

Original Research Article

# A study on platelet count/ spleen diameter ratio and AST/ALT ratio as a marker for detection of esophageal varices in Cirrhosis

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**Abstract: Introduction:** Esophageal varices are a major cause of morbidity and mortality in patients with liver cirrhosis. Esophageal varices can be screened with invasive procedures like esophageal endoscopy which might not be affordable to all in developing countries. This study aimed to find the diagnostic efficacy of some non-invasive markers for detection of esophageal varices in people with cirrhosis.

**Objective:** To assess the feasibility of platelet count/ spleen diameter (PLC/BPD) ratio and Aspartate transaminase / Alanine transaminase (AST/ALT) ratio as a non-invasive marker for esophageal varices in patients with cirrhosis.

**Materials and method:** Platelet count/ bipolar spleen diameter (PLC/BPD) ratio and Aspartate transaminase / Alanine transaminase (AST/ALT) ratio were analysed in hundred patients with cirrhosis admitted in the Medicine Ward of Vinayaka Mission's Medical College and Hospital, Karaikal . The values obtained were co-related to presence or absence of esophageal varices on upper GI endoscopy in these patients.

**Results:** A statistically significant correlation between platelet count/ bipolar spleen diameter (PLC/BPD) ratio and Aspartate transaminase / Alanine transaminase (AST/ALT) ratio and esophageal varices was found in our study group.

**Keywords:** Non-invasive marker; Esophageal varices; Cirrhosis.

## 1. Introduction

Liver cirrhosis is a major cause of morbidity and mortality in underdeveloped countries like India. Analysis of WHO 2014 data indicates that deaths due to liver diseases account for 2.44% of the total deaths in India [1]. Data from multiple studies show both Portal Hypertension and esophageal varices are seen in 24-80% of people with cirrhosis and attribute to the associated high mortality rate. While the prevalence of esophageal varices amongst people with cirrhosis ranges between 60 to 80 %, the mortality due to variceal bleeding is reportedly between 17 to 57%. Hence, detection of esophageal varices and prevention of variceal bleeding is of importance in patients with cirrhosis of liver [1-3].

Both the American Association for the Study of Liver Diseases as well as the Baveno III Consensus Conference on portal Hypertension have recommended since 1996 that all cirrhotic patients should be screened for presence of esophageal varices once the diagnosis of portal hypertension is made [4,5]. Other groups recommend follow-up endoscopy at 2-3 years interval in cirrhotic patients without portal hypertension and 1-2 yearly endoscopy to monitor severity progression in people with varices<sup>4</sup>. Further, Primary prophylactic and screening endoscopy for esophageal varices is recommended in people with high risk of bleeding from esophageal varices. Guidelines also recommend that all patients who have undergone endoscopic esophageal varices ligation should be periodically monitored for Hepatic Venous Pressure Gradient [4-7].

However, this periodic screening is expensive, invasive and cost in-effective, especially in resource challenged communities, thus necessitating need of affordable and non-invasive markers for diagnosis of Portal Hypertension and esophageal varices.

Recently, multiple biochemical, radiological and clinical variables are being evaluated as surrogates for Endoscopic screening for esophageal varices in people with portal hypertension. Some of the prominent variables in the forefront include ascites, splenomegaly, thrombocytopenia and Hepatic enzymes like Aspartate transaminase and Alanine transaminase [8–16].

Splenomegaly in cirrhotic patients is the sequel of portal hypertension related vascular disturbances [11]. Hepatic enzymes like Aspartate transaminase and Alanine transaminase show derangement as the disease progresses but are also subject to residual revivable healthy hepatocyte mass [14–16]. Thrombocytopenia in cirrhotic patients can be due to myriad causes like reduced platelet half-life, low thrombopoietin levels, myelotoxicity of ethanol or hepatotropic viruses or a direct sequel of portal hypertension itself [13].

