

## Original Research Article

# Correlation of platelet count/splenic diameter ratio for the diagnosis of esophageal varices in patients of cirrhosis of liver

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## ABSTRACT

**Background:** In patients with cirrhosis, endoscopic screening for esophageal varices is currently recommended as a gold standard tool at the time of diagnosis of cirrhosis and to institute prophylactic measures in patients with large esophageal varices. Newer methods have been proposed as alternatives to conventional endoscopy for the non-invasive or minimally invasive diagnosis of esophageal varices.

**Methods:** This one year observational study was done in the Department of Medicine at Dr. Prabhakar Kore Hospital MRC Belagavi. A total of 70 patients with cirrhosis of liver were included in the study. Relevant clinical examination, laboratory workup like complete blood count, liver function test, ultrasound abdomen and all patients underwent screening upper gastrointestinal endoscopy. Platelet count to spleen diameter ratio was calculated for all patients.

**Results:** 54 (77.14%) had varices. Males predominated with 64 (91%). Majority patients ranged in between 31-50 years. Evidence of esophageal varices was more common with cirrhosis secondary to alcoholism as compared to hepatitis B virus (HBV) and hepatitis C virus (HCV). The child Pugh score, platelet count, spleen size, platelet count/spleen diameter ratio in patients with varices was significantly different from patients without varices. Platelet count/spleen diameter ratio cutoff value of 909 was obtained with sensitivity of 77% and specificity of 79%. The positive predictive value was 88% and negative predictive value was 62%.

**Conclusions:** The platelet count to spleen diameter ratio may be useful inexpensive tool for diagnosing esophageal varices in liver cirrhosis noninvasively when endoscopy facilities are not available.

**Keywords:** Esophageal varices, Liver cirrhosis, Platelet count to spleen diameter ratio, Endoscopy

## INTRODUCTION

In cirrhosis normal functioning of liver is altered due to destruction and replacement of hepatocytes and liver parenchyma by scar tissue as a result of injury to them. According to the World Health Organization (WHO) data published in May 2014, deaths due to liver diseases accounted for 2.31% of total deaths.<sup>1</sup> Liver disease is the tenth most common cause of death in India.<sup>2</sup>

Portal hypertension usually accompanies cirrhosis.<sup>3</sup> It is a progressive complication of cirrhosis which leads to the

formation of esophageal varices (EV).<sup>4</sup> Patients with gastro esophageal varices (GEV) usually have hepatic vein pressure gradient (HVPG) of 10-12 mm Hg.<sup>5</sup> GEV are the most relevant porto-systemic collaterals that develop in response to portal hypertension and their rupture leads to variceal haemorrhage which is one of the most lethal complication of cirrhosis. EV are present in about 30% patients with compensated and 60% with decompensated cirrhosis.<sup>4</sup>

Their presence usually correlates with the severity of liver disease. The rate of development of new varices is 8% per

year and strongest predictor for development of varices is HVPG more than 10 mm Hg. The progression from small to large varices occurs at rate of 8-10% per year.<sup>7</sup>

To reduce the burden on endoscopic units and to make it more cost-effective to patients by avoiding unnecessary endoscopy, lesser noninvasive alternative to endoscopy have been studied. Various clinical, biochemical and ultrasonography parameters were investigated for non-invasive diagnosis of EV and were found to have good predictive value. Among the parameters studied, the parameter that links EV to portal hypertension was found to have the highest predictive value. Platelet count, spleen diameter are directly or indirectly linked to the presence of EV. The platelet count/spleen diameter ratio (PC/SD), proposed by Giannini et al, is among the best non-invasive predictor of EVs that has been studied till date.<sup>8</sup>

The current study has been done to find the correlation between platelet count, spleen diameter and its ratio with esophageal varices in patients with liver cirrhosis; to validate the diagnostic validity of PC/SD as a non-invasive predictor of varices so that unnecessary endoscopy can be avoided.

## METHODS

The present one year observational study was done in the Department of General Medicine at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre Belagavi from January 2015 to December 2015 after taking proper clearance from the institutional ethical committee.

A total of 70 patients with cirrhosis of liver were included in the study. Patients were subjected to relevant clinical examination, laboratory workup like complete blood count, liver function test, ultrasound abdomen and all patients underwent screening upper gastrointestinal endoscopy. Platelet count to spleen diameter ratio was calculated for all patients.

