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Original Article

Platelet Count/Spleen Diameter Ratio: A Non-Invasive Predictor of Esophageal Varices in Patients with Cirrhosis

Aleem Riaz Qureshi[1], Sundus Aleem[2], Akram Bajwa[3], Riaz Hussain[4], Nandlal Seerani[5], Mohsin Ali[6], Syed Imtiaz Ali[7]

ABSTRACT

Objective: To determine the diagnostic value of platelets count/spleen ratio for detection of esophageal varices in cirrhosis patients.

Methodology: The research was conducted from February 2023 to March 2024 at Liaquat University of Medical & Health Sciences (LUMHS). The sample of 153 cirrhotic individuals of both genders aged 18 to 75 years were incorporated into the research by using non-probability, purposive sampling. Platelet counts, and spleen diameters were measured to calculate the PC/SD ratio. Patients underwent endoscopy to verify the existence of EV. Analysis of data was conducted using SPSS 26.0. The receiver operating characteristic (ROC) curve was performed to evaluate the prediction performance of the PC/SD ratio, with the area under the curve (AUC) computed for sensitivity and specificity.

Results: The mean ± standard deviation of age of the 153 participants was noted as 53.63±9.02 years. Among them 103 (67.3%) were male and 50 (32.7%) were female. Patients with EV showed significantly reduced PC/SD ratio ($p < 0.001$). A cutoff of ≥412.50 demonstrated a sensitivity of 95.1% and a specificity of 79.2%, leading to an AUC of 0.737, indicating moderate accuracy. At this cutoff, the positive likelihood ratio was 4.57. Lower cutoff values increased sensitivity but reduced specificity.

Conclusion: The platelet count-to-spleen diameter (PC/SD) ratio is an easily obtainable, non-invasive predictor of esophageal varices (EV) in liver cirrhosis. These results imply that the PC/SD ratio could be utilized in the routine screening to avoid invasive endoscopy and add an economic value in terms of reducing the cost of healthcare. Additional extensive research with a larger sample size across different study centres in Pakistan is necessary to validate the findings of the current study.

Keywords: Cirrhosis, Esophageal varices, ROC curve, Platelet count, Spleen

INTRODUCTION

Cirrhosis is a progressive liver disease frequently complicated by gastroesophageal varices (GEV) characterized by dilated veins within the esophagus and stomach. GEV develops in approximately 7-8% of cirrhotic patients annually, the transition from tiny to big varices occurs at an annual rate of 10-12%[1]. Variceal bleeding is a severe consequence affecting about 5% of patients per year and is linked with a six-week death rate of 15-25% [2,3].

To address this risk, several non-invasive methods have emerged for predicting GEV. These encompass liver stiffness measurement (LSM), spleen stiffness measurement, and the platelet count to spleen diameter ratio (PSDR)[4]. A systematic meta-analysis reported that endoscopy is the definitive standard for the identification of gastro-esophageal varices (GEV), it is an invasive, costly procedure requiring specialized expertise, making it unsuitable as a routine screening tool in all settings[5]. The Baveno VI consensus recommendations advise against endoscopy in individuals with liver stiffness below 20 kPa and platelet levels over 150 × 10^9/L, as their risk for varices requiring treatment is below 5%[6].

Different studies have investigated non-invasive metrics for GEV prediction, but none have achieved universal acceptance.

Corresponding Author
Aleem Riaz Qureshi
Email: draleemqureshi92@gmail.com

Affiliations:
Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro
Postgraduate Trainee at[1,2,3,5,6,7]
Associate Professor[4]

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Research by Yu et al. also supports PSDR's role as a potential predictor with the area under the curve (AUC) values of 0.907 [7]. Despite promising findings, the accuracy and utility of PSDR remain under-examined due to limited evidence, and no standardized non-invasive tool currently exists for GEV assessment.

Jamil Z, et al and Xu XD, et al stated the effectiveness of PSDR for predicting esophageal varices across different cirrhosis types indicating strong reliability[8,9]. The study by Rahmani et al. extended its application to pediatric patients, emphasizing its versatility[10]. Studies from Mahfuzzaman M, et al and Khadka D, et al found PSDR as a cost-effective tool in resource-limited settings[11,12]. Berger et al. highlighted its practical use where advanced diagnostics are inaccessible[13].

Kothari et al. found PSDR useful in identifying variceal bleeding risk in alcoholic cirrhosis[14] while Mossie et al. confirmed its high sensitivity and specificity[15]. Ozdil et al. linked lower PSDR values to larger varices[16]. Bhattarai et al. provided evidence for its role in risk stratification[17].

