

## Platelet Count/Spleen Diameter Ratio as a Predictor of Esophageal Varices in Patients with Liver Cirrhosis

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### ABSTRACT

**Introduction:** Upper gastro-intestinal endoscopy still remains the gold standard for screening of patients suspected to have esophageal varices but not without limitations. So, this study was conducted to access the diagnostic validity and correlation between non-invasive parameters like platelet count, spleen diameter and their ratio with esophageal varices (EV) in patients with liver cirrhosis. **Methods:** A hospital based descriptive cross-sectional study was carried out in Liver unit of National Academy of Medical Sciences, Bir Hospital, from October 2016 to September 2017. Complete blood count, liver function tests, liver ultrasound and UGI endoscopy were done for all patients included in the study to detect esophageal varices and the platelet count/spleen diameter (PC/SD) ratio was calculated and analyzed to determine whether it can predict the presence of esophageal varices or not. **Results:** Total patients of liver cirrhosis studied after exclusion were 191. EV was present in 125 patients (65.4%). The platelet count/spleen diameter ratio using a cutoff value of  $\leq 909$  to detect EV independent of the grade had 93% sensitivity and 100% specificity and positive and negative predictive values of 100% and 91% respectively. **Conclusions:** PC/SD ratio now can be used as a predictor of presence of esophageal varices in liver cirrhosis.

**Key words:** Esophageal varices, liver cirrhosis, non-invasive markers, portal hypertension, upper gastro-intestinal

### INTRODUCTION

Cirrhosis is the end stage of every chronic liver disease characterized by fibrosis and the replacement of normal liver architectures into structurally abnormal nodules which interferes with liver function and results in portal hypertension. Portal hypertension<sup>1</sup> as a consequence of cirrhosis leads to the formation of esophageal varices (EV) and bleeding EV is one of the major and often lethal complication<sup>2</sup>.

Upper Gastro-intestinal (UGI) endoscopy still remains the gold standard for screening and diagnosing EV, but it has its own limitation like, it is invasive procedure, expensive and needs expertise too, which may be not available in all hospital settings at all times. Therefore, the present study was undertaken to find the correlation between platelet count, spleen diameter and its ratio with presence of esophageal varices in patients with liver cirrhosis which was simple, quick and reproducible so that unnecessary UGI endoscopy can be limited.

### MATERIAL AND METHODS

This hospital based descriptive cross-sectional study was

carried out in Liver unit of National Academy of Medical Sciences, Bir Hospital, Nepal from October 2016 to September 2017. Patients attending Liver unit on outdoor basis and or admitted in ward were enrolled in the study who fulfilled the criteria of liver cirrhosis, namely, one clinical sign of hepatocellular failure and one of portal hypertension along with at least three ultrasonography (USG) findings suggestive of cirrhosis of liver<sup>3</sup>. The following cases with cirrhosis with portal hypertension were excluded from the study: Those patients presenting with variceal bleed or past history of bleeding, patient who had undergone band ligation, patient with hepatocellular carcinoma, cirrhosis with portal vein thrombosis, patient in hepatic encephalopathy grade III or IV and patient refusing for consent.

A detailed history as well as clinical examination was done. Complete blood count was done by automated cell counter, Sysmex 550. Peripheral blood smear was done to rule any other hematological cause of thrombocytopenia. Liver function test was done by Erba XL 300, automated analyzer. Prothrombin time and international normalized ratio was also calculated. All the blood investigations were duly verified by pathologist. All patients underwent 2D ultrasound study of hepatobiliary system for liver architecture and nodularity, spleen bipolar diameter, presence of ascites by Sonosite Micromax doppler ultrasound. UGI endoscopy for all patients was done after overnight fasting with flexible gastroduodenal endoscope (FUJINON). EV were classified as small if varices flattened with insufflations or minimally protrude into the esophageal lumen and large if they protruded into the esophageal lumen and touch each other (presence of confluence), or that filled at least 50% of the esophageal lumen<sup>4</sup>. Child-Turcotte-Pugh (CTP) score was calculated to assess the severity of liver disease<sup>5</sup>. The

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Platelet count/Spleen diameter ratio (PC/SD) cut off value 909, proposed by Giannini et al, is among the best non-invasive predictor of EVs that has been studied till date was taken for reference<sup>6</sup>. Ethical approval was taken from Institutional Review Board (IRB), NAMS and written informed consent was taken from each patient.