### Inclusion criteria

Patients with cirrhosis of liver without any past history of upper gastrointestinal bleeding will be included in the study. Diagnosis of cirrhosis will be based on a combination of- history, clinical findings, impaired liver function tests, deranged clotting profile and abdominal ultrasound.

### Exclusion criteria

Patients with present or previous history of variceal bleed. Patients on previous/current treatment with beta blockers, diuretics (or) anti platelet drugs. Patients who have undergone sclerosis (or) band ligation of esophageal varices, TIPSS (or) surgery for portal hypertension. Patients with history of fever in the past and who are on drugs knowing to cause thrombocytopenia and patients

with asplenia/splenectomy and partial splenectomy will be excluded from the study.

### Statistical analysis

Data was recorded in Microsoft Excel sheet and analysed using statistical package for the social sciences (SPSS) ver. 20 software. The mean, standard deviation and percentages were calculated and tests were applied for parametric and non-parametric data accordingly. P value of <0.05 was considered statistically significant.

**Table 1: Child Pugh classification of cirrhosis.**

Score	1	2	3
<b>Encephalopathy</b>	None	Mild	Marked
<b>Bilirubin (mol/l)</b>	<34	<34-50	>50
<b>Albumin (g/l)</b>	>35	28-35	<28
<b>Prothrombin time (seconds prolonged)</b>	<4	4-6	>6
<b>Ascites</b>	None	Mild	Marked
<b>Add the individual scores</b>	<7=childs' A		
	7-9=childs' B		
	>9=childs' C		

## RESULTS

Out of 70 patients, 64 (91.43%) were male and 6 (8.57%) were females. Male preponderance was seen.

In our study population, patient's age range from 26 to 70 years. Maximum number of patients were in age group of 31-50 years (58.57%), followed by 51-70 years (35.74%).

Abdominal distension with pedal oedema (77.14%) was common presenting symptom followed by jaundice (70.00%), abdominal pain (37.14%) and nausea and vomiting (25.71%).

We observed, 63 (90.00%) patients having splenomegaly on either clinical or radiological examination, 52 (74.29%) with icterus, 14 (20.00%) with signs of chronic liver cell failure, 9 (12.86%) with distended veins over abdomen and 4 (5.71%) with hepatic encephalopathy.

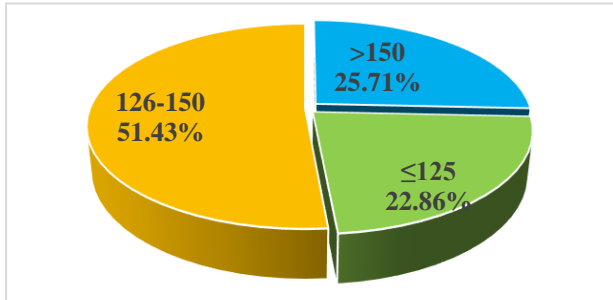
In our study, majority of patients had alcohol induced liver disease (90.00%) and remaining were due to hepatotropic virus infection (10.00%).

On upper gastrointestinal (GI) endoscopy, revealed 54 (77.14%) patients with varying degree of esophageal varices, portal hypertensive gastropathy in 9 (12.85%) patients and 7 (10.00%) were normal.

In our 70 patients, 27 (38.57%) patients had grade 2 esophageal varices, 21 (30.00%) had grade 1 varices, 15 (21.43%) had grade 3 varices and 9 patients with grade 1 and 2 varices also had portal hypertensive gastropathy.

In our study, 35.71% patients belonged to platelet ranging below 100000. 44.28% patients belonged to platelet range from 100000–200000 and 20.00% patients had platelet range above 200000.

Also we observed 36 (51.43%) patients having spleen diameter ranging from 126-150 mm, 18 (25.71%) patients with diameter more than 150 mm and 16 (22.86%) patients having range below or equal to 125 mm (Figure 1).



**Figure 1: Distribution on spleen bipolar diameter.**

And we noted that in 41 (58.57%) patients, ratio of platelet count/spleen diameter was below 1000 and in remaining 29 (41.43%) patients, ratio was more than 1000 (Table 1).

