

ORIGINAL ARTICLE

PREDICTION OF OESOPHAGEAL VARICES BY LIVER RIGHT LOBE DIAMETER TO SERUM ALBUMIN RATIO AMONG PATIENTS WITH CIRRHOSIS OF LIVER

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Abstract:

Background: Oesophageal varix is one of the major complications of liver cirrhosis. Repeated endoscopic examinations are unpleasant for patients and also have cost impact. The aim of the study was to determine the predictive value of liver right lobe diameter to serum albumin ratio, a non-invasive parameter for the prediction of esophageal varices. **Methods:** A Cross-sectional observational study was carried out on cirrhotic patients in Gastroenterology department, Dhaka Medical College Hospital, Dhaka. Patients were subjected to complete blood picture, liver functions, viral markers; abdominal ultrasonography, upper gastrointestinal endoscopy and calculation of the Liver right lobe diameter to serum albumin ratio were done. Statistical analysis was done using SPSS software version 23. **Results:** A total number of 80 patients were included. Age of the patient (mean \pm SD) was 47.00 ± 14.53 years, while 57(71%) were men. Regarding etiology, 40(50%) patients had HBV and 10(12.5%) in HCV. Child-Turcotte-Pugh grades showed 54(67.5%) had CTP grade B, followed by 23(28.7%) grade A. Esophageal varices were observed in 65(81%) of the patients. The mean liver right lobe diameter to albumin ratio was 4.5 ± 0.57 in patients having oesophageal varices and 3.9 ± 0.27 in patients without oesophageal varices which was statistically significant (p values 0.01). The best cut off value of liver right lobe diameter to serum albumin was determined at the highest point of Youden index, which was 4.16. With this cut off value, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy was 73.8 %, 60.6 %, 88.8 %, 34.6% and 71.2% respectively. **Conclusion:** This ratio is a useful noninvasive predictor for the presence of oesophageal varices but cannot be advocated clinically due to low sensitivity and specificity. It may serve for selection of patient who need urgent endoscopy and helps when endoscopy facilities are limited or contraindicated or restricted like Covid-19 pandemic situation.

Keywords: Liver cirrhosis, Oesophageal varices, Serum albumin, Liver Right lobe diameter to serum albumin ratio.

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Introduction:

Cirrhosis of liver is a major health problem. It is characterized by fibrosis of the liver parenchyma and evidence of regenerative activity, resulting in portal hypertension.¹Global prevalence of cirrhosis of liver ranges from 4.5% to 9.5% of general population.²In Bangladesh, the incidence of cirrhosis of liver is increasing day by day. In 1981, the incidence was found 2.6% of admitted patients in Dhaka.³

Cirrhosis of liver has a wide range of complications. Esophageal varix is one of the most common complications with a prevalence of 40% to 80%.⁴ Among cirrhotic patients, the yearly rate of development of new varices is about 5–10% and yearly progression from small to large varices occur in 10% to 20%. All the cirrhotic patients should be screened for the presence of varices at the time of initial diagnosis. Follow-up endoscopy should be performed at 2-3 years intervals in compensated patients with no varices and at 1-2 years intervals in compensated patients with small varices (Garcia-Tsao et al., 2010).⁵Therefore, the sensitivity and specificity of numerous non-invasive parameters have been investigated for assessment of presence of esophageal varices.

There are various types of noninvasive test including platelet count, AST Platelet ratio index (APRI), Fibroindex (based on platelet count, AST and GGT), Fibrosis-4 (based on Age, AST, Platelet count and ALT).Most of them have less sensitivity and specificity to predict the presence of varices, for example, APRI (AST Platelet ratio index) has sensitivity-76%, specificity 72%, Platelet count spleen diameter ratio- sensitivity-85%, specificity-54%, etc.

Ultrasonography is a noninvasive, widely available investigation and routinely done for diagnosis of cirrhosis.Ultrasonogram can evaluate the liver morphology including liver size and surface, the coarseness of the parenchyma, portal vein diameter, direction of blood flow, collateral circulation, thrombosis, and the presence of other signs of portal hypertension.^{6,7} Measurement of serum albumin is also a routine and noninvasive test. Hypoalbuminemia is a good non-endoscopic marker for the presence of esophageal varices.⁸

Endoscopy is a gold standard investigation for diagnosis of Esophageal Varices. It is an invasive procedure with procedural discomfort, for this reason many patients try to avoid this. Moreover, a variable proportion of cirrhotic patient does not develop varices. So, there is a particular need for a noninvasive predictor for the presence of varices to ease the medical, social and economic burden of the

disease.Non-invasive predictors based on routine test can reduce the load and help to diagnosis of esophageal varices alternatively.

