"A study of Non-Endoscopic Predictors of Variceal Bleeding in Patients with Liver Cirrhosis"

S.N. Savitha,[1*] M. Harika,[2] J. Aparna,[3] T. Lokesh [4]

1,2,3 - Assistant professor, General Medicine Department, Sri Venkateshwara Medical College, Tirupati, Andhra Pradesh.

4 – General Physician, Tirupati, Andhra Pradesh.

Corresponding author*:Dr. **M. Harika,**drharika612@gmail.com

ABSTRACT

Background: Esophageal varices, which are caused by portal hypertension in patients with chronic liver disease, affect approximately 50% of patients with cirrhosis of the liver. Present study aimed to identify non-invasive parameters for prediction of esophageal varices in newly diagnosed patients with cirrhosis, without previous upper gastro intestinal bleed.

Material & Method: The present prospective observational study was conducted among the patients attending to medical wards and acute medical care unit, department of medicine, SVRRGGH, Tirupati. From June 2021 to May 2022 with suggestive of liver cirrhosis. Patients with liver cirrhosis with portal hypertension between 18-80yrs of age were included. The study was conducted after obtaining the clearance from ethics committee, and written consent from participants. At the time of admission, all patients underwent a thorough clinical evaluation. Relevant history, etiology of liver disease, and physical characteristics such as age, gender, symptoms and signs of liver failure, hepatomegaly, splenomegaly, and abdominal vein collaterals were all recorded. Endoscopy and ultrasound investigation were performed along with the blood parameter profile. The collected data were analysed using SPSS v23.0 with significance of 0.05.

Result: A fifty patients with mean age of 47.1yrs were included. Among them 14 were female and 36 were male patients (male preponderance). Etiology of liver disease in the study was alcohol for 24 patients, followed by HBV for 2, autoimmune hepatitis for 2, HCV for 1 patient. Severity of liver disease calculated by CTP is as follows, Class A: 6, Class B: 16, Class C: 27, five had suffered with Encephalopathy, 20 had splenomegaly. There was significant association of grade of varices with platelet count, prothrombin time, low albumin level, presence of encephalopathy and presence of portal hypertension. Also the child-pugh score had a linear relation with grade of varices.

Conclusion: It is concluded that non-endoscopic factors like splenomegaly, decreased platelet count, hypoalbuminemia, mean portal vein diameter and mean splenic diameter, Child-Pugh score or a combination of multiple indices, as well as ultrasonographic (US) elastography proved to be the more accurate non-endoscopic predictors of esophageal varices and can also differentiate between the variceal size.

Keywords: CHILD-PUGH, Liver, Cirrhosis, Prediction, Albumin, Platelet.

Introduction:

Esophageal varices, which are caused by portal hypertension in patients with chronic liver disease, affect approximately 50% of patients with cirrhosis of the liver. At the time of diagnosis of liver cirrhosis, approximately 40% of patients with compensated disease and 60% of those with decompensated disease and ascites have esophageal varices. Varices can be found in approximately 85% of people with Child-Pugh C cirrhosis but only in 45% of people with Child-Pugh A cirrhosis.[1] A hepatic venous pressure gradient (HVPG) greater than 10 mm Hg, as well as the presence of decompensated cirrhosis, alcohol aetiology, and red wale signs, are the main predictors of the development of new varices and an increase in their grades at a rate of 8% per year, respectively.[2] Furthermore, varices frequently grow in size over time. Each year, it is estimated that nearly 12% of people with small esophageal varices will develop large varices. 3 Large varices, the presence of red flag symptoms, severe liver disease, and portal pressure greater than 12 mm Hg all predict a higher risk of bleeding. An episode of esophageal variceal bleeding has a 20% mortality rate after six weeks.[3]

Predicting the grade of varices using non-invasive techniques at the time of registration in patients with cirrhosis and portal hypertension is likely to predict the need for prophylactic beta blockers or endoscopic variceal ligation. The current study aims to see how well different clinical, biochemical, and imaging parameters predict the presence and severity of esophageal varices in liver cirrhosis.[4] liver cirrhosis is diagnosed, all cirrhotic patients should be screened for the presence of esophageal varices.[5] A repeat endoscopy is recommended every 1-2 years for patients with small varices to monitor the growth or progression of the condition, and every 2-3 years for those without varices.[3,6]