**Table 1: Distribution of patients with platelet count/spleen diameter ratio.**

Platelet count/spleen diameter ratio	No. of patients	% of patients
<500	9	12.86
501-1000	32	45.71
1001-2000	22	31.43
>2000	7	10.00
<b>Total</b>	<b>70</b>	<b>100.00</b>

In the present study, we observed 40 (57.14%) patients were in grade A child Pugh class, 23 (32.86%) patients in

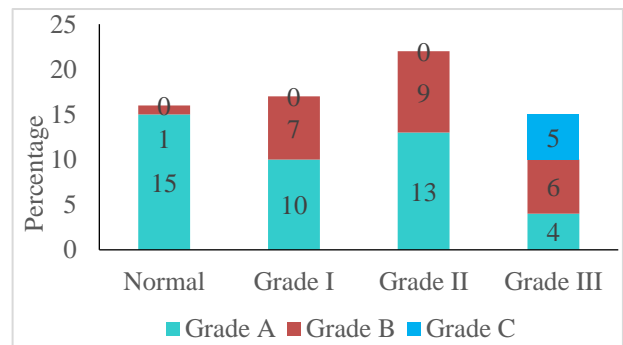
grade B child Pugh class and only 7 (10.00%) in grade C child Pugh class.

In all our 70 patients, when we compared with different parameters (lab/USG) with or without varices, we found significant correlation with platelet count, spleen bipolar diameter, PC/SD ratio, SGPT and serum albumin (Table 2).

Correlation of platelet count, spleen diameter and PC/SD ratio with grades of varices, we found that patients with platelet count ranging from 50000-100000 had more esophageal varices. Similarly, patients with spleen diameter ranging from 126-150 had more varices and patients having PC/SD ratio less than 1000 had more esophageal varices (Table 3).

Majority of patients with ascites had varying degree of esophageal varices (45 patients) as compared to those without ascites.

In our study, correlation of child Pugh class and grades of varices were studied. We found that 42 patients belong child Pugh class A with varying degree of varices. Similarly, 23 patients belong to child Pugh class B and only 5 patients belong to child Pugh class C (Figure 2).



**Figure 2: Correlation of child Pugh class with grades of varices.**

**Table 2: Comparison of different parameters (lab/USG) with varices.**

Variables	Summary	Present varices	Absent varices	Total	t-value	P value
Platelet count	Mean	124351.85	212187.50	144428.57		
	SD	58866.06	114401.18	82987.44	-4.128	0.0001*
Spleen bipolar diameter	Mean	142.52	130.63	139.80		
	SD	13.20	12.85	13.97	3.1840	0.0022*
PLT/spleen diameter ratio	Mean	884.35	1647.88	1058.87		
	SD	439.58	911.85	658.38	-4.641	0.0001*
Serum bilirubin μmol/l	Mean	6.43	4.08	5.90		
	SD	7.32	6.33	7.13	1.1596	0.2502
SGOT U/l	Mean	86.69	135.00	97.73		
	SD	58.09	154.05	90.38	-1.914	0.0598
SGPT U/l	Mean	45.17	282.44	99.40		
	SD	22.11	839.67	404.62	-2.111	0.0384*

Continued.

Variables	Summary	Present varices	Absent varices	Total	t-value	P value
Total protein (g/dl)	Mean	6.53	6.64	6.55		
	SD	1.08	0.92	1.04	-0.361	0.7187
Serum albumin (g/l)	Mean	2.25	2.88	2.39		
	SD	0.65	0.69	0.71	-3.374	0.0012*
INR	Mean	1.73	1.51	1.68		
	SD	0.53	0.55	0.54	1.508	0.1360

\*p&lt;0.05

**Table 3: Correlation of platelet count, spleen bipolar diameter and platelet count/spleen diameter ratio with grades of varices.**

Variables	Normal	%	Grade I	%	Grade II	%	Grade III	%	Total
<b>Platelet counts</b>									
≤50000	1	25.00	2	50.00	1	25.00	0	0.00	4
50000-100000	1	4.76	4	19.05	11	52.38	5	23.81	21
100001-150000	4	20.00	8	40.00	6	30.00	2	10.00	20
150001-200000	2	18.18	1	9.09	3	27.27	5	45.45	11
>200000	8	57.14	2	14.29	1	7.14	3	21.43	14
<b>Spleen bipolar diameter</b>									
≤125	8	50.00	2	12.50	4	25.00	2	12.50	16
126-150	7	19.44	12	33.33	9	25.00	8	22.22	36
>150	1	5.56	3	16.67	9	50.00	5	27.78	18
<b>PLT/spleen diameter ratio</b>									
<500	1	11.11	3	33.33	3	33.33	2	22.22	9
501-1000	4	12.50	11	34.38	12	37.50	5	15.63	32
1001-2000	5	22.73	3	13.64	7	31.82	7	31.82	22
>2000	6	85.71	0	0.00	0	0.00	1	14.29	7
Total	16	22.86	17	24.29	22	31.43	15	21.43	70

