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# Prevention of First Bleeding Episode from Gastroesophageal Varices in Patients with Cirrhosis

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## ABSTRACT

**Background:** Cirrhotic patients with clinically significant portal hypertension (CSPH) have high risk of developing gastroesophageal varices and bleeding. Many invasive and non-invasive tests are used to diagnosis CSPH, hence gastroesophageal varices. Gastroscopy is gold standard, but invasive, costly and not free of complications. In this study, we investigated non-invasive tests platelets count to spleen diameter ratio value in cirrhotic patients, to assess correlation to gastroesophageal varices and their size. **Objective:** In this study, we evaluated whom patients actually needed endoscopy. To determine the diagnostic accuracy of noninvasive tests (platelet count, spleen length, and platelet count-to-spleen length ratio) to identify clinically significant portal hypertension (CSPH) and gastroesophageal varices of any size in adult patients with cirrhosis, irrespective of etiology. **Study Design:** cross sectional study. **Settings:** Gastroenterology Department of Gujranwala Teaching Hospital, Gujranwala Pakistan. **Duration:** One year from January to December 2022. **Methods:** One hundred and ten patients were included. The endoscopy was performed in dedicated endoscopy suite of Gujranwala Teaching Hospital Gujranwala and cirrhotic patient was screened for varices and graded into low and high grade varices. Patient ultrasound was reviewed for spleen diameter and complete blood count for platelets count. Chi-square test was used to determine the relationship of grade of varices with gender. One way ANOVA test was used to compare the mean platelets count, spleen diameter and platelets count to spleen diameter ratio among patient with and without varices. **Results:** The cut-off value for the platelets to spleen diameter ratio 606.9 had the best sensitivity of 96.6% and specificity of 63.0% for exclusion of varices. Platelets to spleen diameter ratio had the best AUC (area under curve) value was 0.880 (95% CI (0.813-0.947, p<0.001) for exclusion of varices. **Conclusion:** In patients with compensated cirrhosis, the platelet count to spleen diameter ratio appears to be best noninvasive test for exclusion of varices. A cut off value 606.9 can be used clinically to avoid gastroscopy in significant proportions of cirrhotic patients.

***Keywords:*** *Cirrhosis, Varices, Platelet count to spleen diameter ratio.*

## INTRODUCTION

Cirrhosis represents an irreversible late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture and the formation of regenerative nodules.[1] Worldwide the most common causes of cirrhosis are chronic viral hepatitis, alcoholic liver disease, and nonalcoholic liver disease.[2,3]

Clinically patient with cirrhosis can categorize into compensated cirrhosis or decompensated cirrhosis.[3] Patients with compensated cirrhosis are asymptomatic

and usually diagnosed on basis of clinical signs, laboratory values and imaging. Patients with decompensated cirrhosis are easier to diagnosis by the presence of any overt complications of cirrhosis such as ascites, hepatic encephalopathy, and/or variceal hemorrhage. In patients with compensated cirrhosis, the severity of portal hypertension correlates with the development of gastroesophageal varices (GEV) and risk of variceal bleeding. GEV usually occur once patients develop clinically significant portal hypertension (CSPH), and patients with CSPH not only have a higher risk of developing varices but also have a higher risk of decompensation.[4] The portal pressure is determined by measuring hepatic venous pressure gradient (HVPG). Gastroscopy is gold standard but invasive procedure for diagnosis of GEV, and patients with GEV on endoscopy have, by definition, CSPH.[4,5] Noninvasive tests can be used to identify patients having CSPH, hence presence of gastroesophageal varices such as liver stiffness measurement by transient elastography, portosystemic collaterals or recanalized umbilical vein or reversal of portal flow on imaging, platelet count, spleen diameter, index of platelet count and spleen diameter. Low platelet count (equal or less than 100000) is associated with presence of varies in cirrhotic patients but not accurate enough alone.[6] However platelet count in association with spleen diameter improves diagnostic accuracy. Platelet count / spleen diameter (millimeters) ratio < 909 was described to have higher sensitivity and specificity for the diagnosis of EV.[7,8,9,10]

Variceal bleeding is one of the most severe complications of liver cirrhosis. When cirrhosis is diagnosed, varices are present in approximately 50 % of compensated patients and in up to 85% patients with decompensated cirrhosis.[5] Gastric varices are present in about 20% of patients with cirrhosis, and they can be of different types.

