

DIAGNOSTIC ACCURACY OF NON-INVASIVE PARAMETERS FOR DETECTING ESOPHAGEAL VARICES IN CIRRHOTIC PATIENTS IN A RESOURCE-LIMITED SETTING

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INTRODUCTION

Global prevalence of hepatic cirrhosis from autopsy studies ranges from 4.5% to 9.5% of the general population.¹ Hence, we estimate that more than fifty million people in the world, in the adult population, would be affected by chronic liver disease (CLD). In 2001, the estimated worldwide mortality from cirrhosis was 771,000 people, ranking 14th and 10th as the leading cause of death in the world and in developed countries, respectively.² Out of the causes of death from CLD, gastrointestinal bleeding accounts for most of the preventable mortality cases, largely driven by the development of oesophageal varices secondary to portal hypertension. Clinically, portal hypertension increases resistance to blood flow, forcing the development of

portosystemic collaterals as the liver's architecture becomes distorted by chronic fibrosis.^{3,4} The most prominent causes of cirrhosis are chronic viral Hepatitis, prolonged excessive alcohol consumption and Non-alcoholic fatty liver disease, with great regional variation.⁵ In Pakistan, studies attribute Hepatitis as the predominant cause of cirrhosis, with Hepatitis C Virus responsible for 41%-52%, followed by Hepatitis B Virus (HBV) for 30% of the cases.⁶ Several studies have demonstrated that parameters obtainable through routine laboratory investigations and imaging, such as AST/ALT ratio, INR, spleen size, portal vein diameter, ascites and platelet-to-spleen diameter ratio, correlate with the presence of oesophageal varices in cirrhotic patients, offering potential tools for non-invasive screening.⁷ In recent literature, platelet count-to-spleen

ABSTRACT

OBJECTIVES

This study evaluates the ability of selected non-invasive markers—portal vein diameter (>13 mm), aspartate aminotransferase (AST), AST-to-platelet ratio index (APRI), platelet-to-spleen diameter ratio, spleen size, and INR to detect oesophageal varices in cirrhotic patients accurately. The goal is to reduce reliance on invasive procedures and lower healthcare costs, particularly in resource-limited settings.

METHODOLOGY

This cross-sectional, prospective study included 165 patients undergoing screening endoscopy, ultrasonography, and laboratory investigations (selected via a non-probability, consecutive sampling technique). The study was conducted at Aga Khan University Hospital, Karachi, from 1st April 2024 to 30th September 2024. Factors associated with oesophageal varices were first analysed using univariable logistic regression analyses. The predictive performance of the final model was evaluated using sensitivity, specificity, positive and negative predictive values, and overall accuracy. Statistical significance was set at $p < 0.05$.

RESULTS

Spleen size remained significantly associated with oesophageal varices (p -value = 0.025). Other variables, including age, gender, PVD >13 mm, Ascites, AST, APRI, platelet-to-splenic diameter ratio, and INR, were not independently associated. The model achieved an overall accuracy of 80%, sensitivity of 84%, specificity of 67%, and positive predictive value of 90%, while the negative predictive value was 55% in predicting oesophageal varices.

CONCLUSION

Among the evaluated non-invasive parameters, spleen size demonstrated the most consistent association with the presence of oesophageal varices, remaining an independent predictor on multivariable analysis. The predictive model incorporating non-invasive markers achieved good overall accuracy with high sensitivity, indicating its usefulness in identifying patients at high risk for oesophageal varices, although specificity and negative predictive value were moderate.

KEYWORDS: Oesophageal Varices, Chronic Liver Disease, Portal Vein Diameter, Non-Invasive Parameters, Diagnostic Accuracy

diameter ratio has emerged as a promising predictor with favourable diagnostic performance in resource-limited clinical settings.⁸ Despite this, to the best of our knowledge, the utility of individual non-invasive parameters such as portal vein diameter >13 mm, aspartate aminotransferase (AST), AST-to-platelet ratio index (APRI), and spleen size for predicting oesophageal varices has not been analysed in Pakistan within a single study. Considering a high disease burden in Pakistan causing financial implications for the healthcare system and in order to minimise unnecessary reliance on endoscopies, this study was conducted to evaluate the diagnostic accuracy of the readily measurable variables.

