

# Platelet Count/Spleen Diameter Ratio in Prediction of Esophageal Varices in Patients with Liver Cirrhosis

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## ABSTRACT

**Background:** Esophageal varices and variceal hemorrhage are common complications of Liver cirrhosis leading to morbidity and mortality. Upper gastrointestinal endoscopy is the gold standard for demonstration of gastro-esophageal varices. Endoscopy facilities are not available in rural areas however the burden of liver cirrhosis is high. Early prediction of esophageal varices through non-invasive means may be life saving. Therefore this study was designed to identify the relationship between platelet count/splenic bipolar diameter ratio for prediction of presence of esophageal varices. **Methodology:** The study was a observational cross sectional study consisting of 53 patients of liver cirrhosis admitted at Bir Hospital, Kathmandu between July 2019 to December 2019. Upper gastrointestinal endoscopy was done to confirm varices. A platelet count/spleen diameter ratio cut-off value of 909 was evaluated for the diagnosis of esophageal varices. Statistical analysis was done using Statistical Package for the Social Sciences 20. **Results:** Esophageal varices were present in 44(83%) of cases. Small and large varices were present in 21(39.6%) and 23(43.4%) respectively. Platelet count to splenic diameter ratio with a cut off value of 909 had sensitivity of 54.5%, specificity of 88.9%, positive predictive value of 96% and negative predictive value of 22.8% ( $p=0.018$ ,  $CI=95\%$ ). **Conclusions:** Platelet count to spleen diameter ratio can be a good predictor of presence of esophageal varices in patient of liver cirrhosis in the resource poor settings.

**Key words:** Platelet count/spleen diameter ratio, liver cirrhosis, esophageal varices

## 1. INTRODUCTION

Portal hypertension is the principal complication of hepatic cirrhosis.[1] More than 80% of patients with cirrhosis will develop esophageal varices (EVs) at some point, and 30% of them have variceal bleeding.[2] 20%-30% of them die due to this bleeding within the first 4-6 weeks.[3] Guidelines recommend endoscopic screening at diagnosis of liver cirrhosis and repeat endoscopy following 2-3 year in patients without varices and at 1-2 year interval in patients with small varices.[4]

Platelet count/Spleen diameter ratio (PC/SD) with cut off value 909 proposed by Giannini et al, is one of the best non-invasive predictor of EVs.[4] Since endoscopy is a invasive procedure requiring expertise and is not readily available throughout the country, objective of our study was to validate the PC/SD ratio as a predictor of presence and absence of esophageal varices in patients with liver cirrhosis.

## 2. METHODOLOGY

The study was a observational cross sectional study conducted from July 2019- Dec 2019 in Department of Medicine of National Academy of Medical Sciences (NAMS), Bir Hospital, Kathmandu, Nepal. Ethical clearance was taken from the Institutional Review of NAMS, Reg. no. 876/ 076/77. The sample size was calculated by

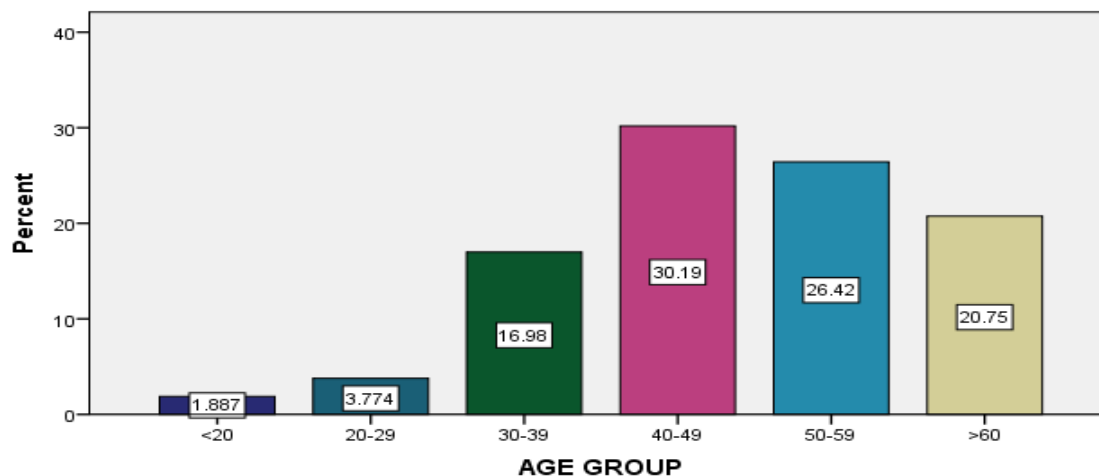
formula:  $n = z^2 p (1-p) / d^2$ . Where proportion (p) = 0.27 which is the overall prevalence of cirrhosis.[5] Confidence level = 95% (z=1.645), Precision (d) = 0.10 which is the maximum tolerable error,  $n = (1.645)^2 0.27 (1-0.27) / (0.1)^2 = 53.34$ . Hence sample size needed for the study was 53 patients. Convenience sampling technique was applied. Patients admitted with diagnosis of liver cirrhosis were included in the study after obtaining informed consent. The patients who were excluded from the study were those presenting with variceal bleed or past history of bleeding, undergone band ligation, hepatocellular carcinoma, cirrhosis with portal vein thrombosis, hepatic encephalopathy grade III or IV and patient refusing for consent.

