Original Article

# Non Endoscopic Predictors of Esophageal Varices in Cirrhotics

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## ABSTRACT

**Objective:** To identify non-invasive predictors of esophageal varices in patients of Liver Cirrhosis.

**Place and duration of study:** First Medical unit, Nishtar Hospital Multan from January 2003 to December 2005.

**Patients and methods:** Sixty five patients diagnosed as Cirrhosis of liver and without any history of hematemesis and/or melena were included in this study. These patients underwent complete clinical, biochemical and ultrasonographic evaluation. Four variables selected to predict the presence of esophageal varices were platelet count, spleen diameter, portal vein diameter and platelet count/spleen diameter ratio. Upper GI endoscopy was done in all these patients to see esophageal varices.

**Results:** Thirty three patients had esophageal varices while varices were not found in 32 patients. Best cut off values of spleen diameter (160 mm, p-value <0.001) and portal vein diameter (13.5 mm, p-value of <0.001) were statistically significant for prediction of presence of varices. Positive and negative predictive values for spleen diameter were 90% and 81% respectively. Positive and negative predictive values for portal vein diameter were 74% and 77% respectively. Best cut off values of platelet count (145 X $10^3$/µL, p-value-0.486), and platelet count/spleen diameter ratio (1200, p-value-0.153) were statistically not significant for prediction of presence of varices.

**Conclusion:** Spleen diameter (cut off value 160 mm) and portal vein diameter (cut off value 13.5 mm) have very good predictive values (positive and negative) and can be used as predictors for presence of varices in patients of cirrhosis with no past history of bleeding.

**Key Words:** Esophageal varices, Spleen diameter, Portal vein diameter, Platelet count, Platelet count/spleen diameter ratio.

## INTRODUCTION

Chronic liver disease is very common in our country. Patients of chronic liver disease ultimately progress to develop cirrhosis of liver and its associated complications like portal hypertension.[1]

Development of esophageal varices is among the major complications of liver cirrhosis, with an estimated prevalence of approximately 50%.[2]

Their presence correlates with the severity of liver disease [3]; while only 40% of Child A patients have varices, they are present in 85% of Child C patients.[4]

Esophageal varices may cause life-threatening bleeding with attendant high hospital cost. Even with modern therapeutic interventions bleeding from esophageal varices carries a mortality of 20%.[5,6] Since effective preventive modalities for variceal hemorrhage have been established, early detection of esophageal varices is critical for primary prevention of bleeding.[7]

The usual clinical practice is to screen all patients with established cirrhosis at the time of diagnosis by upper GI endoscopy for the presence of varices. However, fewer than 50% of cirrhotic patients have varices at screening endoscopy and most have small sized varices, with a low risk of bleeding.[8,9]

Several authors have found that some clinical (splenomegaly), hematologic (thrombocytopenia), radiologic (portal vein diameter) parameters and their combination (platelet count/spleen diameter ratio) are useful predictors for the presence of esophageal varices.[1,2,6,9,14-20]

The aim of the present study was to determine whether some of these non-endoscopic parameters could predict the presence of esophageal varices in our setting.

**Objective:**

To identify noninvasive predictors of esophageal varices in cirrhotic patients admitted to Medical Unit 1 Nishtar Hospital Multan.

## PATIENTS AND METHODS

Consecutive patients admitted to Medical Unit 1 Nishtar Hospital Multan with cirrhosis from January 2003 to December 2005 were considered for inclusion in the study.

**Inclusion criteria:**

All patients diagnosed as cirrhosis of liver on clinical grounds, laboratory investigations and ultrasound, without history of upper GI bleeding were enrolled in this study.

**Exclusion criteria:**
Patients with a past history of hematemesis and/or melena, hemodynamically unstable patients and those with evidence of hepatocellular carcinoma were excluded.
The patients underwent clinical examination, laboratory and Ultrasonographic evaluation. Laboratory tests done included complete blood counts, liver function tests, serum albumin, prothrombin time, HBsAg and anti-HCV antibodies.
Ultrasonographic examination was performed using Toshiba Justvision 200 machine to evaluate echotexture of liver, portal vein diameter, splenic diameter and ascites.
All the patients were classified according to Child-Pugh classification. All the patients were scoped for the presence of esophageal varices using Olympus GIF 160 videoscope. Procedure was done by one of the authors.
**Statistical analysis:**
Patients were divided into two groups based on the presence or absence of esophageal varices. Receiver operating characteristic curve (ROC curve) was applied to find the best sensitivity, specificity and cut off values to discriminate between presence and absence of varices. For all analysis, a p-value $< 0.05$ was considered statistically significant. Data was analysed using SPSS version 13.