Several studies have found platelet count, splenomegaly, advanced Child PUGH status, serum albumin, and high portal vein diameter in ultrasound to be useful indicators of large esophageal varices in cirrhotic patients. Certain clinical, biochemical, and ultrasonographic parameters have good predictive power for determining the risk of variceal bleeding noninvasively, either individually or in combination. However, the variables that predict the presence of varices are not as well defined. Present study aimed to identify non-invasive parameters for prediction of esophageal varices in newly diagnosed patients with cirrhosis, without previous upper gastro intestinal bleed.

Material & Method:

The present prospective observational study was conducted among the patients attending to medical wards and acute medical care unit, department of medicine, SVRRGGH, Tirupati. From June 2021 to May 2022 with suggestive of liver cirrhosis. Patients with liver cirrhosis with portal hypertension between 18-80yrs of age were included. Patients with hepatocellular carcinoma detected by ultrasonography or elevated alpha feto protein, primary hematologic disorder, active gastrointestinal bleeding on admission, taking drug for primary prophylaxis of variceal bleeding, parenteral drug addiction, TIPS, advanced co-morbidity for endoscopy and previous surgical intervention for portal hypertension were excluded.

The study was conducted after obtaining the clearance from ethics committee, and written consent from participants. At the time of admission, all patients underwent a thorough clinical evaluation. Relevant history, etiology of liver disease (alcohol intake, blood transfusion, and so on), and physical characteristics such as age, gender, symptoms and signs of liver failure (spider angioma, palmar erythema), hepatomegaly, splenomegaly, and abdominal vein collaterals were all recorded. None, mild (only detectable on ultrasound), moderate (visible moderate symmetrical abdominal distension), or severe ascites were assigned (marked abdominal distension).

Method: Hemoglobin, total leukocyte count, platelet count, prothrombin time, and serum concentrations of bilirubin (total and conjugated), protein, albumin, alanine transaminase, and aspartate transaminase were all measured. A modified Child-Pugh score was calculated for each patient. To determine the cause of liver cirrhosis, all patients were tested for HBsAg and antibodies to the hepatitis C virus using enzyme immunoassays. Other causes of cirrhosis were only tested for if there was a suggestive clinical clue (serum ceruloplasmin and slit lamp examination for Wilson's disease, autoantibody tests for autoimmune liver disease, and iron studies for hemochromatosis). Ascitic fluid was tapped under aseptic conditions in patients with ascites, and ascitic fluid albumin and serum-ascites albumin gradients were measured. SBP patients were appropriately treated.

Doppler ultrasound: After an overnight fast, all patients underwent ultrasonography, which revealed the following information: nodularity of the liver surface, maximum vertical span of the liver; spleen size (length of its longest axis); diameter of the portal and splenic veins; presence of portal-systemic collaterals; and presence of ascites.

Endoscopic examination: Within 2-3 days of admission, all patients underwent upper gastrointestinal endoscopy to assess esophageal and gastric varices using a video gastroscope

(Pentax). If there were esophageal varices, their size was graded as I-IV using the Paquet grading system. Furthermore, patients were divided into two groups: those who had large esophageal varices (grade III-IV) and those who did not (no varices or grade I-II). Wherever possible, the presence of gastric varices, portal hypertensive gastropathy, duodenopathy, and rectal varices was recorded. Gastric varices were classified as isolated or Gastroesophageal varices, i.e., gastric varices associated with esophageal varices, according to the Sarin classification. The clinical, laboratory, ultrasonographic, and endoscopic evaluations were completed in four weeks. Cirrhosis was diagnosed using clinical, biochemical, and ultrasonographic findings.

Statistical analysis: All the data were entered in excel sheet and analysed using SPSS v23.0. The data were summarised as mean, standard deviation, frequency and percentage. The summarised data were represented using tables, figures, bar diagram and pie chart. The mean difference between continuous data were compared using students t-test and categorical data using chi-square test. A p-value of <0.05 was considered statistically significant.