Esophageal varices (EV) are a severe complication of cirrhosis, associated with significant morbidity and mortality. While endoscopy remains the gold standard for EV detection, its invasive nature and high cost limit its routine use. Non-invasive markers like the platelet count-to-spleen diameter (PC/SD) ratio show promise as reliable alternatives. Despite encouraging results in earlier studies, there remains a lack of population-specific validation and cost-effectiveness analysis in resource-constrained settings. This study aims to evaluate the diagnostic accuracy of the PC/SD ratio in predicting EV among cirrhotic patients, addressing these critical gaps.

METHODOLOGY

The research was carried out in the Department of Gastroenterology at Liaquat University of Medical & Health

Sciences (LUMHS), Jamshoro, from February 2023 to March 2024. The sample of 153 patients was selected through non-probability, purposive sampling. The sample size was determined based on the area under the curve (0.907)[7], margin of error (d)=5%, and confidence interval (C.I) = 95% by using the statistical formula for sample size calculation i.e., $N = \frac{Z^2 \times V(AUC)}{d^2}$ The inclusion criteria included adult patients aged 18 to 70 years of either gender, with liver cirrhosis (characterized by diffuse hepatic fibrosis, nodular transformation of liver architecture, and ultrasonographic findings such as coarse liver echotexture, increased echogenicity, and irregular margins, with or without portal hypertension), a cirrhosis duration of at least six months, and symptoms of hematemesis (vomiting blood) or melena (black tarry stool). Patients with hemophilia, liver malignancies, prior liver surgery or local treatments, splenomegaly, or severe complications like hepatic encephalopathy or hepatorenal syndrome, as well as those taking immunosuppressive or platelet-affecting medications were excluded from the study. Informed written consent about the study was obtained from all the included patients. The same protocols were followed through all steps of data collection to ensure consistency throughout the study. Blood samples (5 cc) were collected by trained phlebotomists, suspected laboratory platelet counts were measured by the laboratory according to standard operating procedures for hematology that are regularly done in order to avoid variability. Spleen diameter was measured by certified radiologists by abdominal ultrasonography using calibrated equipment and standardized protocols. The PC/SD ratio was calculated by dividing the platelet count by the spleen diameter in millimeter, and the method was uniformly reported. Patients then underwent upper gastrointestinal endoscopy to verify the existence of EV which was identified based on established procedural guidelines, defined as visibly dilated submucosal veins in the lower one-third of the esophageal wall projecting into the lumen. The analysis of data was conducted using SPSS version 26.0. Descriptive statistics were used to report the demographic and baseline data of the patients. The receiver operating characteristic (ROC) curve was generated, and the area under the curve (AUC) was calculated, along with optimal cut-off settings for the sensitivity and specificity of the PC/SD ratio.

RESULTS

Table I represent the baseline and clinical characteristics between study participants with and without esophageal varices (EV). The mean age of the participants was noted as 53.11 ± 9.03 years for the EV group and 54.21 ± 9.03 years for the non-EV group, with no significant difference (p = 0.455). Gender distribution also showed insignificant difference (p = 0.123) with male proportion in EV group (72.8%) and non-EV group (61.1%). The Child-Pugh classification shows similar proportions across classes A, B and C between both groups (p = 0.594), but numerically there were more C class patients in the non-EV group (8.6% vs. 11.1%). Lifestyle factors, including smoking (32.1% in EV vs. 30.6% in non-EV, p = 0.837) and alcohol use (11.1% in EV vs. 16.7% in non-EV, p = 0.319), show no significant differences. The incidence of Type 2 Diabetes Mellitus is 13.6% in the EV group and 9.7% in the non-EV group (p = 0.460), which is also non-significant. Laboratory values such as WBC count (3.71 ± 0.74 in EV vs. 3.63 ± 0.73 in non-EV, p = 0.496), RBC count (4.25 ± 0.38 in EV vs. 4.33 ± 0.36 in non-EV, p = 0.174), and hemoglobin levels (125.67 ± 12.69 in EV vs. 124.94 ± 11.99 in non-EV, p = 0.719) show no significant group differences. Liver function indicators, including ALT (38.67 ± 23.53 in EV vs. 37.82 ± 21.17 in non-EV, p = 0.816), AST (47.74 ± 20.60 in EV vs. 46.29 ± 19.03 in non-EV, p = 0.653), AKP (95.43 ± 21.37 in EV vs. 91.94 ± 16.45 in non-EV, p = 0.264), and GGT (41.57 ± 13.59 in EV vs. 47.74 ± 19.51 in non-EV, p = 0.024), are statistically comparable between groups, as are bilirubin (28.91 ± 6.66 in EV vs. 29.35 ± 6.27 in non-EV, p = 0.680), albumin (39.73 ± 3.52 in EV vs. 40.17 ± 3.83 in non-EV, p = 0.462), and creatinine (67.30 ± 7.68 in EV vs. 68.14 ± 7.32 in non-EV, p = 0.490). Blood glucose levels (5.89 ± 0.41 in EV vs. 5.81 ± 0.47 in non-EV, p = 0.324) and mean arterial pressure (91.16 ± 3.99 in EV vs. 91.28 ± 4.11 in non-EV, p = 0.859) are also similar across groups. However, spleen diameter is found to be non-significant difference between groups with a notably high mean in EV group (13.84 ± 1.62 mm) as compared to non-EV group (13.72 ± 1.46 mm) and p value (0.610). The platelet count-to-spleen diameter (PC/SD) ratio was markedly reduced in the non-EV group as compared to the EV group (624.49 ± 208.78 vs 807.23 ± 205.88; P <0.001), indicating that this ratio might be a key predictive marker of EV.

