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Original Research Article

Utility of Non-Invasive Techniques like Portal Vein Diameter, Platelet Count and Fibroscan to Predict the Presence and Extent of Oesophageal Varices in Liver Cirrhosis

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Abstract:

Background: Liver cirrhosis is the end-stage of chronic liver disease. Esophageal variceal bleeding is a potentially deadly consequence of portal hypertension in patients with cirrhosis.

Aim: The present study measured the platelet count, portal vein diameter and Liver Stiffness (fibroscan) to predict the EVs in patients with Liver cirrhosis.

Methods: This was a Cross Sectional comparative study conducted in the outpatient department of Medicine, Hind Institute of Medical Sciences, Safedabad, Barabanki, U.P. Ethical approval was obtained from the HIMS ethical review committee. An independent sample t-test was used for parametric data, whereas the Mann-Whitney U test was used for non-parametric data. The chi square test was used to compare the categorical data of patients with and without EV. Receiver operating characteristic (ROC) analysis was performed to evaluate the cut-off values for the Platelate Count, Portal Vein Diameter, Liver Stiffness, sensitivity, specificity, and area under the curve (AUC).

Results: The study involved 180 patients with (110 cases) and without (70 Cases) EVs, aged 24-90 years; Mean age 48.14±11.52 years; 81.7% males. A total of 110 (61.1%) cases showed presence of esophageal varices. A total of 76 (42.2%) patients had lower grades of varices (Grades 1 and 2) whereas 34 (18.9%) had higher grades of varices. Alcohol (n=104; 57.8%) was the most common etiology followed by NFLD/Chronic illness (n=28; 15.6%), viral (n=26; 14.4%), mixed etiology (n=13; 7.2%) and transfusion (n=9; 5%) respectively. Diabetes (31.1%) and hypertension (21.7%) were the most common comorbid conditions. Platelet count ranged from 0.32 to 2.70 lakhs/cumm. Mild, moderate and severe thrombocytopenia was seen in 44 (24.4%), 67 (37.2%) and 57 (31.7%) patients respectively. There were 57 (31.7%) patients with platelet count in normal range. Mean platelet count was 1.25±0.54 lakhs/cumm. All the patients had ascites. None of the patients had severe ascites. Majority of cases (n=106; 58.9%) had mild ascites. There were 74 (41.1%) cases with moderate ascites. Portal vein diameter ranged from 9 to 19 mm. Majority (70.6%) of cases had portal vein diameter <13 mm. There were 53 (29.4%) cases with portal vein diameter >13 mm. Mean portal vein diameter was 12.83±1.86 mm. Liver stiffness ranged from 16 to 75 kPa. Majority (85.6%) had liver stiffness >21 kPa. There were 26 (14.4%) cases with liver stiffness 14-21 kPa. Mean liver stiffness was 33.87±11.64 kPa. Mean portal vein diameter and liver stiffness values were significantly higher and mean platelet count was significantly lower in cases with esopahgeal varices as compared to those without esophageal varices.

Conclusion: Platelet count at a cut-off <1.045 lakhs/cumm was 62.7% sensitive and 87.1% specific in prediction of esophageal varices. Portal vein diameter at a cut-off >12.5 mm was 70% sensitive and 78.6% specific in prediction of esophageal varices. Liver stiffness at a cut-off >22.95 kPa was 95.5% sensitive and 45.7% specific in prediction of esophageal varices. For detection of higher grades of esophageal varices, portal vein diameter was most sensitive (64.7%) whereas platelet count was most specific (86.8%).

Keywords: Platelet Count, Esophageal Varices, Chronic Liver Disease. Portal Vein Diameter, Fibroscan.

Introduction

Esophageal varices are one of the main complications of liver cirrhosis. Upper gastrointestinal endoscopy is the gold standard for the detection of esophageal varices. Many less invasive methods for screening of varices have been investigated and the most recent Baveno VI guidelines suggest that endoscopy is not necessary in patients with liver stiffness <20 kPa and platelets >150,000/μL [1]. Every year, a percentage of patients with cirrhosis (3-12%) develop esophageal varices and in 8-12% of patients, progression from small to large varices is detected. Spontaneous regression of small esophageal varices can also be observed, mainly following alcohol abstinence in alcoholic cirrhosis [2]. In the setting of variceal bleeding a 6-week mortality rate of 11.1-40% has been reported [3,4]. The presence of red spots, the size of varices, and the severity of cirrhosis are considered to be the most important predictors of variceal bleeding [5]. The esophageal varices are classified as Grade I: straight and unbendable; Grade II: tortuous, occupying < 1/3rd of the esophageal lumen; and Grade III: large, occupying > 1/3rd of the esophageal lumen [6].

Treatment with β-blockers can diminish the probability of bleeding by 50% in patients with medium and large varices [6,7]. Previous reports suggested various non-invasive diagnostic markers for the early prediction of oesophageal varices [8-11]. The non-invasive markers for esophageal variceal prediction described were PC, prothrombin time (PT), albumin concentration, splenic size, and portal vein diameter (on ultrasound) [12]. Previous reports suggested that thrombocytopenia, splenomegaly, and ascites can all independently predict the presence of large oesophageal varices in cirrhotic patients with a higher risk for bleeding [13,14]. Esophageal varices initially appear only when the hepatic venous pressure gradient (HVPG) is >10 Hg. Its size, ranging from small to large, increases by 5 to 10% per year, and its increasing size, with associated increased variceal-wall tension, leads to variceal rupture and bleeding [14].

At present, the method of choice for identifying the presence and estimating the size of varices is esophagogastroduodenoscopy (EGD). However, EGD is an invasive procedure, associated with risk, and not tolerable in all patients [15]. Furthermore, it may not be available in a remote area without an endoscopist. The disadvantages of EGD include the complications associated with endoscopy; especially the need for intravenous sedation [15] and the relatively high cost [16]. These drawbacks have driven the research for new methods of variceal detection. Several minimally or non-invasive methods have been proposed as alternatives to EGD for screening for esophageal varices. The updated Baveno VI guidelines [17] recommend that screening EGD can be avoided in patients with compensated advanced chronic liver disease (cACLD) who have liver stiffness <20 kPa and a platelet count >150,000/μL [18]. Non-invasive methods also currently have a distinct role in clinically significant portal hypertension (CSPH) in patients with cACLD [19]. Portal hypertension is a clinical syndrome characterized by splenomegaly, ascites, gastrointestinal varices, and encephalopathy and is defined by a hepatic vein pressure gradient (HVPG) exceeding 5 mm Hg [20]. Esophageal/gastrointestinal varices happen to be the most common complication resulting from portal hypertension and are seen in nearly 30% of decompensated and 60-70% of patients with decompensated cirrhosis even at the time of diagnosisi [21]. Hepatic venous pressure gradient (HVPG) is also the gold standard hemodynamic measurement for assessing portal hypertension, predicting the risk of hepatic decompensation, and variceal treatment evaluation [15]. It can be used as an alternative tool for detecting EV [22].

