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PLATELET SPLEEN INDEX IS A NON-INVASIVE PREDICTOR OF GASTROESOPHAGEAL VARICES IN PATIENTS WITH CIRRHOSIS.

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ABSTRACT

BACKGROUND: In individuals with liver cirrhosis, the platelet count to spleen diameter (PC/SD) ratio is a reliable, noninvasive predictor of esophageal varices. The goal of this study was to investigate the diagnostic accuracy, sensitivity, and specificity of the platelet spleen index in cirrhotic patients for the identification of esophageal varices. **MATERIAL AND METHOD:** A descriptive comparative cross-sectional study was conducted in the Department of Gastroenterology, Military Hospital, Rawalpindi, Pakistan, from 10 February 2018 to 9 August 2018. The study comprised 170 cirrhotic individuals in total. Necessary investigations, such as complete blood count (platelets count), abdomen ultrasonography, and upper GI endoscopy, were done. Two milliliters of venous blood was taken in an EDTA vacutainer tube for platelets count, which was determined through an automated hematology analyzer (XN-1000, Sysmex, Japan). Abdomen ultrasound and endoscopy were performed at the radiology department. SPSS was used to gather and analyse data, and the findings were presented in tables, graphs, and charts. **RESULTS:** Of the 170 patients, 94 (55.3%) were male and 76 (44.7%) were female, with a mean age of 55.0 ± 9.8 years. The majority of the patients had hepatitis C (142, 83.5%), followed by hepatitis B (20, 11.8%), cryptogenic cirrhosis (8, 4.7%), and Wilson's disease (2, 1.2%). Grades of esophageal varices were as follows: 24 patients (14.2%) were in grade I, 46 patients (27%) were in grade II, 63 patients (37%) were in grade III, and 37 patients (21.8%) had no esophageal varices. There were 118 patients (69.4%) in Child's Pugh stage A, 44 patients (25.9%) in stage B, and 8 patients (4.7%) in grade C. The sensitivity was 73.6%, specificity 100%, positive predictive value 100%, negative predictive value 51.3%, diagnostic accuracy 79.4%, and likelihood ratio 78.3. **CONCLUSION**: Platelet Spleen Index is a straightforward, inexpensive, and non-invasive predictor of varices. The adoption of a non-invasive method to identify gastroesophageal varices might minimise the incidence of invasive esophagogastroduodenoscopies.

KEYWORDS: Esophageal Varices, Cirrhosis, Platelet Spleen Index.

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INTRODUCTION

Cirrhosis and its complications like portal hypertension, variceal bleeding, and hepatic encephalopathy represent major health problems facing our health system today[1]. Though the exact prevalence of cirrhosis worldwide is unknown. In the United States, the prevalence of cirrhosis is around 0.27% and in Pakistan, it is reasonably estimated to be around 1%[2].

Cirrhosis complications including ascites, hypersplenism, hepatic encephalopathy, and esophageal varices are mainly because of portal hypertension[3]. Esophageal varices are commonly found in patients with cirrhosis with the prevalence of 24 to 60 % depending upon the stage of cirrhosis[4]. The mortality rate owing to variceal bleed in cirrhotic patients has been shown to be 17 to 57%, with index bleed accounting for 5 to 10% of deaths[5,6]. As a result, once cirrhosis is confirmed, it is required to test for esophageal varices and give primary prevention with endoscopic variceal band ligation, beta blockers, or both[7]. Baveno and EASL developed recommendations for screening esophageal varices, which has increased medical care costs tremendously, particularly in countries such as Pakistan, where access to modern health facilities such as endoscopy is limited[8]. This load will grow in the future as the number of cirrhotic patients increases, as will patient awareness and survival[9,10]. Different noninvasive approaches for detecting the existence of esophageal varices can distinguish high risk esophageal patients from low risk esophageal patients[11,12]. Various noninvasive methods including CT scan, transient elastography and biomarkers, king score, lok index, Fib-4 score AST/ALT ratio, F1 score and platelet spleen index have been studied[3-6,9]. A review of the literature on platelet spleen ratio for the diagnosis of esophageal varices found that it had a sensitivity of 83% (78% to 0.87%) and a specificity of 63% (76% to 56%)[13]. In Pakistan we have very limited literature on this topic. This study as an attempt to look for platelet spleen ratio for screening varies in our population taking cut off value < 909[14].

