ISSN No:-2456-2165

Non-Invasive Panel for Prediction of Large Esophageal Varices in Patients with HCV-Related Cirrhosis after DAAS Therapy

Mohamed Elsayed Abdelaal[1], Amr Ragab Shalaby[2], Mahmoud Allam[3], Hazem Omar[4],
Elsayed Shaaban Tharwa[5], Hassan Elsayed Zaghla[6]
[1,2,3,5,6]Gastroenterology and Hepatology Department, National Liver Institute, Menoufiya University,
[4]Radiology Department, National Liver Institute, Menoufiya University, Egypt.

Abstract:-

➢ ***Aim:***

This work aim to study sonographic and laboratory parameters as diagnostic non-invasive Indices for prediction and screening of large varices in liver cirrhotic patients post hepatitis C virus after Direct Acting Antiviral Drugs (DAAS).

➢ ***Introduction:***

All cirrhotic patients should be screened for esophageal varices (EV) via endoscopy, as recommended by the guidelines. However, repeated endoscopy is not well accepted by patients and is a costly procedure that places a heavy burden on the endoscopic unit. Therefore, noninvasive predictors of EVs and size discrimination for EVs are of particular importance.

➢ ***Patients and methods:***

A total of 150 post-C liver cirrhosis patients post DAAS, 37 females (24.7%) and 113 males (75.3%). After dividing into three arms: arm 1 with Non-EV, arm 2 grad 1&2 EV (Small Vriceal arm), and arm 3 grade 3 &4 EV (Large Variceal arm). Medical history, physical examination, Standard laboratory tests, Abdominal ultrasound, and Sonographic parameters such as portal vein velocity (PVV). Splenic Index (SI) Splenoportal Index (SPI), platelet count/spleen diameter ratio (PCSDR) and upper gastrointestinal endoscopy were performed for all participants.

➢ ***Results:***

The Noninvasive sonographic and laboratory parameters for prediction of the presence of EVs have demonstrated that low platelet count/spleen diameter ratio (PC/SD) was found to be the most accurate parameter at cut-off (CO) ≤ 1121.43 cu/mm, then SPI at CO >3.98 cm /sec then FIB4 at CO > 2.68 then APRI at CO > 0.6 then PVV at CO ≤ 22.2 cm/sec then SI at CO > 89.7 and lastly Child's-Pugh's score at CO >6 respectively.

The Noninvasive sonographic and laboratory parameters for discrimination of the size of EVs showed that high SPI was found to be the most accurate parameter at CO less than >7.75 cm/sec Then low PC/SD at CO ≤ 514.08 cu/mm then APRI at CO > 1.4 then FIB4 at CO > 7,6 then SI with AUC 0.821 at CO > 122.4 then low PVV at CO < 15 and lastly Child's –Pugh's score at CO> 6 respectively.

➢ ***Conclusions:***

The sonographic and laboratory indices are non-invasive parameters for the prediction of EV & discrimination of its size. And to determine when Upper Endoscopy is done for liver cirrhotic patients post HCV after DAAS

Keywords:- *Liver Cirrhotic Patients Post C after DAAS, Esophageal Varices (EV), Portal Vein Velocity (PVV). Splenic Index (SI) Splenoportal Index (SPI), Platelet Count/Spleen Diameter Ratio (PC/SD), FIB4, APRI,Child–Pugh Score, Upper Endoscopy (UE).*

I. INTRODUCTION

One percent of the world's population is afflicted with chronic hepatitis C virus (HCV) infection, a significant global health concern **(Cooke et al. 2019) (Polaris 2015).**

Currently, Egypt is experiencing the largest HCV epidemic, with an estimated national prevalence of 14.7% **(Guerra et al. 2012).**

The Egyptian government decided at the beginning of 2018 to make a major push to find and treat all HCV-infected people so that the disease could be eliminated as soon as possible **(Waked et al.2020)**.

As with other chronic liver diseases, chronic HCV infection progresses to cirrhosis, which is eventually complicated by portal hypertension (PHT). PHT causes the development of Porto systemic collaterals, which leads to the formation of esophageal varices **(Zhang et al. 2015).**

Varices are present in 60–80 percent of cirrhotic patients, with a 25–35 percent risk of bleeding. **(Amico et al.2004) .**

The variceal wall tension increases with the variceal' size, and when it reaches a critical level, the varices rupture and cause life-threatening bleeding even when treated in a

hospital, the mortality rate from variceal bleeding is about 20% **(D'Amico et al 2003).**

Intravesical pressure is less important than the size and appearance of varices, although a portal pressure of 10 mmHg is required for varices to form and a portal pressure of 12 mmHg is required for them to bleed (Merli et al 2003).