The Platelet Count/Spleen Diameter ratio is used to predict esophageal varices in patients with liver cirrhosis, as indicated by the Receiver Operating Characteristic curve as shown in **Figure 1**. A visual evaluation of the predictive accuracy of the PC/SD ratio is provided by the ROC curve, which plots sensitivity against 1-specificity. The predictive value of the test is increased as the curve approaches the top-left corner. The current study the AUC for the PC/SD ratio was noted as 0.737 and demonstrates moderate accuracy for predicting esophageal varices in this study. An AUC value of 0.737 indicated good discriminative ability of the PC/SD ratio.

Table II shows the data on predictive indices on PC/SD ratio for detecting EV in liver cirrhosis individuals. The area under the curve (AUC) was 0.737±0.040 [95% confidence interval, 0.658 to 0.816]. This value of AUC shows a moderate diagnostic accuracy which indicates that the PC/SD ratio is a fair predictor between patients with and without esophageal varices. Using a cut-off value of ≥412.50, the PC/SD ratio achieved a high sensitivity of 95.1%, indicating that it is highly effective at identifying patients with esophageal varices. A moderate specificity of 79.2% shows that it has limited power to actually rule out the lack of varices. The positive likelihood ratio of 4.57 indicates that individuals with a PC/SD ratio above the cut-off are approximately 4.6 times more likely to have esophageal varices than those who do not achieve the cut-off ratio. The low probability of esophageal varices estimated to be present in the patients having a PC/SD ratio below the cut-off, indicated by the negative likelihood ratio (0.062), indicates that this tool can be used as a helpful non-invasive and reliable screening.

Table III shows sensitivity and specificity values for different cutoff values of the PC/SD ratio, allowing a more detailed approach on assessing diagnosis accuracy based on PC/SD. As shown in Table II, the optimal cutoff at this value is ≥412.50 (sensitivity 95.1%, specificity 79.2%), which relates to the values from Table III at this cutoff (sensitivity 0.951, specificity 0.792). As indicated in table III, this cutoff achieves the most optimal combination of high sensitivity and moderate specificity which fits well for a diagnostic scenario as it is critical to avoid false negatives (high sensitivity). For lower cutoff values, such as 349.00, both sensitivity and specificity are perfect (1.000), but as the cutoff increases, specificity generally decreases while sensitivity remains high, until reaching 412.50, where the balance is optimal. After this point sensitivity begins to drop off significantly with higher cutoffs, indicating that the ability to identify true positive cases declines.