Data were collected using a structured Proforma covering the relevant details. Lab investigations including Platelet count, Liver function tests, HIV, HBsAg and anti HCV were done. Ultrasonogram was used for spleen diameter measurement. UGI Endoscopy was done for confirmation of varices. Statistical analysis was performed using SPSS version 20. Each continuous parameter between the two groups, patient with varices and patient without varices, were analyzed with two tailed Chi square test. Means between various esophageal varices groups were analyzed by one way Anova test. Best cut off value of platelet count to splenic diameter ratio for prediction of presence of esophageal varices was determined by using ROC curve as 909. Sensitivity, specificity, positive predictive value and negative predictive value were determined for platelet count to splenic diameter cut off of 909. P-value of less than 0.05 was considered significant. Multivariate analysis of variables with significant correlation was carried out. Ninety five percent confidence intervals (CIs) were used in all analyses.

### 3. RESULTS

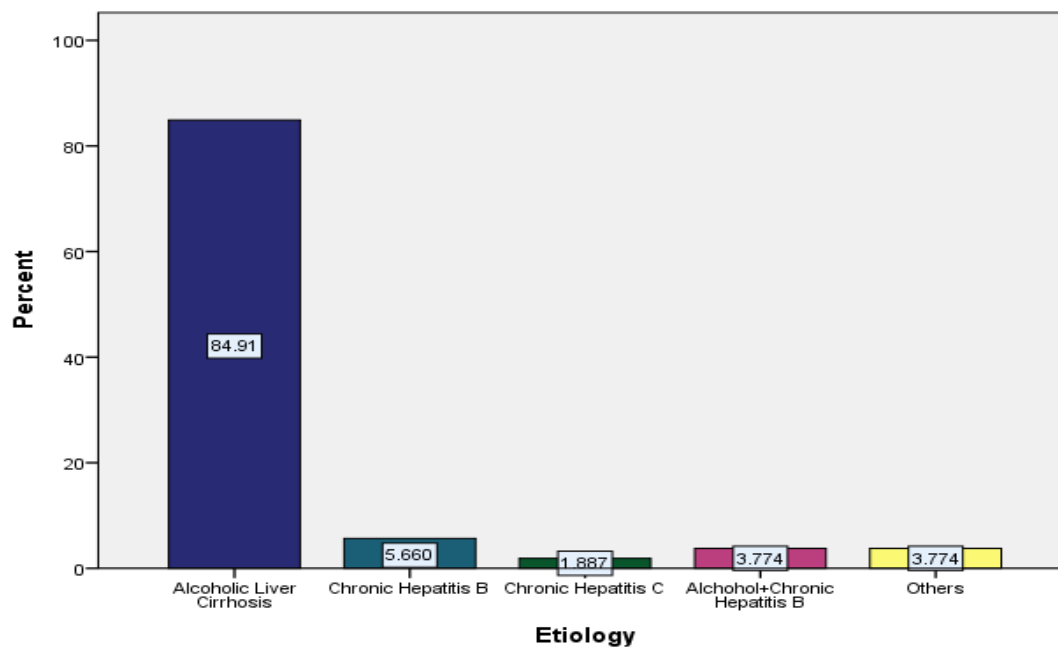
A total of 53 patients of liver cirrhosis were included in the study. Among them 42 (79.25%) patients were male and 11(20.75%) were females. In this study, highest number of patients were found to be 16 (30.19%) in 40-49 age group followed by 14 (26.42) in 50-59 age group, 11 (20.75%) in age group 60 above, 9 (16.96%) in 30-39 age group, 2 (3.77%) in 20-29 age group and 1(1.88%) patient in age group < 20.