METHODOLOGY

The study was a cross-sectional, prospective study conducted after ERC exemption was granted () at Aga Khan University Hospital, Karachi, from 1st April 2024 to 30th September 2024. All male/female patients aged between 18 and 85 years who visited the daycare facility at the Endoscopic Suite of Aga Khan University Hospital, Karachi and were diagnosed with chronic liver disease via abdominal ultrasound as per the operational definition and undergoing screening upper GI (gastrointestinal) endoscopy were included in this study. Patients with a history of variceal bleeding and intervention, cirrhotic patients with hepatocellular carcinoma and patients undergoing liver transplantation were excluded from the study. People who did not consent or who were critically ill were also excluded. A total of 165 patients fulfilling the eligibility criteria were enrolled prospectively using a non-probability, consecutive technique. Sample size was calculated using Dr Lin Naing's calculator, taking sensitivity 71.8%, specificity 55%, prevalence as 64% and margin of error as 0.13%. All stable participants visiting the Ultrasound department at AKUH for CLD follow-up were referred to the Endoscopic suite department at AKUH for their screening endoscopy, and subsequently necessary laboratory investigations were carried out. The record of patients' demographic data (age, gender), laboratory investigations (CBC, LFTs, INR), and initial ultrasonography findings measured using a 4–6 MHz curvilinear probe (portal vein diameter, ascites, spleen size) is carried out by a qualified sonographer or radiology resident. All saved images and electronically mapped callipers are sent via the PACS (Picture Archiving and Communication System) hub to be blindly reviewed and officially validated by a Specialist

Consultant Radiologist trained in hepatic parameters. Organ lengths (like the liver, kidneys, and spleen) are obtained at their maximum longitudinal dimension using outer -margin to outer -margin tracking. At the same time, the portal vein is routinely measured inner -wall to inner -wall to prevent overestimating pathology, and the presence/absence of oesophageal varices is assessed on esophagogastroduodenoscopy performed by the consultant gastroenterologist. Data were analysed using RStudio (version 4.1.2; Boston, USA). Descriptive statistics were used to summarise patient characteristics. Categorical variables, including gender, vein status, and presence of ascites, were reported as frequencies and percentages. Continuous variables, such as age, PVD, and spleen size, were assessed for normality using the Shapiro-Wilk test and were found to be non-normally distributed; therefore, medians with interquartile ranges were reported. Comparisons between patients with and without oesophageal varices were performed using the Chi-square or Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables. Factors associated with oesophageal varices were first examined using univariable logistic regression analyses. Variables with p -values <0.25 in the univariable analyses were included in a multivariable logistic regression model to adjust for potential confounders. Odds ratios (ORs) with 95% CIs were reported to quantify the strength of associations. The predictive performance of the final model was evaluated using sensitivity, specificity, positive and negative predictive values, and overall accuracy. Statistical significance was set at $p < 0.05$.

RESULTS

A total of 165 patients were included in the study. The median age of participants was 61.0 years [Q1: 52.0, Q3: 70.0]. Of the total, 97 (58.8%) were males, and 68 (41.2%) were females. The presence of dilated veins was observed in 77 (46.7%) patients. The median portal vein diameter (PVD) was 12.2 mm [9.8, 14.0]; PVD <13 mm was found in 96 (58.2%) patients, while PVD >13 mm was present in 77 (46.7%). The median spleen size was 137 mm [117, 156]. Ascites was present in 69 (41.8%) of patients, whereas 96 (58.2%) had no ascites. The median AST level was 50.0 U/L [35.0, 85.0], and the median APRI score was 1.40 [0.81, 3.23]. The platelet-to-splenic diameter ratio had a median value of 629 [419, 1180], and the median INR was 1.30 [1.10, 1.60]. (Table 1)

Table 1 Shows Baseline Demographic, Clinical, and Laboratory Characteristics of the Study Population (N = 165)