Sample size was calculated by following formula:

$$n = 4 \left[ \frac{z_{\alpha} + z_{\beta}}{2} \right]^2 \frac{\ln \frac{(1+\rho)}{(1-\rho)}}{\ln \frac{(1+\rho)}{(1-\rho)}} + 3$$

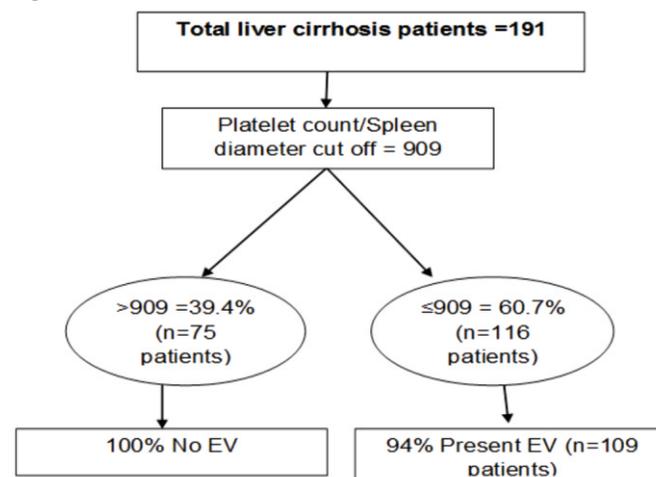
Assuming small effect size of 0.2 at 5% significance level with  $z_{\alpha}=1.96$ , with 80% power with  $z_{\beta}=0.84$ , using formula minimum sample size was 191. Data collected in structured proforma were entered in Microsoft Excel 2007 and statistical analysis was done with SPSS 20 software. Chi-Square test was used for comparisons between categorical variables. Values were expressed as mean±SD, a 95% confidence interval was taken and P values of <0.05 was considered to be statistically significant.

**RESULTS**

Total patients enrolled in the study were 350, among them 159 were excluded and finally 191 patients were studied. During

UGI endoscopy, EV was present in 125 patients (65.4%). Significant relation between CTP class and presence of varices was observed (Chi sq. test statistic=84.808; P=<0.001). Varices were present in majority of cases with CTP class C (Table I).

Platelet count and spleen diameter and their ratio (PC/SD) were calculated as a non-invasive tool for predictor of EV. Significant relation was observed as shown in table II.



**Figure 1: Flow chart showing absence of EV in 100% cases with PC/SD ratio > 909**

CTP Class	NEV	EV	Total	Chi-Square	P value
A	4	6	10	84.808	<0.001
B	40	57	97		
C	22	62	84		
Total	66	125	191		

NEV= No Esophageal varices, EV= Esophageal varices

**Table I: Relation between CTP classes and EV**

Variable	Mean	SD	EV	P value
Platelet (n/mm <sup>3</sup> )	83660.34	31066.45	Yes	<0.0001
	230528.00	210465.76	No	
Spleen size (mm)	143.66	10.85	Yes	<0.0001
	131.19	16.676	No	
PC/SD ratio	579	201	Yes	<0.0001
	1817	1792	No	

EV= Esophageal varices

**Table II: Relationship between Platelet count and Spleen diameter and PC/SD ratio with EV**

PC/SD Ratio Cut off value	Sensitivity	Specificity	Positive predictive value	Negative predictive value
≤ 909	93%	100%	100%	91%

**Table III: PC/SD ratio ≤ 909 have 93% sensitivity and 100% specificity having EV with PPV 100% and NPV 91% as shown below**

