

Non-Invasive Predictors of Esophageal Varices in Patients with Cirrhosis of Liver- A Prospective Study

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Abstract

Background: Liver disease particularly chronic liver disease is one of the major public health problem, accounting for significant morbidity and mortality worldwide. Among the different complications, gastro-esophageal variceal bleeding is the deadliest complications of advanced liver disease and have been described in 50% of patients with liver cirrhosis.

Aim: To identify the non-invasive predictors of esophageal varices in patients with cirrhosis of liver, so as to reduce number of unnecessary endoscopies.

Methods: Ninety two patients with cirrhosis of liver irrespective of etiology were analysed prospectively from October 2019 to March 2020. Appropriate clinical, biochemical and ultrasonographic parameters were selected as variables to compare with esophageal varices. The data were assessed by univariate and multivariate analysis.

Results: Univariate analysis of the studied parameters showed that decreased platelet count, albumin levels and platelet count/splenic diameter ratio and increased bilirubin levels, prothrombin time, splenic size, portal vein size were significantly associated with the presence of esophageal varices and their values correlated with increasing size of varices. On multivariate analysis of variables, the independent predictors for the presence of varices were platelet count/splenic size <1433.1, splenic size >115.75 mm.

Conclusion: Platelet count/splenic size <1433.1, Splenic size >115.75 mm are independent noninvasive predictors of esophageal varices in patients with cirrhosis of liver.

Keywords: Esophageal Varices, Platelet Count/Splenic Size, Ultrasonographic Parameters, Invasive Predictors.

Introduction

Liver disease particularly chronic liver disease is one of the major public health problem, accounting for significant morbidity and mortality worldwide. Among the different complications, gastro-esophageal variceal bleeding is the deadliest complications of advanced liver disease and have been described in 50% of patients with liver cirrhosis. Cirrhosis is responsible for 1.1% of all deaths as estimated by WHO (1). Portal hypertension is a significant complicating feature of decompensated cirrhosis and is responsible for the development of ascites and bleeding from esophagogastric varices, two complications that signify decompensated cirrhosis. Esophageal varices are portosystemic collaterals i.e., vascular channels

that link the portal venous and the systemic venous circulation, that develop as a result of portal hypertension (2). Development of esophageal varices is the major complication of cirrhosis. At the time of diagnosis about 30% of cirrhotic patients have esophageal varices, reaching 90% after approximately 10 years (3). In cirrhotic patients who do not have esophageal varices at initial endoscopy, new varices will develop at a rate of approximately 5% per year. In patients with small varices at initial endoscopy, progression to large varices occurs at a rate of 10% to 15% per year and is related predominantly to the degree of liver dysfunction. Bleeding from varices is most serious and life-threatening complication of cirrhosis which accounts for 10% of all cases of upper gastroin-

testinal bleeding. About one third of cirrhotic patients will bleed from their varices (4). Each episode of variceal hemorrhage carries a 20% to 30% risk of death, 70% of patients not receiving treatment dying within 1 year of the initial bleeding episode (5). Proceedings of the third Baveno international consensus workshop on portal hypertension recommends that all cirrhotic patients should undergo endoscopic screening for varices at diagnosis. Endoscopy should be repeated every 2 to 3 years thereafter in those with compensated disease and no varices, 1 to 2 years for those with small varices and 1 year for those with decompensated disease with or without varices (6). These recommendations imply a considerable burden of endoscopies and related costs; they require that patients repeatedly undergo an unpleasant procedure and also only 9%-36% of patients with cirrhosis found to have varices on screening endoscopy. To reduce the number of unnecessary endoscopies in patients with cirrhosis but without varices, several studies have evaluated possible non-invasive markers of esophageal varices in patients with cirrhosis. The conclusion from most of these studies is that by selecting patients for endoscopic screening based on a few laboratory and/or ultrasonographic variables, an appreciable number of endoscopies may be avoided, while keeping the rate of undiagnosed varices which are at risk of bleeding, acceptably low. Though cirrhosis of liver is today one of the common entity there are no adequate data available for choosing the patients to screening endoscopy in cirrhosis of liver in Bangladesh. Present study is conducted to evaluate validity of non-invasive parameters in predicting esophageal varices in patients with cirrhosis of liver, so as to reduce the number of unnecessary endoscopies and at the same time keeping rate of undiagnosed varices acceptably low.