Nonetheless, it is similarly invasive to EGD. Few studies explore the clinical parameters, such as platelet count [23] and newer blood biomarkers, including serum laminin levels and serum hyaluronic acid [24]. However, the limitations of these tests are their accuracy in predicting EV and their availability. Clinical prediction rules such as FibroTest, APRI, and FIB-4, reflecting liver fibrosis, can help identify high-risk patients; however, they still do not directly predict EV. Ultrasound (US) is one of the noninvasive modalities and has been developed and widely used for the follow-up of chronic liver diseases in identifying cirrhosis and hepatocellular carcinoma [25]. Combined clinical and ultrasound parameters such as platelet count and spleen diameter for predicting EV have good potential [25,26]. Transient elastography (TE, FibroScan®), measuring liver stiffness, has shown promise in predicting EV presence and severity. The Baveno VI criteria suggested the utilization of both TE with a liver stiffness measurement (LSM) value below 20kPa and a platelet count exceeding 150,000 per milliliter (ml) to rule out high-risk varices [27].

Validation and further research are necessary to establish the accuracy and reliability of these noninvasive methods for EV screening in HCV cirrhosis patients. Liver and splenic stiffness measurements using TE or shear wave elastography (SWE) have been widely studied and may represent another potential predictor for EV [25-28]. However, the various machines' different values limit this method's global reproducibility. The Doppler ultrasonography can be used for the hemodynamic evaluation of hepatic vessels like HVPG without invasiveness. Its measuring values

are valid across the machines. The Doppler parameters showed good correlations with portal hypertension and liver stiffness measured by elastography and fibrosis staging obtained from a liver biopsy [26,29]. Doppler ultrasonography can be a useful alternative for EV prediction because of its noninvasiveness, repeatability, and availability [29].

Hence, the present study was planned to evaluate the role of some of the non-invasive techniques like portal vein diameter (USG), platelet count and Fibroscan for prediction of presence and extent of oesophageal varices in liver cirrhosis patients.

Aim and Objectives:

Aim: To assess utility of non-invasive techniques like Portal vein diameter, Platelet count and Fibro scan to predict the oesophageal varices and grade them.

Objectives:

Primary Objectives

1. To examine the association in portal vein diameter with presence and grading of oesophageal varices in patients of Liver Cirrhosis.
2. To examine the association in platelet count with presence and grading of oesophageal varices in patients of Liver Cirrhosis.
3. To examine the association in liver stiffness measured by elastography / Fibroscan with presence and grading of Oesophageal varices in patients of Liver Cirrhosis.

Secondary Objective

1. To compare the diagnostic accuracy of different non-invasive techniques for diagnosis and grading of oesophageal varices in patients of liver cirrhosis.

Materials and Methods:

Materials: Study site: Department of Medicine in collaboration with Department of Radiology, Hind Institute of Medical Sciences (HIMS), Safedabad, Barabanki. HIMS is a tertiary care teaching hospital located in Safedabad, Barabanki a neighbouring city to the state capital, Lucknow. It caters to a wide diversity of rural and urban population of Barabanki, Lucknow, Ayodhya and other adjoining areas, primarily belonging to lower middle and middle socioeconomic classes.

Study subjects: Liver cirrhosis patients attending the OPD or admitted to indoor wards of Department of Medicine, HIMS, Safedabad, Barabanki.

Study Design: Cross-sectional

Study Groups: Patients were endoscopically evaluated for presence of esophageal varices and were divided into two groups:

Group A- Patients with esophageal varices (110 Cases).

Group B- Patients without esophageal varices (70 cases).

Study Period: 18 months.

Sample Size: 180.

Inclusion Criteria:

- Age more than 18 years.
- Confirmed diagnosis of liver cirrhosis by clinical, biochemical and imaging criteria.

Exclusion Criteria

- Past history of upper GI bleeding.
- Known case of bleeding disorders other than those from secondary liver disease.
- Known case of Hepatocellular Carcinoma (evident on USG or on current treatment for it).
- Severe ascites.
- Patients who had undergone endoscopy previously for variceal bleeding.

Sampling Technique: Consecutive sampling.

Methods:

Methods After getting a written consent from all patients, they were asked to undergo the following: 1. Full history taking with special emphasis on previous history of schistosomiasis, history of viral hepatitis or exposure to risk factors (such as anti-schistosomiasis injections, blood transfusion or previous surgical operations), history of jaundice, disturbed conscious level, bleeding tendency, hematemesis or melena.

1. Full clinical examination for stigmata of liver cell failure or signs of portal hypertension was obtained. III. Laboratory investigations included Complete blood count, serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST), total and direct bilirubin, serum albumin, prothrombin time and concentration, Alphafeto protein and HCV
2. Platelet count: A platelet cut off platelet count < 150,000/mm3 is chosen because they represented the median values and offered the best discrimination. (72.5% sensitive and 75% specific predictor of Esophageal varices with positive predictive value of 63.8% and negative predictive value of 70.5%)ii.

Grades of Thrombocytopenia

Mild – 1,00,000/cumm to 1,50,000/cumm

Moderate - 50,000/cumm to 1,00,000/cumm

Severe <50,000/cumm

1. Abdominal ultrasonography Using real time scanning device Toshiba, Aplio MX with convex probe, 3-5uHz to detect the presence of liver cirrhosis(irregular surface, coarse texture, attenuated hepatic veins),Signs of portal hypertension (presence of abdominal collaterals, splenomegaly), ascites and to exclude hepatic focal lesion.
2. upper Gastrointestinal endoscopy Using Olympus GIF 160-Q165 (EXERA II), to evaluate the presence and degree of varices in addition to any relevant upper GIT lesions. Classification of oesophageal varices was done according to Thakeb classification (1988):

Grade 1: Small straight cords of varices confined to the lower third of esophagus.

Grade 2: Moderate sized clubbed varices, with well-defined areas of normal mucosa between them, forming several distinct variceal cords and confined to the lower half of the esophagus. Grade 3: Gross varices extending into the proximal half of the esophagus, normal mucosa might not be visible in between them unless the esophagus is fully distended with air.

