

Prediction of Oesophageal Varices by Serum Albumin Level among Patients with Cirrhosis of Liver

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Abstract

Background: Oesophageal varix is a common complication of liver cirrhosis. Endoscopy is the gold standard test to detect varices but it is unpleasant for patients. The aim of the study was to determine the predictive value of serum albumin for the prediction of oesophageal varices.

Methods: It was a cross-sectional observational study, conducted in gastroenterology department, Dhaka Medical College Hospital, Dhaka on recently diagnosed cirrhotic patients. It was based on routine test for cirrhosis of liver. So, every patient was underwent routine investigations including complete blood count, viral markers, serum albumin, ultra-sonogram of abdomen, upper gastrointestinal endoscopy. Statistical analysis was done using SPSS software version 23.

Results: A total number of 150 patients were included. Age of the patient (mean \pm SD) was 47.89 \pm 14.77 years, while 113 (75.3%) were men. More than half (56.7%) patients had HBV followed by 53(35.3%) was unknown and 12(8.0%) had HCV. Oesophageal varices were observed in 90% of the patients. The mean value of albumin ratio was 2.78 \pm 0.49 in patients having oesophageal varices and 3.11 \pm 0.68 in patients without oesophageal varices which was statistically significant ($p < 0.05$). The correlation of serum albumin with different grades of oesophageal varices was also statistically significant. Considering low serum albumin as below 3.5 gm/dl, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were 82.22%, 20.00%, 90.24%, 11.11%, and 76.00% respectively.

Conclusion: Serum albumin is a useful noninvasive routine test which can predict the presence of oesophageal varices in cirrhotic patients. It can never replace the gold standard endoscopy test but it can help physicians to predict a high probability of esophageal varices. It may also help for selection of patient who need urgent endoscopy when endoscopy facilities are limited like Covid-19 pandemic situation.

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Introduction

Cirrhosis of liver is an increasing cause of morbidity and mortality worldwide. Centers for Disease Control (CDC) estimates that in 2009 chronic liver disease and cirrhosis represented the 12th leading cause of death overall and the fifth leading cause of death for patients aged 45 to 54 years. Among 5500 liver transplants in Europe in each year, cirrhosis is the main indication.¹

The prevalence of cirrhosis is difficult to assess and probably higher than reported, because the initial stages are asymptomatic so the disorder is undiagnosed. Prevalence was estimated at 4.5% to 9.5% worldwide.² In Bangladesh, the incidence of liver diseases is increasing day by day and most are suffering from chronic liver diseases like cirrhosis.

Cirrhosis of liver is a common health problem and has wide range of complications. Oesophageal varices develop in patients with cirrhosis at an annual rate of 5–8%, but the varices are large enough to pose a risk of bleeding in only 1–2% of cases. Approximately 4–30% of patients with small varices will develop large varices each year and will therefore be at risk of bleeding.³

At the time of diagnosis, approximately 30% of cirrhotic patients have oesophageal varices, reaching 90% after approximately 10 years. Bleeding from oesophageal varices is associated with a mortality rate of at least 20% at 6 weeks, although bleeding ceases spontaneously in up to 40% of patients. Variceal hemorrhage is the most common fatal complication of cirrhosis.³

Serum albumin level is often reduced in patients with liver cirrhosis. It may be due to reduced synthesis of albumin (liver parenchyma replaced by fibrous tissue), increased removal by reticuloendothelial

system (spleen) or increased loss through gut in portal hypertensive gastropathy.^{4,5}

Endoscopy of upper GIT is the gold standard investigation to detect the presence or absence of varices. But it causes discomfort and many patients fear to this invasive procedure. So, for this group of patients, non-invasive investigations are required to predict the presence of oesophageal varices. Non-invasive predictors based on routine test can reduce the load and help to diagnosis of oesophageal varices alternatively.

Few studies revealed good predictive value of various non-endoscopic variables for the presence or absence of varices, but available data in our country is limited. Measurement of serum albumin level is easily available and non-invasive test and routine test for cirrhosis of liver patient. There are few published studies on serum albumin and prediction of varices and found it as a good non-invasive predictor for varices. Therefore, this study was conducted for prediction of oesophageal varices by serum albumin level among patients with cirrhosis of liver.