After a variceal bleed, the danger of rebleeding is especially high, ranging from 60 to 70 percent over the subsequent 24 months. However, the greatest risk of rebleeding occurs within hours or days of an acute bleed (Graci 1997). The American Association for the Study of Liver Disease and the Baveno VII Consensus Conference on PHT recommended that all cirrhotic patients must be screened for the presence of EV***(Thomopulos et al 2015 & De Franchis 2022).***

Lack of patient compliance and the invasive nature of upper endoscopy, as well as the policy's lack of cost-effectiveness due to the inability to detect varices in a significant number of patients, limit its use **(Talwalkar et al 2001).**

Several attempts have been made to identify non-invasive clinical, radiological, and biochemical parameters, used singly or in combination, to determine the presence of PHT and EV, such as the ratio of PC to SD, APRI and FIB-4, **(Crisan et al 2012)**. As well as the Splenoportal Index **(Sarangapani et al 2010)**.

➢ ***Aim of the work:***

This Work Aimed to study sonographic and laboratory parameters as a noninvasive diagnostic technique for prediction and screening of large varices in liver cirrhotic patients post hepatitis C virus after direct Acting antiviral drugs (DAAS).

II. PATIENTS AND METHODS

The study was conducted on 150 Egyptian patients with HCV and liver cirrhosis after DAAS presented to the outpatient clinic and endoscopy unit at the National Liver Institute Menofiya University spanning from June 2021 to January 2022. 2023. All patients were consented before enrollment.

All Patients were divided into three arms: **arm 1** (no EV) **arm 2** (grades 1 & 2) and **arm 3** (Grades 3 & 4)

➢ *The Inclusion Criteria for Participants in this Research:*

Patients diagnosed with HCV-related cirrhosis after DAAS are based on clinical evaluation, laboratory findings, and ultrasonography.

➢ *The Exclusion Criteria Consisted of:*

- Patients with cirrhosis of the liver due to causes other than HCV, such as those with hepatitis B virus, autoimmune hepatitis, nonalcoholic steatohepatitis, or Wilson's disease.
- HCC patients.
- Unwilling or unable to sign the consent form.

Every participant in the study was subject to a comprehensive medical history, clinical examination, and laboratory examination, abdominal ultrasound, and sonographic parameters as the size of the liver and spleen, portal-vein-velocity (PVV). Splenic-Index (SI) Splenoportal-Index (SPI),platelet count/spleen diameter ratio (PC/SD) and upper gastrointestinal endoscopy.

Non-invasive parameter calculation (APRI, FIb4, PC /splenic diameter (SD).

➢ *Abdominal Ultrasonography:*

After an overnight fast, ultrasonography was performed on all patients, and the following information was recorded: liver echotexture, ascites, maximum vertical span of the liver, spleen size (length of its longest axis) SI (long axis x transverse axis by Cm), portal vein diameter and PVV by cm/ sec) The TOSHIBA Xario and TOSHIBA Nemio XG are pieces of real-time ultrasound equipment made by the TOSHIBA Corporation of Japan. Both of these devices use a convex array transducer with a frequency of 3.5 MHz.

➢ *Sonographic Parameters:*

The ratio of SI to mean PVV is the definition of SPI, according to the formula, SPI = SI / PVV means, whereby SI is the sonographic calculation of splenic size in square centimeters based on the maximum transverse and longitudinal measurements and PVV mean is the velocity of portal blood flow in cm/s calculated automatically by the machine with time-arranged velocity in two to three cardiac cycles and Platelet Count splenic Diameter Ratio (PCSDR)= platelet count (N/cuL) / the maximum bipolar diameter of spleen (mm).

➢ *Upper Esophagogastroduodenoscopy (EGD):*

Patients with liver cirrhosis were divided into three arms based on endoscopic findings: no varices, small varices, and large varices.