Grade 4: Varices like those of grade 3 but with dilated capillaries on top or in between them and encroaching on esophageal lumen.

Table 1: Soehendra Classification system for Esophageal varices

Grade	Interpretation of Grade
I	• Mild dilatation • Diameter <2 mm • Tortuous • More prominent on flexing the neck forward
II	• Moderate dilatation • Diameter 3–4 mm • Located in the lower part of the esophagus
III	• Total dilatation • Diameter >4 mm • Thin-walled • Varices superimposed on varices • Located in the gastric fundus
IV	• Total dilatation • Found in the entire esophagus • Simultaneous presence of gastric or duodenal varices

1. Liver stiffness measurement (LsM) Using Fibroscan that was performed within days following or preceding upper GI tract endoscopy, the operators was not aware of the results of endoscopy.
2. Interpretation of results of Fibroscan.

1. Up to ten successful acquisitions were performed on each patient. Success rate was calculated as the ratio of the number of successful acquisitions over the total number of acquisitions.

2. The median value of successful measurements was kept as representative of the liver stiffness.

3. Only LSM obtained with 10 successful acquisitions and a success rate of at least 60% was considered reliable [6]. The following table shows the relation between Fibroscan reading in K Pascal and the stage of fibrosis [7]

Fibroscan Cut-off values for liver fibrosis and Portal Hypertension [7]

14-21 kPa - Fibrosis

>21 kPa - Portal hypertension

Statistical Analysis: Data were statistically described in terms of mean ± standard deviation (± SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study Groups was done using Mann Whitney U test for independent samples when comparing 2 Groups and Kruskal Wallis test with posthoc multiple 2-Group comparisons when comparing more than 2 Groups. For comparing categorical data, Chi–square (c2) test was performed. Exact test was used instead when the expected frequency is less than [5]. Accuracy was represented using the terms sensitivity and specificity. Receiver operator characteristic (ROC) analysis was used to determine the optimum cut off value for the studied diagnostic markers. Univariate and multivariate regression models were constructed to determine the significant independent predictors for the occurrence of OV, the grade of OV and occurrence of large OV. p values less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

Results

A total of 180 liver cirrhosis patients were enrolled in the study. The present study was carried out to assess the utility of non-invasive techniques like Portal vein diameter, Platelet count and Fibroscan to predict the oesophageal varices and their grading in liver cirrhosis patients. A total of 110 patients were having oesophageal varices whereas 70 patients were without oesophageal varices. Majority of patients (81.1%) were males.

Age of patients ranged from 24 to 90 years. Majority of patients (n=107/180; 59.4%) were aged between 31 and 50 years. There were 47 (26.1%) cases in age group 51-60 years and 9 (5%) each aged 61-70 and >70 years respectively. A total of 8 (4.4%) patients were aged <30 years. Mean age of patients was 48.14±11.52 years (Median 46 years). As compared to females, males tended to be younger with majority of males being aged <50 years (67.3%) whereas majority of females were aged >50 years (51.5%).

Mean age of males was 47.29±10.85 years (Median 46 years) whereas mean age of females was 51.97±13.65 years (Median 51 years). Statistically, there was a significant difference in mean age of males and females (p=0.034). Table-2 and figure-1 are illustrating the demographic details of the patients.

Table 2: Age and Sex Profile of Patients enrolled in the study (n=180)

Age Group	Male (n=147)		Female (n=33)		Total (n=180)	
	No.	%	No.	%	No.	%
≤ 30 Years	8	5.4	0	0	8	4.4
31-40 Years	32	21.8	7	21.2	39	21.7
41-50 Years	59	40.1	9	27.3	68	37.8
51-60 Years	35	23.8	12	36.4	47	26.1
61-70 Years	6	4.1	3	9.1	9	5.0
>70 Years	7	4.8	2	6.1	9	5.0
Mean age±SD (Range) [Median] Years	47.29±10.85 (24-80) [46]		51.97±13.65 (32-90) [51]		48.14±11.52 (24-90) [46]	

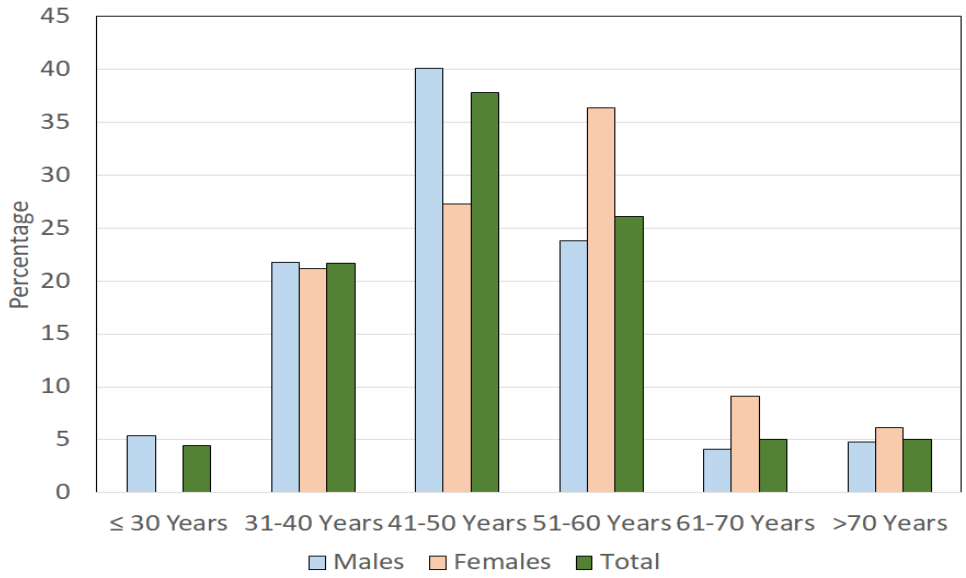

Figure 1: Distribution of cases according to different age groups

It was also observed that, a total of 104 patients (57.8%) and 26 (14.4%) were under alcohol and viral respectively as the major etiologies. There were 50 (27.8%) patients with other etiologies (Table 3).

Table 3: Distribution of cases according to underlying etiology

Etiology	No. of cases	Percentage
Alcohol	104	57.8
Viral	26	14.4
Others	50	27.8

Systemic/chronic illnesses like diabetes, hypertension, chronic kidney disease and coronary artery disease were revealed by 38 (21.1%), 39 (21.7%), 11 (6.1%) and 8 (4.4%) patients respectively. There were 21 (11.7%) cases

with history of hepatitis B and 16 (8.9%) with history of hepatitis C. Alcohol use was the dominant personal habit seen in majority (61.7%) of cases. There were 45 (25%) cases with history of smoking (Table 4).