Objective

The aim of our study was to determine the predictive value of serum albumin for the prediction of oesophageal varices.

Method

This was a cross sectional observational study, conducted at Gastroenterology department in Dhaka Medical College Hospital during the period of June 2019 to February 2020. A total number of 150 adult patients, irrespective of sex, who were recently diagnosed case of liver cirrhosis were enrolled into this study. Purposive sampling technique has been applied.

General and clinical examination were done in each patient. Further routine laboratory investigations including CBC, HBsAg, anti-HCV, serum bilirubin,

AST, ALT, and serum albumin, Prothrombin time (PT), and International normalized ratio (INR) were also collected. Experienced endoscopist had performed the upper GI endoscopy and used the Modified Paquet classification for grading of oesophageal varices.⁶ Laboratory test and endoscopic examinations had been performed within the same week of enrolment.

Data were collected in a pre-designed data collection sheet. All the collected data were analysed 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 unpair t-test. Differences were considered statistically significant if the two-tailed P value was less than 0.05.

Results

Table I shows the clinical characteristics of all patients. It was observed that the mean age was 47.89 ± 14.77 years with ranged from 18 to 82 years. Three fourth (75.3%) patients were male and 37(24.7%) in female. Majority (90.0%) patients had oesophageal varices. More than half (56.7%) patients had HBV followed by 53(35.3%) in unknown and 12(8.0%) in HCV.

Table I: Clinical characteristics of all patients (n=150)

Clinical characteristics	Mean \pm SD	Range (min-max)
Age (in years)	47.89 \pm 14.77	18-82
	Number of Patients	Percentage
Sex		
Male	113	75.3
Female	37	24.7
Oesophageal varices		
Yes	135	90
No	15	10
Etiology		
HBV	85	56.7
HCV	12	8.0
Unknown	53	35.3

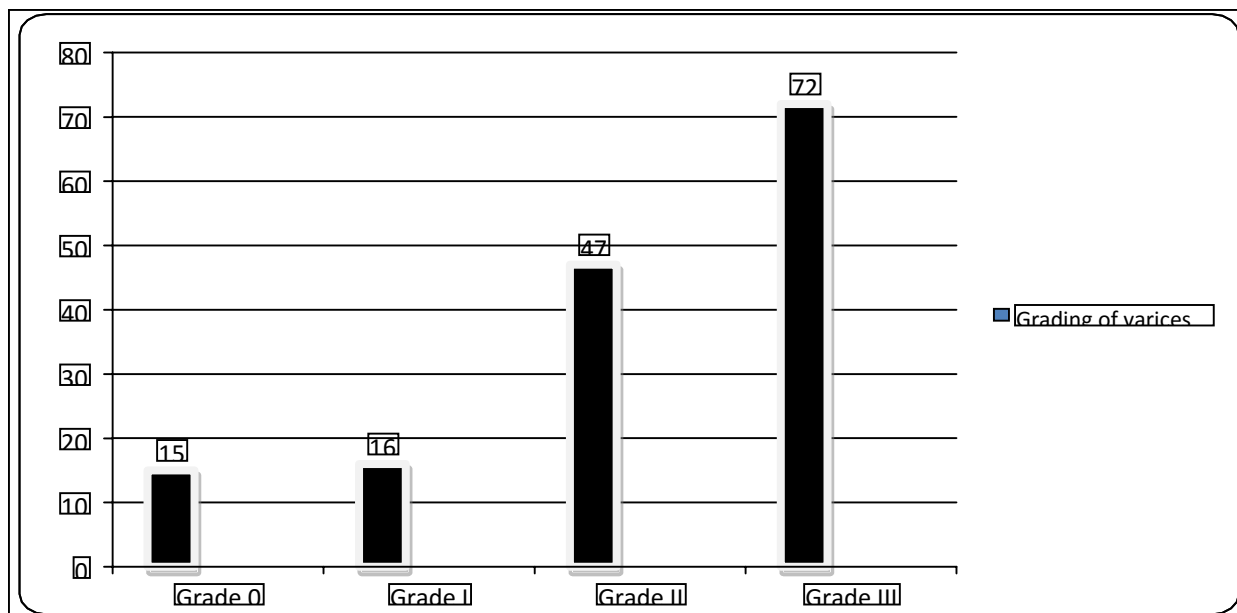


Figure 1. Distribution of grading of varices among cases (n=150)

Figure 1 shows almost half (48%) of patients had grade III oesophageal varices followed by 47 (31.33%) in grade II, 16(10.67%) in grade I and 15 (10.0%) in no varix.