Lastly, we categorized our patients into two group based on a cut-off value of 909 for platelet count/spleen diameter ratio. And same was applied for evidence of esophageal varices. And based on this findings, we calculated sensitivity and specificity.

**Table 4: Comparison between platelet count/spleen diameter ratio with presence of varices.**

Varices	PC/SD ratio		Total
	<909	>909	
Absent	5	11	16
Present	36	18	54
Total	41	29	70

Sensitivity 77%, specificity 79%, positive predictive value 88%, negative predictive value 62%

## DISCUSSION

In the present study of 70 patients with cirrhosis of liver of various aetiologies were studied for correlation of platelet count, spleen bipolar diameter and platelet count/spleen diameter ratio for diagnosis of esophageal varices.

In our study the patient age ranged from 26-70 years, the maximum number of patients that is 41 (58.57%) were in the age group of 31-50 years, followed by 25 (35.71%)

ranging from 51-70 years. This is almost similar to study done by Cherian et al and Sarangapani et al.<sup>13,14</sup>

Taking gender into consideration we observed in our study that males 64 (91.43%) were more compared to females 6 (8.57%), with male to female ratio of 12:1. This similar was studied by Sarangapani et al.<sup>13</sup>

In our study population the majority of the patients presented with abdominal distention and pedal oedema, constituting about 54 (77.14%) patients. Other common symptoms noted were jaundice 49 (70%) and abdominal pain 26 (37.14%) patients. To the best of our knowledge when we tried to search for various studies to compare clinical presentation the information is lacking.

On comparing clinical observation, we found splenomegaly in 63 (90%) patients on either clinical or ultrasound examination followed by clinical signs like ascites in 50 (71.43%), icterus in 52 (74.29%), signs of chronic liver cell failure in 14 (20%) and hepatic encephalopathy in 4 (5.71%) patients. In our study the correlation between ascites and presence of varices was observed. Similar observation was noted in the study by Schwarzenberger et al and in study by Barrera et al.<sup>15</sup>

However, study by Cherian et al and Sarangapani et al did

not find significant difference between ascites and presence of varices.<sup>13,14</sup>

We made an attempt to find out the aetiologies of cirrhosis of liver, we found 63 (90%) patients had cause of alcoholism, 7 (10%) were due to hepatotropic virus infection of which 4 (5.71%) were HbsAg related and 3 (4.28%) HCV related. This is almost similar to study by Cherian et al and Baig et al.<sup>12,14</sup>

However, this is in sharp contrast to study by Schwarzenberger et al and Sarangapani et al who observed hepatotropic viruses as main cause of cirrhosis of liver in this study as compared to alcohol as cause.<sup>13,16</sup>

Among 70 patients of cirrhosis studied 54 (77.14%) had esophageal varices on upper gastrointestinal endoscopy. Varices were graded in 3 grades according to severity. In majority of patients had grade 1 (30%) and 2 (38.57%) esophageal varices. Similar observation were studied by Cherian et al, Sarngapani et al, Baig et al, Abu El Makeram, Taferal et al and Barrera et al.<sup>12-15,17,18</sup> Our study showed similar proportion of varices as many of studies mentioned earlier.

In our study considering platelet count, we observed that 25 (35.71%) patients had platelet ranging below 100000, 31 (44.28%) patients belonged to range from 100000–200000 and 14 (20%) had platelet count above 200000.

Studies by other authors has shown platelet cutoffs from 68000-160000 have sensitivities and specificities ranging from 71-90% and from 36-73% respectively.