Khaled El Mola *et al.*, studied Platelet count / bipolar spleen diameter Ratio as a non-invasive marker for esophageal varices in Egyptian population [17] and proposed that platelet count/ spleen diameter was significantly lower in patients with esophageal Varices. Giannini *et al.*, proposed that the platelet count: spleen diameter ratio be utilized as a non-invasive screening for esophageal varices [12]. Nyblom *et al.*, studied AST/ALT Ratio as an indicator of Cirrhosis in patients with PBC and reported that AST/ALT ratio could be of clinical value in detecting portal hypertension in patients with primary biliary cirrhosis.

Review of literature reveals that prior studies have been subjected to limitations like retrospective nature, narrow study population like transplant wait-listed patients and lack of uniformity in categorization of severity of esophageal varices [10,14,15]. Further, data amongst Indian population which has a significantly different etiology of cirrhosis as well as presentation and facilities as compared to western population is scarce.

It is with this background that our study was undertaken to determine if the platelet count/ spleen diameter and AST/ALT ratio could be used as a cost-effective yet non-invasive parameter to assess presence, severity and likelihood of bleed from esophageal varices in a group of cirrhotic patients in a South-Indian tertiary care centre with and if they could be used to triage the need for invasive treatment like endoscopic varices ligation .

## 2. Method:

### 2.1. Study design and subjects

This study was carried out in the in-patient wards of general medicine department of Vinayaka Mission's Medical College and Hospital, Karaikal between August 2016 and July 2017. Hundred cases of Cirrhosis with Portal Hypertension admitted in the general medical wards were included in this study. The study was initiated after obtaining clearance from the institutional Research Committee and Ethics committee. Informed consent was obtained from all participants after explaining in detail the aims and objectives of the study.

### 2.2. Selection Criteria

#### 2.2.1. Inclusion Criteria

All Male and Non-pregnant Female patients of age more than 18 diagnosed to have cirrhosis with portal hypertension and admitted in medical wards during the study period. The aetiology of Cirrhosis included Alcoholic Cirrhosis, HBV, HCV, Wilson's Disease, Hemochromatosis, Cryptogenic Cirrhosis, Biliary Cirrhosis, Cardiac Cirrhosis, Autoimmune Hepatitis and Non-alcoholic Steato-hepatitis.

#### 2.2.2. Exclusion Criteria

Patients with history of diseases primarily affecting platelet counts like ITP, Short Febrile illnesses like Leptospirosis, Dengue Fever and Malaria, Hematological malignancies like lymphoma and leukemia, other Diseases causing splenomegaly like myelofibrosis and myelodysplasia, EHPVO, patients having acute liver failure, hemodynamically unstable patients, patients on drugs for primary prophylaxis of variceal bleeding or having undergone sclerosis /band ligation of esophageal varices were excluded from the study.

### 2.3. Criterias and normal ranges used in the study

#### 2.3.1. Cirrhosis

Physical Examination (Jaundice, Stigmata of CLD), laboratory investigations (LFT abnormalities), USG or other imaging showing nodular liver with coarse echo-texture.

#### 2.3.2. Portal Hypertension

Ascites, splenomegaly, USG abdomen showing collaterals around gastro-esophageal junction and splenic hilum, splenomegaly, Dilated portal vein >12 mm, dilated splenic vein > 10 mm and demonstration of esophageal varices by upper GI Endoscopy.

#### 2.3.3. Esophageal Varices Grading System

Grade 0: Absent

Grade 1: Small straight varices not disappearing on insufflations.

Grade 2: Medium varices occupying less than 1/3rd of the lumen.

Grade 3: Large Varices occupying more than 1/3rd of the lumen.

#### 2.3.4. Platelet count/Spleen diameter ratio

Platelet number/mm<sup>3</sup> divided by the maximum spleen bipolar diameter in mm as measured by USG Abdomen.

### 2.4. Blood Sample Collection

10 ml of venous blood samples was taken from willing subjects who had given consent. Care was taken during the sample collection by avoiding tourniquets and aggressive veno-suction or sample handling. CBC was estimated on the Asysmex Kx21 3 part haematological Automated Cell counter. The separated serum was tested for serum electrolytes, RFT, LFT and other clinically relevant investigations on the Transasia XL 300 Clinical Chemistry Analyser. USG abdomen was done using GE Volusion 56 machine with 3.5 mega Hz curvilinear probe. Esophageal varices were graded by upper GI Endoscopy using Olympus Flexible Video Endoscope.