**Fig-1: Age Distribution of Patients**



Alcoholic liver cirrhosis was the most common cause of liver cirrhosis 45(84.91%) followed by Chronic Hepatitis B in 3(5.66%) cases, Chronic Hepatitis B along with Alcoholic liver disease in 2(3.77%) cases while 1(1.87) case of Chronic Hepatitis C and 2 being others.

**Fig-2: Etiology of Liver Cirrhosis**



**Table 1: Symptoms and signs observed in enrolled patients**

Symptoms	Present		Absent	
	Frequency	Percentage	Frequency	Percentage
Abdominal Distention	45	84.9	8	15.1
Yellowish Discoloration	22	41.5	31	58.5
Decreased Urine Output	10	18.9	43	81.1
Altered Sensorium	15	28.3	38	71.7
Other	17	32.1	36	67.9
Signs	Present		Absent	
	Frequency	Percentage	Frequency	Percentage
Spider Angioma	29	54.7	24	45.3
Palmer Erythema	16	30.2	37	69.8

Breast Atrophy	2	3.8	51	96.2
Testicular Atrophy	4	7.5	49	92.5
Gynaecomastia	8	15.1	45	84.9

In this study, abdominal distension was present in 45(85%) of the patients. The other common presentations were jaundice in 22 patients (41.5%), altered sensorium in 15 patients (28.3%), decreased urine output in 10 patients (19%) and other symptoms (fever, abdominal pain, etc) in 17 patients (32%). Signs commonly observed were spider nevi in 29 patients (54.7%), palmar erythema in 16 patients (30.2%), breast atrophy in 2 patients (3.8%), gynaecomastia in 8 patients (15.1%), testicular atrophy in 4 patients (7.5%).

**Table 2: Correlation of Esophageal varices with mean platelet count, splenic diameter and mean platelet count to spleen diameter ratio**

<b>Correlation of Esophageal varices with mean platelet count</b>				
<b>Size of Varices</b>	<b>Mean platelet count (/mm<sup>3</sup>)</b>	<b>Number of patients</b>	<b>Std. Deviation</b>	<b>P value</b>
Small	133243	21	68408	0.001
Large	99957	23	60849	
Absent	224889	9	120106	
Total	134360	53	86764	
<b>Correlation of Esophageal varices with mean splenic bipolar diameter</b>				
<b>Size of Varices</b>	<b>Mean Splenic Bipolar diameter in mm</b>	<b>Number of patients</b>	<b>Std. Deviation</b>	<b>P-value</b>
Small	120.7	21	20.6	0.605
Large	124.7	23	14.9	
Absent	127.4	9	19.1	
Total	123.6	53	17.9	
<b>Correlation of Esophageal varices with mean platelet count to splenic diameter ratio</b>				
<b>Size of Varices</b>	<b>Mean</b>	<b>Number of patient</b>	<b>Std. Deviation</b>	<b>P-value</b>
Small	1157.5	21	654.6	

Large	807.3	23	470.8	0.002
Absent	1810.2	9	1108.9	
Total	1116.3	53	757.6	

This table shows that patients with large esophageal varices have low platelet count than the patient without varices. Patients with large esophageal varices have mean platelet count of  $99957 /\text{mm}^3$  with standard deviation of  $60849/\text{mm}^3$  as compared to the mean platelet count of  $224889/\text{mm}^3$  with standard deviation of  $120106/\text{mm}^3$  in patients without varices and is statistically significant.

Table 2 also shows that correlation between esophageal varices and mean splenic diameter is not significantly associated whereas mean platelet count to splenic diameter (PC/SD) ratio was found to be significantly associated with presence of esophageal varices ( $p= 0.002$ ).

