sought for the detection of esophageal varices.

Portal vein is formed by the union of superior mesenteric vein and splenic vein behind the neck of pancreas, in front of the inferior vena cava, and at the level of L2 vertebra[9]. One of the tributaries of the portal vein is the cystic vein which drains the gallbladder[9]. Peculiarity of the portal vein is that the portal vein and its tributaries are devoid of valves[9].Therefore, portal hypertension leads to edema and congestion in gallbladder wall and causes congestivecholecystopathy' resulting into its wall thickening[10]. In a Hamster cirrhosis model, portal hypertension was associated with submucosal edema and areas of dilated vessels in the gallbladder wall. Colour and power Doppler study can identify these dilated venous channels[11, 12]. These histological changes were related to gallbladder wall thickening and associated with impaired wall contractility. Here diffuse wall thickening occurs and wall of the gallbladder is thickened greater than 3mm[13, 14].

Portal hypertensive bleeding prevention remains at the forefront of the long –term management of liver cirrhotic patients[15].Therefore, the challenge is to identify those patients with liver cirrhosis who are at risk of bleeding[16]. Ultrasonography is the method of choice for assessment of the portal system in patient in whom portal hypertension is suspected[17]. It is a non-invasive, cheap and rapid method in comparison with endoscopic procedure. So, gallbladder wall thickening (GBWT) observed at ultrasonography in liver cirrhotic patients may be used as a marker for the presence of esophageal varices[18].

Therefore, the present study has been designed to measure the GBWT by trans abdominal ultrasonography and to find out the association between GBWT and presence of esophageal varices in liver cirrhotic patients.

Material and Methods

It was Descriptive and cross-sectional study. During the study period 50 cases fulfilling inclusion and exclusion criteria were included.*Study place:*Rajshahi Medical College Hospital.

*Duration of study:*January 2013 to December 2014
*Study Population:*All diagnosed cases of chronic liver disease attending in Medicine unit of Rajshahi Medical College Hospital. Chronic liver disease patients were diagnosed on clinical suspicion, liver function tests, by ultrasonography and/or presence of esophageal varices revealed by upper GI endoscopy.*Sampling Method:* Purposive sampling method

Inclusion Criteria:

- All diagnosed cases of chronic liver disease patients.
- Age >18 years.
- Sex-both male and female.

Exclusion criteria:

- Congestive cardiac failure
- Nephrotic syndrome
- Calculus and acalculus cholecystitis
- Liver cirrhotic patients with other complications e.g. hepatic encephalopathy, hepatoma, SBP, hepatorenal syndrome.
- Patients with bleeding episode
- CLD patients with Pregnancy
- Medical contraindication to perform upper GI endoscopy.

Data Analysis Procedure: The data was analyzed with the help of SPSS software program version-16.0 Descriptive analytic techniques involving frequency distribution, computation of percentage, mean, SD etc. were applied. Association between variables was conducted applying appropriate statistical test.

Results

Table-1: Distribution of study population according to age range.

Age group	No. of patients	Percentage(%)
20—29 years	05	10
30—39years	07	14
40—49 years	15	30
50 –59years	14	28
>60 years	9	18
Total	50	100

In this study 50 patients of Liver cirrhosis were included. Mean age(±SD) of the study population was 46.7 (±13.28) years of age. Most of the patients were 40-49 years of age. Among them 34 (68%) were male and 16(32%) were female.

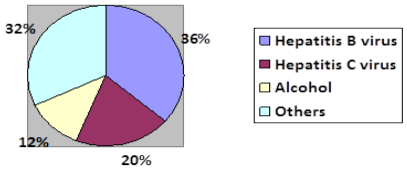

Figure 1: Patients distribution according to cause of cirrhosis

Causative agents were found to be hepatitis B virus in 18 (36%) hepatitis C virus in 10 (20%), alcohol in 6 (12%) cases, whereas no etiology could be detected in the remaining 16 (32%)cases.

Table-II: Patients distribution according to the level of Gall bladder wall thickness.

	Frequency	Percentage (%)
1-3 mm	8	16
3.1-5.9 mm	10	20
6-8.9 mm	16	32
9-12 mm	16	32
Total	50	100
Mean (±SD) =7.09 (±2.90) range: 1.20—11.50 mm		

In this study, all the patients had Gall bladder wall thickness >1.19 mm. The cases were classified by their Gall bladder wall thickness values into four ranges: 1-3 mm; 3.1-5.9 mm; 6-8.9 mm and 9-12 mm. Mean (±SD) Gall bladder wall thickness value was =7.09(±2.90) range: 1.20—11.50 mm. No. of the study population according to calculated level of Gall bladder wall thickness were 8(16%) cases in (1-3 mm), 10 (20%) cases in (3.1-5.9 mm), 16(32%) cases in (6-8.9 mm) and 16(32%) cases in 9-12 mm.

Gall bladder wall thickness up to 3mm was considered as normal[13, 14].