# RESULTS

Total number of patients in the study were 65. Male to female ratio was 1:1.95 (22/43). Mean age of the patients was 45.2 years (range was 13-70). On the basis of clinical examination, biochemical and hematological parameters, patients were classified according to the Child Pugh classification. Six (9.23%) patients were in class A, 31 (47.69%) in class B and 28 (43.07%) in class C. Twenty (30.76%) patients were HBsAg positive, 24 (36.92%) patients were anti-HCV positive, 2 (3.07%) patients were positive both for HBsAg and anti-HCV and 19 (29.23%) patients were negative for anti-HCV and HBsAg.
Characteristics of patients with and without esophageal varices are given in Table No.1. Splenic diameter on the basis of ultrasonography ranged from 118 to 190mm in patients without esophageal varices with a mean diameter of 140mm. In patients with esophageal varices, range was 140 to 190mm with a mean diameter of 163 mm.

**Table No.1: Main characteristics of the 65 patients included in the study, divided according to the presence or absence of esophageal varices.**

| VARIABLE | | NEV ( n = 32 ) | EV ( n = 33 ) |
|---|---|---|---|
| Gender: Male | n (n% ) | 07 (21.8) | 15 (45.5) |
| Female | n (n% ) | 25 (78.1) | 18 (54.5) |
| Age (years) | Mean (Range) | 44.8 (13-70) | 45.5 (22-65) |
| Child grade: A | n (n% ) | 04 (12.5) | 02 (06) |
| B | n (n% ) | 17 (53.1) | 14 (42.4) |
| C | n (n% ) | 11 (34.3) | 17 (51.5) |
| HBsAg +ve | n (n% ) | 09 (28.1) | 11 (33.3) |
| Anti-HCV +ve | n (n% ) | 13 (40.6) | 11 (33.3) |
| Both B & C +ve | n (n% ) | 01 (3.1) | 01 (3.0) |
| Both B & C -ve | n (n% ) | 09 (28.1) | 10 (30.3) |
| Splenomegaly | n (n% ) | 19 (59.3) | 27 (81.8) |
| Ascites | n (n% ) | 22 (68.7) | 32 (96.9) |
| Bilirubin mg/dl | Mean (Range) | 4.7 (.5-24.9) | 5.0 (.8-27.5) |
| SGPT IU/L | Mean (Range) | 113.9 (8-449) | 97.7 (19-395) |
| PT sec | Mean (Range) | 29 (14-89) | 24.6 (15-38) |
| Albumin g/dl | Mean (Range) | 2.9 (1.8-5.8) | 3.1 (1.9-4.6) |
| Spleen diameter (mm ) | Mean (Range) | 140 (118-190) | 163 (140-190) |
| Portal vein diameter (mm ) | Mean (Range) | 12 (8-17) | 13.8 (9-20) |
| Platelet count X $10^3/\mu L$ | Mean (Range) | 159.5 (40-593) | 139.3 (29-536) |
| Platelet/Spleen Diameter ratio | Mean (Range) | 1180.2 (295.4-2949.6) | 878.8 (177-3288.3) |

NEV=Non esophageal varices; EV= Esophageal varices

Portal vein diameters ranged from 8 to 17mm in patients without esophageal varices with a mean portal vein diameter of 12 mm, while in patients with esophageal varices, it ranged from 9 to 20mm with a mean portal vein diameter of 13.8mm.

Platelet count ranged from 40 X $10^3/\mu L$ to 593 X $10^3/\mu L$ in patients without esophageal varices with a mean count of 159.5 X $10^3/\mu L$, while in patients with esophageal varices, it ranged from 29 X $10^3\mu/L$ to 536 X $10^3/\mu L$ with mean platelet count of 139.3 X $10^3/\mu L$.

The ratio between platelet count and splenic size was calculated. The mean ratio for those without esophageal varices was 1180.2 (295.4-2949.6) and for those with esophageal varices was 878.8 (177-3288.3).