**Fig- 3: Receiver operating characteristic curve: Platelet count to Splenic diameter ratio**

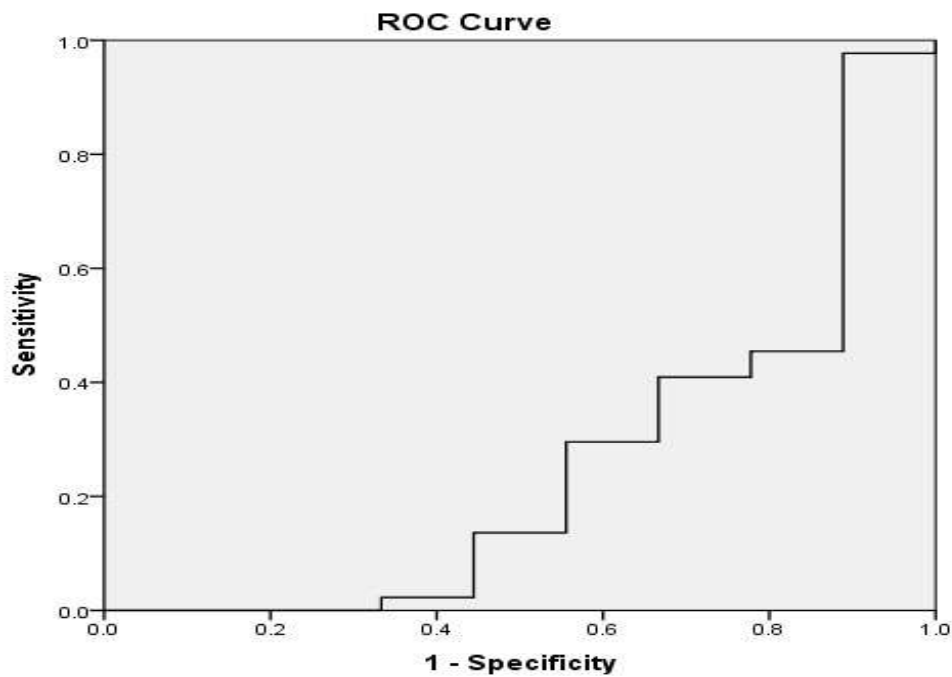


Figure 3. Receiver operating characteristic curve: platelet count to splenic diameter ratio: Area under curve: 0.255 [95% CI]. Best cut off value of platelet count to splenic diameter ratio for predicting the presence of esophageal varices was determined as 909.

**Table 3: Prediction of Esophageal varices from PC/SD cut off value of 909**

PC/SD CUT OFF VALUE	Varices present	Varices absent	Total	P value
<909	24(54.5%)	1 (11.1%)	25 (47.2%)	0.018
>909	20 (45.5%)	8 (88.9%)	28 (52.8%)	
Total	44 (100%)	9 (100%)	53 (100%)	

This table shows that using the cut off value of 909 for platelet count/splenic diameter ratio (PC/SD) has sensitivity of 54.5%, specificity of 88.9%, positive predictive value of 96% and negative predictive value of 22.8% ( $p=0.018$ , CI=95%) for the prediction of esophageal varices which is statistically significant.

#### 4. DISCUSSION

Cirrhosis is the end stage of every chronic liver disease characterized by fibrosis and replacement of normal liver architectures into structurally abnormal nodules which interferes with liver function and results in portal hypertension.[6] One of the major complications of cirrhosis include development of esophageal varices and variceal hemorrhage.[7] Variceal hemorrhage is associated with high mortality rates. In the past, the mortality rate of a single variceal hemorrhage was 30 percent, and only one-third of patients survived for one year.[8,9] According to Child-Turcotte-Pugh (CTP) class A, B, C the one year survival is 100%, 81%, 45% and two year survival is 85%, 57%, 35% respectively.[10,11] Esophageal varices develop when the HVPG exceeds 12mmHg. The annual risk of development of esophageal varices is approximately 5%. However, only a one third of all patients with esophageal varices will bleed.[12] Variceal hemorrhage remains the main cause of hospitalization.[13]

This study showed that patients with large esophageal varices have low platelet count than the patient without varices. Patients with large esophageal varices have mean platelet count of  $99957 /\text{mm}^3$  with standard deviation of  $60849/\text{mm}^3$  as compared to the mean platelet count of  $224889/\text{mm}^3$  with standard deviation of  $120106/\text{mm}^3$  in patients without varices. This was statistically significant ( $p=0.001$ , CI= 95%). This finding was consistent with finding of a prospective study conducted at Kilpauk medical college Chennai. The independent predictor for the presence of large varices were platelet count  $<150000/\text{mm}^3$ . [14] A cross sectional study conducted at Cipto Mangunkusumo Hospital, Indonesia among cirrhotic patients where mean platelet count in the group of patients with varices was  $101000\pm 52000/\text{mm}^3$ , while that of the group without esophageal varices was  $161000\pm 62000/\text{mm}^3$ , with  $\pm 60000/\text{mm}^3$  difference in mean value.[15]

