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COMPARISON OF PLATELET COUNT, LIVER STIFFNESS, SPLENIC STIFFNESS AND SPLENIC DIAMETER IN PREDICTING ESOPHAGEAL VARICES IN THE PAKISTANI POPULATION

Original Research

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ABSTRACT

Background: Esophageal varices (EV) are a life-threatening complication of portal hypertension in cirrhotic patients, often leading to gastrointestinal hemorrhage. Early detection is critical for effective risk stratification and timely intervention. While esophagogastroduodenoscopy (EGD) is the gold standard for diagnosing EV, its invasiveness and limited accessibility in resource-constrained settings necessitate reliable non-invasive alternatives. Platelet count, liver stiffness (LS), splenic stiffness (SS), and splenic diameter (SD) have been proposed as potential predictors of EV, but their comparative diagnostic accuracy remains uncertain, particularly in the Pakistani population.

Objective: To evaluate and compare the diagnostic accuracy of platelet count, LS, SS, and SD in predicting EV in patients with cirrhosis.

Methods: This cross-sectional study was conducted at the Hepatogastroenterology Department of Sindh Institute of Urology and Transplantation from May 2024 to October 2024. A total of 250 cirrhotic patients underwent EGD for EV screening. LS and SS were measured using transient elastography (FibroScan), SD was assessed via ultrasonography, and platelet count was determined using an automated hematology analyzer. The association of these markers with EV was analyzed using independent t-tests and chi-square tests. Receiver Operating Characteristic (ROC) curves were utilized to determine the area under the curve (AUROC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy of each parameter.

Results: EV were detected in 150 patients (60%). Compared to patients without EV, those with EV had significantly lower platelet counts (92,000 ± 38,000/μL vs. 138,000 ± 35,000/μL, $p < 0.001$) and higher LS (27.3 ± 7.5 kPa vs. 20.1 ± 6.2 kPa, $p < 0.001$), SS (61.2 ± 12.8 kPa vs. 40.6 ± 10.2 kPa, $p < 0.001$), and SD (14.1 ± 2.0 cm vs. 12.3 ± 1.8 cm, $p < 0.001$). The AUROC values for EV prediction were 0.72 for platelet count, 0.82 for LS, 0.88 for SS, and 0.65 for SD. SS demonstrated the highest diagnostic accuracy, with a sensitivity of 86%, specificity of 84%, PPV of 90%, and NPV of 79%.

Conclusion: Splenic stiffness emerged as the most accurate non-invasive predictor of EV, surpassing LS, platelet count, and SD. Its superior diagnostic performance suggests potential integration into clinical screening algorithms to reduce the need for unnecessary EGD, particularly in resource-limited settings. Further multicenter validation studies are recommended to confirm these findings.

Keywords: Cirrhosis, esophageal varices, liver stiffness, platelet count, portal hypertension, splenic diameter, splenic stiffness

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INTRODUCTION

Esophageal varices (EV) are a significant complication of portal hypertension in cirrhotic patients, often leading to life-threatening upper gastrointestinal bleeding. Early detection of EV is essential for timely intervention with non-selective beta-blockers or endoscopic variceal ligation (EVL) to prevent bleeding-related morbidity and mortality (1). The gold standard for diagnosing EV is esophagogastroduodenoscopy (EGD); however, its invasive nature, high cost, and limited accessibility in resource-constrained settings underscore the need for reliable, non-invasive predictive markers (2,3). Portal hypertension leads to increased vascular resistance within the liver, triggering the formation of collateral circulation, including esophageal varices. The severity of portal hypertension is reflected in changes such as splenomegaly, thrombocytopenia due to platelet sequestration, and increased liver and splenic stiffness, all of which have been explored as potential non-invasive indicators of EV risk (4,5). Among these, platelet count, liver stiffness (LS), splenic stiffness (SS), and splenic diameter (SD) have garnered particular interest for their diagnostic utility in predicting the presence of varices (6). However, the relative predictive accuracy of these markers remains inconclusive, especially within the Pakistani population, where cirrhosis is predominantly driven by chronic viral hepatitis, particularly hepatitis C virus (HCV) and hepatitis B virus (HBV). Given the high prevalence of these infections in Pakistan, it is critical to evaluate the performance of these non-invasive markers within this specific clinical and demographic context (7).

