



Analysis of Diagnostic Ability of Non – Invasive Parameters to Detect Esophageal Varices in Comparison with Endoscopy in Cirrhosis of Liver with Portal Hypertension

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KEYWORDS

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ABSTRACT:

Introduction: Portal hypertension is a frequent complication of liver cirrhosis and also a significant cause of mortality. It leads to the development of esophageal varices, in about 50% of cirrhotic patients. Screening is crucial, with endoscopy performed every 2-3 years. Non-invasive methods can identify patients at higher risk of bleeding. The study assesses clinical, biochemical, and imaging parameters for predicting esophageal varices.

Aim: The study aims to assess the effectiveness of clinical, biochemical, and imaging parameters in predicting esophageal varices.

Materials and methods: It is cross sectional observational study conducted in the Department General Medicine, at tertiary care hospital in South India, over a period of 1.5 years. Study population 38 patients.

Result: The sensitivity of PC/SD ratio of <1242 and CTP grade B/C in predicting the presence of esophageal varices was 100% with their positive predictive value were 100% and 96.96% respectively. The Portal vein diameter with cut-off of $>12.5\text{mm}$ had a sensitivity of 78.1% and a positive predictive value (PPV) of 58.3%.

Conclusion: Upper gastrointestinal endoscopy is the gold standard for diagnosing esophageal varices in cirrhotic patients, but its limitations include invasiveness and poor availability. Non-endoscopic parameters like platelet count, portal vein diameter, PC/SD ratio, and Child Pugh grade may provide good diagnostic accuracy. A comprehensive multi-centric study is needed to confirm these findings.

INTRODUCTION

Portal hypertension is a common and significant cause of death in patients with liver cirrhosis. [1] Esophageal varices develop as a result of portal hypertension, and they are seen in 50% of patients with liver cirrhosis. The grade of esophageal varices correlates with the severity of liver diseases, estimated by the Child Turcotte Pugh Score. Rupture and bleeding from esophageal varices are associated with a mortality rate

of 20% to 50%, with variceal bleeding accounting for 10-30% of all cases of upper gastrointestinal bleeding. Portal hypertension is caused by an increase in splanchnic blood flow due to vasodilation and increased resistance through the cirrhotic liver. The prevalence of esophageal varices varies from 50-60% in patients with liver cirrhosis, with mortality due to bleeding from gastro esophageal varices being nearly one-third. The risk of initial bleeding is 25-35%,



usually occurring within one year after detection of varices. The reported mortality from the first episode of variceal bleeding ranges from 40-70%. All patients with liver cirrhosis should be screened for the presence of esophageal varices, with check endoscopy being done every 2-3 years in patients without varices and every 1 - 2 years in those with small varices. However, endoscopy is an invasive procedure and its cost-effectiveness is questionable, as only 9-36% of cirrhotic patients have varices on screening endoscopy. It is crucial to routinely screen patients at high risk for the development of esophageal varices with non-invasive parameters and perform endoscopy on them, thereby decreasing the burden and procedure costs. Non-invasive methods can help identify patients at higher risk of bleeding and reduce the social burden on patients. Thomopoulos et al [2] (2003) studied seventeen variables considered relevant to detect the presence of esophageal varices, concluding that thrombocytopenia, splenomegaly, and ascites were independent predictors of large varices. However, in patients with chronic liver disease, thrombocytopenia may be an independent factor other than portal hypertension, such as shortened platelet mean lifetime, decreased thrombopoietin production, or myelotoxic effects of alcohol or hepatitis viruses. Non-invasive methods (platelet count/spleen diameter ratio and Fibroscan) are truly non-invasive, but the former needs proper validation considering other causes of liver cirrhosis, such as Hepatitis B and C, and immunocompromised patients like HIV-AIDS. The study aims to assess the effectiveness of clinical, biochemical, and imaging parameters in predicting esophageal varices.

MATERIALS AND METHODS

Source of data:

Patients with chronic liver diseases with cirrhosis of liver with portal hypertension aged more than 18 years attending OPD/ IPD of General Medicine Department at tertiary care hospital in South India

Methods of Collection of Data:

A. **Study design:** Cross sectional observational study

B. **Study period:** 1.5 years

C. **Place of study:** General Medicine Department at tertiary care hospital in South India

D. **Sample size:** 38 patients

Inclusion Criteria:

- All patients **more than 18 years of age** presenting to General Medicine Department diagnosed with chronic liver diseases based on clinical, biochemical and ultrasonography findings.

F. Exclusion Criteria:

- Established cases of Esophageal Varices with Portal Hypertension on treatment
- Patients with history of upper gastrointestinal bleeding or Bleeding disorders apart from those secondary to liver disease
- Patients who have already received endoscopic or surgical intervention for portal hypertension previously
- Patients with evidence of hepatocellular carcinoma on ultrasonography or previous or current treatment with beta-blockers, nitrates and diuretics.