Table 4: Distribution of cases according to Medical and Personal History

Variables	No. of cases	Percentage
Diabetes	38	21.1
Hypertension	39	21.7
Chronic kidney disease	11	6.1
Coronary artery disease	8	4.4
Hepatitis B	21	11.7
Hepatitis C	16	8.9
Alcohol use	111	61.7
Smoking	45	25.0

It was also observed that the Hemoglobin levels ranged from 6 to 13 g/dl. Maximum number of patients (n=56; 31.1%) had hemoglobin levels in 6.0-8.0 g/dl range followed by 10.1-12.0 g/dl range (n=46; 25.6%) and 8.1-10.0 g/dl range (n=45; 25%). There were 33 (18.3%) patients only having hemoglobin levels >12 g/dl.

Mean hemoglobin was 9.52±2.04 g/dl (Table 4; Fig. 4.1).Platelet count ranged from 0.32 to 2.70 lakhs/cumm. Mild, moderate and severe thrombocytopenia was seen in 44 (24.4%), 67 (37.2%) and 57 (31.7%) patients respectively.

There were 57 (31.7%) patients with platelet count in normal range. Mean platelet count was 1.25±0.54 lakhs/cumm. Mean polymorph, lymphocyte, monocyte and eosinophil count was 52.77±10.10, 41.58±9.97, 2.32±1.60 and 3.33±1.79 respectively. (Table-5 and figure-2).

Table 5: Hematological Profiles

Parameters	No. of cases	Percentage
Hemoglobin		
6.0-8.0 g/dl	56	31.1
8.1-10.0 g/dl	45	25.0
10.1-12.0 g/dl	46	25.6
>12 g/dl	33	18.3
Mean Hb±SD (Range) g/dl	9.52±2.04 (6.0-13.0)	
Platelet count		
<50,000/cumm	57	31.7
50,000-100,000/cumm	67	37.2
100,000-150,000/cumm	44	24.4
>150,000/cumm	57	31.7
Mean Platelet count±SD (Range) Lakhs/cumm	1.25±0.54 (0.32-2.70)	
Mean Polymorph±SD (Range) %	52.77±10.10 (35-70)	
Mean Lymphocyte±SD (Range) %	41.58±9.97 (23-62)	
Mean Monocyte±SD (Range) %	2.32±1.60 (0-6)	
Mean Eosinophil±SD (Range) %	3.33±1.79 (0-9)	

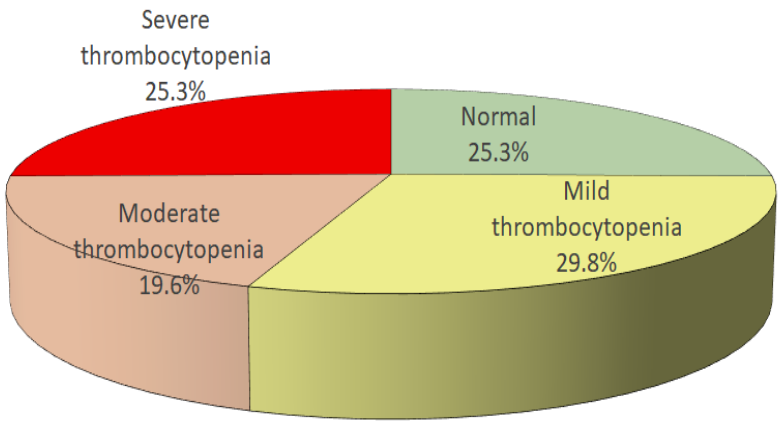

Figure 2: Distribution of cases according to platelet count

It has also observed that the Mean serum bilirubin, SGOT, SGPT and S. albumin were 3.64±5.20 mg/dl, 82.53±96.89 IU/L, 80.78±82.80 IU/L and 2.81±0.52 mg/dl respectively. Mean serum creatinine and BUN were 1.34±0.46 mg/dl and 24.07±11.57 mg/dl (Table-6).

Table 6: Liver and Renal Function Profile

Parameters	Mean	SD	Median	Min	Max
S. bilirubin (mg/dl)	3.64	5.20	1.90	0.39	27.90
SGOT (IU/L)	83.53	96.89	59.40	20	786.0
SGPT (IU/L)	80.78	82.80	54.00	10	456
S. Albumin (mg/dl)	2.81	0.52	2.80	1.67	4.10
S. Creatinine (mg/dl)	1.34	0.46	1.30	0.61	2.09
BUN (mg/dl)	24.07	11.57	23.30	6.9	44.9

In our study it was found that the Majority of cases (n=106; 58.9%) had mild ascites. There were 74 (41.1%) cases with moderate ascites. Portal vein diameter ranged from 9 to 19 mm. Majority (70.6%) of cases had portal vein diameter ≤13 mm. There were 53 (29.4%) cases with portal vein diameter >13 mm. Mean portal vein diameter was 12.83±1.86 mm. Liver stiffness ranged from 16 to 75 kPa. Majority (85.6%) had liver stiffness >21 kPa. There were 26 (14.4%) cases with liver stiffness 14-21 kPa. Mean liver stiffness was 33.87±11.64 kPa (Table-7 and figure-3).

Table 7: Sonographic and Transient Elastography Assessment

Parameter	No. of cases	Percentage
Ascites		
Mild	106	58.9
Moderate	74	41.1
Portal vein diameter		
≤13 mm	127	70.6
>13 mm	53	29.4
Mean PV Diameter±SD (Range) mm	12.83±1.86 (9-19)	
Liver stiffness (Fibroscan)		
14-21 kPa (Fibrosis)	26	14.4
>21 kPa (PH)	154	85.6
Mean LS±SD (Range) kPa	33.87±11.64 (16-75)	

