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Original Research Article

Evaluation of platelet count/spleen diameter ratio for detection of oesophageal varices in patients with cirrhosis of liver: a cross-sectional study

Ashok Mysore Lakshminarayana[1], Shweta Mallikarjun Kumbar[1]*, Manohara Melur Chandregowda[1], Kiran Warrier[2]

[1]Department of General Medicine, Bangalore Medical College, Bengaluru, Karnataka, India
[2]Department of Pharmacology, Bangalore Medical College, Bengaluru, Karnataka, India

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***Correspondence:**
Dr. Shweta Mallikarjun Kumbar,
E-mail: dr.shwetamkumbar@gmail.com

ABSTRACT

Background: Gastroesophageal varices due to portal hypertension in patients with liver cirrhosis is an important cause of morbidity and mortality. Gold standard investigation for varices is esophagogastroduodenoscopy and patients are advised to undergo regular follow up based on the risk stratification. But the invasive nature, risk of procedure-related complication and lack of accessibility and affordability makes it important to identify simpler methods to screen patients. Platelet count/spleen diameter (PSD) ratio has been validated as a marker for oesophageal varices (OV) in multiple studies but with varying results. The present study was conducted to evaluate the accuracy of PSD ratio in OV.
Methods: A cross-sectional study was conducted in patients diagnosed with liver cirrhosis. Clinical examination, relevant laboratory investigations, abdominal ultrasound and endoscopy were performed and data were recorded. PSD was calculated. Receiver-operator characteristics curves were plotted to determine cut-off values. Sensitivity, specificity, positive and negative predictive values were calculated.
Results: Total 100 patients were included in this study, out of which 25% of patients did not have varices on endoscopy. The mean PSD was for patients without varices 1242.82 (253.45) and 883.51 (582.38467) for patients with OV. The area-under-curve was 0.823, 95% CI=0.734-0.912, p value=0.000001. The cut-off value for PSD was calculated from the ROC analysis was 1077. The sensitivity, specificity, positive and negative predictive values were 76%, 88%, 95% and 55% respectively.
Conclusions: PSD ratio is not an efficient parameter for detection of varices in patients with liver cirrhosis. The current evidence does not support its role as a screening test for identification of patients with OV.

Keywords: Oesophageal varices, Platelet count/splenic diameter ratio, Liver cirrhosis, Endoscopy

INTRODUCTION

Gastro-oesophageal varices due to portal hypertension are a frequent complication of liver cirrhosis irrespective of the underlying etiology. These varices especially OV have a high prevalence of 60-80% and have an increased tendency to bleed, causing various complications like hemorrhage which can lead to higher morbidity and mortality in cirrhotic patients despite the advancement in the pharmacological and surgical management of variceal bleeding. Thus, the existing guidelines for management of liver cirrhosis advocate screening of such patients for OV

at the time of diagnosis using upper gastro-intestinal (UGI) endoscopy, which is the investigation of choice for OV. These patients may also require frequent follow up which may be annual in case of decompensated and every 2-3 years in case of compensated cirrhosis.[1,2]

UGI endoscopy, though a frequently performed medical procedure with good track record of safety is not without inherent risk on the accord of being an invasive procedure. These may include aspiration pneumonitis, perforation and hospital acquired infections. The invasive nature of this investigation may also lead to poor compliance of the patients with screening schedules. Moreover, the requirement for repeated follow up puts a great strain on the healthcare set-up especially in resource poor settings where these facilities may not be readily accessible or easily available. Thus, there is a need to identify simpler and less invasive methods for screening and follow-up of patients of liver cirrhosis with OV.[3-5]

Multiple comparative studies have attempted to correlate various laboratory, sonological and radiological parameters with the severity of the varices and attempt to simplify the follow up process of patients with liver cirrhosis due to various etiologies. These include fibrosis-4 score (FIB-4), aminotransferase-to-platelet ratio index (APRI), Doppler ultrasound which aim to correlate the liver status and portal venous flow and pressure with severity of varices have been shown to have reasonable accuracy.[6,7]

Various studies have shown that PSD is an excellent predictor of OV in cirrhosis. This method is based on the hypothesis that portal hypertension leading to splenic enlargement can cause hypersplenism resulting in thrombocytopenia.[8] A study by Gianni et al has proposed that the platelet count (per mm^3) divided by the spleen diameter (in mm) less than 909 increases the likelihood that the patient has large varices with increased potential for variceal bleeding.[4] There is considerable variability in current scientific literature regarding the usefulness of PSD ratio in predicting the presence of varices in patients with liver cirrhosis.[9]

Therefore, the present study was conducted with the aim of determining the utility of PSD in predicting presence and its relationship with the severity of oesophageal varices in patients with liver cirrhosis.

METHODS

The present cross-sectional study was conducted in the tertiary care hospitals attached to Bangalore medical college and research institute, Bengaluru over a period of 18 months from (November 2018) to (May 2020) after obtaining clearance from the institutional ethics committee. Patients above the age of 18 years, with a diagnosis of liver cirrhosis confirmed based on history, clinical findings, liver function tests and ultrasound abdomen were included in the study after obtaining written informed consent. Patients with prior history of upper gastro-intestinal bleeding, on treatment with beta blockers, diuretics and antiplatelet drugs, history of fever with thrombocytopenia, on drugs known to cause thrombocytopenia were excluded.