Variable	Overall (N=165)
Age	
Median [Q1, Q3]	61.0[52.0,70.0]
Gender	
Female	68 (41.2%)
Male	97 (58.8%)
Vein	
No	88 (53.3%)
Yes	77 (46.7%)
PVD Size (mm)	
Median [Q1, Q3]	12.2[9.80,14.0]
PVD <13MM	
No	69 (41.8%)
Yes	96 (58.2%)
PVD >13MM	
No	88 (53.3%)
Yes	77 (46.7%)
Spleen Size (mm)	
Median [Q1, Q3]	137[117,156]
Ascites	
Absent	96 (58.2%)
Presence	69 (41.8%)
AST	
Median [Q1, Q3]	50.0[35.0,85.0]
APRI	
Median [Q1, Q3]	1.40[0.813,3.23]
Platelet to Splenic Diameter	
Median [Q1, Q3]	629[419,1180]
INR	
Median [Q1, Q3]	1.30[1.10,1.60]

Among the 165 patients, 129 (78.2%) had oesophageal varices, while 36 (21.8%) did not. The median age was slightly lower among patients with varices (60.0 years [50.0, 70.0]) compared to those without (63.5 years [53.8, 75.3]), though this difference was not statistically significant ($p = 0.073$). Males were more frequently affected by varices (60.5%) than females (39.5%), but this difference was also not significant ($p = 0.447$). The median PVD was significantly higher in patients with varices (12.3 mm [10.0, 14.0]) than in those without (10.9 mm [8.85, 13.2], $p = 0.027$). Similarly, spleen size was markedly larger among patients with varices (142 mm [124, 161]) compared with those without (113 mm [91.8, 144], $p < 0.001$). Although the proportion of patients with ascites was higher in the varices group (45.7% vs 27.8%), the difference approached but did not reach statistical significance ($p = 0.059$). No significant differences were observed in AST levels ($p = 0.191$), APRI scores ($p = 0.297$), or INR values ($p = 0.319$) between the two groups. However, the platelet-to-splenic diameter ratio was significantly lower in patients with varices (582 [419, 1060]) than in those without (1160 [440, 1600], $p = 0.034$). (Table 2) In univariable analysis, spleen size (OR 1.04, 95% CI 1.02–1.05,

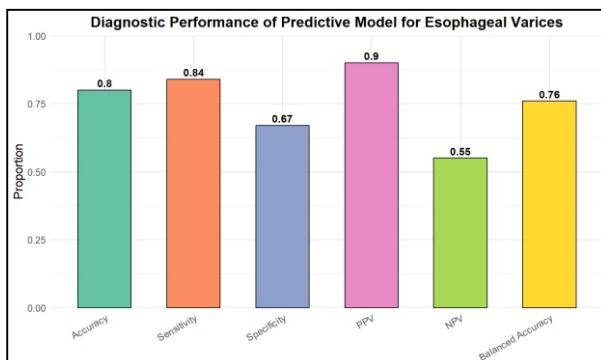
$p < 0.001$) and platelet-to-splenic diameter ratio (OR 1.34, 95% CI 1.10–1.90, $p = 0.005$) were significantly associated with higher odds of oesophageal varices. Age (OR 0.97, 95% CI 0.94–1.00, $p = 0.058$) and PVD size (OR 1.13, 95% CI 1.00–1.28, $p = 0.056$) showed borderline associations. Ascites showed a trend toward increased odds of varices (OR 2.19, 95% CI 1.00–5.11, $p = 0.057$). Other factors, including gender, PVD >13 mm, AST, APRI, and INR, were not significantly associated with oesophageal varices in univariable analysis. (Table 3) After adjustment for all factors, spleen size remained significantly associated with oesophageal varices (OR 1.02, 95% CI 1.01–1.05, $p = 0.025$). Other variables, including age, gender, PVD >13 mm, Ascites, AST, APRI, platelet-to-splenic diameter ratio, and INR, were not independently associated. Ascites, which showed a trend in univariable analysis, was not significant in the multivariable model (OR 1.57, $p = 0.358$). (Table 3) The model achieved an overall accuracy of 80% (95% CI: 74–86%) in predicting oesophageal varices. It showed high sensitivity (84%), indicating a strong ability to correctly identify patients with varices, and moderate specificity (67%), reflecting its performance in correctly identifying those without varices. The positive predictive value was 90%, suggesting that most patients predicted to have varices actually had the condition, while the negative predictive value was 55%, indicating a moderate ability to rule out disease. (Figure 1)