Table I: Baseline Characteristics of Study Participants (n=153)				
Variables		**Esophageal Varices**		**P-Value**
		Yes, (n=81)	**No**, (n=72)	
Age in years, Mean ± SD		53.11 ± 9.03	54.21 ± 9.03	0.455
Gender	Male, n (%)	59 (72.8)	44 (61.1)	0.123
	Female, n (%)	22 (27.2)	28 (38.9)	
Child Pugh Class	A, n (%)	58 (71.6)	46 (63.9)	0.594
	B, n (%)	16 (19.8)	18 (25.0)	
	C, n (%)	7 (8.6)	8 (11.1)	
Smoking History, n (%)		26 (32.1)	22 (30.6)	0.837
Alcohol Use, n (%)		9 (11.1)	12 (16.7)	0.319
Type 2 Diabetes Mellitus, n (%)		11 (13.6)	7 (9.7)	0.460
WBC in 10^3/L, Mean ± SD		3.71 ± 0.74	3.63 ± 0.73	0.496
RBC in 10^{12}/L, Mean ± SD		4.25 ± 0.38	4.33 ± 0.36	0.174
Hemoglobin in g/l, Mean ± SD		125.67 ± 12.69	124.94 ± 11.99	0.719
INR, Mean ± SD		1.03 ± 0.18	1.01 ± 0.14	0.424
Prothrombin time in second, Mean ± SD		12.16 ± 1.10	12.27 ± 1.15	0.564
ALT in IU/l, Mean ± SD		38.67 ± 23.53	37.82 ± 21.17	0.816
AST in IU/l, Mean ± SD		47.74 ± 20.60	46.29 ± 19.03	0.653
AKP in IU/l, Mean ± SD		95.43 ± 21.37	91.94 ± 16.45	0.264
GGT in IU/l, Mean ± SD		41.57 ± 13.59	47.74 ± 19.51	0.024
Total bilirubin in umol/l, Mean ± SD		28.91 ± 6.66	29.35 ± 6.27	0.680
Albumin in g/l, Mean ± SD		39.73 ± 3.52	40.17 ± 3.83	0.462
Creatinine in umol/l, Mean ± SD		67.30 ± 7.68	68.14 ± 7.32	0.490
Blood glucose in mmol/l, Mean ± SD		5.89 ± 0.41	5.81 ± 0.47	0.324
MAP in mmHg, Mean ± SD		91.16 ± 3.99	91.28 ± 4.11	0.859
Platelets in 10^9/L, Mean ± SD		81.62 ± 21.77	83.33 ± 23.25	0.638
Spleen Diameter (SD) in mm, Mean ± SD		13.84 ± 1.62	13.72 ± 1.46	0.610
PC/SD ratio, Mean ± SD		807.23 ± 205.88	624.49 ± 208.78	0.0001

WBC, white blood cell; RBC, red blood cell; INR, international normalized ratio; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AKP, alkaline phosphatase; GGT, γ-glutamyl transpeptidase; MAP, mean arterial pressure; PC/SD, Platelet count/diameter of the spleen.

Figure-1

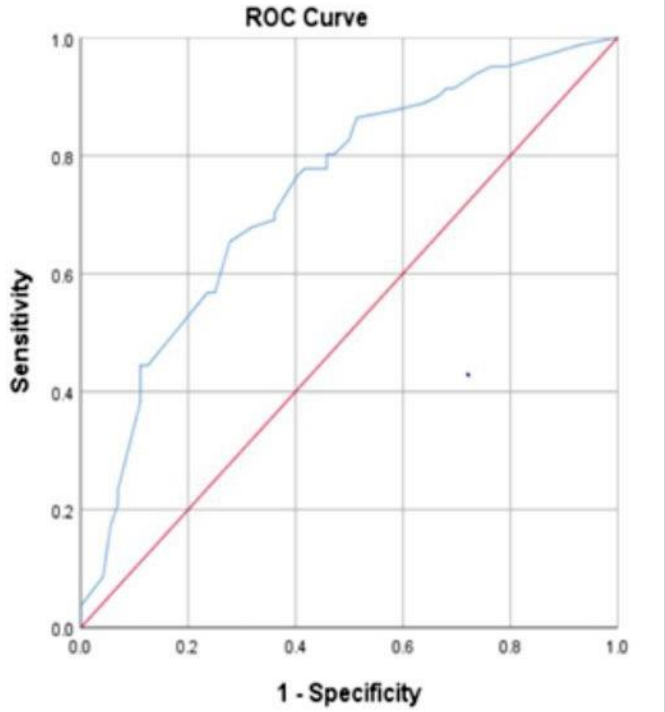

Table II: Predictive Value of PC/SD Ratio for Esophageal Varices in Liver Cirrhosis (n=153)

Area under the curve (AUC)	0.737
Std. Error	0.040
95% Confidence Interval	0.658----0.816
P-Value	0.0001
Cut off value	≥412.50
Sensitivity	95.1%
Specificity	79.2%
Positive Likelihood Ratio	4.57
Negative Likelihood Ratio	0.062

Table III: Coordinates of the Curve (n=153)