Ultrasonogram of liver and measurement of serum albumin are routinely done in evaluation of cirrhotic patient. There are few published studies in abroad on the liver right lobe diameter to serum albumin ratio and found it as a good noninvasive predictor for varices.Alempijevic Tamara et al. (2007) from Serbia first conducted a study on liver right lobe diameter to albumin ratio: a new non-invasive parameter for prediction of oesophageal varices in patients with liver cirrhosis and with the cut off value of their ratio 4.42. They found the sensitivity and specificity of prediction of varices are 83.1% and 73.9% respectively.⁹Sanjay Raj et al. (2015) from India and Akram et al. (2018) from Pakistan also found a positive correlation between this ratio and grade of oesophageal varices.^{10,11}There is no such type of published article in our country.So, this study was conducted to explore the noninvasive, easily available,routine test-based ratio in prediction of presence of varix in patients with liver cirrhosis. The aim of the study was to determine the role of liver right lobe diameter to serum albumin ratio in prediction of presence of esophageal varices among patients with cirrhosis of liver.

Methods:

This was a cross sectional observational study, conducted in Gastroenterology department of Dhaka Medical College Hospital, Bangladesh, during the period of June 2019 to February 2020.A total number of 80 adult patients, irrespective of sex, who were recently diagnosed case of liver cirrhosis, based on history, physical examination, liver biochemistry and ultrasonogram, were the target population and who fulfilled the inclusion, and exclusion criteria and gave consent were considered as study population. Purposive sampling technique has been applied. Patients with history of variceal bleeding, history of endoscopic band ligation or variceal sclerosis and having ultrasonographic evidence of hepatic focal lesion or portal vein thrombosis or hepatic vein outflow obstruction were excluded from this study.

General and clinical examination parameters were collected. Further routine laboratory investigations including complete blood tests, HBsAg, anti-HCV, serum bilirubin, asparate aminotransferases (AST), alanine aminotransferases (ALT), and serum albumin, Prothrombin time (PT), and International normalized ratio (INR) were also collected. All studied subjects underwent ultrasonogram of abdomen by confined experienced sonologist. While patient lying in a supine position, a curvilinear probe of a high-

resolution real-time scanner was placed sub-costally in the right mid-clavicular line in a sagittal plane. The cranio-caudal right lobe diameter at mid-clavicular line was measured from the diaphragm to the liver edge. This measurement was taken for three times in the same sitting and the mean value was recorded. Experienced endoscopist had performed the upper GI endoscopy and used the Modified Paquet classification for grading of esophageal varices.¹² Laboratory test and ultrasonographic and endoscopic examinations had been performed within the same week of enrollment.

Data were collected in a pre-designed data collection sheet. All the collected data were analyzed and correlated. Statistical analysis had been performed by using the Statistical Package for Social Sciences (SPSS, version 23.0). Basic descriptive statistics included means, standard deviations, ranges and percentages. Associations among predictors with or without varices were done by unpaired t-test. Differences were considered statistically significant if the two-tailed P value was less than 0.05. Sensitivity and specificity of the ratio of liver right lobe diameter to albumin, for the presence of varices were calculated by using ROC curve. The best cut off value was determined at the highest point of Youden index (sensitivity + specificity - 1).

Results:

Table I
Demographic profile of study population (n=80)

Variables	n (%)	
Age	Range (years)	18-82 (years)
	Mean ± SD	47.00 ±14.53
Sex	Male	57 (71.3 %)
	Female	23 (28.7%)
Oesophageal varices	Yes	65(81.2%)
	No	15(18.8%)
Etiology	HBV	40(50%)
	HCV	10(12.5%)
	Others	30(37.5%)
Child Pugh grade	A	23(28.7%)
	B	54(67.5%)
	C	03(3.8%)

Table I shows, mean age 47 years, 57(71%) patients were male, 65(81%) had oesophageal varices, HBV and HCV were 40(50%) and 10(12%) respectively, 54(67.5%) had CTP grade B, followed by 23(28.7%) grade A.

Table II
Liver right lobe diameter, serum albumin and their ratio among the study population (n=80).

Variables	Oesophageal varices present (n=65), Mean ± SD	Oesophageal varices absent (n=15), Mean ± SD	p value
Liver Right lobe Diameter (cm)	12.4± 1.40	12.1± 1.47	0.51
Serum Albumin (gm/dl)	2.8± 0.23	3.1± 0.43	0.02*
Liver Right liver Diameter to albumin ratio	4.5± 0.57	3.9± 2.7	0.01*

* Significant, P value reached from unpaired t-test

The mean liver right lobe diameter was 12.4±1.40 cm in patients having oesophageal varices and 12.1±1.47 cm in patients without oesophageal varices which was not significant. The mean serum albumin was 2.8±0.23 g/dl in patients having oesophageal varices and 3.1±0.43 g/dl in patients without oesophageal varices which was statistically significant. The mean liver right lobe diameter to albumin ratio was 4.5±0.57 in patients having oesophageal varices and 3.9±2.7 in patients without oesophageal varices which was also statistically significant.