The study's rationale is to utilise platelet spleen index to predict esophageal varices since it is noninvasive and less expensive[15]. In resource-scarce nations such as Pakistan, where availability and cost are major impediments to the health-care system, it will help to avoid 50 to 60% negative screening endoscopies[9] which is more expensive and invasive. It will reduce the cost and potential complications of the procedure[16].

MATERIAL AND METHOD

The Department of Gastroenterology, Military Hospital, Rawalpindi, Pakistan, did a descriptive comparative cross-sectional study. Following informed consent and ethical committee approval, 170 patients included. For the study variables, detailed demographic data was gathered. Cirrhosis was defined using the operational notion. The data was collected by the researcher and recorded in a standardised questionnaire (attached). A complete blood count was conducted on patients' blood samples at the hospital lab, an ultrasound abdomen was performed in the Department of Radiology, and an upper GI endoscopy was performed in the endoscopic suite to screen for varices.

SPSS version 24 was used to enter and analyse data. The mean and standard deviation were used to summarise numerical information such as age, platelet count, and spleen size. Qualitative variables, like gender, cause of cirrhosis, and grade of esophageal varices, were presented in the form of frequency and percentages. Data were stratified for age, gender, cause, and stage of cirrhosis, and grade of varices, and post-stratification 2x2 tables were constructed to calculate diagnostic accuracy. ROC and likelihood ratio were calculated.

RESULTS:

Out of 170 patients, 94 (55.3%) were male and the remaining 76 (44.7%) were female, with a mean age of 55.0 ± 9.8 years. The majority of the patients had hepatitis C (142, 83.5%), followed by hepatitis B (20, 11.8%), non-cryptogenic cirrhosis (8, 4.7%), and Wilson's disease (2, 1.2%). Grades of esophageal varices were as follows: 24 patients (14.2%) had grade I, 46 patients (27%) had grade II, 63 patients (37%) had grade III, and 37 patients (21.8%) had no esophageal varices. There were 118 patients (69.4%) in Child's Pugh stage A, 44 patients (25.9%) in stage B, and 8 patients (4.7%) in grade C.

The sensitivity was 73.6%, the specificity was 100%, the positive predictive value was 100%, the negative predictive value was 51.3%, the diagnostic accuracy was 79.4%, and the likelihood ratio was 78.3. A receiver operating characteristic (ROC) curve was also created as presented in Figure 01. Stratification based on age, gender, cause of

cirrhosis, and stage of cirrhosis was also performed and as shown in Table 1.

Table 1: Descriptive analysis of different variables in current study

Variables		Frequencies
		Number (%)
Gender	Male	94 (55.3)
	Female	76 (44.7)
	Total	170 (100)
Age Groups	21-50	57 (33.5)
	51-70	113 (66.5)
	Total	170 (100)
Causes of Cirrhosis	HBV	20 (11.8)
	HCV	142 (83.5)
	Wilson Disease	2(1.2)
	Non-cryptogenic cirrhosis	8 (4.7)
	Total	170 (100)
Child's Pugh Stage	Stage A	118 (69.8)
	Stage B	44 (25.9)
	Stage C	8 (4.7)
	Total	170 (100)