Methodology:

After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling the inclusion criteria will be enrolled for the study after obtaining written informed consent in English and local language.

Detailed history, relevant clinical examination, basic biochemical investigations followed by ultrasonography and endoscopy will be done. Modified Child Turcotte Pugh score will be applied (to classify the severity of cirrhosis) and the duration of portal hypertension and related symptoms will be recorded. Those who are at risk of developing varices shall receive appropriate prophylactic treatment at the earliest. The results obtained will help to demonstrate the correlation of endoscopic detection of esophageal varices with non-invasive parameters in Cirrhosis of Liver with Portal Hypertension. Clinical and Demographic parameters and existence of co-morbidities will also be recorded,



according to a predesigned proforma – Case Record Form.

STATISTICAL ANALYSIS:

The data is collected and tabulated using Microsoft Excel. Later it is analysed using SPSS Software Version 19. Chi square test for proportions and Student ‘t’ test for quantitative data will be applied. P < 0.05 is considered to as statistically significant. The appropriate statistical test will be applied and data will be analysed.

Sensitivity, Specificity, Positive predictive value (PPV), Negative predictive value (NPV) and hence diagnostic accuracy of non-invasive methods to detect esophageal varices as compared to endoscopy will be calculated in patients of cirrhosis of liver with portal hypertension.

RESULT

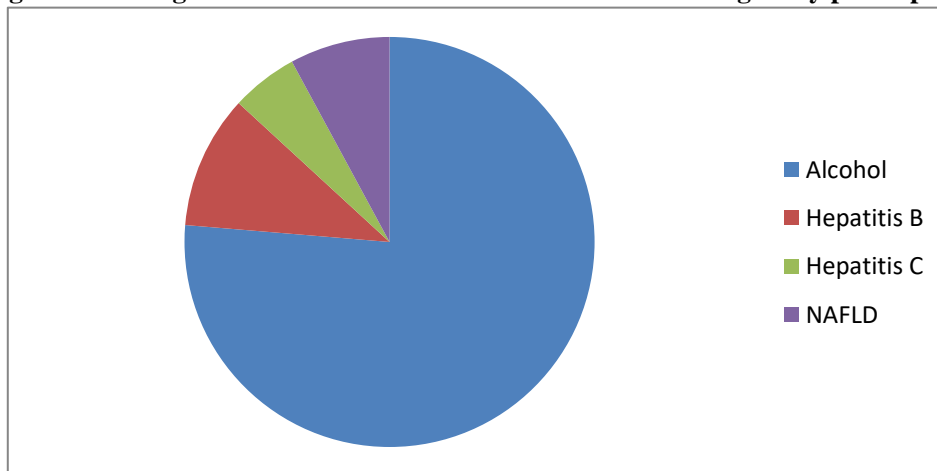
Thirty eight eligible patients with cirrhosis of the liver were included in the study. All patients were offered upper GI endoscopy and all were screened for esophageal varices. All were male(100%).

Table 1: Mean values of various clinical and laboratory factors for varices

Variable	Mean	Standard Deviation
Age in years	43.4	11.9
Hemoglobin (g/dl)	11.9	2.8
Platelet Count (PC) (per µl)	134582	73408.6
Spleen diameter (SD) (mm)	124.3	27.5
PC/SD ratio	1206.6	853.4
Prothrombin Time (seconds)	22.3	7.3
INR	1.7	0.7
Portal Vein diameter (mm)	16.6	5.6
Albumin (g/dl)	2.61	0.7
Total Bilirubin (mg/dl)	3.05	2.9

Table Shows the mean and standard deviation of clinical and laboratory parameters in our study. The mean age of our study participants is 43.4 years. The mean hemoglobin is 11.9g/dl. Mean platelet count is 134581.6 per µl with mean spleen diameter 124.3 mm.

Figure 1: Etiological risk factors for chronic liver disease among study participants





Those who had significant alcohol intake as the risk factor, accounted for 29 (76.3%) of the studied population. There were 4 (10.5%) subjects with hepatitis B surface antigen positive status, while

those with anti HCV Positive status were 2 (5.3%). There were 3 (7.9%) of subject with non-alcoholic fatty liver disease in our study.