Cut Off Values	Sensitivity	Specificity
349.00	1.000	1.000
375.00	.988	.931
412.50	.951	.792
430.00	.951	.764
442.50	.938	.736
452.50	.914	.694
457.50	.914	.681
465.00	.901	.667
497.50	.889	.639
537.50	.877	.583
555.00	.864	.514
567.50	.827	.500
582.50	.802	.472
600.00	.802	.458
620.00	.778	.458
635.00	.778	.417
645.00	.765	.403
651.00	.704	.361
701.00	.691	.361
770.00	.679	.319
795.00	.654	.278
815.00	.568	.250
840.00	.568	.236
869.00	.444	.125
894.00	.444	.111
925.00	.383	.111
953.50	.235	.069
968.50	.210	.069
990.00	.173	.056
1015.00	.086	.042
1115.00	.037	.000
1201.00	.000	.000

DISCUSSION

This research assesses the predictive significance of the platelet count-to-spleen diameter (PC/SD) ratio as a non-invasive indicator for esophageal varices (EV) in individuals with hepatic cirrhosis, demonstrating its potential clinical utility. By establishing a cut-off value of ≥412.50, this study achieved a high sensitivity of 95.1% and specificity of 79.2%, indicating that the PC/SD ratio can effectively identify patients with EV while moderately ruling out those without it. This finding is consistent with earlier studies such as those by Yu et al.[7] and Basha et al.[3] The study of Basha et al.[3] stated the cut-off value of ≤1014, with a sensitivity of 92.77% and specificity of 64.71%, whereas Yu et al.[7] reported sensitivity of 86.4% and specificity of 77.1% with cut-off value of ≤909[7]. Both studies noted similar predictive accuracies for PC/SD ratio, suggesting it, as an efficient substitute to invasive endoscopic procedures for routine EV screening. The area under the curve (AUC) of 0.737 found in this study supports these findings, AUC values ranging from 0.7 to 0.8 indicate reasonable diagnostic accuracy[4]. Yu et al. found in the study an AUC of 0.884[7] while the study by González-Ojeda A, et al. reported an AUC of 0.802[23]. In clinical practice, where reducing unnecessary endoscopies is critical, a reliable non-invasive marker like the PC/SD ratio could alleviate patient burden and lower healthcare costs, aligning with the Baveno VI consensus recommendation to avoid endoscopies in low-risk cirrhotic patients with low liver stiffness and high platelet counts[6]. Jamil Z, et al noted AUC of 0.883 with a cutoff value of ≤1077.42, sensitivity of 88.75%, and specificity of 81.43%[8].

Different studies have noted the need for the PC/SD ratio emphasizing its diagnostic relevance. For example, Alam, et al reported comparable AUC values for the PC/SD ratio to predict EV underscoring its diagnostic need in diverse populations[5]. Cho, et al.[1] suggested that this combination with other non-invasive markers (like liver stiffness) could complement the information on diagnostic accuracy although simplicity in calculation and interpretability make the PC/SD ratio attractive for clinical practice. Still, Mattos et al. pointed out that the PC/SD ratio is likely to miss potential improvements in accuracy possibly provided by a multi-parametric approach[4]. The simplicity-precision trade-off supports a potential limitation of this study, wherein future research could explore additional biomarkers in parallel to ratio of PC/SD.

The strength of recent study is its relatively large sample size which enhances the reliability of findings. The present investigation was a single-center study, and this may restrict generalization to the populations. A collection of patient studies led by Kraja B and associates[18] illuminated wide-ranging efficacy of the platelet count to spleen diameter ratio across diverse demographic and clinical circumstances, highlighting the necessity for multi-center investigations to authenticate the test's predictive power globally. Moreover, this analysis neglected other confounding elements influencing esophageal varices evolution such as liver ailment origins and portal hypertension as pointed out in works from Faheem HA, et al., Patil S, et al. and corroborated in research by Elatty EA and colleagues as well as Kumar P and partners[19-22].

Evaluating these additional parameters may enhance the understanding of variceal risk and increase the relevance of the platelet count to spleen diameter ratio across diverse patient groups.

CONCLUSION

The platelet count-to-spleen diameter (PC/SD) ratio is an easily obtainable, non-invasive predictor of esophageal varices (EV) in liver cirrhosis. These results imply that the PC/SD ratio could be utilized in the routine screening to avoid invasive endoscopy and add an economic value in terms of reducing the cost of healthcare. Additional extensive research with a larger sample size across different study centres in Pakistan is necessary to validate the findings of the current study.

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