

Original Research Article

Are non invasive predictors of esophageal varices reliable?

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ABSTRACT

Background: One of the most serious complications of portal hypertension is the development of esophageal varices and variceal bleeding due to the rupture of varices. The purpose of the study was to assess the efficacy of various clinical and laboratory parameters in predicting the presence and severity of esophageal varices in cirrhotic patients.

Methods: This is an observational cross-sectional study done in the department of medicine in Vydehi Institute of Medical Sciences, Bengaluru over a period of one year. Total of 76 patients above the age of 18 years with the diagnosis of cirrhosis of any etiology were included. Multivariate Backward method was applied and Portal vein diameter, Platelet count, PT INR, FIB-4 score, APRI, AST/ALT ratio were included as predictors in the model.

Results: No statistically significant correlation was found between platelet count, portal vein diameter, FIB 4 score, APRI, AST/ALT ratio and presence of esophageal varices.

Conclusions: Present study showed that the non invasive markers such as platelet count, portal vein diameter, FIB 4 score, APRI and AST/ALT ratio are not reliable in predicting the presence of esophageal varices.

Keywords: Esophageal varices, Non invasive predictors, Portal hypertension

INTRODUCTION

Cirrhosis is characterised by the disorganization of liver architecture and nodule formation and development of portal hypertension.¹ Portal hypertension is initially asymptomatic in the vast majority of patients (around 80-90%).² One of the most serious complications of portal hypertension is the development of esophageal varices and variceal bleeding is still the most common lethal complication of cirrhosis.³

Primary prophylaxis clearly reduces mortality in these patients thus making it essential to make an early diagnosis of esophageal varices (EV). The most important predictor of variceal bleeding is the variceal size, with the highest risk of first hemorrhage about 15% per year occurring in patients with large varices.⁴ Upper gastrointestinal endoscopy remains the gold standard test

for detection of EV. However, endoscopy is an invasive and uncomfortable procedure which may not be acceptable for all the patients and routine endoscopy screening may not be cost-effective, as less than 50% of all patients with cirrhosis have EV.³

Hence, predicting the presence of EV through non-endoscopic and non invasive markers is important in order to identify the patients who benefit from routine endoscopy screening. The conclusions of previous studies vary in different populations and in different etiologies of liver cirrhosis and their utility in clinical practice is uncertain.

The present study has been undertaken to assess the efficacy of various clinical and laboratory parameters in predicting the presence and severity of esophageal varices in cirrhotic patients.

METHODS

This is an observational cross-sectional study done in the department of medicine in Vydehi Institute of Medical Sciences, Bengaluru over a period of one year.

Inclusion criteria

Total 76 patients above the age of 18 years with the diagnosis of cirrhosis of any etiology were included.

Exclusion criteria

- Patients who had undergone endoscopic banding or sclerotherapy and
- Patients who were on beta blockers.

Liver cirrhosis was diagnosed based on clinical data, laboratory test and liver imaging.

All the patients were subjected to clinical examination, biochemical investigations, ultrasound abdomen with portal vein Doppler and upper GI endoscopy. Endoscopy was done by a gastroenterologist. Ethical clearance was obtained from institutional ethics committee. Informed written consent was taken from all the participants included in the study. Laboratory data included hemoglobin, platelet count, AST and ALT levels, serum albumin, total serum bilirubin, prothrombin time with international normalized ratio (INR) and serum creatinine. All patients were classified according to the Child-Turcotte-Pugh (CTP) class. Model for end-stage liver disease (MELD), aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio (AST/ALT),

AST to platelet ratio index (APRI), fibrosis-4-index (FIB-4) were measured for all participants.

Statistical analysis

Data was entered in MS Excel and analyzed in SPSS V22. Descriptive statistics were represented with percentages, mean, standard deviation. Chi square test or Fischer exact test was applied for finding significance in qualitative data. Independent t test was applied to find significance in quantitative data. Logistic regression with backward method was applied as multivariate model. In all the cases $P < 0.05$ was considered as statically significant.

RESULTS

Total of 76 patients were included in the study of which 63 were males (82.89%). The mean age was 48.28 ± 12.36 years in patients without varices and 43.91 ± 9.08 years in patients with varices. The etiology of cirrhosis was alcohol in 40 (52.6%) patients, hepatitis B in 10 (13.1%) patients and hepatitis C in 7 (9.21%) patients. Ascites and splenomegaly were present in all the study participants.

Hepatic encephalopathy was present in 16 patients (21.05%) and spider naevi in 23 (30.26%) patients. Out of 76 patients of cirrhosis included in the study, 58 patients were detected to have esophageal varices on upper GI endoscopy. Eighteen of these patients had large varices. Among the 58 patients with esophageal varices only 6 patients (10.3%) gave H/O hematemesis and all these patients had large varices. Twenty four patients (41.4%) gave H/O melena.

Table 1: Comparison of non-invasive parameters in study population.