Demographic data and results of laboratory investigations (including platelet count) were recorded. Bipolar diameter of spleen was calculated using ultrasound and presence or absence of varices was confirmed using upper GI endoscopy performed as per standard protocols. PSD was calculated as PSD=platelet count (PC) to spleen diameter (SD) ratio, PC (N/ml)/the maximum bipolar diameter of the spleen (mm).[10] Severity of liver disease was assessed using Child-Pugh score.

Sample size was calculated based on a similar study done by Giannini et al using prevalence of 60% and a relative precision of 10%.[6]

Data was summarized as percentage, proportions and mean. Sensitivity, specificity, positive and negative predictive values for PSD were calculated in comparison to UGI endoscopy findings and receiver-operator characteristics curve was plotted. Microsoft excel for Microsoft 365 (Microsoft corporation, Redmond, Washington, USA) and statistical package for social sciences version 20 (IBM Corporation, Armonk, New York, USA) were used for statistical analysis.

RESULTS

A total of 100 patients were included in the study. The demographic details, grading of varices, clinical characteristics, ultrasonography and UGI endoscopy are summarized in Table 1.

Table 1: Summary of demographic details, clinical characteristics and results of laboratory investigation, ultrasound and UGI endoscopy findings.

Patient characteristics	Number (%)
Mean age (in years) (SD)	46.65 (10.34)
Gender	
Male	76 (76)
Female	24 (24)
Viral markers positive	
HBsAg	5 (5)

Continued.

Patient characteristics	Number (%)
Ascites	76 (76)
Encephalopathy	29 (29)
Grading of varices	
Grade 0	25 (25)
Grade 1	17 (17)
Grade 2	27 (27)
Grade 3	21 (21)
Grade 4	10 (10)
Cause of cirrhosis	
Alcoholic	73 (73)
Non-alcoholic	27 (27)

Table 2: Results of laboratory investigation and sonological examination in patients with various grades of varices (AST-aspartate aminotransferase; ALT-alanine amino transferase; ALP-alkaline phosphatase; INR-international normalized ratio).

Grades	0 (N=25)	1 (N=17)	2 (N=27)	3 (N=21)	4 (N=10)
Mean PSD (SD)	1242.82 (253.45)	1008.58 (523.40)	888.38 (410.72)	1040.54 (786.09)	328.02 (105.69)
MeanAST (SD)	0.6304 (0.45)	5.13 (5.77)	1.79 (2.18)	0.88 (0.63)	1.93 (0.50)
Mean ALT (SD)	45.76 (19.95)	23.06 (18.00)	41.44 (32.42)	35.48 (31.34)	47.70 (14.83)
Mean ALP (SD)	89.08 (19.77)	29.91 (110.00)	109.74 (39.36)	95.71 (31.69)	117.80 (19.14)
Mean serum bilirubin (SD)	3.54 (2.44)	8.64 (7.79)	4.29 (4.29)	3.47 (4.71)	5.39 (0.80)
Mean serum albumin (SD)	2.92 (0.58)	2.79 (0.52)	2.54 (0.57)	2.54 (0.83)	2.57 (0.23)
Mean INR (SD)	0.47 (1.83)	1.60 (0.30)	.57.00 (0.65	1.40 (0.30)	1.66 (0.12)
Mean Child-Pugh score (SD)	7.80 (1.91)	9.88 (1.27)	9.33 (1.14)	10.19 (1.94)	12 (0.00)

Table 3: Receiver operator characteristics for PSD ratio (AUC-area under the curve; CI-confidence interval).

AUC	95% CI	P value
0.823	0.734-0.912	0.000001
ROC for detection of high grade varices		
0.745208	0.627-0.863	0.000093

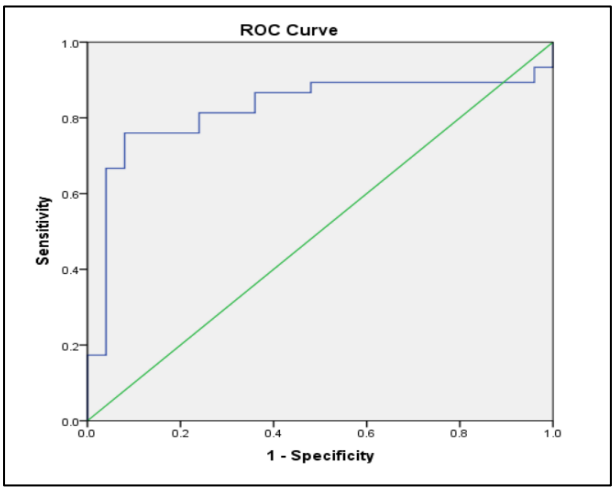

Figure 1: ROC curve for PSD<909 in comparison with endoscopy.