Despite extensive research on surrogate markers of portal hypertension, the comparative effectiveness of platelet count, liver stiffness, splenic stiffness, and splenic diameter in predicting EV has not been well established. Addressing this gap, the present study aims to determine which of these markers serves as the most reliable predictor of EV in Pakistani patients with cirrhosis. By identifying the most accurate non-invasive indicator, this research seeks to refine risk stratification strategies, minimize unnecessary endoscopic procedures, and optimize resource allocation in healthcare settings with limited endoscopic availability (8).

METHODS

This cross-sectional study was conducted at the Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation, from May 1, 2024, to October 31, 2024, after obtaining ethical approval from the Institutional Review Board. Informed written consent was obtained from all participants prior to their enrollment. Patients diagnosed with liver cirrhosis based on clinical, biochemical, radiological, and elastographic criteria were included. A total of 250 patients were recruited, considering previous studies estimating the prevalence of esophageal varices at 60%, with a power of 80% and a confidence level of 95% (9). Eligibility criteria included adult patients aged over 18 years who had a confirmed diagnosis of cirrhosis and underwent transient elastography for liver and splenic stiffness assessment. Additionally, only those patients who underwent esophagogastroduodenoscopy (EGD) for esophageal varices screening were included. Patients were excluded if they had a prior history of gastrointestinal bleeding, were on beta-blockers, had previously undergone endoscopic variceal ligation, or had hepatocellular carcinoma (HCC) or portal vein thrombosis. Cases with incomplete clinical records or elastographic data were also excluded to ensure data integrity and accuracy (10).

Data collection involved a comprehensive assessment of esophageal varices using EGD as the reference standard. Platelet count was determined through an automated hematology analyzer. Liver stiffness and splenic stiffness measurements were performed using transient elastography (FibroScan), while splenic diameter was assessed via ultrasonography. All procedures were conducted by trained specialists to minimize inter-observer variability (11). Statistical analysis was carried out using SPSS software, with continuous variables analyzed through independent t-tests and categorical variables compared using the Chi-square test. Receiver Operating Characteristic (ROC) curves were utilized to determine the area under the ROC curve (AUROC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy of each non-invasive parameter in predicting esophageal varices. Statistical significance was set at a p-value of <0.05.

RESULTS

A total of 250 patients diagnosed with cirrhosis were included in the study, with a mean age of 54.2 ± 10.8 years. Males comprised 62% of the study population. The predominant etiology of cirrhosis was hepatitis C virus (HCV) infection (58%), followed by hepatitis B virus (HBV) (22%) and non-alcoholic fatty liver disease (NAFLD) (12%). The mean platelet count was 110,000 ± 42,000/µL, liver stiffness measured 24.6 ± 8.2 kPa, splenic stiffness was 53.1 ± 15.6 kPa, and the average splenic diameter was 13.4 ± 2.1 cm. Esophageal varices were identified in 150 patients (60%), while 100 patients (40%) had no varices. Patients with esophageal varices exhibited significantly lower platelet counts (92,000 ± 38,000/µL vs. 138,000 ± 35,000/µL, $p < 0.001$) and higher values of liver stiffness (27.3 ± 7.5 kPa vs. 20.1 ± 6.2 kPa, $p < 0.001$), splenic stiffness (61.2 ± 12.8 kPa vs. 40.6 ± 10.2 kPa, $p < 0.001$), and splenic diameter (14.1 ± 2.0 cm vs. 12.3 ± 1.8 cm, $p < 0.001$) when compared to those without esophageal varices.

The area under the receiver operating characteristic (AUROC) curve for predicting esophageal varices was 0.72 for platelet count, 0.82 for liver stiffness, 0.88 for splenic stiffness, and 0.65 for splenic diameter. Among all parameters, splenic stiffness demonstrated the highest predictive accuracy with an AUROC of 0.88. The sensitivity, specificity, positive predictive value (PPV), negative predictive

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value (NPV), and overall diagnostic accuracy varied among the markers, with splenic stiffness showing the highest sensitivity (86%) and specificity (84%), followed by liver stiffness, platelet count, and splenic diameter.