Materials and Methods

Ninety-two patients with liver cirrhosis irrespective of etiology who were admitted in Medicine ward, Sheikh Russel National Gastroenterology Institute & Hospital, Mohakhali, Dhaka, Bangladesh from October 2019 to March 2020 were prospectively studied after taking written informed consent. All the patients were subjected to a detailed clinical evaluation, biochemical investigations such as complete blood count, liver function tests, kidney function tests, serum electrolytes, prothrombin time, international normalized ratio, hepatitis B surface antigen and antibody to hepatitis C virus were analyzed. Ultrasonography of abdomen was done to assess liver size and structure, maximum splenic bipolar diameter and portal vein diameter. Child-Pugh score was calculated for all patients to assess severity of cirrhosis. Upper gastrointestinal endoscopic examination was done to identify esophageal varices. Esophageal varices were classified into small and large varices based on the following findings. Small esophageal varices were defined as those that flatten with insufflation or minimally protrude into the oesophageal lumen. Large varices were defined as those which protrude into the esophageal lumen and touch each other (or) fill at least 50% of the esophageal lumen (7).

Inclusion Criteria: Patients with cirrhosis of liver without any past history of gastrointestinal bleed were included in study. The diagnosis of cirrhosis was made on the basis of clinical, biochemical and ultrasonographic findings.

Exclusion Criteria: Patients with present or previous history of bleeding disorders, previous/current treatment with beta block-

ers, who had undergone sclerosis or band ligation of oesophageal varices, TIPSS or surgery for portal hypertension were excluded from study.

Statistical Analysis: Statistical analysis was performed using SPSS 15.0 software. Results were expressed as mean±S.D. Qualitative data were tabulated in frequencies and percentages. Quantitative data were given in mean and standard deviation. Association between qualitative data and grade of varices were analysed using Pearson chi-squared test. Association between qualitative data and grade of varices were analysed using one way analysis of variance (ANOVA), F-test and student t-test. P value of <0.05 was considered to be significant. Then multivariate analysis of variables with significant correlation was carried out using stepwise logistic regression analysis to detect the independent predictors for presence of varices.

Results

There were 92 eligible liver cirrhosis patients. Majority of them are in the age group of between 41-60 years. Among them 77(76.1%) were males and 22(23.9%) were females [Figure-1]. The etiology of cirrhosis was alcoholic liver disease in 59 patients. HCV, HBV and autoimmune hepatitis constituted rest of the etiology. Esophageal varices were found in 90 patients. 45 had small varices and 35 had large varices. Univariate analysis of the studied parameters was carried out and it was found that decreased platelet count, albumin levels and platelet count/splenic diameter ratio and increased bilirubin levels, prothrombin time, splenic size, portal vein size were significantly associated with the presence of esophageal varices and their values correlated with increasing size of varices as shown in [Table 1]. On multivariate analysis of variables, the independent predictors for the presence of varices were platelet count/splenic size <1433.1, splenic size >115.75 mm as shown in [Table 2]. It was also found that there was a positive correlation between grading of oesophageal varices and splenic size [Figure-2]. That means when portal vein diameter increases, esophageal varices also increase in size. There was also negative correlation between platelet count/splenic size and grades of varices [Figure-3].

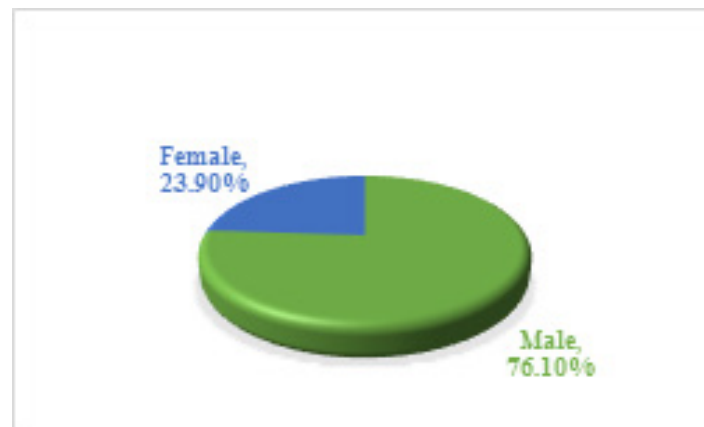


Figure-1: Sex distribution of patients.

Table 1: Association of parameters with esophageal varices (N=92)

Parameter	Nil	Small Varices	Large Varices	P Value
Prothrombin time(secs)	13.5±1.24	15.44±2.22	19.41±2.52	<0.001
Serum bilirubin(mg/dL)	4.10±1.14	6.02±4.12	9.98±5.62	<0.001
Serum albumin(g/dL)	2.94±0.39	2.68±0.38	2.25±0.41	<0.001
Platelet count (x103/MI)	165.58±37.90	106.44±25.78	85.514±19.68	<0.001
Portal vein diameter(mm)	11.92±0.710	12.84±0.88	14.52±1.24	<0.001
Splenic size(mm)	115.75±3.52	130.69±9.52	146.97±9.56	<0.001
Platelet count/splenic size	1433.1±332.19	824.6±231.16	587.5±149.17	<0.001

Table 2: Multivariate analysis (N=92)

Parameter	Significance	Odds ratio	Confidence interval
Spleen size	0.018	2.305	1.154-4.605
Platelet count/Splenic size	0.029	0.983	0.967-0.998
Portal vein	0.086	34.77	0.606-1.996