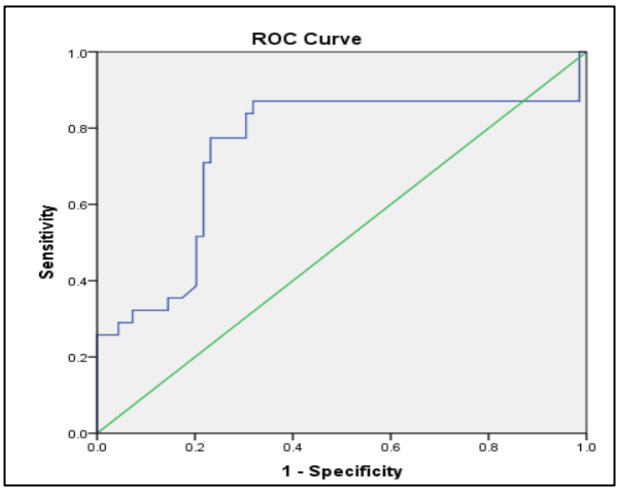

Figure 2: ROC curve for PSD<806.93 in comparison with varices grade on endoscopy.

The mean age of the patients was 46.65 (10.34) years. More than three-fourth (76%) of the patients included were male. Total 5 (5%) patients had viral marker hbsag positive. The most common cause of cirrhosis was alcohol abuse (73%). The results of laboratory investigations are summarized in table 2. The mean child-pugh score in grade 3 and grade 4 varices population was >10 putting them in class c (<45% chance of 1 year survival). The roc curves are represented in figure 1 and 2 and show a linear relationship between the psd ratio and presence of ov. Area under the curve (auc), its 95% confidence intervals and asymptotic significance values are represented in table 3. The cut-off values for psd ratio for detection of ov from roc analysis was set at ≤1077 (p=0.000001).

DISCUSSION

Gastroesophageal varices are present in about 34% to 80% in liver cirrhosis patients with portal hypertension and hemorrhage from varices is among the most important causes of morbidity and mortality in these patients.[11] Therefore, it is recommended that all liver cirrhosis patients should undergo screening for gastroesophageal varices at the time of diagnosis and continue regular follow up using UGI endoscopy. This invasive procedure requires a good clinical set-up, technical expertise and places a heavy burden on the healthcare resources especially in places with poorer infrastructure and can also lead to reduced compliance with follow up guidelines. Hence, there is a need to utilize simpler, economical and less invasive methods to effectively follow up the progress of gastroesophageal varices in these patients thereby helping assess and stratify the risk of bleeding.

Male patients constituted the majority (76%) of cases this can be attributed to the fact that the important risk factor of alcohol consumption as well as alcohol abuse is more prevalent in males than in females. In majority of the cases included in the present study, the cause for cirrhosis was alcohol abuse (73%), 27% cases had other etiologies for cirrhosis and hepatitis B surface antigen (HBsAg) being positive in 5% of the cases. This correlates with previous studies done in patients with liver cirrhosis which shows that the majority of cases of cirrhosis and the associated morbidity and mortality were related to alcohol abuse.[12]

The cut-off values for PSD ratio was determined to be ≤1077. At this value, the sensitivity and specificity of the PSD ratio was 76% and specificity was 88%. Multiple studies have shown similar results with overall reported sensitivity ranging from 64% to 100% and specificity ranging from 63% to 97%. The positive and negative predictive values were 95% and 55%. The positive and negative likelihood ratios were 6.33 and 0.27, respectively.[9,13,14] The sensitivity and specificity of the PSD ratio ≤1077 for predicting higher grade OVs was 87.1% and 62.08% respectively. A study by Giannini et al reported the sensitivity of 75% and specificity of 47.8% in patients with liver cirrhosis due to hepatitis C infection.[3] The positive and negative predictive values were 45% and 90%. The positive and negative likelihood ratios were 1.82 and 0.25.

From the above results it is evident that though a useful tool, PSD ratio lacks the diagnostic accuracy to be used as a screening tool for patients with OVs due to liver cirrhosis as a single parameter. Previous studies have utilized different cut-off rates for PSD ratio for detection of varices achieving different results and a lot of variation remains in the published literature. Therefore, further comparative studies need to be done on a larger scale to establish this simple investigation as an effective screening tool for diagnosis of OVs.

The results of the present study should be considered in the light of certain limitation. The study sample size was small and the proportion of patients with grade 3 and grade 4 OV was lower. which may have led to a reduced ability of the study to detect a difference. PSD ratio may also be limited by the fact that multiple co-factors like infection and cirrhosis itself can adversely affect the platelet count in patients with cirrhosis.

CONCLUSION

Though a useful tool, PSD ratio lacks the diagnostic accuracy to be used as a screening tool for patients with oesophageal varices due to liver cirrhosis as a single parameter. PSD ratio is not an efficient parameter for detection of varices in patients with liver cirrhosis. The current evidence does not support its role as a screening test for identification of patients with oesophageal varices. Therefore, further comparative studies need to be done on a larger scale to establish this simple investigation as an effective screening tool for diagnosis of OVs.

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