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Criteria for the non-invasive prediction of large esophageal varices based on clinical, laboratory, and imaging data

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Abstract
Introduction: A portal pressure gradient over 5-10 mm Hg is indicative of portal hypertension, which is a defining feature of cirrhosis. Varices form in individuals with portal hypertension when the flow of blood through the portal circulation is redirected by portosystemic collaterals.
Methods: This prospective study included all consecutive newly diagnosed patients at our tertiary referral center, Department of Paediatrics, D.D. Medical College and Hospital, Thiruvallur, Tamil Nadu, India, between August 2011 and July 2012, with or without gastrointestinal bleeding. Informed permission was signed by patients before to enrollment in the trial.
Results: In all, eighty people took part in the study. The population's age range spans from 15 to 70 years old, with a median age of 45. There were 2.11 male patients for every female patient. The patients were sixty-two men. Ninety days was the average duration of symptoms (range, 10-230 days). Of the patients, 43 exhibited pedal edoema and 50 had evident ascites.
Conclusion: If this method is proven to be effective, it would obviate the necessity for costly and invasive procedures such as gastrointestinal endoscopy. Additionally, it would enable the utilization of beta-adrenergic antagonists as preventive measures against primary variceal hemorrhage in patients suffering from liver cirrhosis.

Keyword: Clinical, imaging criteria, non-invasive, large esophageal varices, gastrointestinal endoscopy

Introduction

Variceal hemorrhage is a major contributor to illness and death in individuals with cirrhosis. Primary prophylaxis using nonselective beta-blockers and endoscopic band ligation can decrease the likelihood of variceal hemorrhage. Thus, it is advisable for individuals diagnosed with cirrhosis to undergo endoscopic screening for esophageal varices (EV) upon diagnosis. Esophageal varices and internal hemorrhage are two perilous consequences that can arise in patients suffering from portal hypertension [1-3]. At the time of diagnosing liver cirrhosis, approximately 40% of patients with compensated disease and 60% of patients with decompensated disease and ascites have esophageal varices [4]. Annually, approximately 5% of the population will acquire cirrhosis of the liver without producing esophageal varices. Approximately 4% of patients with hepatic cirrhosis experience a variceal hemorrhage annually [4, 5]. The occurrence of large esophageal varices in

individuals without bleeding issues is exceedingly uncommon. Consequently, a significant number of unnecessary invasive endoscopic procedures are being conducted on cirrhotic patients who have not experienced any bleeding episodes. Therefore, it is necessary to use non-invasive techniques to ascertain the presence of substantial esophageal varices.

Increased availability of these alternatives could potentially reduce the frequency of using endoscopic procedures for detecting significant esophageal varices [6, 7]. Patients with cirrhosis who have a high platelet count, splenomegaly, an advanced Child status, elevated blood albumin levels, or a large portal vein diameter on ultrasonography are all noninvasive markers of large esophageal varices. Differences in the causes of cirrhosis, the degree of liver disease, and the nutritional state of different populations can result in specific predictive indicators [8]. Despite the late presentation, lower nutritional status, and higher proportion of viral cause, there is a lack of research on Indians with liver cirrhosis. The aim of this study is to evaluate the accuracy of several clinical, biochemical, and ultrasonographic indicators in predicting the occurrence of significant esophageal varices in patients with portal hypertension. The objective of this inquiry is to determine the prevalence of esophageal varices of different sizes in individuals with liver disease.

Various techniques can be employed to identify significant esophageal varices at an early stage, including clinical examination, biochemical analysis, and ultrasonic imaging [9,11]. The objective is to identify the most accurate and precise diagnostic indicators for predicting the existence of large esophageal varices. The clinical evaluation of the 909 platelet count to spleen diameter ratio as a predictor for the presence of large esophageal varices.

Methodology

From August 2011 to July 2012, we conducted a prospective analysis of all consecutive patients who arrived at our institution, Department of Paediatrics, D.D. Medical College and Hospital, Thiruvallur, Tamil Nadu, India. These patients were referred to our tertiary center and had a diagnosis of liver disease, with or without a history of gastrointestinal bleeding. Prior to engaging in the trial, patients were obligated to sign a document known as an informed consent form.

Inclusion Criteria

- Age ranges from 15-70 years.
- The topic of discussion is hepatitis and portal hypertension.

Exclusion Criteria

- Challenges in the field of primary hematology.
- Upon arrival, there was a gastrointestinal hemorrhage.
- Administering medicine as a preventive measure against variceal hemorrhage.
- Prior history of parenteral drug addiction.
- History of band ligation or EST and TIPS.
- Advanced co-morbidity for endoscopy.
- Prior surgical intervention for portal hypertension.