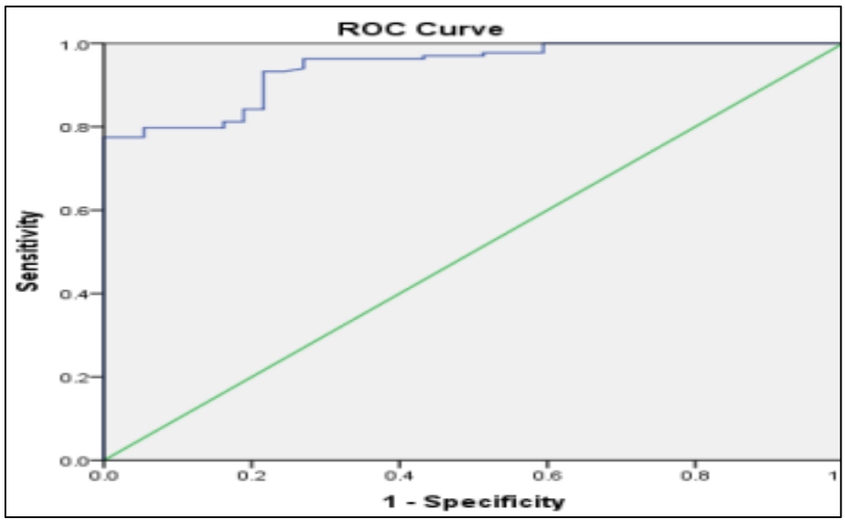

Figure: 1 The count of platelets has a different receiver operating Curve (ROC).

Table 2: Esophageal diagnosis through platelet spleen index using video endoscopy.

Platelet spleen index	Video Endoscopy		Total
	Negative	Positive	
Negative	37 (TN) d	35 (FN) c	72
Positive	0 (FP) b	98 (TP) a	98
Total	37 b+d	133 a+c	170

Sensitivity: 73.6% , Specificity: 100%, PPV: 100% , NPV: 51.3% , Accuracy: 79.4% , Likelihood ratio 78.3%

Table 3: Age-wise stratification of the platelet spleen index for esophageal cancer using a video endoscopy.

Age	Platelet spleen index	Video Endoscopy		Total
		Negative	Positive	
21-50 years	Negative	13 (TN) d	8 (FN) c	21
	Positive	0 (FP) b	36 (TP) a	36
	Total	13 b+d	44 a+c	57
51-70 year	Negative	24 (TN) d	27 (FN) c	51
	Positive	0 (FP) b	62 (TP) a	62
	Total	24 b+d	89 a+c	113

1. Stratification for age (21-50 year); Sensitivity: 81.2% , Specificity: 100%, PPV: 100% , NPV: 91.9% , Accuracy: 85.9% , Likelihood ratio 33.3%
2. Stratification for age (51-70 year); Sensitivity: 69.6, Specificity: 100%, PPV: 100%, NPV: 47.0%, Accuracy 76.1%, Likelihood ratio: 46.3%

Table 4: Gender-wise stratification of the platelet spleen index, for esophageal cancer using a video endoscopy.

Gender	Platelet spleen index	Video Endoscopy		Total
		Negative	Positive	
Male	Negative	17 (TN) d	23 (FN) c	40
	Positive	0 (FP) b	54 (TP) a	54
	Total	17 b+d	77 a+c	94
Female	Negative	20 (TN) d	12 (FN) c	32
	Positive	0 (FP) b	44 (TP) a	44
	Total	20 b+d	56 a+c	76

1. Male: Sensitivity: 70.1% , Specificity: 100%, PPV: 100% , NPV: 42.5% , Accuracy: 75.5% , Likelihood ratio: 34.3%
2. Female: Sensitivity: 79.5% , Specificity: 100%, PPV: 100% , NPV: 62.5% , Accuracy: 84.2%, Likelihood ratio: 45.2%

Table 5: Etiological-wise (Hepatitis C vs Non-crytogenic) stratification of the platelet spleen index for esophageal cancer using a video endoscopy.

Causes	Platelet spleen index	Video Endoscopy (Gold Standard)		Total
		Negative	Positive	
Hepatitis C	Negative	30 (TN) d	25 (FN) c	55
	Positive	0 (FP) b	87 (TP) a	87
	Total	30 b+d	112 a+c	142
Non-cryptogenic	Negative	1 (TN) d	4 (FN) c	5
	Positive	0 (FP) b	3 (TP) a	3
	Total	1 b+d	7 a+c	8

1. Hepatitis C: Sensitivity: 77.6% , Specificity: 100%, PPV: 100% , NPV: 54.5% , Accuracy: 82.3% , Likelihood ratio: 70.6%.
2. Non-cryptogenic: Sensitivity: 42.8% , Specificity: 100%, PPV: 100% , NPV: 20% , Accuracy: 50% , Likelihood ratio 1.02%

Table 6: Stage-wise (Child Pugh A, B & C) stratification of of the platelet spleen index for esophageal cancer using a video endoscopy.