Table 2: Relationship between ascites and presence of varices

Ascites	Varices Present	Varices absent	Chi Square value	P value
Present	30 (93.8)	2 (6.2)	13.871	<0.001
Absent	2 (33.3)	4 (66.7)		

Those who had ascites on ultrasound were 32 (32/38=84.2%). Those who have varices and also had ascites were 30 (30/32=93.8%) and those who did not have varices were 2 (2/32=6.2%). When Fischer

exact test was applied to see the difference in proportions between ascites and presence of varices, the difference was found statistically significant. (p<0.001)

Table 3: Relationship between Child Pugh score and presence of varices

Child Pugh score	Varices Present	Varices Absent	Chi-Square Value	P value
Grade A	0	5 (100)	30.875	<0.001
Grade B	18 (94.7)	1 (5.3)		
Grade C	14 (100)	0		

The Patients were grouped based on the child-Pugh classification for severity of liver disease; Grade A had 13.2% of the population while B and C had 50% and 36.8% respectively. It shows relationship between presence of varices and Child Pugh score. Those in grade A who had varices were 0 of 5, those

in Grade B who had varices were 18 (94.7%) of 19 and those in grade C were 14(100%) of 14. When fischer exact test was applied to see the difference in proportions between various grades and presence of varices, the difference was found statistically highly significant. (p<0.001)

Table 4: Relationship between laboratory parameters and presence of varices

Variable	Varices Present (n=32) Mean (SD)	Varices absent (n=6) Mean (SD)	P value
Platelet Count	118878.13 (64912.8)	218333.33 (61294.9)	0.001
Spleen Diameter	126 (26.9)	112.5 (30)	0.26
Hemoglobin	11.44 (2.75)	14.5 (1.2)	0.01
Total Bilirubin	4.5 (6.27)	1.5 (1.05)	0.25
Direct Bilirubin	2.31 (3.08)	0.67 (0.52)	0.21
Albumin	2.53 (0.72)	3 (0.63)	0.14
Spleen Diameter	126 (26.9)	112.5 (30)	0.26
PC/SD Ratio	1041.5 (733.9)	2087.3 (971.9)	0.004
Portal Vein Diameter	17.6 (5.5)	11.2 (1.17)	0.007



On univariate analysis, platelet count, prothrombin time, portal vein diameter and platelet count /spleen diameter ratio and hemoglobin were significantly associated with the presence of esophageal varices.

On multivariate analysis, the presence of esophageal varices was significantly associated with only portal vein diameter > 13 mm (OR 7.27; 95% CI, 1.07-49.17)

Table 5: Sensitivity, specificity, positive and negative predictive values for Noninvasive parameters

Parameter	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
PC/SD ratio (<1242)	100%	75%	100%	57%
Portal Vein Diameter (>12.5mm)	78.10%	83.30%	58.30%	96.20%
CTP grade (B/C)	100%	83.33%	96.96%	0

The sensitivity of both, PC/SD ratio of <1242 and CTP grade B/C in predicting presence of esophageal varices was 100% with their positive predictive value were 100% and 96.96% respectively. The Portal vein diameter with cut off of >12.5mm had a sensitivity of 78.1% and positive predictive value (PPV) of 58.3%.

Table 6: Area under the curve for different predictors of varices

Variables	Area Under the Curve (AUC)
Platelet count	0.859
Spleen diameter	0.651
portal vein diameter	0.935
PC/SD ratio	0.879
Prothrombin time	0.776

Portal vein diameter is an excellent predictor of varices with AUC 0.935. Platelet count and PC/SD ratio have good predictive value for varices with AUC of 0.859 and 0.879 respectively.

DISCUSSION

The development of varices in cirrhosis occurs at a rate of 8% per year. Esophageal varices are present in almost half of patients with liver cirrhosis at the time of diagnosis. Worldwide the prevalence and incidence of varices varies. Among cirrhotic patients in the Western world the prevalence is 40%, [3]

Diagnosis of oesophageal varices is either by barium swallow or upper gastrointestinal tract endoscopy. The latter has an advantage over the former in that direct visualization of the varices is feasible, and at the same

time grading of the lesion and instituting intervention procedures. The general guidelines for management of cirrhotic patients include routine endoscopy to detect varices and hence initiate prophylactic measures against bleeding from such varices.

The gold standard for diagnosis of esophageal varices is endoscopy. It is however a costly and invasive procedure. Endoscopy is an invasive procedure and not all eligible patients are likely to give consent for the procedure beside cost issue, thus it becomes necessary to seek for other non-invasive procedures that are likely to predict the presence of varices especially in patients who are not eligible for an upper gastrointestinal tract endoscopy.

Certain clinical, radiologic and laboratory parameters have been reported to be associated with the presence of esophageal varices. These are low platelet count, spleen diameter, ratio of platelet count/splenic diameter, portal vein diameter and Childs Pugh grade. [4, 5, 6,7]

The non-invasive predictors of esophageal varices may become instruments for prioritizing surveillance endoscopy. Bleeding from ruptured varices remains a very important complication in patients with chronic liver disease because of the mortality associated with each event. In this study some non-invasive markers of portal hypertension were evaluated as predictors of presence of varices at endoscopy which is the current gold standard.