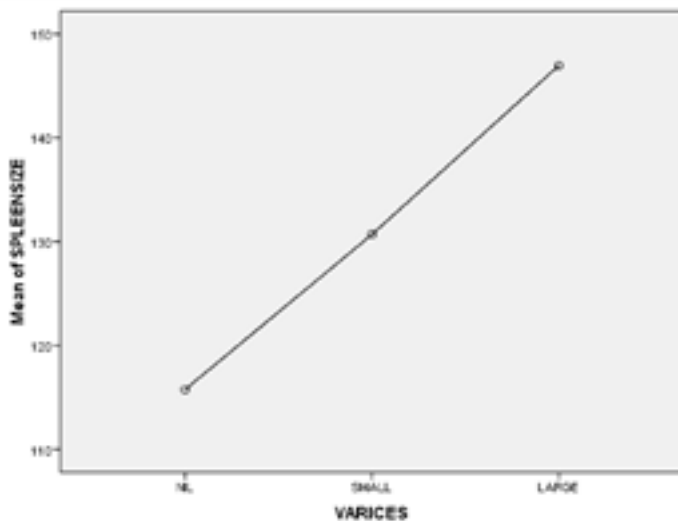


Figure-2: Correlation of splenic size with esophageal varices.

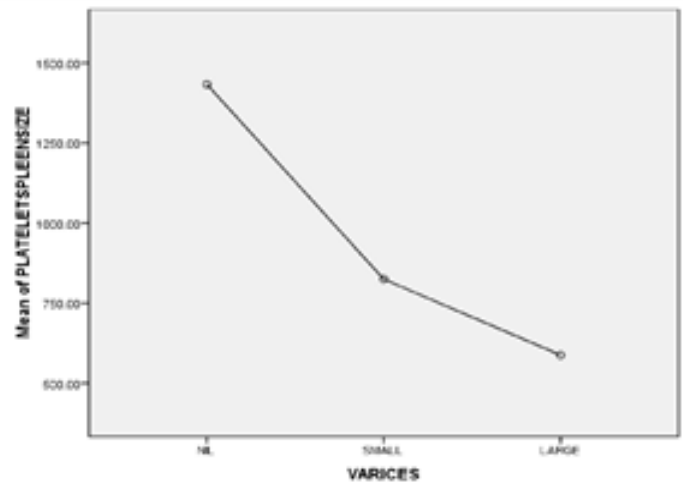


Figure-3: Correlation of platelet count/splenic size with esophageal varices.

Discussion

Esophageal varix is the leading cause of mortality in patients with cirrhosis of liver. Hence early identification of varices is necessary to reduce significant suffering. There is a particular need for non-invasive predictors of the presence of esophageal varices as they might help reduce medical, social and economic costs. There are number of studies in the past which shows significant correlation between presence of esophageal varices and platelet count, albumin, portal vein diameter, splenic size and platelet count/splenic size. In our study splenic size of >115.75mm and platelet count/splenic size of <1433.1 were significant independent predictors for the presence of esophageal varices in cirrhosis of liver. A splenic diameter of 115.75 mm and platelet count/splenic size of 1433.1 were chosen because they represented the median values and offered the best discrimination. There was a correlation between increasing grade of varices and increasing splenic size

and decreasing platelet count/splenic size. Splenic size and thrombocytopenia consequent to hypersplenism are indirect determinants of raised portal hypertension. Identification of splenomegaly and thrombocytopenia as predictors of raised portal hypertension and its complication, development of esophageal varices is well studied and supported by many studies. Platelet count and splenic size in combination as a ratio is a better indicator for presence of varices. Studies by E.Giannini et al (8), and W W Baig et al (9), showed platelet count/splenic size of <909 and <1014 respectively were independent predictors for presence of varices in cirrhosis. Splenic size of >131.5mm and >131.29mm were associated with presence of esophageal varices in cirrhosis as studied by Serag Esmat et al (10). And Lopamudra Mandal et al (11), respectively. In addition, platelet count is also independently correlated with the prevalence and grade of GEV in several studies, suggesting that it could be of help in avoiding unnecessary endoscopies (12, 13).

Again, another noninvasive quantitation of liver stiffness (LS) by ultrasound based TE using Fibro Scan has revolutionary role in the early diagnosis of liver cirrhosis and high values of liver stiffness at TE are strongly predictive of the presence of CSPH, as well as varices (14).

Conclusion

A splenic diameter of >115.75 mm and platelet count/splenic size of <1433.1 are independent predictors for presence of esophageal varices in patients with cirrhosis of liver. Increasing size of spleen and decreasing ratio of platelet count/splenic size were associated with increasing grade of varices. So upper GI endoscopy can be considered in patients with cirrhosis of liver with increased splenic size and decreased platelet count/splenic size to avoid this unpleasant procedure and economic burden, while keeping the rate of undiagnosed varices acceptably low.

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