Result: A fifty patients with mean age of 47.1yrs were included. Among them 14 were female and 36 were male patients (male preponderance). Etiology of liver disease in the study was alcohol for 24 patients, followed by HBV for 2, autoimmune hepatitis for 2, HCV for 1 patient. Severity of liver disease calculated by CTP is as follows, Class A: 6, Class B: 16, Class C: 27, five had suffered with Encephalopathy, 20 had splenomegaly.

Table 1: Demographic details of the patients			
		Frequency	**Percent**
Gender	Male	36	72
	Female	14	28
Etiology	Alcohol	24	48
	Hepatitis B virus	2	4
	Hepatitis C virus	1	2
	Autoimmune hepatitis	2	4
	Others	21	42
Child-Pugh class	A	6	12
	B	16	32
	C	28	56

Clinical presentation	Pallor	34	68
	Jaundice	32	64
	Pedal edema	21	42
	Bleeding	28	56
Ascites	None	6	12
	Mild	7	14
	Moderate	33	66
	Severe	4	8
Encephalopathy		5	10
Splenomegaly		20	40
Endoscopic findings	Grade 0 (No varices)	7	14
	Grade 1	15	30
	Grade 2	15	30
	Grade 3	13	26
CTP Class	A	6	12
	B	16	32
	C	28	56

Out of Fifty patients, seven had no oesophageal varices, fifteen had Grade-1 oesophageal varices, 15 had Grade-2 oesophageal varices, and thirteen had Grade-3 oesophageal varices.

Table 2: Comparison of the variables with endoscopy grade of varices							
Variable	**Endoscopy grade of varices**						**Total**
			0	1	2	3	
Gender (p=0.056)	Female	No of patients	1	6	3	4	14
		% within gender	7.14	40	14.29	35.71	100.0
		% within endoscopy	14.29	12	18.18	29.14	20.0
	Male	No of patients	6	9	12	9	36
		% within	7.1	60	26.8	23.2	100.0

		gender					
		% within endoscopy	85.71	18	81.82	70.59	80.0
Age group (p=0.156)	<39yrs	No of patients	3	3	1	4	11
		% within Age group	27.27	27.27	9.09	36.36	100.0
		% within endoscopy	42.86	20	6.67	30.77	22.0
	40-49	No of patients	1	7	10	3	21
		% within Age group	4.76	33.33	47.62	14.29	100.0
		% within endoscopy	14.29	46.67	66.67	23.08	42
	50-59	No of patients	1	5	4	5	15
		% within Age group	6.67	33.33	26.67	33.33	100.0
		% within endoscopy	25	25.8	26.3	50.0	31.4
	>60yrs	No of patients	2	0	0	1	3
		% within Age group	66.67	0	0	33.3	100.0
		% within endoscopy	28.57	0	0	7.69	6
Platelet count/μL (p=0.01*)	<=100000	No of patients	3	6	3	9	21
		% within Platelet	14.29	28.57	14.28	42.86	100.0
		% within endoscopy	42.85	40	20	69.23	42

	100001-150000	No of patients	1	1	6	3	11
		% within Platelet	14.3	9.1	54.54	27.26	100.0
		% within endoscopy	0	6.67	40	23.08	22
	150001-200000	No of patients	0	2	2	0	4
		% within Platelet	0	50	50	0	100.0
		% within endoscopy	0	13.33	13.33	0	8
	>200000	No of patients	3	6	4	1	14
		% within Platelet	21.43	42.86	28.57	7.14	100.0
		% within endoscopy	42.85	40	26.67	7.69	28
PT (p=0.01*)	<=15	No of patients	2	6	8	4	20
		% within gender	10	30	40	20	100
		% within endoscopy	28.57	40	53.33	30.77	40
	16-25	No of patients	5	7	7	9	28
		% within gender	17.86	25	25	32.14	100.0
		% within endoscopy	71.43	46.67	46.67	69.23	56
	26-35	No of patients	0	2	0	0	2
		% within	0	100	0	0	100