Applying the receiver operating curves (ROC) best sensitivity and specificity cutoff values of different variables for the presence of varices were calculated. For spleen diameter best cutoff value of 160mm had sensitivity of 79% and specificity of 91%. Positive predictive value (PPV) was 90% and negative predictive value (NPV) was 81%. For portal vein diameter best cut off value of 13.5mm had sensitivity of 79% and specificity of 72%. PPV and NPV were 74 and 77% respectively. For platelet count best cutoff value of 145 X $10^3$/µL had sensitivity of 70% and specificity of 44%. PPV was 56% and NPV was 58%. For platelet count/spleen diameter ratio cut off value of 1200 had sensitivity of 82% and specificity of 31%. PPV and NPV were 55 and 63% respectively. Spleen diameter and portal vein diameter were statistically significant (p-values <0.001) while platelet count and platelet count/spleen diameter ratio were statistically insignificant (p-values 0.486 and 0.153 respectively) (Table No.2 and 3).

**Table No.2: Spleen size, portal vein diameter, platelet count and platelet count/spleen diameter ratio of 65 patients subdivided according to the presence or absence of EV.**

| Variable | | n | Minimum | Maximum | Mean ± SD | *P - value* |
|---|---|---|---|---|---|---|
| Spleen diameter (mm) | NEV | 32 | 118 | 190 | 140 ± 15.3 | *< 0.001** |
| | EV | 33 | 140 | 190 | 163 ± 16 | |
| | | | | | | |
| Portal vein diameter (mm) | NEV | 32 | 8 | 17 | 12 ± 2 | *< 0.001** |
| | EV | 33 | 9 | 20 | 13.8 ± 1.9 | |
| | | | | | | |
| Platelet count X $10^3$/µL | NEV | 32 | 40 | 593 | 159.5 ± 125.9 | *0.486* |
| | EV | 33 | 29 | 536 | 139.3 ± 109.7 | |
| | | | | | | |
| Platelet count/ spleen diameter ratio | NEV | 32 | 295.4 | 2949.6 | 1180.2 ±1008.3 | *0.153* |
| | EV | 33 | 177 | 3288.3 | 878.8 ± 684.4 | |

*Statistically significant at P-value <0.05

**Table No.3: Sensitivity, specificity, positive and negative predictive values according to cut off values of spleen diameter, portal vein diameter, platelet count and platelet count/spleen diameter ratio of 65 patients.**

| Variable | Cut off | Total | EV (n=33) | NEV (n=32) | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|---|---|
| Spleen diameter (mm) | > 160 | 29 | 26 | 3 | 79% | 91% | 90% | 81% |
| | ≤ 160 | 36 | 7 | 29 | | | | |
| | | | | | | | | |
| Portal vein diameter (mm) | > 13.5 | 35 | 26 | 9 | 79% | 72% | 74% | 77% |
| | ≤ 13.5 | 30 | 7 | 23 | | | | |
| | | | | | | | | |
| Platelet count x$10^3$/µL | ≤ 145 | 41 | 23 | 18 | 70% | 44% | 56% | 58% |
| | > 145 | 24 | 10 | 14 | | | | |
| | | | | | | | | |
| Platelet count/spleen diameter ratio | ≤ 1200 | 49 | 27 | 22 | 82% | 31% | 55% | 63% |

# DISCUSSION

The Baveno 111 Consensus conference on portal hypertension recommended that "all cirrhotic patients should be screened for the presence of varices at the time of initial diagnosis of liver cirrhosis.[10] However, fewer than 50% of cirrhotic patients have varices at screening endoscopy and most have small sized varices with low risk of bleeding.[9] Endoscopically, the most consistent findings associated with increased risk of bleeding are the size of varices and the presence of red wale markings.[11] These

endoscopic findings, in combination with Child class, form the North Italian Endoscopic club index, which predicts the risk of esophageal bleeding.[12] Since the prevalence of varices at risk of bleeding is relatively low in compensated cirrhotic patients, the AASLD single topic symposium[13] suggested performing an upper gastrointestinal endoscopy only on those patients with clinical evidence of portal hypertension to avoid an invasive and unnecessary procedure.

Many studies have been performed to identify any clinical or biochemical parameters which can be used as predictors of presence of esophageal varices.[1,2,9,14-20] These parameters include spiders, platelet count, spleen diameter, platelet/spleen diameter ratio, portal vein diameter, ascites, prothrombin time, bilirubin and albumin. Some of them have been claimed to have significant predictive value e.g., platelet count and platelet count/spleen diameter ratio.

In our study we selected 4 variables, splenic diameter, portal vein diameter, platelet count and platelet count/spleen diameter ratio.