Moderate thrombocytopenia is a frequent finding in cirrhosis of liver and well tolerated in most instances. The pathophysiology of thrombocytopenia in liver disease has been associated with hypersplenism, where portal hypertension was thought to cause pooling and sequestration of all corpuscular elements of the blood, predominantly thrombocytes in the enlarged spleen. Thrombopoietin (TPO) production in human is dependent on functional liver cell mass and is reduced when liver cell mass is severely damaged. This leads to reduced thrombopoiesis in the bone marrow and consequently to thrombocytopenia in advanced-stage liver disease.[16,17] In alcohol related liver disease, ethanol may directly suppress platelet production and folate deficiency, which further impairs platelet production.[18]

In this study, mean platelet count to splenic diameter (PC/SD) ratio was found to be associated with presence of esophageal varices. The patients without esophageal varices had mean PC/SD ratio of 1810.2 with standard deviation of 1108.9 whereas patients with small and large varices have mean PC/SD of 1157.5 and 807.3 with standard deviation of 654.6 and 470.8 respectively. This finding was statistically significant to predict the presence of esophageal varices ( $p= 0.002$ , CI=95%). The result of this study indicated that the PC/SD ratio with an area under receiver operating characteristic curve of [95% CI (0.255-1.00)] could be valuable predictor of

esophageal varices in liver cirrhosis patients. The ideal reference point under the curve was 1.00. In this study a cut off value of 909 was determined using ROC curve and analyzing the various coordinate points to maximize the difference of sensitivity value and 1-specificity value. This cut off had the sensitivity of 54.5%, specificity of 88.9%, positive predictive value of 96% and negative predictive value of 22.8% ( $p=0.018$ ,  $CI=95\%$ ) for the prediction of esophageal varices. This finding was supported by a study conducted in patients from ambulatory care clinic of Brazilian hospital. They used a cut off of 909 for the platelet count / spleen diameter ratio, as previously published. The platelet count/spleen diameter ratio had sensitivity of 77.5%, positive predictive value of 79.5% and negative predictive value of 42.6% and accuracy of 68.9% ( $p<0.05$ )[19] In an analytical study conducted at Hospital Civil de Guadalajara “Fray Antonio Alcalde” in Mexican patients with hepatic cirrhosis, showed platelet count/spleen diameter ratio for prediction of esophageal varices using a cut off value of  $\leq 884.3$ , had 84% sensitivity, 70% specificity, and positive and negative predictive values of 94% and 40% respectively. These findings are close to the findings of this study.[20]

In a prospective study conducted at Kasturawa medical college, India showed that the platelet count to spleen diameter ratio had the highest accuracy among platelet count, spleen diameter and PC/SD ratio. As the liver disease advances, platelet count decreases and spleen size increases, as a result PC/SD ratio also gradually becomes less. This study shows negative correlation of PC/SD ratio with presence of esophageal varices with regression coefficient ( $r = -0.707$ ). The possible relationships between splenomegaly and portal hypertension have been analyzed in patients with cirrhosis. Splenomegaly is not only caused by portal congestion, but it is mainly due to tissue hyperplasia and fibrosis. The increase in spleen size is followed by an increase in splenic blood flow, which participates in portal hypertension actively congesting the portal system.[21]

## 5. CONCLUSIONS

Upper Gastro Intestinal endoscopy is the gold standard for diagnosis of esophageal varices. However, the platelet count to spleen diameter ratio can be a useful non-invasive method for identifying patients with esophageal varices especially when resources are limited and endoscopy facilities are not available. The use of PC/SD ratio and other non-invasive markers will definitely reduce unnecessary endoscopies for screening purposes and lower the medical expenditures. Those cirrhotic patients who have high risk of esophageal varices (low PC/SD ratio  $< 909$ ) can be referred to higher centers for further management.

## 6. ACKNOWLEDGEMENT

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## 7. Conflicts of interest: None

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