To evaluate EV and its grades, upper gastrointestinal endoscopy was performed on all patients. EV was assigned a 0-4 grade under the Paquet grading system (Paquet et al 2016).

- No varices: Grade **0**
- Grade 1:Varices, disappearing with insufflations.
- Grade 2: Larger, clearly visible, usually straight varices, not disappearing with insufflations.
- Grade 3: More prominent varices, locally coil-shaped and partly occupying the lumen.
- Grade 4:Tortuous, sometimes grape-like varices occupying the esophageal lumen.

ISSN No:-2456-2165

III. STATISTICAL ANALYSIS

➢ *Statistical Analysis of the Data*

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative data were described using numbers and percentages. The Kolmogorov-Smirnov test // Shapiro-Wilk test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, and standard deviation, median and interquartile range (IQR). The significance of the obtained results was judged at the 5% level.

IV. RESULTS

There were 37 females (24.7%) and 113 males (75.3%). The age ranged between 43 - 83 years, presented to the outpatient clinic and endoscopy unit at the National Liver Institute Menofiya University throughout the period from June 2021 to Jan. 2023. All patients were consented before enrollment.

According to the absence & size of EV, three arms are described. Arm 1 without varices included 30 male (78.9%) and 8 female (21.1%) with mean age 60.79 ± 3.76 years, arm 2 with small EV included 52 male (82.5%) and 11 female (17.5%) with mean age 60.27 ± 5.77 years, arm 3 with Large EV included 31 male (63.3%) and 18 female (36.7%) with mean age 63.59 ± 8.20 years, EV were more predominant in male gender among three arms without statistically significant.

There was a significant correlation between EV Size and Age in the three arms. and significantly greater in large EVs (arm 3) than in Small EVs (arm II).

There was a statistically significant difference between the three arms in terms of spleen size, presence of ascites and presence of edema.

There were significantly higher variceal arms 2 &3 than arm 1 concerning the size of the spleen, between arms 3 than arm 1 concerning ascites, and between arms 3 than both arms 1 and 2 concerning Edema.

Table 1 Comparison between the Studied Arms According to Biochemical Liver Profile

Biochemical liver profile	Esophagus			Test of Sig.	P	Sig. bet. Grps.		
	Free (arm1) (n = 38)	Small EV(arm2) (n = 63)	Larg EV(arm3) (n = 49)			1 vs. 2	1 vs. 3	2 vs. 3
Bilirubin								
Min. – Max.	0.43 – 1.20	0.29 – 4.60	0.30 – 8.40	H=25.177*	<0.001*	0.010*	<0.001*	0.004*
Mean ± SD.	0.78 ± 0.22	1.23 ± 0.95	2.94 ± 2.72					
Median (IQR)	0.80 (0.61 – 0.95)	0.85 (0.67 – 1.29)	1.20(0.95 – 6.20)					
AST								
Min. – Max.	20.0 – 56.0	15.0 – 240.0	21.0 – 195.0	H=29.466*	<0.001*	0.036*	<0.001*	<0.001*
Mean ± SD.	38.82 ± 8.55	49.97 ± 30.68	79.35 ± 44.12					
Median (IQR)	39.5 (34.0 – 46.0)	45.0 (36.0 – 55.0)	66.0(45.0 – 110.0)					
ALT								
Min. – Max.	16.0 – 50.0	7.0 – 86.0	13.0 – 96.0	H=13.152*	0.001*	0.421	0.001*	0.004*
Mean ± SD.	29.74 ± 7.91	33.14 ± 14.97	43.31 ± 20.17					
Median (IQR)	28.5 (26.0 – 37.0)	31.0 (22.0 – 42.0)	42.0 (29.0 – 54.0)					
AST/ ALT ratio								
Min. – Max.	1.04 – 1.56	0.73 – 5.33	0.96 – 3.60	H=25.165*	<0.001*	0.088	<0.001*	<0.001*
Mean ± SD.	1.33 ± 0.14	1.58 ± 0.66	1.86 ± 0.62					
Median (IQR)	1.36(1.20 – 1.44)	1.35(1.19 – 1.76)	1.72(1.47 – 2.14)					
ALP								
Min. – Max.	46.0 – 112.0	44.0 – 147.0	42.0 – 184.0	H=2.950	0.229	>0.05	>0.05	>0.05
Mean ± SD.	71.63 ± 19.38	73.24 ± 23.16	80.53 ± 27.77					
Median (IQR)	71.0 (54.0 – 87.0)	67.0 (56.0 – 83.0)	74.0 (62.0 – 92.0)					
Albumin								
Min. – Max.	3.0 – 4.30	2.10 – 4.50	1.80 – 4.70	F=22.598*	<0.001*	<0.001*	<0.001*	0.016*
Mean ± SD.	3.89 ± 0.38	3.35 ± 0.63	3.05 ± 0.64					
Median (IQR)	4.0 (3.80 – 4.10)	3.50 (2.85 – 3.90)	3.0 (2.60 – 3.40)					
Prothrombin time								
Min. – Max.	49.50 – 76.55	43.10 – 82.50	38.0 – 71.90	F=23.704*	<0.001*	0.601	<0.001*	<0.001*
Mean ± SD.	64.42 ± 8.49	62.72 ± 9.01	53.16 ± 8.09					
Median (IQR)	66.5 (55.8 – 72.2)	64.2 (57.7 – 68.7)	52.1 (48.3 – 56.5)					