Table 2: Comparison of Clinical and Laboratory Characteristics Between Patients with and without Oesophageal Varices

Variable	Oesophageal Varices		p-value
	Yes (N=129)	No (N=36)	
Age			
Median [Q1, Q3]	60.0 [50.0, 70.0]	63.5 [53.8, 75.3]	0.073
Gender			
Female	51 (39.5%)	17 (47.2%)	0.447
Male	78 (60.5%)	19 (52.8%)	
PVD Size (mm)			
Median [Q1, Q3]	12.3 [10.0, 14.0]	10.9 [8.85, 13.2]	0.027
PVD <13MM			
No	58 (45.0%)	11 (30.6%)	0.131
Yes	71 (55.0%)	25 (69.4%)	
PVD >13MM			
No	66 (51.2%)	22 (61.1%)	0.347
Yes	63 (48.8%)	14 (38.9%)	
Spleen Size (mm)			
Median [Q1, Q3]	142 [124, 161]	113 [91.8, 144]	<0.001
AST			
Median [Q1, Q3]	51.0 [39.0, 85.0]	43.5 [26.8, 101]	0.191
APRI			
Median [Q1, Q3]	1.55 [0.884, 2.97]	1.01 [0.451, 4.92]	0.297
Platelet to Splenic Diameter			
Median [Q1, Q3]	582 [419, 1060]	1160 [440, 600]	0.034
INR			
Median [Q1, Q3]	1.30 [1.10, 1.60]	1.20 [1.10, 1.73]	0.319

Table 3: Univariable and Multivariable Logistic Regression Analyses for Factors Associated with Oesophageal Varices

Factor	Univariable	Multivariable
	OR (95% CI), P-value	OR (95% CI), P-value
Age	0.97 (0.94-1.00, p=0.058)	0.99 (0.96-1.03, p=0.628)
Gender		
Female	Ref-1.00	-
Male	1.37 (0.65-2.88, p=0.408)	-
Vein		
No	Ref-1.00	-
Yes	1.30 (0.62-2.77, p=0.497)	-
PVD Size (mm)	1.13 (1.00-1.28, p=0.056)	1.12 (0.87-1.45, p=0.383)
PVD >13MM		
No	Ref-1.00	-
Yes	1.50 (0.71-3.25, p=0.292)	-
Spleen Size (mm)	1.04 (1.02-1.05, p<0.001)	1.02 (1.00-1.05, p=0.025)
Ascites		
No	Ref-1.00	Ref-1.00
Yes	2.19 (1.00-5.11, p=0.057)	1.57 (0.61-4.28, p=0.358)
AST	1.10 (0.99-1.30, p=0.219)	1.00 (0.99-1.01, p=0.964)
APRI	0.94 (0.83-1.00, p=0.180)	0.83 (0.63-1.00, p=0.167)
Platelet to Splenic Diameter	1.34 (1.10-1.90, p=0.005)	1.02 (0.99-1.05, p=0.169)
INR	1.02 (0.79-1.63, p=0.876)	-

**Figure 1: Diagnostic Performance of the Predictive Model for Oesophageal Varices**

DISCUSSION

Multiple clinical studies have provided significant evidence supporting the correlation between non-invasive predictors of oesophageal varices in patients with chronic liver disease. Early identification of patients at risk remains a cornerstone of management; however, reliance on endoscopic screening is often impractical in resource-limited settings, which results in rising mortality. This study evaluated the diagnostic performance of routinely available non-invasive parameters to identify oesophageal varices among cirrhotic patients and demonstrated that spleen size