Table II: Serum albumin level in study population (n=150)

Serum Albumin	Frequency	Percentage (%)
<2.8	75	50%
2.8-3.5	48	32%
>3.5	27	18%

Table II shows 18% patients have normal serum albumin and 82% patients have low serum albumin. Among them, 50% patients have very low serum albumin that is below 2.8 gm/dl.

Table III: Association of serum albumin with and without varices (n=150)

	Oesophageal varices		p value
	Present (n=135) Mean±SD	Absent (n=15) Mean±SD	
Serum Albumin	2.78±0.49	3.11±0.68	0.019 ^s

s=significant, P value reached from unpaired t-test

The mean serum albumin was 2.78±0.49 g/dl in oesophageal varices present and 3.11±0.68 g/dl oesophageal varices absent. The difference of serum albumin was statistically significant (p<0.05) among the parameters with and without varices.

Table IV: Correlation of serum albumin and grades of varices (n=150)

Serum Albumin	Oesophageal varices on Endoscopy				Total	P value
	Grade 0	Grade I	Grade II	Grade III		
<2.8	8	7	25	35	67	0.04
2.8-3.5	4	6	12	26	44	
>3.5	3	3	10	11	24	
Total	15	16	47	72	135	

S = significant, P value reached from ANOVA test

Table IV shows the correlation of serum level with different grades of oesophageal varices, which was statistically significant.

Table V: Performance of serum albumin for the prediction of presence of oesophageal varices considering endoscopy as gold standard

Serum Albumin	Endoscopy OV		Total
	OV+	OV -	
<3.5	111 TP	12 FP	123
>3.5	24 FN	3 TN	27
Total	135	15	150

Table V shows the performance of low serum albumin for the prediction of presence of oesophageal varices. Considering low serum albumin as below 3.5 gm/dl, the validity of the test was sensitivity-82.22%, specificity-20.00%, Positive Predictive Value (PPV)-90.24%, Negative Predictive Value (NPV)- 11.11%, Accuracy-76.00%

Discussion

In this study, a total 150 participants were enrolled. Regarding the cirrhotic patients enrolled in the study, their age ranged from 18 to 82 years with a mean value of 47.89 ± 14.77 . Among the study population, there were 113 male and 37 female. In this study, 135 (90%) patients had oesophageal varices (OV) and 15 patients had no varices. Among 135 patients, 16 patients had grade 1 OV, 47 patients had grade 2 OV, and 72 patients had grade 3 OV. Regarding etiology, more than half (56.7%) patients had HBV followed by 53(35.3%) was unknown and 12(8.0%) had HCV.

In this study, 18% patients have normal serum albumin and 82% patients have low serum albumin. Among them, 50% patients have very low serum albumin that is below 2.8 gm/dl.

The mean serum albumin was 2.78 ± 0.49 g/dl in oesophageal varices present and 3.11 ± 0.68 g/dl oesophageal varices absent. The difference of serum albumin was statistically significant ($p < 0.05$) among the parameters with and without varices.

Regarding correlation of serum albumin and different grades of varices, ANOVA test showed a significant relation between serum albumin and OV grades. which was statistically significant.

In this study, the performance of serum albumin for the prediction of presence of oesophageal varices considering endoscopy as Gold standard was done. Considering low serum albumin as below 3.5 gm/dl, the validity of the test was sensitivity- 82.22%, specificity-20.00%, Positive Predictive Value

(PPV)-90.24%, Negative Predictive Value (NPV)- 11.11%, Accuracy-76.00%.

This study revealed that the mean age value of the enrolled patients was 47.89 ± 14.77 years with the age ranged from 18 to 82 years. In a study by Dewa Gde Agung Budiayasa at Sanglah General Hospital, Indonesia, reported the mean age 49.98 ± 1.62 years and age ranged from 13 to 77 years which are consistent with our study.⁷

In this study, 75.3% patients were male and 37(24.7%) in female. 90.0% patients of this study had oesophageal varices. Dewa Gde Agung Budiayasa et al also found 73.8% male and 26.2% female patients in their study. They also found 86.9% patient having oesophageal varices. So, the reports of our study are near about similar with this Indonesian study.