Table-III: Patients distribution according to the presence of esophageal varices.

Esophageal varices	No. of patients	Percentage (%)
Presence	42	84
Absence	8	16
Total	50	100

Table-IV: Patients distribution according to grade of esophageal varices.

Grade of Esophageal varices	No. of patients	Percentage (%)

Grade-I	9	21.4
Grade-II	17	40.5
Grade-III	16	38.1
Total	42	100

Esophageal varices were found in 42(84%) cases and 8(16%) cases had no varix.

Among 42 cases of esophageal varices 9 (21.4%) cases had grade-I, 17 (40.5%) cases had grade-II and 16 (38.1%) cases had Grade-III esophageal varices(table-5).The grading of esophageal varices were done according to Japanese classification.

Table V: Patients distribution according to the presence or absence of esophageal varices and level of Gall bladder wall thickness

		Grading of esophageal varix				Total
		Grade I	Grade II	Grade III	Absent	
Gall bladder	Normal(1-2.9 mm)	0	0	0	8	8
		(0%)	(0%)	(0%)	(100%)	16%
	Mild(3-5.9 mm)	9	1	0	0	10
		(90%)	(10%)	(0%)	(0%)	20%
	Moderate (6-8.9 mm)	0	16	0	0	16
		(0%)	(100%)	(0%)	(0%)	32%
	(Severe) 9-12 mm	0	0	16	0	16
		(0%)	(0%)	(0%)	(0%)	32%
Total		9	17	16	8	50
		18.0%	34.0%	32.0%	16.0%	100.0%

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Gall bladder wall thickness in mm * Grading of esophageal varix	Between Groups (Combined)	52.235	3	17.412	212.750	0.000
	Within Groups	3.765	46	0.082		
	Total	56.000	49			

Gall bladder wall thickness (GBWT) value between normal(1-3 mm) 8 cases had no EV; GBWT value between mild (3.1-5.9) mm ,10 cases had EV(9 cases had grade 1 and 1 case had grade 11 EV); GBWT value between moderate(6-8.9 mm) , 16 cases had grade 11 EV and GBWT value between severe (9-12 mm) 16 cases had grade 111 EV. In this table it was shown that the more the level of GBWT the more the presence of EV. So there is positive correlation with the presence of EV and the level of GBWT. ANOVA test was applied to see the statistical significant. A significant positive statistical correlation was found between the level of GBWT and EV (P<0.001).

Table VI: Patients distribution according to the level of Mean Gall bladder wall thickness with or without esophageal varices.

Grading of esophageal varix	Gall bladder wall thickness in mm Mean	N	% of Total N
Absent	2.3125	8	16.0%
Grade I	5.4333	9	18.0%
Grade II	7.3563	17	34.0%
Grade III	9.9824	16	32.0%
Total	7.0960	50	100.0%

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Gall bladder wall thickness in mm * Grading of esophageal varix	Between Groups (Combined)	350.646	3	116.882	85.163	0.000
	Within Groups	63.133	46	1.372		
	Total	413.779	49			

In this table it was shown that grade of varices numerically increases with the level of mean Gall baldder wall thickness. ANOVA test was applied to see the statistical significant. A significant positive statistical correlation was found between level of GBWT and EV (P<0.001).

Here df=49 and variance ratio (F)=85.163.

Discussion

Liver cirrhosis can occur with or without the development of portal hypertension. Individual who develops portal hypertension presents with splenomegaly and varices in addition to other clinical symptoms and signs. As the portal vein drains the lower end of esophagus as well as gall bladder so increase in portal pressure is reflected in the gall bladder. The reflected retrograde pressure is manifested by thick, edematous gall bladder and also venous engorgement of this organ and causes congestive cholecystopathy' resulting into its wall thickening.

In the above context, this study was designed to make a relation between gall bladder wall thickening (GBWT) and esophageal varices (EV) in cirrhotic patients. This will permit the use of GBWT as a preliminary indirect parameter that will indicate the presence of esophageal varices (EV) as manifestation of PHTN especially where endoscopy facilities are not available.

In this study 50 patients of Liver cirrhosis were included. Mean age (±SD) of the study population was 46.7 (±13.28)years of age. Most of the patients were 40-49 years of age. Among them 34 (68%) were male and 16(32%) were female. Liver cirrhosis patients were diagnosed on clinical suspicion, liver function tests and by ultrasonography and/or presence of esophageal varices revealed by upper GI endoscopy. For the diagnosis of liver cirrhosis ultrasound has 87% sensitivity[19].

Causative agents were found to be hepatitis B virus in 18, hepatitis C virus in 10, alcohol in 6 cases, whereas no etiology could be detected in the remaining 16 cases.