Clinical Evaluation

Every patient underwent a comprehensive medical checkup upon registration. We documented the patient's age, gender, medical history, and the etiology of their liver disease, along with any indications or manifestations of liver failure, such as hepatomegaly, splenomegaly, and abdominal vein collaterals.

Results

The study included a grand total of 80 individuals. The population has a median age of 45, with an age distribution ranging from 15 to 70. The male-to-female patient ratio was 2.11:1. There were a total of 62 patients that were male. The average duration of symptoms was 90 days, with a range of 10 to 230 days. A total of 50 individuals exhibited evident ascites, while an additional 43 patients displayed pedal edema. Out of the total number of patients, specifically fifty-three individuals experienced gastrointestinal bleeding, which included symptoms like hematemesis (Vomiting blood) or melena

(passing dark, tarry stools). A total of fifty-three individuals were found to have jaundice throughout the presentation. The primary cause of liver illness was found to be alcohol consumption, with hepatitis B virus, autoimmune hepatitis, and hepatitis C virus being secondary causes. Here, we provide CTP's assessment of the seriousness of liver illness. Table 1 provides a list of demographic and clinical characteristics, including the severity of the disease and the root cause of liver cirrhosis.

Table 1: Endoscopic findings of portal hypertension

Sr. No.	Endosciopic findings	Number
1.	No varices	04
2.	Small varices	24
3.	Large varices	29
4.	Esophagogastric varices	02
5.	Portal hypertensive gastropathy	21
	Total	80

The endoscopy results are summarized above, revealing that two individuals were diagnosed with esophagogastric varices. Out of the total number of patients, 21 individuals had both esophageal varices and portal hypertensive gastropathy. Each individual never has only one stomach varix.

Table 2: Varicose vein presence classification (CTP)

Sr. No.	CTP class	Varices	Large varices
1.	A=25	15	10
2.	B=32	24	08
3.	C=23	20	03

Examining a Single Variable Sequentially There was a significant correlation between the presence of big varices and raised bilirubin levels, low platelet counts, a high complete blood count time point (CTP) score, a small spleen, and enlarged portal and splenic veins.

Table 3: Identification of factors associated with the presence of big esophageal varices using a multivariate logistic regression

Sr. No.	Predictor	P-value
1.	Bilirubin	0.08
2.	Palpable spleen	0.001
3.	Platelet count	0.0001
4.	Spleen size	0.0003
5.	Portal vein size	0.0001
6.	Splenic vein size	0.0001

Table 3 presents the outcomes of a logistic regression analysis performed on a sample of 80 patients, utilizing the predictors that were identified as statistically significant in the univariate study. Statistically significant findings were observed in the existence of a palpable spleen, platelet count in the blood, size of the portal vein, and size of the splenic vein.

By comparing the dimensions of the platelets with those of the spleen, it is possible to determine the presence or absence of significant esophageal varices. The AUC (Area Under the Curve) of the prediction function's receiver operating characteristic was 0.95. At a threshold of 908, the sensitivity and specificity were both 99%.

Discussion

There will be a higher need for OV screens in the near future as more patients are anticipated to receive a diagnosis of chronic liver disease. Due to the serious medical, societal, and financial ramifications that come with varices, researchers are actively looking for non-invasive predictors of the condition's progression. Only one research examined individuals with compensated illness, and several studies lacked homogeneity in OV classification or appropriate statistical analysis [12, 13]. Moreover, a small patient sample was used in the majority of investigations on the non-invasive diagnosis of OV. There was one prospective study, and the results aligned with the findings of the retrospective studies. Low platelet counts and

splenomegaly are reliable non-invasive markers of ova. We solely took into account standardized, widely recognized, and repeatable criteria as a result. Six criteria were found to have univariate predictive value for the incidence of large esophageal varices based on data from 106 people with portal hypertension, 51 of whom had these conditions. Only four of these factors-a low platelet count, splenomegaly, a large portal vein, and a large splenic vein-were found to be predictive by a multivariate analysis. In the investigations [14, 15], the areas under the ROC curve for platelet count and splenomegaly were only moderately effective, at 0.701 and 0.883, respectively. One of the main causes of morbidity and death in patients with portal hypertension is internal bleeding from varices.

On the other hand, compared to those with larger varices, those with smaller varices have a significantly lower risk of developing this illness. It is important to identify patients who have significant esophageal varices and would benefit most from preventative interventions, since pharmaceutical medications, such as beta-adrenergic receptor antagonists, can minimize the risk of variceal bleeding [16]. Examining for the presence of substantial esophageal varices at the time of first diagnosis and at frequent intervals throughout life is crucial for people with liver cirrhosis. Nevertheless, this approach results in significant cost burdens for patients and strains endoscopic centers. Thus, studies have been carried out to determine whether clinical, laboratory, and imaging features of a patient may be used to accurately predict the presence or absence of substantial esophageal varices. Aetiology of liver disease, portal vein diameter, thrombocytopenia, ascites, spider naevi, hepatic encephalopathy, serum albumin concentration, serum bilirubin levels, prothrombin time, Child-Pugh score, and derived measures such as the ratio of platelet count to splenic size have all been demonstrated to be beneficial in this regard [17, 18].