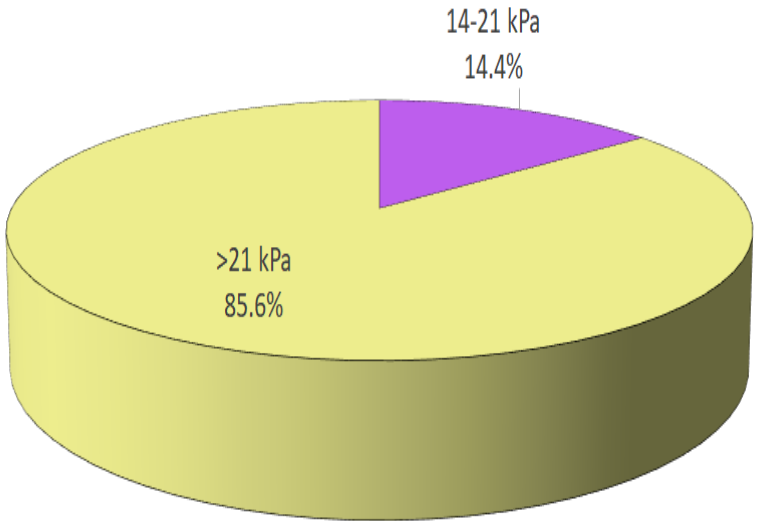

Figure 3: Distribution of cases according to Liver Stiffness

A total of 70 (38.9%) cases were not having esophageal varices. Remaining 110 (61.1%) cases showed esophageal varices. There was a dominance of those with lower grades of varices (Grades 1 and 2) (n=76; 42.2%). There were 29 (16.1%) patients with Grade 3 and 5 (2.8%) with Grade 4 varices (Figure-4).

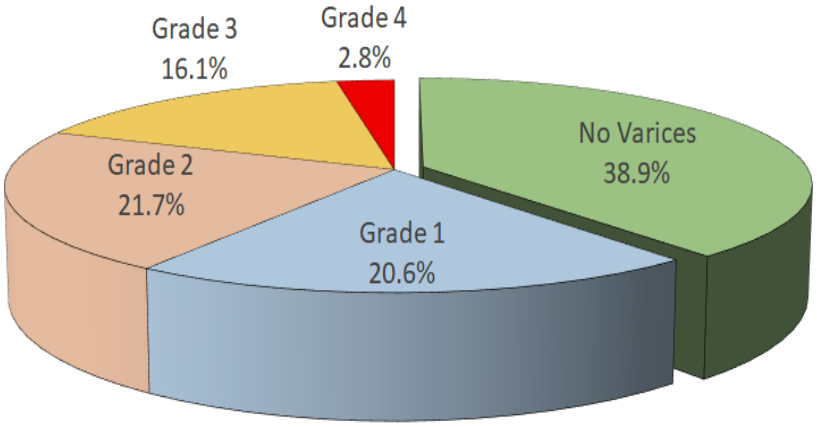

Figure 4: Endoscopic Findings

Statistically, there was no significant difference between the two groups with respect to age, sex, etiology, hemoglobin, differential count, liver and renal function parameters. However, mean portal vein diameter and liver stiffness values were significantly higher and mean platelet count was significantly lower in cases with esopahgeal varices as compared to those without esophageal varices ($p<0.001$) (Table- 8).

Table 8: Association of different Clinicodemographic and sonographic variables with Esophageal Varices

Variables/ Parameters	Esophageal varices present (n=110)	Esophageal varices absent (n=70)	Statistical significance
Mean age±SD (years)	48.11±10.62	48.20±12.89	t=0.051; p=0.959
Male:Female	89 (80.9%): 21 (19.1%)	58 (82.9%): 12 (17.1%)	χ^2=0.108; p=0.742
Etiology			
Alcohol	64 (58.2%)	40 (57.1%)	χ^2=0.411; p=0.814
Viral	17 (15.5%)	9 (12.9%)	
Others	29 (26.4%)	21 (30.0%)	
Mean Hb±SD (g/dl)	9.32±1.97	9.83±2.12	t=1.664; p=0.098
Mean PC±SD (Lakhs/mm^3)	1.03±0.43	1.61±0.51	t=8.194; p<0.001
PC<1.0 Lakhs/cumm	51 (46.4%)	5 (7.1%)	χ^2=30.70; p<0.001
Mean polymorph±SD (%)	53.53±9.97	51.59±10.25	t=1.260; p=0.209
Mean lymphocyte±SD (%)	40.90±9.96	42.64±9.97	t=1.144; p=0.254
Mean monocyte±SD (%)	2.21±1.59	2.49±1.61	t=1.131; p=0.260
Mean Eosinophil±SD (%)	3.36±1.86	3.29±1.70	t=0.284; p=0.209
Mean S. Bilirubin±SD (mg/dl)	3.19±4.42	4.36±6.19	t=1.471; p=0.143
Mean SGOT±SD (IU/L)	76.57±84.53	94.47±113.4	t=1.210; p=0.228
Mean SGPT±SD (IU/L)	73.33±77.81	92.48±88.40	t=1.518; p=0.131
Mean S. albumin±SD (mg/dl)	2.82±0.57	2.78±0.43	t=0.623; p=0.534
Mean S. creatinine±SD (mg/dl)	1.30±0.47	1.39±0.44	t=1.205; p=0.230
Mean S. BUN±SD (mg/dl)	23.33±11.79	25.23±11.21	t=1.074; p=0.284
Portal vein diameter			
≤13 mm	64 (58.2%)	63 (90.0%)	χ^2=20.85; p<0.001
>13 mm	46 (41.8%)	7 (10.0%)	
Mean PV±SD (mm)	13.45±1.84	11.87±1.43	t=6.076; p<0.001
Liver stiffness (FibroScan)			
14-21 (Fibrosis)	5 (4.5%)	21 (30.0%)	χ^2=22.43; p<0.001
>21 (PH)	105 (95.5%)	49 (70.0%)	
Mean LS±SD (kPa)	36.83±11.93	29.22±9.34	t=4.499; p<0.001

It was also found that the Mean platelet count was significantly higher in patients without varices and lower variceal grades (Grades 1/2) as compared to higher variceal grades (Grades 3/4) ($p<0.001$).Portal vein diameter and liver stiffness showed a significant incremental trend with increasing grades of varices ($p<0.001$) (Figure-5).