## DISCUSSION

Varices usually develop in cirrhosis when portal pressure, measured as hepatic venous pressure gradient (HVPG) reached up to 10-12 mmHg<sup>1</sup>. Once varices develop, rate of enlargement from small to large is at a rate of 5–12% per year and bleed at a rate of 5–15% per year<sup>7</sup>. Early diagnosis of varices before the first bleed is essential because the risk of variceal hemorrhage can be reduced from 50% to about 15% for large esophageal varices if timely primary prophylaxis initiated timely<sup>8</sup>. UGI endoscopy remains the gold standard for screening, but this test is not without its own limitations. To overcome this problem some non-invasive parameters have been developed like platelet count, spleen size and ratio PC/SD which are simple, quick, reproducible, and cost effective too.

In our study, majority of patients with EV were in CTP class C ( $P < 0.0001$ ). Garcia-Tsao et al, also reported EV were more common in CTP class C (85%) as compared to class A (40%)<sup>1</sup>. As liver disease severity score reflected by CTP class, higher the score, more the disease severity and thus more the incidence of EV.

In this study, mean platelet count of  $83660.34 \pm 31066.45/\text{mm}^3$  was associated with presence of EV and with no EV group it was  $230528 \pm 210465.76/\text{mm}^3$  ( $P < 0.0001$ ). Chalasani et al, in their study also reported low platelet count ( $< 88,000/\text{mm}^3$ ) as an independent predictor of EV<sup>9</sup>. Thomopoulos et al, observed platelet count of  $< 118,000/\text{mm}^3$  as a predictor for presence of EV with sensitivity of 95% and specificity of 73%<sup>10</sup>.

In our study showed that average spleen size in patients without EV was  $131.19 \pm 16.67$  mm and with varices was  $143.66 \pm 10.85$  mm ( $P < 0.0001$ ). Thomopoulos et al, also reported splenomegaly ( $> 135$  mm) as a predictor of EV<sup>10</sup>. In the study by Agha et al, the mean spleen diameter of EV group was 147 mm and no EV group was 109 mm<sup>11</sup>. Splenomegaly in cirrhosis is mainly related to development of portal hypertension as a consequence of cirrhosis.

In our study PC/SD ratio  $579 \pm 201$  was associated with EV and ratio of  $1817 \pm 1792$  was not associated with EV which is also statistically significant ( $P < 0.0001$ ). Compare to Giannini et al, platelet count/spleen diameter ratio 1638 (545–3500) was not associated with EV and 533 (77–909) was associated with EV ( $P < 0.0001$ ) with cut off value of 909 in their study with sensitivity of 100% and specificity of 93% and positive predictive value of 96% and negative predictive value of 100<sup>6</sup>. Comparable results were obtained in our study too with sensitivity of 93% and specificity of 100% and positive and negative predictive value of 100% and 91% respectively. Tiwari et al reported the sensitivity and specificity keeping the PC/SD ratio cut-off 909, the values obtained were, sensitivity and specificity of 81.8% and 100%, respectively, the positive and negative predictive values for PC/SD ratio were 100% and

73.91%, respectively which were comparable to our study too<sup>12</sup>. With similar cutoff value of PC/SD Chawla et al, also demonstrate a diagnostic accuracy of cut-off 909 for PC/SD ratio as a predictor of EV<sup>13</sup>. González-Ojeda A et al, demonstrate PC/SD ratio  $824.56 \pm 412.27$  was related to EV and ratio of  $1390 \pm 905.49$  was not related to presence of EV (0.018)<sup>14</sup>.

Limitation of our study was measurement of portal pressure as hepatic venous pressure gradient (HVPG) was not done in our study. Diagnostic accuracy of PC/SD ratio as a predictor of EV may be further validated by multicenter study.

## CONCLUSIONS.

The PC/SD ratio can be a useful noninvasive predictor for esophageal varices in patients with liver cirrhosis and thereby may help reducing the number of unnecessary endoscopies.

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