Prediction of large esophageal varices in cases with cirrhosis of liver: A non-invasive approach

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Abstract
Esophageal variceal bleeding is a severe lethal complication of cirrhosis due to its high rate of mortality. Non-invasive procedures like clinical, biochemical and USG have immense predictive value in the diagnosis of esophageal varices. The present study was designed to evaluate non-invasive predictors for esophageal varices. A total of 100 clinically diagnosed cases with cirrhosis of liver were recruited. Laboratory parameters like serum bilirubin, serum albumin, platelet count and prothrombin time, Clinical parameters like child Pugh class, ascites and splenomegaly and USG parameters like portal vein diameter and spleen diameter along with echo texture of the liver, spleen size and direction of blood flow, portal vein diameter and platelet count/spleen diameter ratio was determined. Among the study cases, 57% cases had small (Grade I-II) varices and 43% cases had large varices (Grade III-IV). Alcohol was the most common etiology in 48.8% cases with large varices and 28.57% cases with small varices, followed by HBV. In large varices group, 55.8% were in CTP-C, 27.9% were in CTP-B and 16.2% were belonged to CTP-A. The Grade III-IV large esophageal varices were significantly correlated with the total bilirubin levels, low albumin levels, elevated prothrombin time, increased portal vein diameter, increasing spleen size, low platelet count, lower values of platelet count and spleen diameter ratio. The above parameters are the significant predictors of large esophageal varices.

Keywords: Esophageal varices, portal hypertension, non-invasive procedures

Introduction
Esophageal variceal bleeding is a common lethal complication of portal hypertension in chronic liver disease cases. Esophageal varices exists approximately 50% of cases with cirrhosis of the liver and is developing in cirrhotic cases at an annual rate of 5% [1]. The incidence of esophageal varices is more common in child pugh class C (85%) cases than child pugh class A (40%) cases. The rate of progression from small to large varices is approximately 5-12% per year and bleed at a rate of 5-15% per year [2]. The upper gastrointestinal endoscopy is the gold standard diagnostic tool for esophageal varices [3]. Even though it has few limitations i.e. discomfort while performing procedure, increases health care cost. In order to restrict upper gastrointestinal endoscopy, some non-invasive procedures have been used in the prediction of esophageal varices. Several studies suggested that clinical, biochemical and Ultrasonographic parameters alone or together have good predictive value for noninvasively assessing the presence of esophageal varices [4]. The present study was designed to evaluate non-invasive predictors for esophageal varices.

Materials and Methods
The present cross-sectional study was conducted in the Department of General Medicine in association with Department of Biochemistry and Department of Radiology at MNR Medical College and Hospital, Sangareddy from April 2019 to May 2020. A total of 100 clinically diagnosed cases with cirrhosis of liver were recruited. The written informed consent was obtained from all the study participants and the study protocol was approved by the institutional ethics committee. Cases confirmed clinically, biochemically and ultrasonographically with Esophageal varices were included. Cases with variceal bleed, portal vein thrombosis, hepatoma and history of esophageal varices were excluded. A detailed history was taken on details and duration of alcoholism, jaundice, ascites, oliguria, pedal edema and gastrointestinal bleed. Presence or absence of jaundice, ascites, splenomegaly and hepatic encephalopathy was noted. Platelet count, prothrombin time and
liver function tests including serum bilirubin, serum transaminases and serum albumin was estimated. Modified Child-Turcotte-Pugh (CTP) class was calculated for each patient. At ultrasonogram abdomen and Doppler study of portal venous system, the portal vein and spleen diameter along with echo texture of the liver, spleen size and direction of blood flow, ascites was noted. The portal vein diameter and platelet count/spleen diameter ratio was determined. At UGI endoscopy, the esophageal varices was graded as large (Grade III-IV) or small (Grade I-II), based on Paquet’s grading system.

The SPSS version 23 software was used to carry out statistical analysis relevant to the study. The frequency and percentage (%) were calculated for cardiac manifestations in patients with pulmonary tuberculosis. The chi-square test was used to compare the variables and p-value of <0.05 was considered statistically significant.

**Results**

A total of 100 clinically diagnosed cases with cirrhosis of liver with 57% grade III-IV large esophageal varices and 43% cases with grade I-II small esophageal varices were included.

![Fig 1: Grade wise distribution of esophageal varices based on Paquet’s grading system](image)

| Table 1: Demographic parameters of cases with esophageal varices |
|---------------------------------------------------------------|
| Parameter | Grade I-II (Small varices) | Grade III-IV (Large varices) |
|-----------|---------------------------|-----------------------------|
| **Age (In years)** | | |
| <20 | 04 (7.07%) | 03 (6.97%) |
| 21-40 | 11 (19.29%) | 09 (20.9%) |
| 41-60 | 20 (35%) | 16 (37.20%) |
| 61-70 | 14 (24.5%) | 10 (23.2%) |
| >70 | 08 (14.03%) | 05 (11.62%) |
| **Gender** | | |
| Male | 31 (54.7%) | 23 (53.4%) |
| Female | 26 (45.6%) | 20 (46.5%) |
| **Etiological distribution** | | |
| HBV | 11 (19.2%) | 08 (18.6%) |
| HCV | 06 (10.5%) | 02 (4.6%) |
| Alcohol | 16 (28%) | 21 (48.8%) |
| Alcohol+HBV | 07 (12.2%) | 04 (9.3%) |
| Alcohol+HCV | 05 (8.77%) | 03 (6.9%) |
| Other complications | 12 (21%) | 05 (11.6%) |
| **Child PUGH class** | | |
| Class A | 42 (73.6%) | 07 (16.2%) |
| Class B | 10 (17.5%) | 12 (27.9%) |
| Class C | 05 (8.7%) | 24 (55.8%) |
| **Grade of ascites** | | |
| None | 27 (47.3%) | 12 (27.9%) |
| Mild | 20 (35%) | 09 (20.9%) |
| Moderate | 08 (14%) | 15 (34.8%) |
| Huge | 02 (3.5%) | 07 (16.2%) |
Table 2: Correlation of the study parameters with varices grade