In this study Gall bladder wall thickness of all patients was measured by ultrasonography. Ultrasonographic examination was performed after fasting for eight hours. Gallbladder wall thickness was measured in its thickest portion preferably at the anterior wall. In this study, all the patients had Gall bladder wall thickness >1.19 mm. The cases were classified by their Gall bladder wall thickness values into four ranges: 1-3 mm; 3.1-5.9 mm; 6-8.9 mm and 9-12 mm. Mean (±SD) Gall bladder wall thickness value was =7.09(±2.90) range: 1.20—11.50 mm. No. of the study population according to calculated level of Gall bladder wall thickness were 8(16%) cases in (1-3 mm), 10 (20%) cases in (3.1-5.9 mm), 16(32%) cases in (6-8.9 mm) and 16(32%) cases in 9-12 mm. Gall bladder wall thickness up to 3mm was considered as normal[13, 14].

In this study, esophageal varices were accepted as an indicator of portal hypertension as done by Saverymuttuin 1990[10], Galip in 1997[18], Begum in 2012[20]. Esophageal varices were found in 42(84%) cases and 8(16%) cases had no varix. Among 42 cases of esophageal varices 9(21.4%) cases had grade-I, 17 (40.5%) cases had grade-II and 16(38.1%) cases had Grade-III esophageal varices(table-5).The grading of esophageal varices was done according to Japanese classification.

In this study 4 cases had Gall bladder wall thickness (GBWT) value more than 3 mm and had Esophageal varices(EV) but no ascites. Among them two patients had GBWT value 5mm and had grade-1 EV; one had GBWT value 7.2mm and had grade-11 EV and another had GBWT value 8mm and had grade-111 EV. All of them had no ascites.So it was suggested that EV was the contributing factor for developing GBWT. This finding is consistent with the study done byGalip in 1997[18].

In this study Gall bladder wall thickness (GBWT) value between normal (1-3 mm) 8 cases had no EV; GBWT value between mild (3.1-5.9) mm ,10 cases had EV(9 cases had grade 1 and 1 case had grade 11 EV); GBWT value between moderate(6-8.9 mm) , 16 cases had grade 11 EV and GBWT value between severe (9-12 mm) 16 cases had grade 111 EV. It was shown that the more the level of GBWT the more the presence of EV. So, there is positive correlation with the presence of EV and the level of GBWT. Chi-square test was applied to see the statistical significant. A significant statistical correlation was found between the level of GBWT and EV (p=0.000).

In this study, it was shown that grade of varices numerically increases with the level of mean Gall baldder wall thickness. ANOVA test was applied to see the statistical significant. A significant statistical correlation was found between level of GBWT and EV (P<0.001). Here df=49 and variance ratio (F)=85.163.

This finding is consistent with the study done by Saverymuttu et al.[10] in the Departments of Medicine and Radiology, St George's Hospital and Medical School, London, andGalip et al.[18].

So, this result reveals that that Gall bladder wall thickening (GBWT) measured by ultrasonography may be considered as an important marker for the presence of esophageal varices (EV) done by endoscopy as manifestation of portal hypertension

(PHTN).Endoscopic screening is an invasive, less available ,costly investigation and there are also so many contradictions of this procedure . On the other hand, ultrasonogram is noninvasive, easily available, less costly investigation having no contraindication. So, by measuring GBWT by ultasonography we can stat prophylactic treatment of varices of liver cirrhotic patients and this will reduce mortality, cost of treatment of these patients and will be also convenient to these patients. Patients with cirrhosis, treatment with propranolol reduces variceal bleeding by 47%, death from bleeding by 45%) and overall mortality by 22%[6].

Conclusion

Liver cirrhosis is an emerging health problem in our country. Liver cirrhosis results in liver damage and development of portal hypertension. One of the main features of portal hypertension is the development of Gastro-esophageal varices. As bleeding from esophageal varices is a life-threatening condition, an early prediction and detection of esophageal varices is important. Currently endoscopy of upper GIT is the best method to detect EV. Endoscopic examination is an invasive as well as expensive procedure for the detection of esophageal varices. Therefore, alternative non-invasive procedure is sought for the detection of esophageal varices.

As the portal vein drains the lower end of esophagus as well as gall bladder so increase in portal pressure is reflected in the gall bladder.The reflected retrograde pressure is manifested by thick, edematous gall bladder and also venous engorgement of this organ. So, this study was designed to make a relation between gall bladder wall thickening (GBWT) measured by ultrasonogram and esophageal varices (EV) in chronic liver disease patient. GBWT measured by ultrasonogram may be used as an important marker for the diagnosis of esophageal varices compared to the invasive and expensive upper gastrointestinal endoscopic procedure.

This study shows that the presence of EV is directly related to the level of GBWT and there is also association with the grade of EV and level of GBWT. It is remarkable that all of the patients with a GBWT value >3 mm had esophageal varices. This finding will permit the use of GBWT as a preliminary indirect parameter that will predict the presence of esophageal varices (EV). It can help clinicians in determining the urgency of care, especially where endoscopy facilities are not available.

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