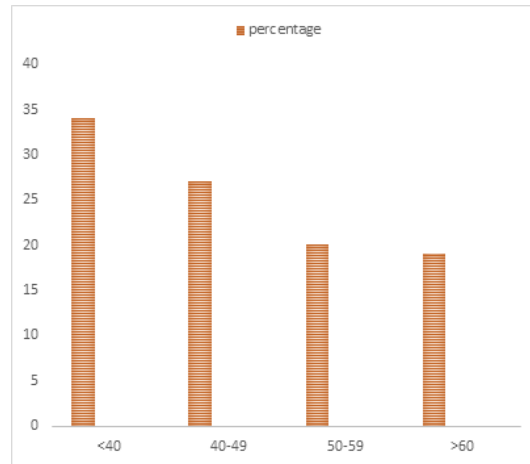
Data was entered into excel sheet and analysis done by using SPSS version 16. The ratios namely Platelet count/Bipolar spleen diameter and AST/ ALT Ratio were analysed using receiver operating characteristics (ROC) curves and its statistical significance was calculated using tests like Mann- Whitney U and p Value. Qualitative variables were summarised using proportions. Quantitative variables using mean with standard deviation / median.

### 3. Results

In our study, 100 cases were identified as per the Inclusion and exclusion Criteria mentioned earlier and of these, 94% patients were of Male gender. Maximum patients belonged to the age group of less than 40 years.

**Table 1.** Age Distribution

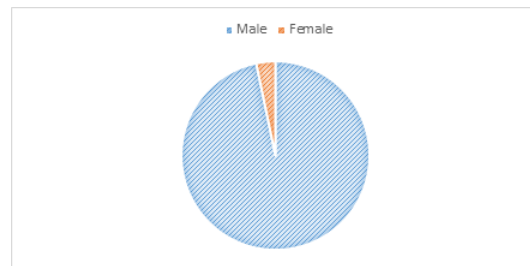
Age in years	Frequency	Percent (%)
<40	34	34
40-49	27	27
50-59	20	20
>60	19	19
Total	100	100



**Figure 1.** Age Group Distribution as Percentage

**Table 2.** Sex Distribution

Gender	Frequency	Percent (%)
Male	94	94
Female	6	6
Total	100	100

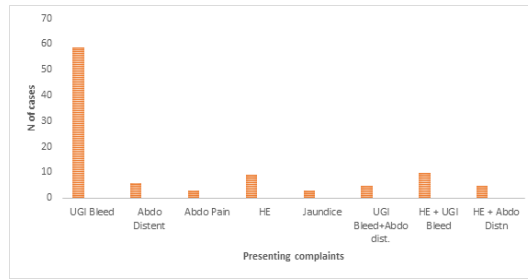


**Figure 2.** Gender Distribution as Percentage

In our study population, the most common presenting complaint was upper GI Bleed while the least common presentation was Hepatic encephalopathy. The other presentations included abdominal pain, abdominal distention and jaundice.

**Table 3.** Presenting Complaints

Presenting Complaints	Frequency	Percent (%)
Upper GI Bleed	59	59
Abdominal Distention	6	6
Abdominal Pain	3	3
Hepatic Encephalopathy ( HE)	9	9
Jaundice	3	3
Upper GI Bleed + Abdominal Distention	5	5
HE + Upper GI Bleed	10	10
HE + Abdominal Distention	5	5
Total	100	100

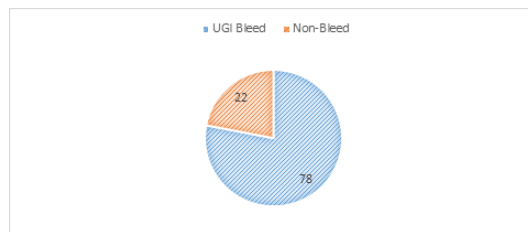


**Figure 3.** Spectrum of Presenting Complaints

The most common presentation in our study group was Upper GI Bleed while the least common were non bleed causes like abdominal pain.