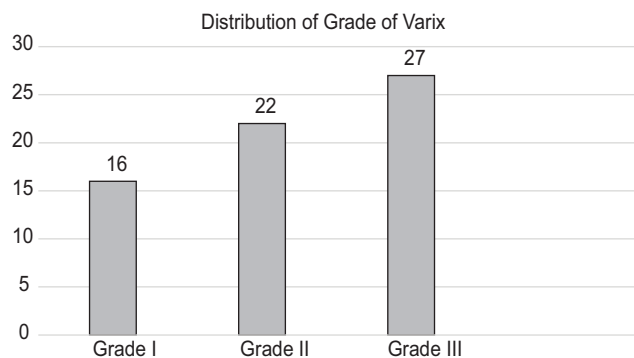


Figure 1: Distribution of different grade of varices among study population (n=65).

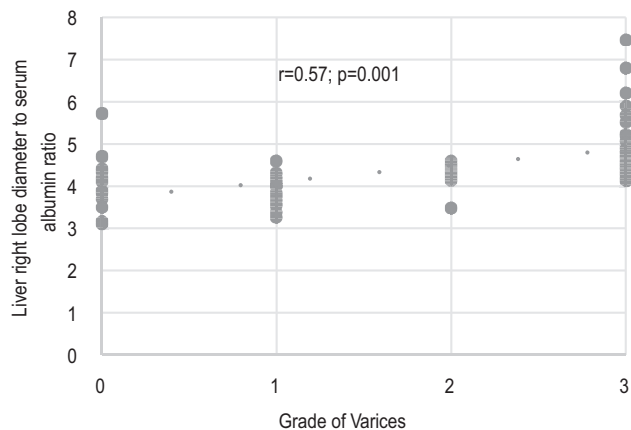


Fig.-2: Correlation between liver right lobe diameter to serum albumin ratio and grade of varices

Scatter diagram showing positive significant spearman’s rank correlation ($r=0.57$; $p=0.001$) between liver right lobe diameter to serum albumin ratio and grade of varices.

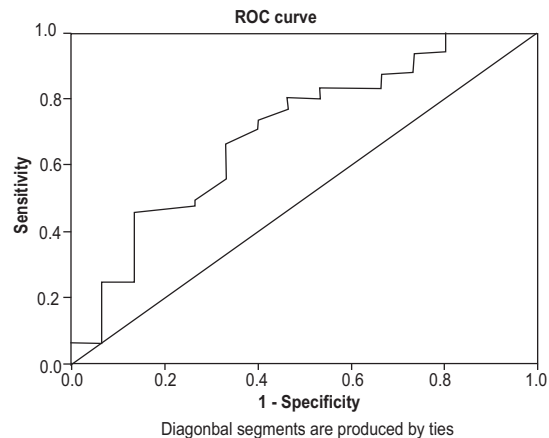


Fig.-3: ROC curve for sensitivity and specificity of liver right lobe diameter and albumin ratio for prediction of Varices.

Receiver-operator characteristic (ROC) curve was constructed by using liver right lobe diameter to serum albumin and the presence of oesophageal varices. The area under the receiver-operator characteristic (ROC) curves was 0.699. The best cut off value of liver right lobe diameter to serum albumin was determined at the highest point of Youden index, which was found 4.16.

Table III

Performance of liver right lobe diameter to serum albumin ratio at cut off value of 4.16 for diagnosis of presence of varices considering endoscopy as Gold standard.

Ratio	Gold standard (Endoscopy)		Total
	Endoscopy OV+	Endoscopy OV-	
≥ 4.16	48 (TP)	6 (FP)	54
< 4.16	17 (FN)	9 (TN)	26
Total	65	15	80
Sensitivity =	TP/ (TP+FN) x 100 =		73.8%
Specificity =	TN/ (FP+TN) x 100 =		60.6%
Positive Predictive value =	TP/ (TP+FP) x100 =		88.8%
Negative Predictive value =	TN/ (FN+TN) x 100 =		34.6%
Accuracy =	(TP+ TN) x 100 / Population =		71.2%

Discussion:

In this study, a total 80 participants were enrolled. The mean age of the enrolled patients was 47.00 ± 14.53 years with the age ranged from 18 to 82 years. In a study by S. Esmat et al., (2012) in Egypt, reported the mean age 49.23 ± 7.99 years and age ranged from 20 to 70 years which are consistent with our study.¹³

Among the study population, 57(71%) patients were male and 23(29%) in female, 65(81%) patients of this study had oesophageal varices. Sanjay Raj et al.,

(2015) in India found (88%) male and (12%) were female in their study. They also found approximately 90% patient having oesophageal varices. So, the reports of our study are near about similar with this Indian study.¹⁰

Among the study population having oesophageal varice, 27(33.8%) patients had grade III oesophageal varices followed by 22(27.5%) in grade II, 16(20%) in grade I oesophageal varix, 15 (19%) in no varix.