➢ *Bilirubin:*

The mean level of Bilirubin for arm 1 was 0.78 ± 0.22, 1.23 ± 0.95 for arm 2, and 2.94 ± 2.72 for arm 3 with the significant value among three arms and a significant value greater in variceal arms 2 &3 than arm 1 (Non-variceal arm). And variceal arms 3 than 2 (larger than small variceal arms).

➢ *AST:*

The mean level of AST for arm 1 was 38.82 ± 8.55, 49.97 ± 30.68 for arm 2, and 79.35 ± 44.12 for arm 3 with a significant value among three arms and a significant value greater in variceal arms 2 and 3 compared to arm 1, and arm 3 compared to arm 2.

➢ *ALT:*

The mean level of ALT for arm 1 was 29.74 ± 7.91, 33.14 ± 14.97 for arm 2, and 43.31 ± 20.17 for arm 3 with a significant value among three arms and a significant value higher in (arm 3 than arm 1 and with an insignificant value between arm 2 and arm 1.

➢ *AST/ALT Ratio:*

The mean level of AST for arm 1 (no varices) were 1.33 ± 0.14, 1.58 ± 0.66 for arm 2 (small varices) and 1.86 ± 0.62 for arm 3 (large Varices) with a significant value among three arms and significant value higher in variceal arms 2 and 3 than arm 1 and arm 3 than 2.

➢ *Alkaline phosphatase:*

The mean levels for arm 1 were 71.63 ± 19.38, 73.24 ± 23.16 for arm 2, and 80.53 ± 27.77 for arm 3 without any significant value among three arms and insignificant value between arm 1 and variceal arms 2 &3 and Between arm 3 and arm 2.

➢ *Albumin:*

The Mean level of Albumin for arm 1 (no varices) was 3.89 ± 0.38, 3.35 ± 0.63 for arm 2 (small varices) And 3.05 ± 0.64 for arm 3 (large Varices) with a significant value among the three arms and a significant value reduced in variceal arms 2 and 3 than arm 1 and Also between arm 3 and arm 2.

➢ *Prothrombin time:*

The Mean level of Prothrombin time concentration for arm 1 was 64.42 ± 8.49, 62.72 ± 9.01 for arm 2 and 53.16 ± 8.09 for arm 3 with a significant value among three arms and statistically significant value lower in arm 3 than arm I, with insignificant value between arm 2 and arm 1 and there was significant value lower value between arm 3 and arm.

There were significant values among the three arms concerning elevated Bilirubin, AST, ALT, AST/ ALT, and reduced levels of Albumin and prothrombin time concentration, and insignificant values among the three arms concerning ALP.

There were significant values higher in arm 2 (Small variceal arm) than in arm 1 (Non-variceal arm) concerning elevated Bilirubin, AST, AST/ALT, and reduced Albumin and in arm 3 (Large variceal arm) than in arm 1 (Non-variceal arm) and arm 2 (Small variceal arm) concerning elevated Bilirubin, AST, ALT, AST/ ALT and reduced level of Albumin and prothrombin time concentration.