Stage of Cirrhosis	Platelet spleen index	Video Endoscopy (Gold Standard)		Total
		Negative	Positive	
Child Pugh A	Negative	35 (TN) d	27 (FN) c	62
	Positive	0 (FP) b	56 (TP) a	56
	Total	35 b+d	83 a+c	118
Child Pugh B	Negative	1 (TN) d	6 (FN) c	7
	Positive	0 (FP) b	37 (TP) a	37
	Total	1 b+d	43 a+c	44
Child Pugh C	Negative	1 (TN) d	2 (FN) c	3
	Positive	0 (FP) b	6 (TP) a	6
	Total	1 b+d	8 a+c	9

1. Stage A: Sensitivity: 67.4% , Specificity: 100%, PPV: 100% , NPV: 56.4% , Accuracy: 77.1% , Likelihood ratio: 58.5%.
2. Stage B: Sensitivity: 86% , Specificity: 100%, PPV: 100% , NPV: 14.2% , Accuracy: 86.3% , Likelihood ratio 3.8%
3. Stage C: Sensitivity: 75% , Specificity: 100%, PPV: 100% , NPV: 33.3% , Accuracy: 77.7%, Likelihood ratio: 2.2%

DISCUSSION

There are no replacement indicators for detecting the existence and extent of esophageal varices, according to recent recommendations, and esophagogastroduodenoscopy remains the gold standard for diagnosing them[17]. However, esophagogastroduodenoscopy and other resources are inadequate in impoverished nations. Due to a lower proportion of people do not have varices, the reported percentage of esophageal varices from 24-80%[18]. If noninvasive methods for predicting the existence of esophageal varices were available, endoscopic examinations would be confined to individuals at high risk of having varices. All patients with cirrhosis should be evaluated through endoscopy in order to varify the varices presence[19].

Previous reports show that the non-invasive techniques were used for identificaiton of patients and were tried to avoid endoscopy[20]. It has been demonstrated that various predictors of the occurrence of varices exist. However, heterogeneity in the research groups and illness spectrum make it challenging to construct a broadly applicable prediction model[20].

According to Giannini et al., the platelet count (PC)/spleen diameter (SD) ratio was employed as a non-invasive procedural strategy for determining the occurrence of varices. The diagnostic precision of PC/SD was established using endoscopy for diagnosis and was also utilised for patient follow-up until esophageal varices were free[21]. The PC/SD ratio may be the most effective non-invasive detector for esophageal varices due to its excellent sensitivity and specificity in patients with liver cirrhosis. Furthermore, in individuals with portal hypertension, the PC/SD ratio may play an important role[22].

The present literature does not consistent to replace endoscopy technique with any other procedure for identification of esophageal varices, whereas the PC/SD ratio has own benefits for assessing the cirrhotic patients into different categories of risk. PC/SD ratio is more essential in few patients having any health issues which exclude the invasive techniques procedure[23]. The PC/SD along with the maximum size of the spleen in diameter can measure in millimetres through abdominal ultrasonography procedure were also employed in present investigation to determine the non-invasive predictors[24]. In the current study, the sensitivity and specificity were 73% and 100%,

respectively. These findings are congruent with those of a previous meta-analysis research, which revealed sensitivity and specificity of 89% and 74%, respectively. These diagnostic tests are regularly performed in cirrhotic individuals at no additional cost[25]. Positive predictive value (PPV) was 100 percent, while negative predictive value (NPV) was 51.3%. The PC/SD ratio will aid in the development of a low-cost, effective, and time-consuming method for detecting esophageal varices in patients with portal hypertension. The PC/SD ratio should be examined in individuals who are at high risk of developing esophageal varices[26].

CONCLUSION

Platelet Spleen Index is a straightforward, inexpensive, and non-invasive predictor of varices. The adoption of a non-invasive method to identify gastroesophageal varices might minimise the incidence of invasive esophagogastroduodenoscopies.

ETHICS APPROVAL: The ERC gave ethical review approval.

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

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