Variable	Without varices (N=18) Mean±SD	With varices (N=58) Mean±SD	P value
Platelet count	93.5±58.57	113.53±76.65	0.312
PT/INR	1.49±0.39	1.73±0.57	0.099
AST	84.89±73.07	82.45±52.66	0.876
ALT	55.44±50.53	54.79±39.73	0.955
Total bilirubin	4.45±3.13	6.3±5.06	0.149
Direct bilirubin	2.20±1.68	2.95±2.75	0.279
Portal vein diameter	13.44±1.10	13.47±1.37	0.925
MELD score	21.11±5.94	23.83±7.40	0.160
FIB 4 score	6.68±4.23	6.55±5.70	0.929
APRI	3.03±3.27	2.62±2.56	0.581
AST/ALT ratio	1.86±1.60	1.81±1.08	0.874

The mean platelet count among the patients without varices was $93,500/\text{mm}^3$ and it was $1,13,534/\text{mm}^3$ among the patients with varices with no statistically significant difference among the 2 groups in platelet count (p value 0.312). There was also no statistically significant

difference found in PT/INR, AST, ALT, albumin among the patients with and without varices (Table 1).

The mean portal vein diameter was 13.44 mm in patients without varices and 13.47 mm in patients with varices.

This too did not correlate with the size of varices. MELD score, FIB 4 score, APRI score and AST/ALT ratio were found to be comparable among the patients with and without varices.

Multivariate Backward method was applied and Spider nevi, Portal vein diameter, Platelet count, PT INR, FIB- 4 score, APRI, AST/ALT ratio were included as predictors in the model. All variables were eliminated by the backward regression model except spider nevi with Odds ratio 0.1 (0.01-0.85). Sensitivity 100% and specificity 0%, Area under the curve is 0.65 in ROC curve but it is not statistically significant (Figure 1).

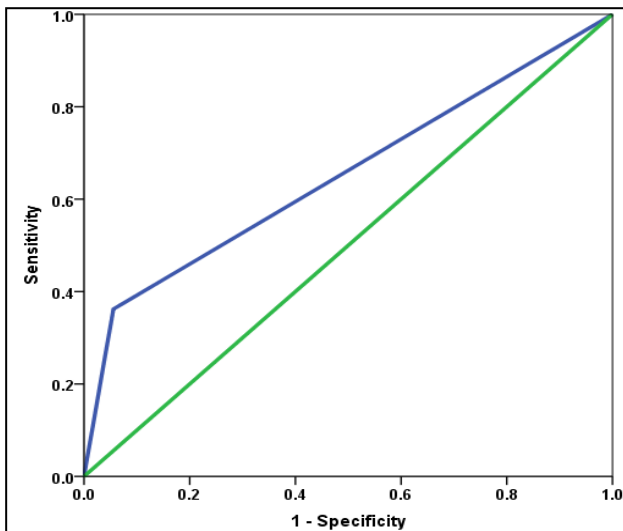


Figure 1: Area under the curve.

DISCUSSION

In a study by Nada L et al, involving 372 patients with viral liver cirrhosis, five variables considered relevant to the presence and grade of varices were tested using univariate analysis. On univariate analysis, platelet count with a cutoff point of $100000/\text{mm}^3$ ($p=0.0011$), prothrombin time ($p=0.04$) and abundance of ascites ($p=0.006$) were significantly associated with the presence of esophageal varices. Portal vein diameter did not correlate with the presence of esophageal varices. In multivariate analysis, only grade of ascites was associated with large size varices.⁵

Similarly, in another study, a significant correlation was found between platelet count and esophageal varices. 70% (28/40) patients with esophageal varices had platelet count $<1,00,000/\text{cu mm}$, while 80% (8/10) of patients without esophageal varices had platelet count above $1,00,000 \text{ cu mm}$.⁶ Some other studies also showed low platelet count as independent risk factor for the presence of large esophageal varices.⁷⁻¹⁰ However, in present study no statistically significant difference in platelet count was found between the patients with and without esophageal varices. 53.44% (31/58) patients with esophageal varices had platelet count $>1\text{lakh}/\text{mm}^3$ and out of 18 patients

with large varices, 9 (50%) patients had platelet count $>1\text{lakh}/\text{mm}^3$. Platelet count was $<1\text{lakh}/\text{mm}^3$ in 12 out of 18 patients in whom varices were absent.

In concordance with other studies no significant correlation was noted between portal vein diameter and the presence and severity of varices.^{5,6} Similarly, Prothrombin time, serum bilirubin and liver enzymes like ALT, AST, ALP failed to show any significant correlation with size and presence of esophageal varices.

In a study done by Kraja B et al, there was a significant association between esophageal varices and FIB 4 score (OR = 1.18 for one unit increment; 95%CI: 1.01-1.38), and MELD score (OR = 1.11 for one unit increment; 95%CI: 1.01-1.22). On the other hand, there was no evidence of any significant association of esophageal varices with the other non-invasive markers (fibrosis index, King's score, APRI, PL/SD and AST/ALT). FIB-4, which was shown a powerful predictor of esophageal varices, was nevertheless a very poor predictor of esophageal variceal bleeding (the area under the curve was only 51%) for a cut-off value of 5.02. None of the non-invasive markers appeared to be a useful predictor of esophageal variceal bleeding.³ The present study did not show association between FIB 4 score, AST/ALT ratio and APRI on multivariate analysis.

The limitations of present study are the small sample size. The same study needs to be done on a larger group of patients for further confirming the results.

CONCLUSION

Non invasive markers such as platelet count, PT/INR, Portal vein diameter, MELD score, FIB 4 score, AST/ALT ratio and APRI may not reliably predict the presence or severity of esophageal varices.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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