		gender					
		% within endoscopy	0	13.33	0	0	4
Serum albumin (g/dL) (p=0.01*)	<=3	No of patients	2	8	5	10	25
		% within gender	8	32	20	40	100
		% within endoscopy	28.57	53.33	33.33	76.92	50
	3-3.5	No of patients	2	4	8	2	16
		% within gender	12.5	25	50	12.5	100
		% within endoscopy	28.57	26.67	53.33	15.38	32
	>3.5	No of patients	3	3	2	1	9
		% within gender	33.33	33.33	22.22	11.11	100
		% within endoscopy	42.86	20	13.33	7.69	18
Encephalopathy (p=0.01*)	Yes	No of patients	0	2	0	3	5
		% within gender	0	40	0	60	100
		% within endoscopy	0	13.33	0	23.08	10
	No	No of patients	7	13	15	10	45
		% within gender	15.56	28.89	33.33	22.22	100
		% within endoscopy	100	86.67	100	76.92	90

Portal vein diameter (cms) (p=0.01*)	<1.00	No of patients	3	0	0	0	3
		% within gender	100	0	0	0	100.0
		% within endoscopy	42.86	0	0	0	6
	1.00-1.10	No of patients	2	1	0	0	3
		% within gender	66.67	33.33	0	0	100.0
		% within endoscopy	28.57	6.67	0	0	6
	1.20-1.3	No of patients	2	9	1	0	12
		% within gender	16.67	75	8.33	0	100
		% within endoscopy	28.57	60	6.67	0	24
	1.40-1.50	No of patients	0	1	6	0	7
		% within gender	0	14.29	85.71	0	100.0
		% within endoscopy	0	6.67	40	0	14
	1.60-1.70	No of patients	0	4	8	0	12
		% within gender	0	33.33	66.67	0	100.0
		% within endoscopy	0	26.66	53.33	0	24
	>1.80	No of patients	0	0	0	13	13
		% within	0	0	0	100.0	100.0

		gender					
		% within endoscopy	0	0	0	100.0	26
CTP score (p=0.01*)	A	No of patients	3	2	1	0	6
		% within gender	50	33.33	16.67	0	100.0
		% within endoscopy	42.86	13.33	6.67	0	12
	B	No of patients	0	5	8	3	16
		% within gender	0	31.25	50	18.75	100.0
		% within endoscopy	0	33.33	53.33	23.08	32
	C	No of patients	4	8	6	10	28
		% within gender	14.29	28.57	21.43	35.71	100.0
		% within endoscopy	57.14	53.33	40	76.92	56

Discussion:

The American College of Gastroenterology (ACG) recommended screening endoscopy for cases with established cirrhosis who were medical therapy candidates in 1997. In addition, the American Association for the Study of Liver Diseases (AASLD) recommended screening endoscopy for varices to be routine in Child Pugh Class B and C patients, but limited to patients with evidence of portal hypertension (thrombocytopenia or large portal vein/collaterals on abdominal imaging) in child Pugh Class A.[7]

More than half of cirrhotic patients will develop varices. The risk of bleeding is 20-35% after two years. According to reports, the mortality rate from the first episode of variceal bleeding ranges between 17 and 57%. Recurrent bleeding occurs in approximately 66% of those who survive the first episode of bleeding and do not receive active treatment, and it usually occurs

within 6 months of the first episode. Because cirrhotic patients with large esophageal varices are more likely to bleed, efforts to prevent bleeding have focused on identifying cirrhotic patients with large varices.

When large varices were discovered during a screening endoscopy, prophylactic therapy was initiated, which reduced the incidence of bleeding and had an effect on bleeding-related mortality. Endoscopic screening yield and cost-effectiveness must be improved by identifying clinical features that can accurately predict esophageal varices and assist in identifying patients at highest risk.[8]

Varices can occur in the lower, middle, or upper thirds of the oesophagus. The size of the varices in the lower third of the oesophagus is the most important descriptors. During the withdrawal of the endoscope, the size of the varices in the lower third of the oesophagus is determined. Small varices have a diameter of less than 5 mm, whereas large varices have a diameter greater than 5 mm.[9] Patients with large esophageal varices, Child-Pugh class C cirrhosis, and varices with red colour signs have the highest risk of variceal bleeding within a year. The presence of red wale marks at baseline endoscopy (longitudinal dilated venules resembling whip marks on the variceal surface) is associated with decompensated cirrhosis (Child-Pugh B/C) of Alcoholic etiology.[10]