**Table 4.** Presence of Upper GI Bleed

Presenting Complaints	Frequency	Percent (%)
UGI Bleed	78	78
Non-Bleed	622	22
Total	100	100

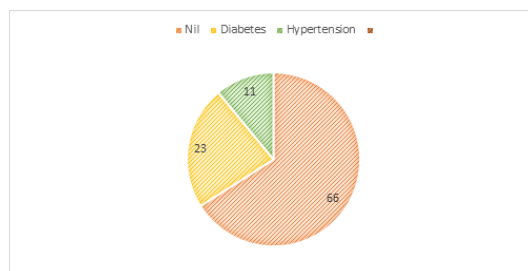


**Figure 4.** Upper GI Bleed as presenting Complaint

The most common coexistent disease in our study population was Diabetes Mellitus followed next by Systemic Hypertension.

**Table 5.** Associated Comorbidities

Comorbidities	Frequency	Percent (%)
None	66	66
Diabetes Mellitus (DM)	23	23
Hypertension (HTN)	11	11
Total	100	100

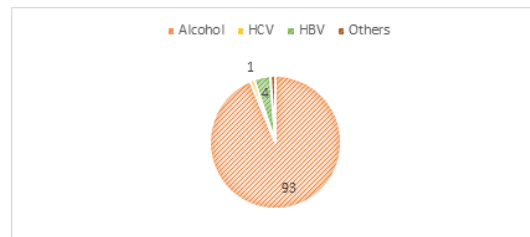


**Figure 5.** Co-morbidities Distribution

In our study population, the most common cause of Cirrhosis was alcohol followed by Hepatitis B infection.

**Table 6.** Etiology Of Cirrhosis

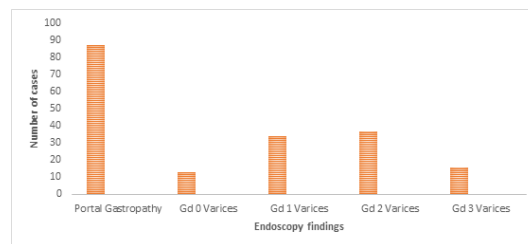
Etiology	Frequency	Percent (%)
Alcohol	93	93
HCV	1	1
HBV	4	4
Others	2	2
Total	100	100

**Figure 6.** Etiology of Cirrhosis

On upper GI Endoscopy, portal hypertensive gastropathy was found in 87 subjects. Esophageal Varices were not seen in 13 cases while Grade 1 and Grade 2 varices were seen in 13 and 34 cases respectively.

**Table 7.** Upper GI Endoscopy Findings

Endoscopy Findings	Frequency	Percent (%)
Portal Gastropathy	87	87
Grade 0 Varices	13	13
Grade 1 Varices	34	34
Grade 2 Varices	37	37
Grade 3 Varices	16	16

**Figure 7.** Upper GI Endoscopy Findings

**Table 8.** Descriptive Statistics of the Study Group

Sr No	Variable	N	Minimum	Maximum	Mean	Standard Deviation
1	Hemoglobin (gm %)	100	2	14	1.0259	1.92485
2	Platelet ( /mm <sup>3</sup> )	100	30,000	2,22,000	1.06	43368.064
3	Direct Bilirubin (gm %)	100	0.4	3.9	1.06	.7278
4	Indirect Bilirubin	100	0.3	4.0	1.130	.7023
5	AST (IU)	100	29	220	83.76	39.681
6	ALT (IU)	100	17	195	61.88	35.468
7	Albumin (Gm %)	100	1.8	4.3	2.968	.6361
8	PT/INR	100	.9	2.2	1.424	.3094
9	Bipolar Diameter Spleen BPD(cm)	100	90	180	133.64	24.048
10	Liver Span( cm)	100	9	16	12.47	1.672
11	Portal Vein (cm)	100	2	15	11.762	1.8761
12	Splenic Vein (cm)	100	4	14	9.09	2.454
13	Platelet/ BPD Ratio	100	164.0	2111.1	819.804	402.1647
14	AST/ALT Ratio	100	1.0	131.0	2.738	12.9580

**Table 9.** Test result Variable(s): PLC/BPD Ratio

			Aymptomatic 95% CI	
Area	Std Error <sup>d</sup>	Asymptomatic Sig <sup>b</sup>	Lower Bound	Upper Bound
0.908	0.036	0.000	0.839	0.978