Table: Baseline Characteristics of the Study Population (n-250)

Variables	EV Present (n=150)	EV Absent (n=100)	p-value
Age (years)	55.1 ± 9.8	52.3 ± 11.5	0.02
Male (%)	64	58	0.18
HCV (%)	61	54	0.21
Platelet count (x10^3/µL)	92 ± 38	143 ± 45	<0.001
Liver stiffness (kPa)	27.3 ± 7.5	18.9 ± 6.2	<0.001
Splenic stiffness (kPa)	61.2 ± 12.8	43.5 ± 10.3	<0.001
Splenic diameter (cm)	14.1 ± 2.0	11.8 ± 1.9	<0.001

Table: Comparison of Continuous and Categorical Variables in Terms of Esophageal Varices

Parameter	EV Present (n=150)	EV Absent (n=100)	p-value
Platelet count (x10^3/µL)	92 ± 38	143 ± 45	<0.001
Liver stiffness (kPa)	27.3 ± 7.5	18.9 ± 6.2	<0.001
Splenic stiffness (kPa)	61.2 ± 12.8	43.5 ± 10.3	<0.001
Splenic diameter (cm)	14.1 ± 2.0	11.8 ± 1.9	<0.001

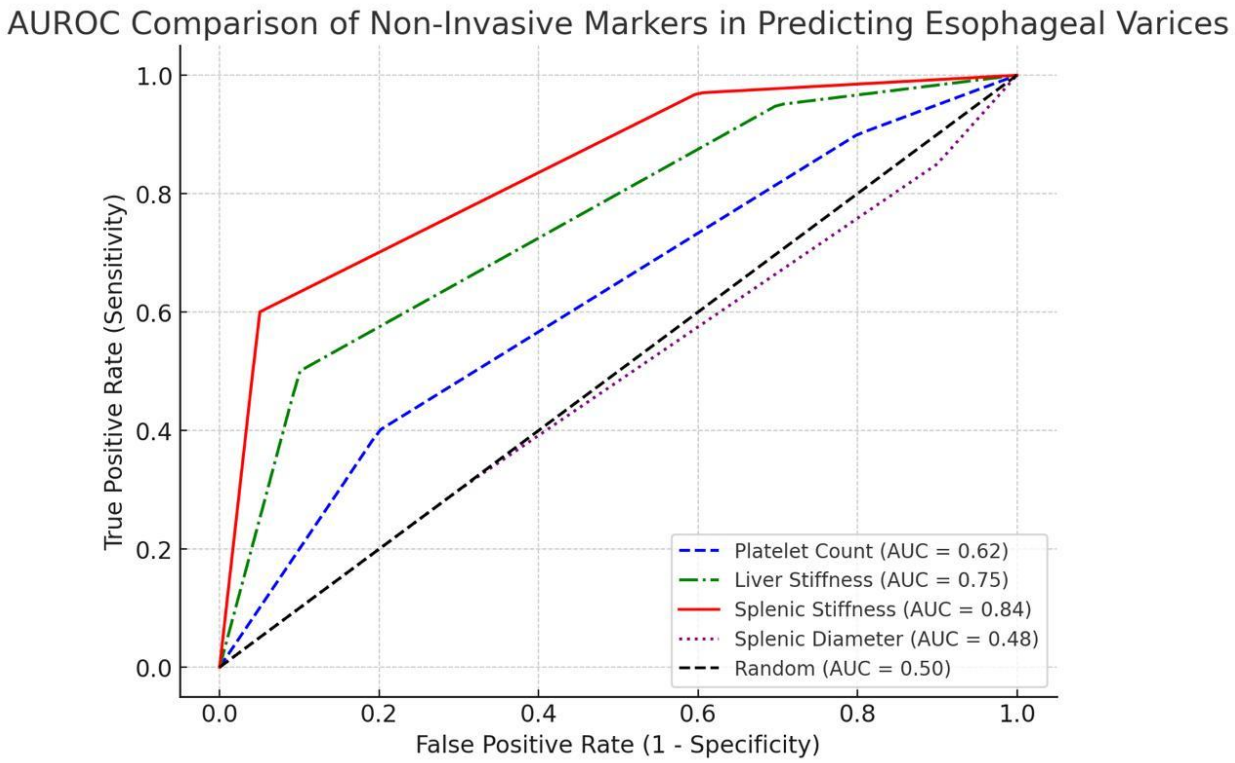
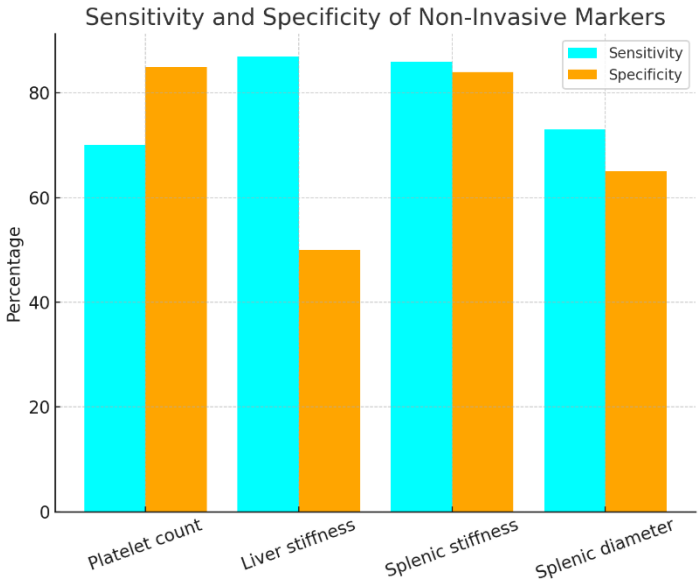
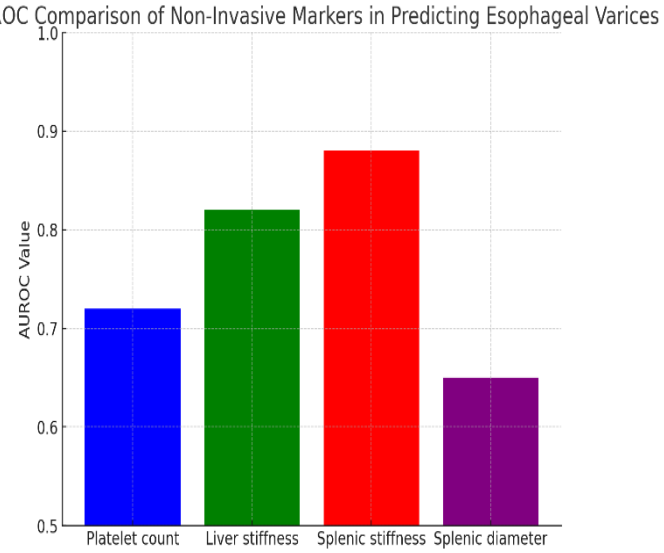


Figure: AUROC Comparison of Non-Invasive Markers in Predicting Esophageal Varices

Table: Sensitivity, Specificity, PPV, NPV, and Diagnostic Accuracy

Parameter	AUROC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Platelet count	0.72	70	85	88	64	76
Liver stiffness	0.82	87	50	72	73	73
Splenic stiffness	0.88	86	84	90	79	85
Splenic diameter	0.65	73	65	76	61	69





DISCUSSION

The findings of this study provide valuable insights into the predictive accuracy of non-invasive markers for esophageal varices in cirrhotic patients, highlighting splenic stiffness as the most reliable predictor. The diagnostic performance of splenic stiffness surpassed that of liver stiffness, platelet count, and splenic diameter, reinforcing its potential role as a primary screening tool for esophageal varices in clinical practice. The ability to predict esophageal varices through non-invasive assessments is particularly relevant in resource-limited settings, where access to esophagogastroduodenoscopy remains constrained (12,13). The results align with existing literature that has explored the utility of non-invasive markers in detecting portal hypertension and esophageal varices. Platelet count, a well-established surrogate marker, demonstrated moderate predictive ability, consistent with prior studies that have suggested its association with variceal development. However, while a threshold platelet count has been proposed for varices prediction, its lower predictive accuracy compared to elastography-based parameters limits its standalone clinical utility. Liver stiffness, a widely validated marker of portal hypertension, exhibited high predictive accuracy in this study, reinforcing its role as an important diagnostic tool. The observed AUROC for liver stiffness was comparable to previously reported values, supporting its reliability in varices prediction. However, its specificity was lower, which may be attributed to factors such as hepatic congestion and inter-individual variations in liver stiffness measurements (14,15).