Table 2 Comparison between the Studied Arms According to CBC

CBC	Esophagus			Test of Sig.	P	Sig. bet. Grps.		
	Free (arm1) (n = 38)	Small EV(arm2) (n = 63)	Large EV(arm3) (n = 49)			I vs. II	I vs. III	II vs. III
HB								
Min. – Max.	9.0 – 13.0	6.90 – 15.70	5.40 – 15.80	F= 17.871*	<0.001*	0.021*	<0.001*	0.001*
Mean ± SD.	11.24 ± 1.18	10.26 ± 1.91	8.98 ± 1.96					
Median (IQR)	11.3 (10.5 – 12.0)	9.80 (8.80 – 11.3)	8.70 (7.70 – 10.2)					
WBC								
Min. – Max.	3.0 – 10.0	1.60 – 15.40	1.50 – 14.0	H= 19.106*	<0.001*	<0.001*	<0.001*	0.531
Mean ± SD.	6.56 ± 1.93	5.06 ± 2.49	4.79 ± 2.57					
Median (IQR)	6.60 (5.20 – 8.0)	4.20 (3.40 – 6.55)	4.20 (3.10 – 5.50)					
PLT								
Min. – Max.	143.000 –221.000	160.0 – 1790.0	90.000 – 57.000	H= 121.10*	<0.001*	<0.001*	<0.001*	<0.001*
Mean ± SD.	178000.405 ± 194.8	110000.709 ± 214.1	54000,609 ± 237.9					
Median (IQR)	178.000 (168.000 191,000)	112.000 (970.0 – 121.000)	53.000 (39.000 – 68.000)					

➢ *Hemoglobin:*

The Mean levels of Hemoglobin for arm 1 were 11.24 ± 1.18, 10.26 ± 1.91 for arm 2 and 8.98 ± 1.96 for arm 3 with a significant value among the three arms and a significant value lower in variceal arms 2 and 3 than arm 1 and Also between arm 3 and arm 2.

➢ *White Blood Cells (WBCs):*

The Mean level of WBCs for arm 1 was 6.56 ± 1.93, 5.06 ± 2.49 for arm 2 and 4.79 ± 2.57 for arm 3 with statistically significant values among the three arms and significant values lower in variceal arms 2 and 3 than arm 1 and Also between arm 3 and arm 2.

➢ *Platelets:*

The Mean level of Platelets count for arm 1 was 178.000 (168.000 ± 194.8), 110000.709 ± 214.1for arm 2, and 54000,609 ± 237.9 for arm 3 with a significant value among the three arms and statistically significant value lower in variceal arms 2 and 3 than arm 1 and Also between arm 3 and arm 2. There was a significant value among the three arms in relation to low levels of hemoglobin (HB), white blood cells (WBC), and Platelets (PLT). There was a significant value lower in variceal arms 2 and 3 than in arm 1 and also between arm 3 and arm 2 (large and small variceal arm) in relation to low levels of HB, WBCs, and PLT.

Table 3 Child-Pugh Score in Three Arms:

	Esophagus						Test of Sig.	p	Sig. bet. Grps.		
	Free (arm1) (n = 38)		Small EV(arm2) (n = 63)		Large EV(arm3) (n = 49)				I vs. II	I vs. III	II vs. III
	No.	%	No.	%	No.	%					
Child pough score											
A	33	86.8	35	55.6	3	6.1	χ^2= 63.789*	<0.001*	MCp= 0.003*	<0.001*	<0.001*
B	5	13.2	25	25	33	67.3					
C	0	0.0	3	4.8	13	26.5					
Min. – Max.	5.0 – 7.0		5.0 – 11.0		5.0 – 12.0		F= 33.014*	<0.001*	0.005*	<0.001*	<0.001*
Mean ± SD.	5.76 ± 0.68		6.65 ± 1.40		8.10 ± 1.69						
Median (IQR)	6.0(5.0 – 6.0)		6.0(6.0 – 7.50)		7.0(7.0 – 10.0)						

➢ *Child-Pugh score:*

Arm 1 showed that Thirty-Three (86.8 %) had Child's A class liver disease, 5 (13.2%) had Child's class B disease while no patient had Child's C class disease. Arm 2 showed 35 (55.6%) had Child's A class liver disease, 25 (25%) had Child's B class disease and 3 (4.8%) patients had Child's C class disease. Arm 3 showed 3 (55.6 %) had Child's A class liver disease, 33(67.3%) had Child's B class disease, and 13 (26.5%) patients had Child's C class disease.