decreased platelet count and splenomegaly were identified as non-invasive predictors of the presence of EV. Variceal gastrointestinal bleeding is a serious complication of portal hypertension that can be fatal.[5] This complication, however, is more common in patients with large oesophageal varices and less common in those with small varices. Because variceal bleeding can be prevented with pharmacological agents such as beta-adrenergic receptor antagonists, it is critical to identify patients with large oesophageal varices who are at a higher risk of developing variceal bleeding and are likely to benefit from such interventions. As a result, it has been recommended that patients with liver cirrhosis be screened for the presence of large oesophageal varices at the time of initial diagnosis and at regular intervals thereafter for the rest of their lives. However, this recommendation places a significant burden on endoscopy units and incurs significant costs for patients.[11]

The aetiology included alcohol (24 patients, 48%), Hepatitis virus (2 patients, 4%), and Hepatitis c (1 patient, 2%), autoimmune (2 patients,4%) other causes (21patients, 42%). In a recent study, Ankouane et al., discovered that the average age of patients with HBV-related hepatocellular carcinoma was 38.5 years. The mean age at presentation of HCV-related

cirrhosis, on the other hand, was 66.17%. also reported that the majority of patients with hepatitis C virus-related hepatocellular carcinoma were over the age of 50 (mean 61.5 years old). [12]

In total, seven patients (14%) had no oesophageal varices, fifteen (30%) had Grade-1 oesophageal varices, fifteen (30%) had Grade-2 oesophageal varices, and thirteen (26%) had Grade-3 oesophageal varices. This finding is consistent with the findings of Cherian et al.[13] A similar result was found in the study of Ismail et al, where many ascites were found based on clinical examination results on patients with large varices, while radiological examination results did not differ between patients with large and small varices. Goh et al., and Limquiaco et al., discovered ascites with varying percentages in their study of oesophageal variceal bleeding.[14,15] Six patients had CTP CLASS A, sixteen had CTP CLASS B, and twenty-eight had CTP CLASS C. Jijo et al., conducted a study that found significance and a sensitivity of 95% for Child-Pugh Class B and C in predicting oesophageal varices and proposed an algorithm in which patients with Child-Pugh Class B and C were given primary prophylaxis and for Class A, platelet count and spleen diameter were measured and prophylaxis was initiated accordingly.[16] Goh et al., discovered that the Child Pugh score was not a predictive factor for oesophageal varices.[15]

Garcia-Tsao et al., (180 patients), Pilette et al., (116 patients), reported anaemia as a risk factor for the presence of varices on its own.[17,18] Mohammad Khuram et al., found esophageal varices in 146 of 200 patients, with 121 suffering from thrombocytopenia (94.5%).[19] In 346 patients, Chalasani et al., discovered that splenomegaly (OR, 2.0; 95% CI, 1.1-3.8) and a platelet count less than 88103/L (OR, 1.6; 95% CI, 1.0-3.0) were independent risk factors for the presence of large varices.[20] According to Singh M et al., patients in the varices group had a lower mean platelet count, higher mean bilirubin levels, a larger mean spleen diameter, and a larger mean portal vein diameter.[21]

The higher the Prothrombin time, the more severe the varices. Prothrombin activity less than 70% predicted the presence of oesophageal varices, according to Filippo Schepis et al., (odds ratio [OR]: 5.83; 95% CI: 2.6-12.8).[22] In a study of 116 patients with cirrhosis, Pilette et al. discovered that a low platelet count, a high Prothrombin time, and the presence of spider angiomata were independent risk factors for the presence of varices.[19] KJ Paquet et al. High Prothrombin time and its association with varices were demonstrated in a prospective controlled trial.[9]

Our research discovered a link between serum albumin and varices. The lower the serum albumin levels, the more severe the varices. The presence of spider naevi, a low albumin level, and a low platelet count were independent risk factors for the presence of varices in a logistic regression study of 63 of 180 patients by Garcia-Tsao et al.[18] Also, study found a link between Portal vein diameter and the severity of varices. The grade of varices increases as the portal vein diameter increases. Varices of grade 2,3 were seen when the portal vein diameter exceeds 1.8cm. Arulprakash Sarangapani and colleagues, 2009, The study looked at 106 people who had liver disease. On multivariate analysis, spleen size >13.8 mm, portal vein >13 mm, and splenic vein >11.5 mm were independent predictors of the presence of Large varices.[23]