Along with a low platelet count, a wide portal vein, and a short splenic vein, previous research has consistently shown that the presence of an enlarged spleen is a predictor [19]. This study discovered that, in contrast to other research, none of these additional traits were even remotely important in predicting success. All things considered, the results of this inquiry aligned with the previously mentioned information. Research by K. C. Thomopoulos *et al*. revealed that 50% of patients had esophageal varices, with 17% of those patients (33/92) having severe varices. Using a dataset of 22 variables, univariate analysis showed that large esophageal varices were independently associated with the incidence of ascites, splenomegaly, and high bilirubin levels [19-21].

Multivariate analysis showed that the size of the oesophageal varices was independently correlated with a large spleen, a high platelet count, and the presence of ascites by ultrasound. Of the 39 patients with platelets below 118 (109/l), spleen length below 135 mm, and no ascites, 5/39 (12.8%) met the median value cutoffs for the absence of varices. Furthermore, the varicose veins in the patients weren't too bad. Fifteen (83.3%) of the eighteen patients who had ascites, a spleen length greater than 135 mm, and a platelet count of 118 109/l also experienced varices. Of the eighteen patients, five (28.1%) developed severe varices. Thrombocytopenia, splenomegaly, and ascites were independent predictors of large oesophageal varices in individuals with cirrhosis [22].

A platelet count of 88,000 was the only factor linked to the development of large esophageal or stomach varices, according to univariate and multivariate studies done by Zaman A. *et al*. ($p < 0.05$). 33 High platelet counts and a Child-Pugh class are independent risk factors for varices, and the occurrence of large varices in particular, according to investigations done by Zaman A. *et al*. A Child-Pugh score of advanced was associated with a platelet count of 90,000. Extensive varices were independently associated with a severe Child-Pugh class and a platelet count of 80,000 [23].

Prihatini J *et al*. discovered that the prevalence of varices was 76.6% after looking into 47 cases. 35 Using bivariate analysis, we found that a splenic size of 10.3 cm had 83.3% sensitivity and 63.0% specificity, a portal vein diameter of 1.15 cm had 75% sensitivity and 54.5% specificity, and a

platelet count of 82,000/ul had 90.9% sensitivity and 41.7% specificity as a predictor of esophageal varices in liver cirrhosis. Noninvasive assays, such as portal vein width, anteroposterior splenic measurement, and platelet count, can be used to diagnose esophageal varices in individuals with cirrhosis.

According to studies by Jeon SW *et al*., esophageal varices affect 48% of the population.

In univariate analysis, 41 biomarkers were shown to have significant relationships, including serum albumin, total bilirubin, prothrombin time, platelet count, spleen size, portal vein velocity, and portal vein diameter. In a multivariate analysis, the independent variables included the platelet count, the spleen diameter, and the ratio between the two. Varices can be seen in a patient with cirrhosis and splenomegaly during an endoscopic evaluation. The 909 value that Giannini *et al*. established as the ideal platelet-spleen diameter ratio limit is supported by this study. It was discovered that the ratio of 909 between the diameters of the spleen and platelets was highly specific (99%) and sensitive (98.5%) in identifying the existence of large esophageal varices. The ROC curve was determined to have an AUC of 0.95. One can approximate the degree of clinically severe portal hypertension by dividing the platelet count by the diameter of the spleen [24].

Conclusion

Severe esophageal varices were identified in 48.1% of the population. Large esophageal varices are independently associated with low platelet counts, splenomegaly, portal vein size, and splenic vein size in individuals with liver cirrhosis. These tests may be helpful in determining whether an upper GI endoscopy is necessary for patients without severe esophageal varices. Both the patient's discomfort and the endoscopic unit's cost may decrease as a result. The prevalence of big esophageal varices was only partially explained by these variables. By comparing the size of the platelets to the spleen, portal hypertension can be identified. The "platelet count/spleen diameter ratio technique" seems to be a more economical method of detecting OV than the "scope all strategy." The validity of the platelet count/spleen diameter ratio as a noninvasive diagnostic tool for varices requires more investigation. If successful, individuals with liver cirrhosis may be able to avoid initial variceal bleeding by using beta-adrenergic antagonists rather than gastrointestinal endoscopy, which would be less invasive and costly.

Funding

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Conflict of Interest

None.