The mean Child–Pugh score in arm 1 was 6.0(5.0–6.0) while in arm 2 was 6.0 (6.0–7.50) and in arm 3 was 7.0 (7.0–10.0) with a significant value among three arms in the prediction of the presence of EV and significant value in prediction of large varices with an advanced score.

There was a significant value between variceal arms 2 and 3 than Arm 1 in the prediction of the presence of EV with advanced score and a significant value between Arm 3 and Arm 2 in the prediction of large varices.

➢ *Portal vein diameter:*

The mean Portal vein diameter in arm 1 was 12.23 ± 0.57 mm, arm 2 was 13.27 ± 2.18 mm and arm 3 was 12.98 ± 2.18 mm with a significant value greater in arm 2 than arm I, with insignificant value between arm 3 and arm 1 and between arm 3 and arm 2.

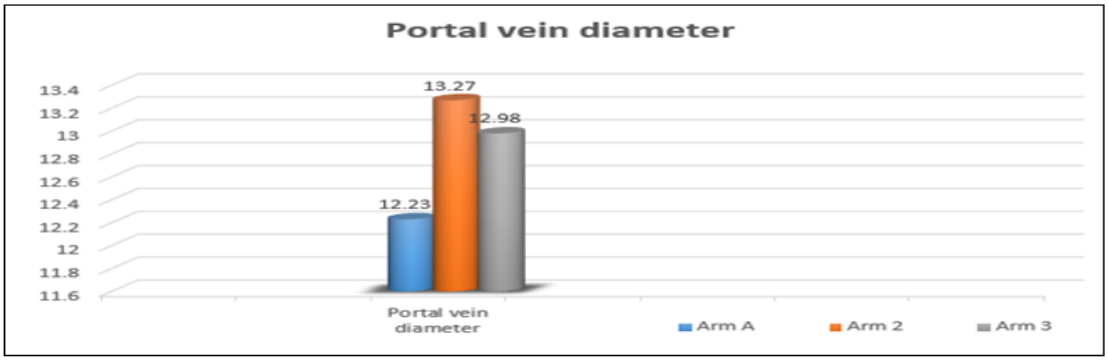

Fig 1 The Mean Value for Portal Vein Diameter in 3 Arms

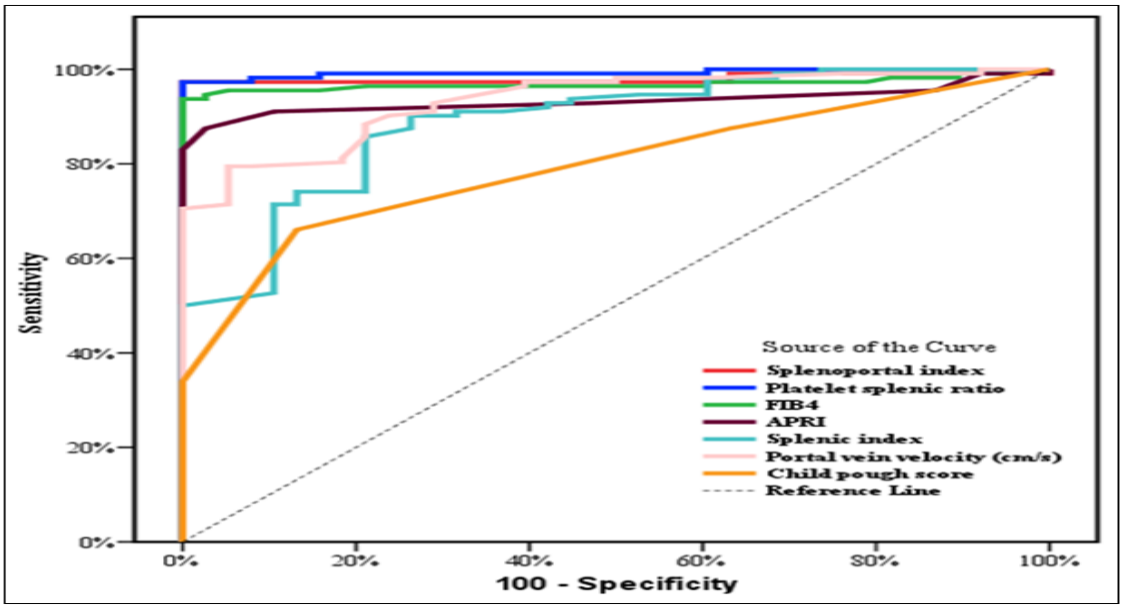

Fig 2 ROC Curve for Different Scores as Regards their Ability to Predict the Presence of EV (n = 112) from Non- EV (n = 38)