The Pugh score of a child had a linear relationship with the grade of varices. According to Atif Zaman et al., patients with CTP score B or C are nearly three times more likely to have large varices on upper endoscopy than those with CTP score A.[24] Cales and colleagues.[25] Multivariate analysis revealed that the initial size of varices and interval worsening of the Child- Pugh score predicted the development of varices in their study. The presence of an enlarged spleen in liver cirrhotic patients was associated with an increased risk of complications related to portal hypertension. In decompensated cirrhosis, the spleen diameter was significantly larger than in compensated cirrhosis. A systematic review found that bipolar spleen diameters greater than 150 mm on ultrasonography could be used as an alternative tool for EV diagnosis in liver cirrhosis. Splenomegaly is caused by a variety of mechanisms, including portal congestion, fibrosis, and tissue hyperplasia.[26]

Platelet count less than 6 lakhs, serum albumin less than 2.2 g/dl, and portal vein diameter greater than 13 mm on ultrasound are independent and significant predictors of esophageal varices on endoscopy, according to his findings. As a result, all patients with liver cirrhosis who have no history of GI bleeding but any of these predictors should undergo screening endoscopy. The use of these non-invasive predictors may reduce the need for endoscopic screening in cirrhotic patients, with endoscopy reserved for patients at high risk of developing varices. Endoscopic screening for varices should be performed on all patients when cirrhosis is diagnosed, and then every 2 to 3 years in those with compensated disease and no varices; the recommended time intervals between endoscopies for those with small varices were 1 to 2 years and 1 year for those with decompensated disease, with or without varices. These recommendations imply a significant burden of endoscopies and associated costs; they require patients to repeatedly undergo an unpleasant procedure, despite the fact that up to

50% of them may not have developed esophageal varices 10 years after being diagnosed with cirrhosis.

Conclusion: It is concluded that non-endoscopic factors like splenomegaly, decreased platelet count, hypoalbuminemia, mean portal vein diameter and mean splenic diameter, Child-Pugh score or a combination of multiple indices, as well as ultrasonographic (US) elastography proved to be the more accurate non-endoscopic predictors of esophageal varices and can also differentiate between the variceal size. These predictors may be of help to the physicians practicing in rural areas where endoscopy facilities are not readily available, in helping them to initiate appropriate primary pharmacological prophylaxis in these patients. In an urban setting where the endoscopy workload is high, a non-invasive predictor, as in this study, can help one to initiate drug therapy while waiting for the endoscopy procedure.

Funding: Nil

Conflict of interest: Nil

Reference:

1. Herrera JL, Rodríguez R. Medical care of the patient with compensated cirrhosis. Gastroenterol Hepatol (N Y). 2006;2(2):124-26.

2. Tripathi D, Stanley AJ, Hayes PC, Patch D, Millson C, Mehrzad H, et al. U.K. guidelines on the management of variceal haemorrhage in cirrhotic patients. Gut. 2015;64(11):1680–704.

3. Triantos C, Kalafateli M. Endoscopic treatment of esophageal varices in patients with liver cirrhosis. World J Gastroenterol WJG. 2014;20(36):13015.

4. Dyson JK, Anstee QM, McPherson S. Non-alcoholic fatty liver disease: a practical approach to diagnosis and staging. Frontline Gastroenterol. 2014;5(3):211–8.

5. Jakab SS, Garcia-Tsao G. Screening and surveillance of varices in patients with cirrhosis. Clin Gastroenterol Hepatol. 2019;17(1):26–9.

6. Rajoriya N, Gorard DA. Endoscopic Management of Oesophageal and Gastric Varices. In: Endoscopy of GI Tract. IntechOpen; 2013.

7. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W. Practice Guidelines Committee of the

American Association for the Study of Liver D, Practice Parameters Committee of the American College of G. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology. 2007;46(3):922–38.

8. Cordon JP, Torres CF, García AB, Rodriguez FG, de Parga JMS. Endoscopic management of esophageal varices. World J Gastrointest Endosc. 2012;4(7):312.