This study revealed that, almost half (48%) of patients had grade III oesophageal varices (OV) followed by 47 (31.33%) in grade II, 16(10.67%) in grade I and 15 (10.0%) in no varix. Dewa Gde Agung Budiayasa et al studied on only 61 patients and they found 8(13.1%) patients without varices, 14 (23.0%) patients with Varix grade I, 21 (34.4%) patients with grade II and 18 (29.5%) patients with grade III. In our study, study population was comparatively higher and we got more patient with grade III varices.

Regarding etiology, this study showed that 56.7% patients had HBV followed by 35.3% had unknown and 8 % patient had 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.⁸ Akbar SMF et

al., (1997) in Bangladesh who found more than 5% prevalence of HCV in apparently healthy Bangladeshis.⁹ So, our etiology of cirrhosis is consistent with the previous report from Bangladesh.

In this study, 18% patients have normal serum albumin (>3.5 gm/dl) and 82% patients have low serum albumin (≤ 3.5 gm/dl). Among them, 50% patients have very low serum albumin that is below 2.8 gm/dl.

Rajanna, et al., in Bengaluru, India conducted a study where they found that the albumin value of <2.8 mg/dL was seen in a high number of study subjects (76%), followed by an albumin level of 2.8–3.5 mg/dL (23%) and >3.5 mg/dL (1%).¹⁰

The mean serum albumin was 2.78 ± 0.49 g/dl in oesophageal varices present and 3.11 ± 0.68 g/dl oesophageal varices absent. The difference of serum albumin was statistically significant ($p < 0.05$) among the parameters with and without varices. Dewa Gde Agung Budiayasa et al, found that Serum albumin level ranged between 1.10-3.60 mg/dL, and the average value was 2.21 ± 0.451 mg/dL. Regarding correlation of serum albumin and different grades of varices, ANOVA test showed a significant relation between serum albumin and OV grades., which was statistically significant.

In this study, considering Endoscopy as Gold standard for detection of oesophageal varices, performance of low serum albumin (below 3.5 gm/dl) was calculated and the validity of the test was sensitivity- 82.22%, specificity-20.00%, Positive Predictive Value (PPV)-90.24%, Negative Predictive Value (NPV)-11.11%, Accuracy-76.00%. Muhammad Zaman Baloch et al, conducted a study at Isra University Hospital Hyderabad in collaboration with department of Gastroenterology, AIMS Hospital,

Hyderabad, and they found the sensitivity of oesophageal varices on serum albumin (<3.4) was 81.08% with specificity of 84.48%. The PPV value was 76.92%, NPV value was 87.5% and diagnostic accuracy of oesophageal varices on serum albumin was 83.16% taking oesophageal varices on EGD as gold standard.¹¹ In another study in our country conducted by S F Hossain et al, 2010 found that hypoalbuminaemia (<3.5gm/dl) and Oesophageal varices is significant and they found the Sensivity: 56%, Specificity: 83.8%, positive predictive value (PPV): 62.06%, negative predictive value (NPV): 80.2%.¹² So, the finding of this study is consistent with the finding of previous study of our country.

Khan H et al. in their study found 57 patients (28.9%) out of 197 have hypoalbuminemia (<3.5gm/dl) and among them, 35 patients (61.4%) have Varices, while 140 patients (71.1%) had albumin level >3.5 gm/dl with 28 having Varices (20%). They found hypoalbuminemia (<3.5 gm/dl) has 53.2% sensitive & 91% specific predictor of EV with positive predictive value of 73.3% and negative predictive value of 80.8%.¹³ So, the finding of this study is consistent with the finding of other study.

Conclusion

serum albumin is a useful non-invasive routine indicator of oesophageal varices in cirrhotic patients. However, due low sensitivity of hypoalbuminemia, the absence of hypoalbuminemia does not rule out varices. So, It can never replace the gold standard endoscopy test but it can help physicians to predict a high probability of oesophageal varices. It may also help for selection of patient who need urgent endoscopy when endoscopy facilities are limited like Covid-19 pandemic situation.

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