There are no published studies describing the prevalence of GE varices in liver cirrhosis among Gujranwala and its periphery areas and also there are no published studies highlighting importance of non-invasive tests in identifying patients with CSPH and hence GE varices. Hence by this study we have determined the diagnostic accuracy of noninvasive tests (platelet count, spleen length, and platelet count-to-spleen length ratio) to identify clinically significant portal hypertension (CSPH) and gastroesophageal varices of any size in adult patients with cirrhosis, irrespective of etiology and also prevalence of GE varices. We have also determined if and when an upper endoscopy is needed in patients with cirrhosis.

## METHODS

This Cross-Sectional study was carried out in Gastroenterology Department of Gujranwala Teaching Hospital, Gujranwala, in period of study one year January to December 2022. One hundred and ten patients were recruited in this study. After the approval of the Ethics Review Committee. The sample size was calculated by using WHO software "Sample Size Determination in Health Studies" with 95% confidence interval and 5% margin of error. Considering proportions 93 % sensitivity of Platelet count/spleen diameter ratio as a non-invasive marker for the presence or absence of esophageal varices and the sample size is 110 patients. Non-probability convenience sampling technique was used**.** Patients of either sex between ages of 20 to 75 years presenting in OPD with cirrhosis as per operational definition were included**.** Patients with previous or present history of upper GI bleed and features of hepatic encephalopathy were excluded. Patients with previous history of endoscopic banding or injection sclerotherapy were also excluded. Patients who were already on non-selective beta blockers drugs were excluded. Patients who were not willing for endoscopy or have any contraindication for endoscopy were excluded.

## RESULTS

The mean age of the patients was 51.0 ± 11.2 with age range from 22 to 75 years. Majority of the patients were female (59.1%). High grade varices were observed in 58 (52.7%) patients, low grade varices were observed in 23 (20.9%) patients. No varices were observed in 29 (26.4%) patients.

**Table 1: Showing distribution of gender and grade of varices among study participants**

| Variable | | Frequency | Percentage |
|---|---|---|---|
| **Gender** | Male | 45 | 40.9 |
| | Female | 65 | 59.1 |
| **Varices** | No | 29 | 26.4 |
| | Low | 23 | 20.9 |
| | High | 58 | 52.7 |

**Table 2: showing descriptive statistics for platelets, spleen and platelets to spleen diameter ration among study participants**

| Variable | Mean ± SD | Min. | Max. |
|---|---|---|---|
| **Platelets** | 104481.8 ± 36074.0 | 40000.0 | 210000.0 |
| **Spleen** | 130.8 ± 20.3 | 90.0 | 180.0 |
| **Platelet to spleen diameter ratio** | 837.7 ± 361.6 | 266.7 | 1890.0 |

**Table 3: showing association of grade of varices with gender**

| Variables | Category | | Grade of Varices | | | p-value |
|---|---|---|---|---|---|---|
| | | | No | Low | High | |
| Gender | Male | n | 10 | 9 | 26 | 0.640 |
| | | % | 34.5% | 39.1% | 44.8% | |
| | Female | n | 19 | 14 | 32 | |
| | | % | 65.5% | 60.9% | 55.2% | |

Chi-squares test revealed no significant association of gender and grade of varices.

**Table 4: comparison of platelets, spleen and platelet to spleen diameter ratio among patient with and without varices**

| Variables | Grade | Mean ± SD | Range | p-value |
|---|---|---|---|---|
| **Platelets** | No | 133724.1 ± 16153.1 | 103000 – 167000 | < 0.001* |
| | Low | 120304.3 ± 34446.8 | 75000 – 210000 | |
| | High | 83586.2 ± 30364.5 | 40000 – 189000 | |
| **Spleen** | No | 116.3 ± 20.7 | 90.0 – 180.0 | < 0.001* |
| | Low | 123.4 ± 17.7 | 90.0 – 165.0 | |
| | High | 140.9 ± 15.0 | 100.0 – 173.0 | |
| **Platelet to spleen diameter ratio** | No | 1183.9 ± 246.0 | 600.0 – 1670.1 | < 0.001* |
| | Low | 979.2 ± 256.3 | 681.0 – 1521.7 | |
| | High | 608.4 ± 269.1 | 266.7 – 1890.0 | |

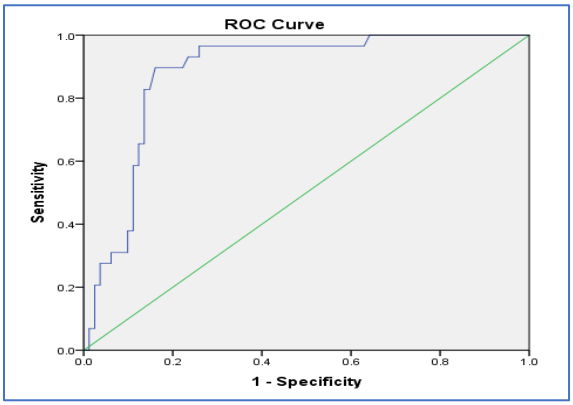
One way ANOVA test showed that there was significant difference in mean platelets, spleen and platelet to spleen diameter ratio among patients with low and high grade varices and without varices. The platelets and platelets to spleen diameter ratio were significantly lower in patients with low grade and high grade varices. However, the spleen size was significantly higher in patients with low grade and high-grade varices as shown in Table 4.