Elshazly Abd Elhady Sheta et al., (2016) in Egypt reported a study where they enrolled 100 cirrhotic patients, among them, 32 were found to have grade III oesophageal varices, 15 patients were found to have grade II, 10 patients were found to have grade I and 43 patients had no varices. The Patterns of grade of oesophageal varices in enrolled patients are consistent with our study.¹⁴

Regarding etiology, 40(50%) patients had HBV followed by 30(37.5%) in others and 10(12.5%) in HCV. Mamun-Al-Mahtab et al., (2015) from Bangladesh published an original article where they reported HBV is the leading cause of CLD in the country. They found HBV attributed to 61.15% cases of cirrhosis of liver in this country. They also reported as HCV was the second commonest cause of CLD responsible for 4.1% in Sylhet and 5% in Barisal divisions, respectively.¹⁵ Akbar SMF et al., (1997) in Bangladesh who found more than 5% prevalence of HCV in apparently healthy Bangladeshis.¹⁶ So, our etiology of cirrhosis is consistent with the previous report from Bangladesh.

In this study, it is found that mean liver right lobe diameter was 12.4 ± 1.40 cm in patients having oesophageal varices and 12.1 ± 1.47 cm in patients without oesophageal varices which was not statistically significant. The mean serum albumin was 2.8 ± 0.23 g/dl in patients having oesophageal varices and 3.1 ± 0.43 g/dl in patients without oesophageal varices which was statistically significant. The mean liver right lobe diameter to albumin ratio was 4.5 ± 0.57 in patients having oesophageal varices and 3.9 ± 0.27 in patients without oesophageal varices which was also statistically significant. Sanjay Raj, et al, in India published a similar article where they found that right liver lobe diameter was 12.85 ± 2.34 cm in patients' group having oesophageal varices and 11.20 ± 2.20 cm in patients' group having no oesophageal varices which was not statistically significant. Serum albumin was 2.61 ± 0.61 g/dl in patients' group having oesophageal varices and 2.68 ± 0.29 g/dl in patients' group having no oesophageal varices which was statistically significant. Right liver lobe diameter/albumin ratio was 5.06 ± 1.02 in patients having oesophageal varices and 4.17 ± 0.72 in patients having no oesophageal varices which was also statistically significant. So, the reports of our study are consistent with this Indian study.¹⁰

Receiver-operator characteristic (ROC) curve was constructed by using liver right lobe diameter to serum albumin and the presence of oesophageal varices. The area under the curves was 0.699. The best cut off value of liver right lobe diameter to serum

albumin was determined at the highest point of Youden index, which was found 4.16. With this cut off value, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and Accuracy was 73.8 %, 60.6 %, 88.8 %, 34.6% and 71.2% respectively. Alempijevic T., et al. (2007) concluded for the first time that the liver right lobe diameter to albumin ratio can be used as a noninvasive predictor of oesophageal varices. In that study, at a cut-off value of 4.42, the sensitivity was 83.1%, and the specificity was 73.9%.⁹ Mohamed Salem et al. (2018) from Egypt conducted a similar study where they found the best cut off value of the ratio > 4.1 , area under the curve = 0.7, with sensitivity of 62 %, specificity of 73.3 %, positive predictive value of 73.9 % and negative predictive value of 59.4 %.¹⁷ So, the reports of this study are consistent with the Egyptian study.

Conclusion:

In this study, the best cut off value of the ratio was 4.16, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were 73.8%, 60.6%, 88.8%, 34.6% and 71.2% respectively. This ratio can be a useful non-invasive predictor for the presence of oesophageal varices in cirrhotic patients at initial stage. It cannot be advocated clinically due to low sensitivity and specificity. This routine test-based ratio may serve for the purpose of selection of patient who need urgent endoscopy and help the physicians where or when endoscopy facilities are limited or contraindicated or restricted like Covid-19 pandemic situation.

Conflict of Interest:

The author stated that there is no conflict of interest in this study

Funding:

No specific funding was received for this study.

Ethical consideration:

The study was conducted after approval from the ethical review committee. The confidentiality and anonymity of the study participants were maintained

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