References

1. Qamar AA, Grace ND, Groszmann RJ, Garcia-Tsao G, Bosch J, Burroughs AK, *et al*.
2. Platelet count is not a predictor of the presence or development of gastroesophageal varices in cirrhosis. Hepatology, 2008, 47(9).
3. Gluud LL, Klingenberg S, Nikolova D, Gluud C. Banding ligation versus beta-blockers as primary prophylaxis in esophageal varices: systematic review of randomized trials. Am J Gastroenterol, 2007, 102(8).
4. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology. 2007;46(38).
5. Merli M, Neri G, Amoroso A, *et al*. Incidence and natural history of small varices in cirrhotic patients. J Hepatol. 2003;38:266-72.
6. Poynard T, Cales P, Pasta L, *et al*. Beta adrenergic-antagonist drugs in the prevention of gastrointestinal bleeding in patients with cirrhosis and esophageal varices. An analysis of data and prognostic factors in 589 patients from four randomized clinical trials. Franco-Italian Multicenter Study Group. N Engl J Med. 1991;324:1532-1538.
7. D'Amico G, Pagliaro L, Bosch J. The treatment of portal hypertension: A meta-analytic review. Hepatology. 1995;22:332-54.
8. Merkel C, Zoli M, Siringo S, *et al*. Prognostic indicators of risk for first variceal bleeding in

cirrhosis: a multicenter study in 711 patients to validate and improve the North Italian Endoscopic Club (NIEC) index. Am J Gastroenterol. 2000;95:2915-20.
9. Nevens F, Bustami R, Scheys I, Lesaffre E, Fevery J. Variceal pressure is a factor predicting the risk of a first variceal bleeding: a prospective cohort study in cirrhotic patients. Hepatology. 1998;27:15-19.
10. D'Amico G, Pagliaro L. The clinical course of portal hypertension in liver. In: Rossi P, ed. Diagnostic Imaging and Imaging Guided Therapy. Berlin: Springer-Verlag; c2000. p. 15-24.
11. D'Amico G, Pagliaro L, Bosch J. Pharmacological treatment of portal hypertension: an evidence-based approach. Semin Liver Dis. 1999;19:475-505.
12. Pilette C, Oberti F, Aube C, *et al*. Non-invasive diagnosis of esophageal varices in chronic liver diseases. J Hepatol. 1999;31:867-73.
13. Zaman A, Becker T, Lapidus J, Benner K. Risk factors for the presence of varices in cirrhotic patients without a history of variceal hemorrhage. Arch Intern Med. 2001;161:2564-70.
14. Thomopoulos KC, Labropoulou-Karatza C, Mimidis KP, Katsakoulis EC, Iconomou G, Nikolopoulou VN. Non-invasive predictors of the presence of large oesophageal varices in patients with cirrhosis. Dig Liver Dis. 2003;35:473-8.
15. Zein CO, Lindor KD, Angulo P. Prevalence and predictors of esophageal varices in patients with primary sclerosing cholangitis. Hepatology. 2004;39:203-209.
16. Cottone M, D'Amico G, Maringhini A, *et al*. Predictive value of ultrasonography in the screening of non-ascitic cirrhotic patients with large varices. J Ultrasound Med. 1986;5:189-192.
17. Zaman A, Hapke R, Flora K, *et al*. Factors predicting the presence of esophageal varices or gastric varices in patients with advanced liver disease. Am J Gastroenterol. 1999;94:3292-6.
18. Sarwar S, Khan AA, Alam A, *et al*. Non-endoscopic prediction of presence of esophageal varices in cirrhosis. J Coll Physicians Surg Pak. 2005;15(9):528-31.
19. Prihatini J, Lesmana LA, Manan C, Gani RA. Detection of esophageal varices in liver cirrhosis using non-invasive parameters. Acta Med Indones. 2005;37(3):126-31.
20. Amarapurkar DN, Parikh SS, Shankaran K, *et al*. Correlation between splenomegaly and oesophageal varices in patients with liver cirrhosis. Endoscopy. 1994;26:563.
21. Sharma SK, Aggrawal R. Prediction of large esophageal varices in patients with cirrhosis of the liver using clinical, laboratory, and imaging parameters. J Gastroenterol Hepatol. 2007;22:1909-1915.
22. Fagundes ED, Ferreira AR, Roquete ML, *et al*. Clinical and laboratory predictors of esophageal varices in children and adolescents with portal hypertension syndrome. J Pediatr Gastroenterol Nutr. 2008;46(2):178-83.
23. Giannini EG, Zaman A, Kreil A, *et al*. Platelet Count/Spleen Diameter Ratio for the Noninvasive Diagnosis of Esophageal Varices: Results of a Multicenter, Prospective, Validation Study. Am J Gastroenterol. 2006;101(11):2511-2519.
24. Jeon SW, Cho CM, Tak WY, *et al*. The value of Doppler-ultrasonography and laboratory tests as non-invasive predictors of the presence of esophageal varices in patients with chronic liver disease. Korean J Gastroenterol. 2006;48(3):180-7.