When we attempted to correlate platelet count with esophageal varices, it was observed that there was significant correlation between platelet count and evidence of esophageal varices. P value being statistically significant ( $p < 0.0001$ ) (i.e. those who had low platelet count has significant evidence of esophageal varices). Studies by Giannini et al, Sarangapani et al, Cherian et al, Barrera et al, Schwarzenberger, Baig et al, Abu El Makeram, Tafarel et al and Sharma et al had similar observation.<sup>8,10,12-18</sup>

This is in sharp contrast to study by Abbasi et al in which there was inverse correlation between platelet count with varices ( $r = 0.321$ ,  $p < 0.001$ ).

In present study, we took spleen bipolar diameter into consideration, we observed that 36 (51.43%) patients having spleen diameter ranging from 126-150 mm and 18 (25.71%) had diameter more than 150 mm.

Similarly, when we made an attempt to correlate spleen diameter with varices, we found significant correlation between splenic bipolar diameter and esophageal varices p value being statistically significant ( $p < 0.0022$ ).

Similar observations were drawn by Giannini et al,

Sarangapani et al, Cherian et al, Barrera et al, Schwarzenberger et al, Baig et al, Abu El Makeram and Tafarel et al in this study.<sup>8,12-17</sup>

Platelet count/spleen diameter ratio has been shown by several studies to correlate well with the presence of varices. Several studies have been performed to validate this new parameter.

When attempt was made to correlate between platelet count/spleen diameter ratio with varices, we observed that 41 (58.57%) patients had ratio below 1000 and 29 (41.43%) had ratio more than 1000. Many authors had observed the similar results.

Child Pugh classification was taken into consideration, we observed 40 (57.14%) patients were in grade A child Pugh class, 23 (32.86%) in class B and only 7 (10%) in child Pugh class C.

When same was compared with the presence of varices, we observed significant correlation of presence of varices with child Pugh classification (there is significant varices in class A and class B as compared to class C). Similar observation were drawn by Cherian et al and Abu El Makeram et al.<sup>14,17</sup>

In our study, we also correlated platelet count, spleen diameter and PC/SD ratio with grades of varices, we found that patients with platelet count ranging from 50000-100000 had more varying grades of varices. Similarly, patients with spleen bipolar diameter ranging from 126-150 had more varices and patients having PC/SD ratio less than 1000 had more varying grades of esophageal varices. Similar study was done by Schwarzenberger et al and Mattos et al.<sup>16,19</sup>

When an attempt was made to correlate ascites with grades of varices, we found that majority of patients with ascites had varying degree of esophageal varices as compared to those without ascites. Similar finding was noted in the study by Schwarzenberger et al and in study by Barrera et al.<sup>15,16</sup> This was statistically significant in our study.

Lastly, considering the PC/SD ratio cut off 909 as suggested by Giannini et al (which yielded 100% sensitivity and 93% specificity).<sup>8</sup>

In our study, we categorized our patients into two groups based on this cutoff value of 909 for platelet count/spleen diameter ratio. And same was applied for evidence of esophageal varices. And based on this findings, we calculated sensitivity and specificity which yielded a sensitivity of 77% and specificity of 79%.

Other studies which are carried out with the same ratio of 909 were compared and following observation were made.

Baig et al showed cut off of 909 with sensitivity 80% and specificity of 89%.<sup>12</sup> Giannini et al showed cut off of 909



with sensitivity 100% and specificity 93%.<sup>8</sup> Sarangapani et al showed cut off of 909 with sensitivity 88.5% and specificity 83%.<sup>13</sup>

### Limitations

To the best of our knowledge, there are no randomized-controlled trials in the published literature to find out efficacy of the PC/SD ratio and its relevance in these patients.

These non-invasive and cost effective parameters can overcome the lack of availability of endoscopy units and expertise in peripheral centers. Owing to small sample size (70 patients), a large sample size may be required to overcome these limitations.

### CONCLUSION

In patients with cirrhosis, aetiology was more attributable to alcoholism as compared to HBV and HCV. There is strong evidence of esophageal varices with thrombocytopenia, splenomegaly and low platelet count/spleen diameter ratio. Comparison with other lab parameters like SGPT, serum albumin has statistical significance. We did not find significant correlation with gender and clinical presentation. There is also strong correlation between platelet count, splenic diameter and platelet count/spleen diameter ratio with various grades of esophageal varices. With this study, use of the platelet count/spleen diameter ratio may be proposed as a safe and reproducible as it is easily available in any hospital setup including peripheral centers.

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