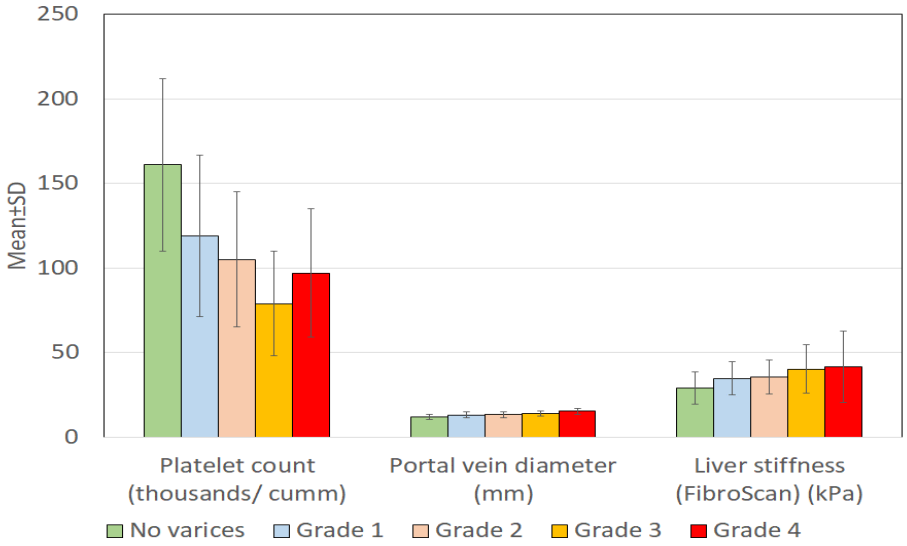

Figure 5: Comparison of Platelet count, Portal vein and Liver Stiffness in different grades of Esophageal Varices

ROC analysis was done in total 180 cases and it was observed that the area under the curve values derived for platelet count, portal vein diameter and liver stiffness for detection of esophageal varices were 0.82±0.03, 0.77±0.04 and 0.69±0.04 respectively. For platelet count the optimum cut-off value (J=0.499) was <1.045 lakhs/cumm which was projected to be 62.7% sensitive and 87.1% specific. The positive and negative predictive values of platelet count criteria were 85.5% and 59.8% respectively. Platelet count criteria had an accuracy of 72.2%. For portal vein diameter, the optimum cut-off value (J=0.486) was >12.5 mm which was projected to be 70% sensitive and 78.6% specific. The positive and negative predictive values of portal vein criteria were 83.7% and 62.5% respectively. Portal vein diameter criteria had an accuracy of 73.3%. For liver stiffness, the optimum cut-off value (J=0.312) was >22.95 kPa which was projected to be 95.5% sensitive and 45.7% specific. The positive and negative predictive values of liver stiffness criteria were 73.4% and 86.5% respectively. Liver stiffness criteria had an accuracy of 76.1% (Table-9).

Table 9: Derivation of Study Specific Cut-off values of Platelet count, Portal vein diameter and Liver Stiffness for diagnosis of esophageal varices (ROC Analysis) (n=180)

ROC Statistic	Platelet count	Portal vein diameter	Liver Stiffness
AUC±SE (p-value)	0.82±0.03 (p<0.001)	0.77±0.04 (p<0.001)	0.69±0.04 (p<0.001)
Projected cut-off value	≤1.045 L/mm^3	≥12.5 mm	≥22.95 kPa
Youden index (J) at the selected cut-off value	0.499	0.486	0.312
Sensitivity	62.7%	70.0%	95.5%
Specificity	87.1%	78.6%	45.7%
Positive predictive value	85.5%	83.7%	73.4%
Negative predictive value	59.8%	62.5%	86.5%
Accuracy	72.2%	73.3%	76.1%

ROC analysis was done in 110 cases (EV) and it was found that the area under the curve values derived for platelet count, portal vein diameter and liver stiffness for differentiation of high grade from low grade esophageal varices were 0.68±0.06, 0.67±0.06 and 0.59±0.07 respectively. For platelet count the optimum cut-off value (J=0.310) was <0.715 lakhs/cumm which was projected to be 44.1% sensitive and 86.8% specific. The positive and negative predictive values of platelet count criteria were 60.0% and 77.6% respectively. Platelet count criteria had an accuracy of 73.6% .For portal vein diameter, the optimum cut-off value (J=0.331) was >13.5 mm which was projected to be 64.7% sensitive and 68.4% specific. The positive and negative predictive values of portal vein criteria were 47.8% and 81.3% respectively. Portal vein diameter criteria had an accuracy of 67.3%. For liver stiffness, the optimum cut-off value (J=0.267) was >45.25 kPa which was projected to be 41.2% sensitive and 85.5% specific. The positive and negative predictive values of liver stiffness criteria were 56.0% and 76.5% respectively. Liver stiffness criteria had an accuracy of 71.8% (Table 10).

Table 10: Derivation of Study Specific Cut-off values of Platelet count, Portal vein diameter and Liver Stiffness for discrimination of higher and lower grades of esophageal varices (ROC Analysis) (n=110)

SN	ROC Statistic	Platelet count	Portal vein diameter	Liver Stiffness
1.	AUC±SE (p-value)	0.68±0.06 (p=0.003)	0.67±0.06 (p=0.004)	0.59±0.07 (p=0.121)
2.	Projected cut-off value	≤0.715 L/mm^3	≥13.5 mm	≥45.25 kPa
3.	Youden index (J) at the selected cut-off value	0.310	0.331	0.267
4.	Sensitivity	44.1%	64.7%	41.2%
5.	Specificity	86.8%	68.4%	85.5%
6.	Positive predictive value	60.0%	47.8%	56.0%
7.	Negative predictive value	77.6%	81.3%	76.5%
8.	Accuracy	73.6%	67.3%	71.8%

Discussion:

Chronic liver disease an outcome of a spectrum of liver diseases that are generally progressive in nature and finally end up in cirrhosis and portal hypertension[30]. With recent advances in imaging modalities, there has been increasing interest in using imaging-based methods to diagnose and assess liver cirrhosis patients [31]. Sonography along with transient elastography has emerged as a useful imaging modality for assessment of liver cirrhosis patients for complications like portal hypertension and esophageal varices. Moreover, role of platelet count in prediction of esophageal varices in suspicious patients has also been recognized. Hence the present study was carried out to assess the usefulness of non-invasive techniques like Portal vein diameter, Platelet count and Fibro scan to predict the oesophageal varices and their grading. A total of a total of 180 patients with diagnosis of liver cirrhosis (age range 24-90 years; Mean age 48.14 years; 81.7% males) were enrolled in the study. Many similar studies were in concordance our patients demographic profiles [30-32].In the present study, alcohol (57.8%), and viral hepatitis (14.4%) were the most common liver cirrhosis etiologies. A previous study found as many as 80% of the patients to have alcoholic etiology, where as in another study, alcoholic cirrhosis was detected in as many as 85% of the patients[33].In the present study, there were 31.1% patients having a history of diabetes and 27.1% having a history of hypertension. Majority of patients had hemoglobin levels <12 g/dl (81.7%).In previous studies, prevalence of low hemoglobin in chronic liver disease patients, particularly liver cirrhosis has been reported to range from 61.5% to 100% [34].In our study, platelet count ranged from 0.32 to 2.70 lakhs/cumm. Mild, moderate and severe thrombocytopenia was seen in 44 (24.4%), 67 (37.2%) and 57 (31.7%) patients respectively. There were 57 (31.7%) patients with platelet count in normal range. Mean platelet count was below the cut-off of thrombocytopenia (<1.5 lakhs/cumm). Fall in platelet count is another complication associated with chronic liver disease and cirrhosis. In most of the previous studies, exploring esophageal varices in liver cirrhosis patients, generally a low platelet count has been documented and subsequently accordance with our results[33-35].In the present study, portal vein diameter ranged from 9 to 19 mm. Majority (70.6%) of cases had portal vein diameter <13 mm. There were 53 (29.4%) cases with portal vein diameter >13 mm. Mean portal vein diameter was 12.83±1.86 mm. Liver stiffness ranged from 16 to 75 kPa. Majority (85.6%) had liver stiffness >21 kPa. There were 26 (14.4%) cases with liver stiffness 14-21 kPa. Mean liver stiffness was 33.87±11.64 kPa. esophageal varices were seen in 110 (61.1%) cases. There was a dominance of those with lower grades of varices (Grades 1 and 2) (n=76; 42.2%). Mean portal vein diameter and liver stiffness values were significantly higher and mean platelet count was significantly lower in cases with esopahgeal varices as compared to those without esophageal varices. Moreover, we also found that mean portal vein diameter and liver stiffness values were significantly higher and mean platelet count was significantly lower in cases with higher grades of esopahgeal varices as compared to those having lower grades of esophageal varices. These findings were mostly in consistence with other studies[28-29,36].

In the present study, we found that platelet count at a cut-off <1.045 lakhs/cumm was 62.7% sensitive and 87.1% specific in prediction of esophageal varices, portal vein diameter at a cut-off >12.5 mm was 70% sensitive and 78.6% specific in prediction of esophageal varices and liver stiffness at a cut-off >22.95 kPa was 95.5% sensitive and 45.7% specific in prediction of esophageal varices, portal vein at a cut-off value of >12.5 mm was only 70% sensitive and 78.6% specificity However, a previous study at a cut-off value >12.25 mm, found it to be 92.7% sensitive and 90% specificity, thus showing its performance to be better than that achieved in the present study. The above results were agreeable with the previous results [37]. A high sensitivity of liver stiffness as observed in the present study (95.5%) A similar study had reported (91%) however at a higher cut-off (>27.3 kPa)[37]. Another study however, used the cut-off value

>22.4 kPa which was similar to that in the present study[38]. The findings in the present study were encouraging and showed a promising use of non-invasive and easy-to-assess markers like platelet count, liver stiffness and portal vein diameter as predictors of esophageal varices and their grading. One of the limitations of the present study was sample size and smaller representation of higher grades of esophageal varices.

Conclusion

The present study evaluated the usefulness of platelet count, portal vein diameter and liver stiffness for prediction of esophageal varices and their grades in liver cirrhosis patients. A total of 110 (61.1%) cases showed presence of esophageal varices. A total of 76 (42.2%) patients had lower grades of varices (Grades 1 and 2) whereas 34 (18.9%) had higher grades of varices. Platelet count, portal vein diameter and liver stiffness were found to be significantly associated with esophageal varices and their grades. Among these three parameters, liver stiffness was most sensitive (95.5%) whereas platelet count was most specific (87.1%). For detection of higher grades of esophageal varices, portal vein diameter was most sensitive (64.7%) whereas platelet count was most specific (86.8%). The findings of the study show that platelet count, portal vein diameter and liver stiffness are important in prediction of esophageal varices. Further studies on a larger sample size with inclusion of more parameters are recommended.

References:

1. Kim MY, Choi H, Baik SK et al., Portal hypertensive gas tropathy: correlation with portal hypertension and prognosis in cirrhosis, Digestive Diseases and Sciences, 2010; 55 (12): 3561–3567.
2. Garcia-Tsao G and Lim JK, Management and treatment of patients with cirrhosis and portal hypertension: recommenda tions from the Department of Veterans Affairs Hepatitis C Resource Center Program and the Na-tional Hepatitis C Program, The American Journal of Gastroenterology, 2009; 104(7): 1802–1829.
3. Garcia-Tsao G, Sanyal AJ, N. D. Grace ND, Carey W, Practice Guidelines Committee of the American As-sociation for the Study of Liver Diseases, the Practice Parameters Committee of the American College of Gastroenterology, Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis, Hepatology, 2007; 46 (3): 922 -938.
4. D'Amico G, Upper digestive bleeding in cirrhosis. Post therapeutic outcome and prognostic indicators, Hepatology, 2003; 38(3): 599–612.
5. Merli M, Nicolini G, Angeloni S et al., Incidence and natural history of small esophageal varices in cirrhotic patients, Journal of Hepatology, 2003; 38(3): 266–272.
6. Garcia-Tsao Sanyal AJ, Grace ND, Carey WD, The Practice Guidelines Committee of the American Association for the Study of Liver Diseases and the Practice Parameters Committee of the American College of Gastroenterology, Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis, The American Journal of Gastroenterology, 2007;102(9): 2086–2102.
7. Fukui H, Saito H, Ueno Y et al., Evidence-based clinical practice guidelines for liver cirrhosis 2015, Journal of Gastro enterology, 2016; 51(7): 629–650.
8. Charoenchue P, et al. Prediction of Esophageal Varices in Viral Hepatitis C Cirrhosis: Performance of Combined Ultrasonography and Clinical Predictors. International Journal of Biomedical Imaging, 2023, Article ID 7938732, 1-10
9. Patil, S.; Patnaik, S.K.; Kanungo, M.; Uthansingh, K.; Narayan, J.; Pradhan, S.; Mishra, D.; Sahu, M.K.; Pati, G.K. Platelet Count/Spleen Diameter Ratio as a Non-Invasive Predictor of Esophageal Varices in Cirrhotic Patients: A Single-Center Experience. Gastroenterol. Insights 2024; 15: 98–106.
10. Gorka W.; AlMulla A.; AlSebayel M.; Altraif I.; Gorka T.S. Qualitative hepatic venous Doppler sonography versus portal flowmetryinpredicting the severity of esophageal varices in hepatitis C cirrhosis. Am. J. Roentgenol. 1997; 169: 511–515.
11. Ishibashi, H.; Higuchi, N.; Shimamura, R.; Hirata, Y.; Kudo, J.; Niho, Y. Sonographic assessment and grading of spleen size. J. Clin. Ultrasound JCU, 1991; 19: 21–25.
12. Thomopoulos, K.C.; Labropoulou-Karatza, C.; Mimidis, K.P.; Katsakoulis, E.C.; Iconomou, G.; Ni-kolopoulou, V.N. Non-invasive predictors of the presence of large oesophageal varices in patients with cirrhosis. Dig. Liver Dis. 2003; 35: 473–478.
13. Sharma, S.K.; Aggarwal, 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.
14. 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: 2564–2570.
15. Baig, W.W.; Nagaraja, M.V.; Varma, M.; Prabhu, R. Platelet count to spleen diameter ratio for the diagnosis of esophageal varices: Is it