The prevalence of varices in the studied population was 84.2%. Considering that this is a surveillance study in patients who have never bled, this prevalence is very high but similar to results of previous studies done in Jos where a prevalence of 75% was obtained and some



other studies elsewhere, were 76.6 % was seen in Ivory Coast and 84% in Egypt. [7,8]

The high prevalence of varices in this study buttresses the need for surveillance of patients with chronic liver disease and also underscores the need for non-invasive predictors of the presence of varices, considering the high cost of endoscopy, and poor availability of upper gastrointestinal tract endoscopy services in the country.

Variceal grading

Varices were graded according to the Modified Paquet Classification system [9] and grade I and II had the highest frequency of 12 (37.5%) and 14 (43.8%) respectively.

Gender with Varices

There were 100% males in the studied population. A total 32 (84.2%) had varices and 6 (15.8%) without varices. In a study done in Egypt to evaluate non-invasive predictors of varices there were 115 men and 60 women while another study done in Ivory coast the male to female ratio was 2.1. [10,11,12].

Age with Varices

The mean age of the studied population was 43.4±11.9 years and those within the age group 31-40 were the highest occurring age group in our study. The mean age was similar to that of this study in studies done by Sarangapani A et al (mean age 45 years) (2010) [4]

Child Pugh score with varices

Patients were grouped according to Child Pugh Classification of cirrhosis. 19 (50%) of patients were in Grade B while 36.8% were in Grade C. Shobhana Bitey et al [14] also reported varices were found to be more common among class B and class C.

Portal vein diameter with varices

The patients who had varices at endoscopy had a mean portal vein diameter that was significantly larger than in those who did not have varices at endoscopy in this study, 17.6±5.5 mm versus 11.2±1.17mm with a P value 0.007. This is a reflection of the impact of portal hypertensive pressure on the size of the portal vein. The study done by Shateri K et al (2012)[15], where they showed that portal vein diameter was significantly

different between those who had varices and those who did not, and portal vein diameter also predicted the presence of varices at endoscopy.

Spleen bipolar length with varices

In our study, Spleen diameter of 111 mm showed a sensitivity of 75% and specificity of 66.6% with AUC of 0.651 and 95% CI (0.397-0.905). Abdulgafoor Kassim et al [13] showed that spleen longitudinal diameter had a sensitivity and specificity, of 79.6% and 33.3%.

Platelet count with varices

In our study, at the cut-off value of 152500 platelet count had a sensitivity of 83.3% and specificity of 81.2%, AUC of 0.859. The sensitivities for thrombocytopenia fluctuate from 62% to 100%, and the specificities range from 18% to 77% [2]. In a study by Abdulgafoor Kassim et al [13] at a cut-off point of 100×10^6 platelet count sensitivity, specificity was of 26.56%, 87.18%, respectively. This wide range of sensitivities and specificities may be explained by using a different cut off points and the different etiology of CLD in different studies.

Platelet count to spleen diameter ratio (PC/SD) with varices

In our study, at the cut-off value of PC/SD ratio <1242, the sensitivity and PPV was 100% and specificity was 75%. Shobhana Bitey et al. [14] reported that the PC/SD cut off of <957 had a sensitivity of 78.75% and positive predictive value (PPV) of 95.92% and the sensitivity of PC/SD ratio of <909 in predicting presence of esophageal varices was 74% with its PPV was 86%. In a study by Nada L et al, platelet count with a cut-off point of 100000/mm³ (p=0.0011), prothrombin time (p=0.04) and abundance of ascites (p=0.006) were significantly associated with the presence of esophageal varices.[16]

We believe that these predictors may be of help to the physicians practicing in rural areas where endoscopy facilities are not readily available, in helping them to initiate appropriate primary pharmacological prophylaxis in these patients. In an urban setting where the endoscopy workload is high, a non-invasive



predictor, as in this study, can help one to initiate drug therapy while waiting for the endoscopy procedure.

CONCLUSION

Upper gastrointestinal endoscopy is the gold standard for diagnosing esophageal varices in cirrhotic patients, but it has limitations such as being invasive and having poor availability in peripheral areas. Patients at high risk can be screened using clinical, hematological, biochemical, and radiological markers. There is no consensus set of non-endoscopic parameters that can predict esophageal varices in cirrhotic patients. However, a combination of two or more non-endoscopic parameters may provide better diagnostic accuracy. A comprehensive multi-centric study is needed to confirm these findings and identify more robust non-endoscopic predictors. Platelet count, a simple, inexpensive, and available investigation, can be used as a suitable predictor of varices presence. Portal vein diameter can also be used to predict varices non-invasively, but the technicality may limit its widespread use in the future. The ratios of platelet count to spleen bipolar diameter (PC/SD ratio) are another accessible measurement. The Child Pugh grade can determine the incidence of higher grades of varices and identify patients who require endoscopy for prophylactic management.

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