ROC analysis was applied for exclusion of varices, the AUC (area under curve) value was 0.880 (95% CI (0.813-0.947, p<0.001) (Figure 1) and the cut-off value for platelets to spleen diameter ratio was 606.9 with a sensitivity of 96.6% and specificity of 63.0%. (Table 5)

**Table 5: ROC analysis and sensitivity and specificity of platelets to spleen diameter ratio in prediction of no varices**

| Area under curve | p-value | 95% Confidence Interval | |
|---|---|---|---|
| | | Lower | Upper |
| 0.880 | < 0.001 | 0.813 | 0.947 |
| **Varices** | **Cut-off value** | **Sensitivity** | **Specificity** |
| No vs. (low + high grade varices) | ≥ 606.9 | 96.6% | 63.0% |

**Figure 1: ROC for platelets to spleen diameter ratio in prediction of varices**




## DISCUSSION

Cirrhosis represents an irreversible late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture and the formation of regenerative nodules.[1] Worldwide the most common causes of cirrhosis are chronic viral hepatitis, alcoholic liver disease, and nonalcoholic liver disease.[2,3]

In patients with compensated cirrhosis, the severity of portal hypertension correlates with the development of gastroesophageal varices (GEV) and risk of variceal bleeding.

Gastroscopy is gold standard but invasive procedure for diagnosis of GEV, and patients with GEV on endoscopy have, by definition, CSPH.[4,5] Noninvasive tests can be used to identify patients having CSPH, hence presence of gastroesophageal varices such as liver stiffness measurement by transient elastography,[11] portosystemic collaterals or recanalized umbilical vein or reversal of portal flow on imaging, platelet count, spleen diameter, index of platelet count and spleen diameter.[11] Low platelet count (equal or less than 100000) is associated with presence of varies in cirrhotic patients but not accurate enough alone.[6] However platelet count in association with spleen diameter improves diagnostic accuracy. Platelet count / spleen diameter (millimeters) ratio < 909 was described to have higher sensitivity and specificity for the diagnosis of EV.[7,8,9,10]

Sami *et al* have performed a systemic review and meta-analysis of twenty-one studies on compensated cirrhosis patients to identify noninvasive tests for detection of esophageal varices, to estimate diagnostic accuracy and clinical utilization of these noninvasive tests. Sami *et al* have found that PSR for detection of varices in patients with compensated cirrhosis has sensitivity 0.87 %and specificity 0.71% and highest summary AUC 0.85. They have also found PSR 909 cut off value clinically useful to avoid gastroscopy in significant proportions of patients.[13]

Cherian *et al*. have conducted a study on cirrhotic patients to identify non-endoscopic methods that could predict presence of esophageal varices and found that PSR was not predictive for presence of esophageal varices, however cut off value of ≤ 606 had sensitivity 66.3 %and specificity 80.4% for presence of varices.[14]

Amoak *et al* have done a cross sectional study on liver cirrhotic patients at Korleu-Bu teaching hospital Gana and have found best cutoff value ≤ 833.3 an independent predictor of esophageal varices with diagnostic accuracy of 72.62 %.[15] Mahassadi *et al* conducted a similar study in Cote d'Ivoire and found similar results.[16]

Abu El Makarem have found that best cutoff value of PSR was 939.7 and diagnostic accuracy 96.5 %.[17]

## CONCLUSION

The best cut-off value of platelet count and spleen diameter ratio in our study is 606.9 as determined by ROC and is independent predictor in prediction of varices. The sensitivity and specificity of this cut-off value is 96.6% and 63.0% in our population. PSD ≥ 606.9 can be used as noninvasive marker in cirrhotic patients for excluding esophageal varices and help in decision making which patients may need beta-blockers as primary prophylaxis and gastroscopy in resource limited country areas.

## LIMITATIONS

There may be interobserver variation in assessing spleen size.

## SUGGESTIONS / RECOMMENDATIONS

Further exploration in this dimension for facilitation of patient's management and diseases prognosis.

## CONFLICT OF INTEREST / DISCLOSURE

There is no conflict of interest.

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