feasible? Can. J. Gastroenterol. 2008; 22: 825–828.
16. Garcia-Tsao G, Bosch G, J. Management of varices and variceal hemorrhage in cirrhosis. N. Engl. J. Med. 2010; 362: 823.
17. Miceli G.; Calvaruso V.; Casuccio A.; Pennisi G.; Licata M.; Pintus C.; Basso M.G.; Velardo M.; Daidone M.; Amodio E.; et al. Heart rate variability is associated with disease severity and portal hypertension in cirrhosis. Hepatol. Commun. 2023; 7: e0050.
18. Schwarzenberger E.; Meyer T.; Golla V.; Sahdala N.P.; Min A.D. Utilization of Platelet Count/Spleen Diameter Ratio in Predicting the Presence of Esophageal Varices in Patients with Cirrhosis. J. Clin. Gastroenterol. 2010; 44: 146–150.
19. Sarangapani A.; Shanmugam C.; Kalyanasundaram M.; Rangachari B.; Thangavelu P.; Subbarayan J.K. Non-invasive prediction of large esophageal varices in chronic liver disease patients. Saudi J. Gastroenterol. 2010; 16: 38–42.
20. Chawla S.; Katz A.; Attar B.M.; Gupta A.; Sandhu D.S.; Agarwal R. Platelet count/spleen diameter ratio to predict the presence of esophageal varices in patients with cirrhosis. Eur. J. Gastroenterol. Hepatol. 2012; 24, 431–436.
21. Chalasani N.; Imperiale T.F.; Ismail A.; Sood, G.; Carey M.; Wilcox M.C.; Madichetty H.; Kwo P.Y.; Boyer T.D. Predictors of large esophageal varices in patients with cirrhosis. Am. J. Gastroenterol. Suppl. 1999; 94: 3285–3291.
22. Ng F.H.; Wong S.Y.; Loo C.K.; Lam K.M.; Lai C.W.; Cheng C.S. Prediction of esophageal varices in patients with liver cirrhosis. J. Gastroenterol. Hepatol. 1999; 14: 785–790.
23. GarciaTsao G.; Escorsell A.; Zakko M.; Patch D.; Matloff D.; Grace N.; Burroughs A.; Bosch J.; Groszmann R.J. Predicting the presence of significant portal hypertension and varices in compensated cirrhotic patients. Hepatology 1997; 26: 257–275.
24. Goh S.H.; Tan W.P.; Lee S.W. Clinical predictors of bleeding esophageal varices in the ED. Am. J. Emerg. Med. 2005, 23: 531–535.
25. Bacon B.R. Cirrhosis and its complications. In Chapter 308. Harrison's Principles of Internal Medicine, 18th ed.; McGraw-Hill: New York, NY, USA, 2014; 1971–1974.
26. Gupta T.K.; Chen L.; Groszmann R.J. Pathophysiology of portal hypertension. Clin. Liver Dis. 1997; 1: 1–12.
27. DeFranchis F.; Primignani M. Naturalhistory of portal hypertension in patients with cirrhosis. Clin. Liv. Dis. 2001; 5: 645–663.
28. Rigo G.P.; Merighi A.; Chahin N.J.; Mastronardi M.; Codeluppi P.L.; Ferrari A.; Armocida C.; Zanasi G.; Cristani A.; Cioni G.; et al. A prospective study of the ability of three endoscopic classifications to predict hemorrhage from esophageal varices. Gastrointest. Endos. 1992; 38: 425–429.
29. DeFranchis R.; Bosch J.; Garcia-Tsao G.; Reiberger, T.; Ripoll C.; Abraldes J.G.; Albillos A.; Baiges A.; Bajaj J.; Bañares R.; et al. Baveno VII-Renewing consensus in portal hypertension. J. Hepatol. 2022; 76: 959–974.
30. D'amico G.; Pagliaro L.; Bosch J. The treatment of portal hypertension, ameta-analysis review. Hepatology. 1995; 22: 332–354.
31. Spiegel B.M.; Targownik L.; Dulai G.S.; Karsan H.A.; Gralnek, I.M. Endoscopic screening for esophagealvarices in cirrhosis: Is it ever cost effective? Hepatology 2003; 37: 366–377.
32. DeFranchis R.; Dell'Era A.; Primignani M. Diagnosis and monitoring of portal hypertension. Dig. Liver Dis. 2008; 40: 312–317.
33. Boregowda U.; Umapathy C.; Halim N.; Desai M.; Nanjappa A.; Arekapudi S.; Theethira T.; Wong H.; Roytman M.; Saligram S. Update on the management of gastrointestinal varices. World J. Gastrointest. Pharmacol. Ther. 2019; 10: 1–21.
34. Pilette C.; Oberti F.; Aubé C.; Rousselet M.C.; Bedossa P.; Gallois Y.; Rifflet H.; Calès P. Non-invasive diagnosis of esophageal varices in chronic liver disease. J. Hepatol. 1999; 31: 867–873.
35. Ong J.; Younossi Z.M. Clinical predictors of large esophageal varices: How accurate are they? Am. J. Gastroenterol. 1999; 94: 3103–3105.
36. Madhotra R.; Mulcahy H.E.; Willner I.; Reuben A. Prediction of esophageal varices in patients with cirrho-sis. J. Clin. Gastroenterol. 2002; 34: 81–85.
37. Giannini E.; Botta F.; Borro P.; Risso D.; Romagnoli P.; Fasoli A.; Mele M.R.; Testa E.; Mansi C.; Savarino V.; et al. 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: 1200–1205.
38. D'Amico G.; Morabito A. Noninvasive markers of esophageal varices: Another round, not the last. Hepa-tology 2004; 39: 30–34.