| Parameter                        | Grade I-II varices | Grade III-IV varices | p-value |
|----------------------------------|--------------------|----------------------|---------|
|                                  | Median             | Range                | Median  |
|                                  |                    |                      | Range   |
| Total bilirubin (mg/dl)          | 1.3                | 0.39-18.1            | 2.5     | 0.34-11.4 | <0.005* |
| Albumin (g/dl)                   | 3.68               | 2.4-4.6              | 2.41    | 1.8-4.0   | <0.005* |
| Prothrombin time                 | 2.12               | 0.5-11.9             | 3.52    | 1.0-11.3  | <0.005* |
| Portal vein diameter (mm)        | 11.5               | 7.8-14.5             | 13.8    | 10.6-20.2 | <0.005* |
| Platelet count                   | 200000             | 41000-438000         | 912000  | 27500-248000 | <0.005* |
| Spleen size (mm)                 | 144.7              | 94-216               | 169.4   | 143-267   | <0.005* |
| Platelet count/Spleen diameter ratio | 1428.0            | 289-4687            | 502.4   | 138.5-165.8 | <0.005* |

Discussion

Esophageal variceal bleeding is the deadliest complications of cirrhosis due to its high mortality. Approximately 60-80% cases with cirrhosis have varices and 25-35% has risk of bleeding [3]. The present study was designed to evaluate the non-invasive predictors of large esophageal varices in cases with cirrhosis. A total of 100 clinically diagnosed cases with cirrhosis of liver were recruited. Among the study cases, 57% cases had small (Grade I-II) varices and 43% cases had large varices (Grade III-IV) (Graph 1). Among the study cases in grade I & II varices, majority cases were in between 41-60 years i.e. 35%, followed by 24.5% in between 61-70 years and 19.29% in between 21-40 years. Whereas in grade III-IV varices, majority cases were in between 41-60 years (37.20%), followed by 23.2% in 61-70 years and 20.9% in 21-40 years. Males were predominant than females in both grades.

Alcohol was the most common etiology in 48.8% cases with large varices and 28% cases with small varices, followed by HBV in 18.6% cases with large varices and 21% cases with small varices. In large varices group, 55.8% were in CTP-C, 27.9% were in CTP-B and 16.2% were belonged to CTP-A. In small varices group, 73.6% cases were in CTP-A, 17.5% were belonged to CTP-B and 8.7% cases were belonged to CTP-C. A study by Jijo V. Cherian et al. noticed that 42 cases were in CTP-A and 187 cases were belonged to CTP-B and CTP-C [10].

The Grade III-IV large esophageal varices were significantly correlated with the total bilirubin levels, low albumin levels, elevated prothrombin time, increased portal vein diameter, increasing spleen size, low platelet count, lower values of platelet count and spleen diameter ratio. A study by Chalasani et al. found that a platelet count < 88,000 was an independent risk factor for the presence of large varices [3]. A study by Arulprakash Sarangapani et al. stated that platelet count, palpable spleen, splenic size, portal vein size, and a platelet spleen diameter ratio were found to be predictors of large EVs [1]. Studies by Garcia-Tsao et al., Pilette et al., and Thomopoulos KC et al. stated that the low platelet count to be an independent risk factor for the presence of varices [7,8]. A study by Jijo V. Cherian et al. stated that CTP class (B/C), platelet count, prothrombin time, spleen diameter, portal vein diameter and platelet count/spleen diameter ratio were significantly associated with the presence of esophageal varices. The predictor for large varices were CTP class B/C, platelet count, spleen bipolar diameter, portal vein diameter and platelet count/spleen diameter ratio [10]. A study by Jijo V. Cherian et al. stated that child pugh class B/C, low platelet count and spleen diameter emerged as significant predictors for the presence of large esophageal varices. These predictors are much helpful for the clinicians where endoscopy facilities not available [10]. A study by Arulprakash Sarangapani et al. concluded that use of platelet count/spleen diameter ratio is the significant parameters in discriminating small and large esophageal varices. It may avoid unnecessary endoscopy in cases without significant risk of missing esophageal varices [3]. A study by Chandail VS et al. concluded that portal vein size and spleen diameter can be used effectively as a screening test without subjecting cases to EGD [11]. A study by Kumar P et al. concluded that clinically palpable spleen, thrombocytopenia, portal vein size, splenic vein size, spleen size, and the presence of portosystemic collaterals have a significant association with the presence of LEV [12]. A study by Maria Andrea Penaloza-Posada et al. concluded that portal vein diameter >13mm is a non-invasive parameter related to high risk of variceal bleeding [13].

Conclusion

Esophageal variceal bleeding is most severe complication of portal hyper tension in chronic liver disease cases. The results of this study concluded that Low platelet count, child pugh class B and child pugh class c, elevated prothrombin time, high spleen size, high portal vein diameter, low platelet count/spleen diameter ratio are the most useful significant determinants of large esophageal varices.

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