Splenic stiffness emerged as the most accurate non-invasive predictor of esophageal varices, demonstrating superior sensitivity and specificity. This finding corroborates emerging evidence suggesting that splenic stiffness may better reflect the hemodynamic changes associated with portal hypertension than liver stiffness alone. The spleen undergoes significant architectural changes in response to increased portal pressure, including fibrosis and congestion, making splenic stiffness a robust surrogate marker of clinically significant portal hypertension. Given its superior diagnostic performance, splenic stiffness may serve as a primary screening tool for esophageal varices, potentially reducing the need for unnecessary endoscopic evaluations (16,17). Among the markers assessed, splenic diameter exhibited the lowest predictive accuracy. While splenomegaly is a recognized feature of portal hypertension, its diagnostic reliability is affected by variability in splenic enlargement across different cirrhosis etiologies. This limitation aligns with previous research, which

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has suggested that splenic diameter alone may not be a strong predictor of varices. Its incorporation into multi-parameter predictive models may enhance risk stratification, but its standalone diagnostic utility remains suboptimal (18,19).

The clinical implications of these findings emphasize the importance of incorporating non-invasive assessments into routine risk stratification protocols for cirrhotic patients. The high diagnostic accuracy of splenic stiffness suggests that it may be integrated into screening algorithms, particularly in centers equipped with transient elastography. The combination of splenic stiffness, liver stiffness, and platelet count may provide a comprehensive non-invasive approach to predicting esophageal varices, allowing for targeted endoscopic evaluations and optimizing healthcare resource utilization (20). Despite the strengths of this study, including a robust sample size and a direct comparison of multiple non-invasive markers, certain limitations should be considered. The single-center nature of the study may limit the generalizability of findings to broader populations with varying cirrhosis etiologies. Additionally, transient elastography measurements may be influenced by operator expertise and patient-specific factors such as obesity and ascites, which could affect the reliability of liver and splenic stiffness assessments. Future multicenter studies with larger sample sizes are warranted to validate these findings across diverse patient populations and to explore the integration of these markers into standardized risk assessment protocols.

CONCLUSION

This study underscores the significance of splenic stiffness as the most reliable non-invasive predictor of esophageal varices in cirrhotic patients, demonstrating superior diagnostic accuracy compared to liver stiffness, platelet count, and splenic diameter. The findings highlight its potential integration into clinical risk stratification models, offering a valuable alternative to invasive procedures and optimizing the utilization of esophagogastroduodenoscopy. By enhancing early detection strategies, splenic stiffness may contribute to improved patient management and resource allocation in settings with limited endoscopic availability. Further research is warranted to validate these findings across diverse populations and explore its broader implementation in routine clinical practice.

AUTHOR CONTRIBUTIONS

Author	Contribution
Abdul Wahid Balouch	Conceptualization, Methodology, Formal Analysis, Writing - Original Draft, Validation, Supervision
Azhar Ali	Methodology, Investigation, Data Curation, Writing - Review & Editing
Ali Hyder	Investigation, Data Curation, Formal Analysis, Software
Khalid Tareen	Software, Validation, Writing - Original Draft
Raja Taha Yaseen Khan	Formal Analysis, Writing - Review & Editing
Abbas Ali Tasneem	Writing - Review & Editing, Assistance with Data Curation
Nasir Hasan Luck	Investigation, Data Curation, Formal Analysis, Software
Huraira Ali	Software, Validation, Writing - Original Draft
Syeda Maryam Mehdi	Formal Analysis, Writing - Review & Editing
Abdullah Nasir	Writing - Review & Editing, Assistance with Data Curation

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