9. Paquet KJ. Prophylactic endoscopic sclerosing treatment of the esophageal wall in varices-a prospective controlled randomized trial. Endoscopy. 1982;14(01):4–5.

10. Giannini E. Platelet count/spleen diameter ratio: proposal and validation of a non-invasive parameter to predict the presence of oesophageal varices in patients with liver cirrhosis. Gut. 2003;52(8):1200–5.

11. El-Kassas M, Elakel W, Alboraie M, Ezzat R, Abdelhakam S, Hassany M, et al. Egyptian revalidation of non-invasive parameters for predicting esophageal varices in cirrhotic patients: A retrospective study. Arab J Gastroenterol. 2022;23(2):120–4.

12. Andoulo FA, Noah DN, Djapa R, Kowo M, Talla P, Medjo EH, et al. Epidemiology of hepatitis C: related hepatocellular carcinoma in Cameroon. Pan Afr Med J. 2014;19(1).

13. Cherian J V, Deepak N, Ponnusamy RP, Somasundaram A, Jayanthi V. Non-invasive predictors of esophageal varices. Saudi J Gastroenterol Off J Saudi Gastroenterol Assoc. 2011;17(1):64.

14. Limquiaco J, De Lusong M, Pilapil J, Feir S, Prodigalidad P, Cabanayan E, et al. Clinical predictors of bleeding from esophageal varices a retrospective study. J Gastroenterol Hepatol. 2006;21:A38–A38.

15. Goh S-H, Tan W-P, Lee S-W. Clinical predictors of bleeding esophageal varices in the ED. Am J Emerg Med. 2005;23(4):531–5.

16. Peck-Radosavljevic M. Thrombocytopenia in chronic liver disease. Liver Int. 2017;37(6):778–93.

17. Pilette C, Oberti F, Aubé C, Rousselet MC, Bedossa P, Gallois Y, et al. Non-invasive diagnosis of esophageal varices in chronic liver diseases. J Hepatol. 1999;31(5):867–73.

18. GarciaTsao G, Escorsell A, Zakko M, Patch D, Matloff D, Grace N, et al. Predicting the presence of significant portal hypertension and varices in compensated cirrhotic patients. Hepatology. 1997;26(4):927–32.

19. Khuram M, Khan NY, Arif M, Irshad MM, Hammatul Bushra K, Hassan Z. Association of platelet count to splenic index ratio with presence of esophageal varices in patients with hepatitis C virus related compensated cirrhosis. Pak J Gastrenterol. 2006;20:37–42.

20. Chalasani N, Imperiale TF, Ismail A, Sood G, Carey M, Wilcox MC, et al. Predictors of large esophageal varices in patients with cirrhosis. Off J Am Coll Gastroenterol ACG. 1999;94(11):3285–91.

21. 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(21):2564–70.

22. Schepis F, Cammà C, Niceforo D, Magnano A, Pallio S, Cinquegrani M, et al. Which patients with cirrhosis should undergo endoscopic screening for esophageal varices detection? Hepatology. 2001;33(2):333–8.

23. Sarangapani A, Shanmugam C, Kalyanasundaram M, Rangachari B, Thangavelu P, Subbarayan J. Noninvasive Prediction of Large Esophageal Varices in Chronic Liver Disease Patients. Saudi J Gastroenterol. 2010;16:38–42.

24. Zaman A, Hapke R, Flora K, Rosen HR, Benner K. Factors predicting the presence of esophageal or gastric varices in patients with advanced liver disease. Am J Gastroenterol. 1999;94(11):3292–6.

25. D´ Amico G, García-Tsao G, Calés P, Escorsell A, Nevens F, Cestari R. Diagnosis of portal hypertension. How and when? In: De Franchis R, editor. Portal hypertension III. Proceedings of the Third Baveno International Consensus Works-hop on Definitions, Methodology and Therapeutic Strategies. Oxford. 2001;

26. Abu El Makarem MA, Shatat ME, Shaker Y, Abdel Aleem AA, El Sherif AM, Moaty MA, et al. Platelet count/bipolar spleen diameter ratio for the prediction of esophageal varices: The special Egyptian situation: Noninvasive prediction of esophageal varices. Hepat Mon. 2011;11(4):278–84.