remained statistically significant after multivariable adjustment. Previously, Habibullah Jan D et al. and Sarangapani A et al. have corroborated these findings.^{9,10} This finding is pathophysiologically plausible, as splenomegaly directly reflects sustained portal hypertension. Recent studies and consensus guidelines continue to emphasise spleen size as a robust surrogate marker of clinically significant portal hypertension, particularly in settings where electrography and hepatic venous pressure gradient measurements are unavailable.¹¹ Our results reinforce spleen size as a simple, reproducible, and cost-effective marker that can be easily incorporated into routine ultrasonography assessment. Portal vein diameter and platelet-to-splenic diameter ratio demonstrated significant associations with oesophageal varices on univariable analysis; however, these associations did not persist after adjustment for confounding factors. Although PVD is traditionally considered a marker of portal hypertension, its diagnostic reliability has been inconsistent in contemporary literature.¹² Since ultrasound findings are operator-dependent, its utility is limited as a standalone predictor. The platelet-to-splenic diameter ratio, which integrates thrombocytopenia and splenomegaly, has been proposed as a non-invasive screening tool in several studies.^{10,13} Failure to be statistically significant might be due to the multifactorial nature of thrombocytopenia in cirrhosis, including bone marrow suppression, viral Hepatitis, nutritional deficiencies, and medication effects, which can confound its relationship with portal hypertension, particularly in resource-limited populations. Biochemical markers, including AST levels, APRI scores and INR, were not significantly associated with oesophageal varices. Although these indices are widely used for fibrosis assessment and prognostication in chronic liver disease, emerging evidence suggests that they have limited utility in predicting portal hypertension-related complications.^{7,14} These markers primarily reflect hepatic necroinflammatory activity and synthetic dysfunction rather than portal pressure, which may account for their limited discriminatory ability in identifying varices in this study. The predictive model incorporating non-invasive parameters achieved good overall accuracy with high sensitivity, indicating a strong capacity to identify patients with oesophageal varices. However, the model demonstrated acceptable but limited specificity and negative predictive value, suggesting that while it is effective for identifying patients who require endoscopic evaluation, it may be less reliable for safely excluding varices. Similar diagnostic performance patterns have been reported in recent validation studies of non-invasive models, underscoring the ongoing challenge of replacing endoscopy with non-invasive tools.^{15,16,17,18}

LIMITATIONS

This study is limited by its cross-sectional design, which precludes causal inference, and by its single-centre setting, which may limit generalizability. The endoscopy-based sampling strategy may also have introduced selection bias, as patients who underwent endoscopic assessment may have differed systematically from those who did not. Although ultrasonography is non-invasive, portal vein diameter measurements are operator-dependent and may be influenced by patient positioning, respiratory phase, measurement technique, and interobserver variability; details regarding operator training, blinding to endoscopic findings, and measurement reproducibility were not reported. In addition, the study did not include internal or external validation of the proposed predictive threshold or diagnostic performance estimates. Advanced non-invasive modalities, such as transient elastography, were unavailable, and potentially relevant confounding factors, including disease aetiology, severity, and hemodynamic or treatment-related variables, may not have been fully accounted for. These limitations mean that portal vein diameter should be interpreted as a supportive screening marker rather than a replacement for endoscopic evaluation. Future multicenter prospective studies integrating dynamic markers and longitudinal outcomes are warranted to validate these findings and refine non-invasive screening strategies.

CONCLUSIONS

In this study, oesophageal varices were common, occurring in 129 (78.2%) patients. Portal vein diameter was significantly greater in patients with varices than in those without; however, PVD greater than 13 mm was not significantly associated with varices in either univariable or multivariable analysis. Spleen size was the only parameter that remained independently associated with oesophageal varices after adjustment for other clinical and laboratory factors. The predictive model demonstrated good sensitivity and positive predictive value but only moderate specificity and a limited negative predictive value.

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Maria Danish Khan - Concept & Design; Data Acquisition; Data Analysis/Interpretation; Critical Revision; Supervision; Final Approval

Angheen Aqeel - Concept & Design; Data Acquisition; Drafting Manuscript; Final Approval

Samar Fatima - Concept & Design; Drafting Manuscript; Critical Revision; Final Approval

Tahir Munir - Concept & Design; Data Analysis/Interpretation; Drafting Manuscript; Final Approval

The authors accept responsibility for all aspects of the work and will ensure that any concerns regarding the accuracy or integrity of any part are properly investigated and resolved.



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