The first variable was spleen size. The best cut off value for spleen size to predict presence of varices was 160 mm with p value of <0.001 (which is significant). Positive predictive value (PPV) was 90% and negative predictive value (NPV) was 81%. This is similar to the findings of other workers.

Thomopoulos et al[9] found that spleen length of 135 mm (with a significant p-value of 0.01) is cutoff value for prediction of esophageal varices. Sethar et al[1] observed that spleen diameter of 130 mm (p-value of 0.001) is the cut off value. Ismail et al [14] found splenic size ≥158 mm to be independent noninvasive predictor of large varices.

Second variable in our study was portal vein diameter. Its best cut off value for prediction of presence of varices was 13.5 mm and it was significant (p value <0.001). PPV was 74% and NPV was 77%.

Sarwar et al[15] observed that patients with portal vein diameter of >11mm (p-value of 0.038) were more likely to have high grade varices. Schepis et al[16] concluded that compensated cirrhotic patients should be screened by upper gastrointestinal endoscopy if ultrasonographic portal vein diameter greater than 13 mm (p-value was 0.001) was observed. This is again in confirmation with our findings. Cherian et al[17] also found portal vein diameter of 13 mm (p-value was 0.026) as an independent predictor for the presence of esophageal varices.

Third variable was platelet count. We observed that best cutoff value of platelet count for the presence of varices was 145,000 X $10^3/\mu L$ (with p value of 0.486 which was not significant), with PPV of 56% and NPV of 58%. Hence we conclude that platelet count alone is not a useful predictor of presence of varices. This is against the observation of many workers.

Schepis et al[16] concluded that compensated cirrhotic patients should be screened by upper gastrointestinal endoscopy if platelet count was less than $100 \times 10^9/L$ (with a significant p-value of 0.01). Thomopoulos et al[9] found that platelet count of 118,000 (p-value of 0.0001 which is very significant) is the cutoff value for prediction of esophageal varices.

Sanyal et al [18] in a study on 1016 patients observed that a minimum platelet count of $150,000/mm^3$ was a cut off value that excluded medium and large esophageal varices with a sensitivity of 90%.

Sarwar et al[15] in a study observed that patients with platelet count of less than $88,000/mm^3$ (p-value of 0.156 in a multivariate analysis which is not significant) were more likely to have esophageal varices. This confirms our finding.

To assess the validity of Schepis study Riggio et al[19] conducted a study on 215 patients. Esophageal varices were detected in 104 patients. It was found that 58 patients classified as those with the lowest probability of having varices (PLT ≥100 X $10^9/L$; PT ≥70%; P ≤13mm) 20 (34.4%) had varices. On the other hand among the 24 patients with high probability of having varices, 10 had no varices at endoscopy (with a lower AUC (area under the curve) of 0.63 ± 0.03).

Fourth variable in our study was platelet count/spleen diameter ratio. The cut off value for platelet count/spleen diameter was 1200 (with a p value of 0.153 which is insignificant, PPV of 55% and NPV of 63%). This parameter is also not useful for the purpose and this observation is against the conclusion of some other studies. Sethar et al[1] observed that cutoff value for platelet count/spleen diameter of 1445 (with p value of 0.001) to predict the presence of varices.

Giannini et al [20] found that mean platelet count/spleen diameter ratio cut off value of 909 had 100% negative predictive value for a diagnosis of varices.

Alempijevic et al[2] in their study concluded that the mean platelet count/spleen diameter ratio was 1017.75 ± 729 was a non-invasive parameter providing accurate information pertinent to determination of presence of esophageal varices but this was not significant (p-value 0.686).

# CONCLUSION

Out of 65 cirrhotics without any history of upper GI bleed, 33 patients had varices while 32 patiens had no varices on upper GI endoscopy.We selected four variables to predict the presence of varices. Cut off values for prediction of varices were: spleen diameter 160 mm (p-value of <0.001), portal vein diameter 13.5 mm (p-value of <0.001), platelet count 145 X $10^3/\mu L$ (p-value of 0.486), and platelet count/spleen diameter ratio 1200 (p-value of 0.153).

Out of four variables we studied, spleen diameter and portal vein diameter turned out to be statistically

significant non invasive parameters to predict the presence of varices. While other two variables (platelet count and platelet count/spleen diameter ratio) were not statistically significant.

We conclude that only those patients of liver cirrhosis without history of bleeding should be scoped for varices who have spleen diameter of ≥160 mm or portal vein diameter of ≥13.5mm or both.

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