**Table 10.** Test Statistics

Test	PLC/BPD Ratio
Mann Whitney U	191.500
Wilcoxon W	7817.500
Z	-5.448
Asymptomatic Sig (2 -Tailed)	.000

**Table 11.** Test result Variable(s): AST/ALT Ratio

			Aymptomatic 95% CI	
Area	Std Error <sup>d</sup>	Asymptomatic Sig <sup>b</sup>	Lower Bound	Upper Bound
0.794	.066	.000	.665	.923

**Table 12.** Test Statistics

Test	AST/ALT Ratio
Mann Whitney U	430.500
Wilcoxon W	583.500
Z	-3.924
Asymptomatic Sig (2 -Tailed)	.000

#### 4. Discussion

This study was conducted on 100 patients meeting the inclusion criteria in the wards of Department of General Medicine, Vinayaka Mission's Medical college and Hospital, Karaikal. Majority of the population were between 40-59 years and of male gender. Estrogen may have a protective role against fibrosis in viral hepatitis by stellate cell inhibition as proven in other studies. Our findings are similar to that reported in other studies [18]. The major presenting complaint in our study group was Upper GI Bleed (51%) with or without other associated complaints like abdominal distention, abdominal pain, hepatic Encephalopathy or jaundice. Similar findings have been reported in other studies (Longstreth GF *et al.*)

In our study group, the main aetiology of Cirrhosis was alcohol, followed by HBV infection. However, these findings are different from studies in developed countries where Viral Hepatitis was the most common cause of Cirrhosis [19].

In our study, 37 patients had grade 2 esophageal varices, 34 had grade 1 varices and 16 had grade 3 varices. 84 of the 100 cirrhotic patients had portal gastropathy. In our study, the ROC curve showing PLC/ BPD ratio had an area under curve of 0.906, cut off value 0.919, sensitivity of 74%, specificity of 88% and a p Value < 0.001, all of which are statistically significant. Similar findings have been reported in other studies like that by Giannini *et al.*, and Khaled El Mola *et al.*, [12,17].

The ROC curve showing AST/ALT ratio was also plotted in the present study, with area under curve of 0.794, cut off value 1.30, sensitivity of 74%, specificity of 82% and a statistically significant p Value < 0.001. Nyblom *et al.*, reported in their retrospective study that significantly higher AST/ALT ratios were seen in people with esophageal varices as compared to those without varices. Castera *et al.*, reported an AUROC 0.83 with sensitivity of 68% and specificity of 89% of AST/ALT ratio for predicting presence of esophageal Varices in people with cirrhosis.

## 5. Conclusion

Our study again reiterated the diagnostic efficacy of Platelet count/ Bipolar Spleen Diameter ratio and AST/ALT Ratio as an inexpensive and non-invasive marker for presence of Esophageal Varices in patients with Cirrhosis of liver. Of the 100 cirrhotic patients included in the study, majority were of male gender, had alcoholism as the cause of cirrhosis and presented as Upper GI Bleed. On Upper GI Endoscopy, 87% had portal hypertensive gastropathy, 37%, 34% and 16% had Grade 2, Grade 1 and Grade 3 Esophageal Varices and 13% had no varices. The Platelet count/ Bipolar Spleen Diameter ratio (PLC/BPD) and AST/ALT Ratio had statistically significant sensitivity, specificity and p Value.

Thus, these two Non-endoscopic parameters- Platelet count/ Bipolar Spleen Diameter ratio and AST/ALT Ratio may be used as surrogate markers to predict the presence of esophageal varices and empirical treatment be started to prevent variceal bleeding, where endoscopic facilities are not readily available with the proviso that Upper GI endoscopy is needed without too much delay for diagnosis and therapeutic interventions.

## 6. Limitations

Our study had a small sample size and thus larger studies should be carried out to confirm the findings and practical implications regarding the general population.

**Author Contributions:** All authors contributed equally to the writing of this paper. All authors read and approved the final manuscript.

**Conflicts of Interest:** "Authors declare that they do not have any conflict of interests."

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