ISSN No:-2456-2165

Table 4 Prediction Power Criteria for Different Scores to Predict EV

	AUC	P	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV	Accuracy
Splenoportal index	0.980	<0.001*	0.958 – 1.0	>3.98	97.32	86.84	95.6	91.7	94.67
Platelet splenic ratio	0.992	<0.001*	0.981 – 1.0	≤1121.43	98.21	92.11	97.3	94.6	97.98
FIB4	0.969	<0.001*	0.940 – 0.998	>2.68	95.54	92.11	97.3	87.5	94.67
APRI	0.933	<0.001*	0.892 – 0.974	>0.6	91.07	89.47	96.2	77.3	90.66
Splenic index	0.887	<0.001*	0.830 – 0.944	>89.7	85.71	78.95	92.3	65.2	84.0
Portal vein velocity (cm/s)	0.932	<0.001*	0.894 – 0.971	≤22.2	91.07	71.05	90.3	73.0	86.0
Child pough score	0.795	<0.001*	0.724 – 0.867	>6	66.07	86.84	93.7	46.5	71.33

EV (n = 112) from Non- EV (n = 38)

ROC (Receiver operator characteristic) curve for sonographic and laboratory parameters to find out the best cut-off (CO) of Platelets count/ SD ratio, SPI, FIB4 and APRI, SI and PVV & detection of sensitivity & specificity at this point that could predict EV in cirrhotic post-HCV after direct-acting antiviral drugs (DAAS)

- *(PCSDR)***:**

The area under the curve (AUC) was calculated to be 0.992%.with a significant value greater in the variceal arm than non-variceal arm (P < 0.001) with the best CO to be ≤ 1121.43, The sensitivity was (98.21%), specificity (92.11%), and diagnostic Accuracy (97.98%).

- *SPI***:**

We found that the AUC was 0.980 with a significant value higher in the variceal arm than non-variceal arm (P < 0.001) with the best CO to be > 3.98, The sensitivity was (97.32%), specificity (86.84%), and diagnostic Accuracy (94.67%).

- *FIB4:*

We found that the AUC was 0.969 with a significant value greater in the variceal arm than non-variceal arm (P < 0.001) with the best CO to be >2.68, the sensitivity was (95.54%), specificity (92.11and Diagnostic Accuracy (94.67%).

- *APRI:*

We found that the AUC was 0.933 with a significant value greater in the variceal arm than non-variceal arm (P < 0.001) with the best CO to be > 0.6, the sensitivity was (91.07%), specificity (89.47%), and diagnostic Accuracy (90.66%).

- *SI:*

We found that the AUC was 0.887 with a significant value greater in the variceal arm than non-variceal arm (P < 0.001) with the best CO to be >89.7 As shown in figure (2)

The sensitivity was (85.71%), specificity (78.95%), positive predictive value (PPV) (92.3%), negative predictive value (NPV) (65.2%), and diagnostic Accuracy (84.0%).

- *PVV:*

We found that the AUC was 0.932 with a significant value higher in the variceal arm than non-variceal arm (P < 0.001) with the best CO to be ≤22.2, The sensitivity was (91.07 %), specificity (71.05 %), PPV (90.3 %), NPV (73.0 %) and diagnostic Accuracy (86.0%).

We found that the child–Pugh score AUC was 0.795 with a significant value higher in the variceal arm than non-variceal arm (P < 0.001) with the best CO to be >6, The sensitivity was (66.07 %), specificity (66.07%), PPV (93.7 %), NPV (46.5 %) and diagnostic Accuracy (71.33 %). When predicting EV, a Child-Pugh score came six.

- *In Conclusion*

The AUC and diagnostic Accuracy for Platelet/splenic ratio was > SPI > FIB4, APRI > PVV > SI >Child–Pugh score for prediction EV in post-HCV liver cirrhotic patients after DAAs.

ISSN No:-2456-2165

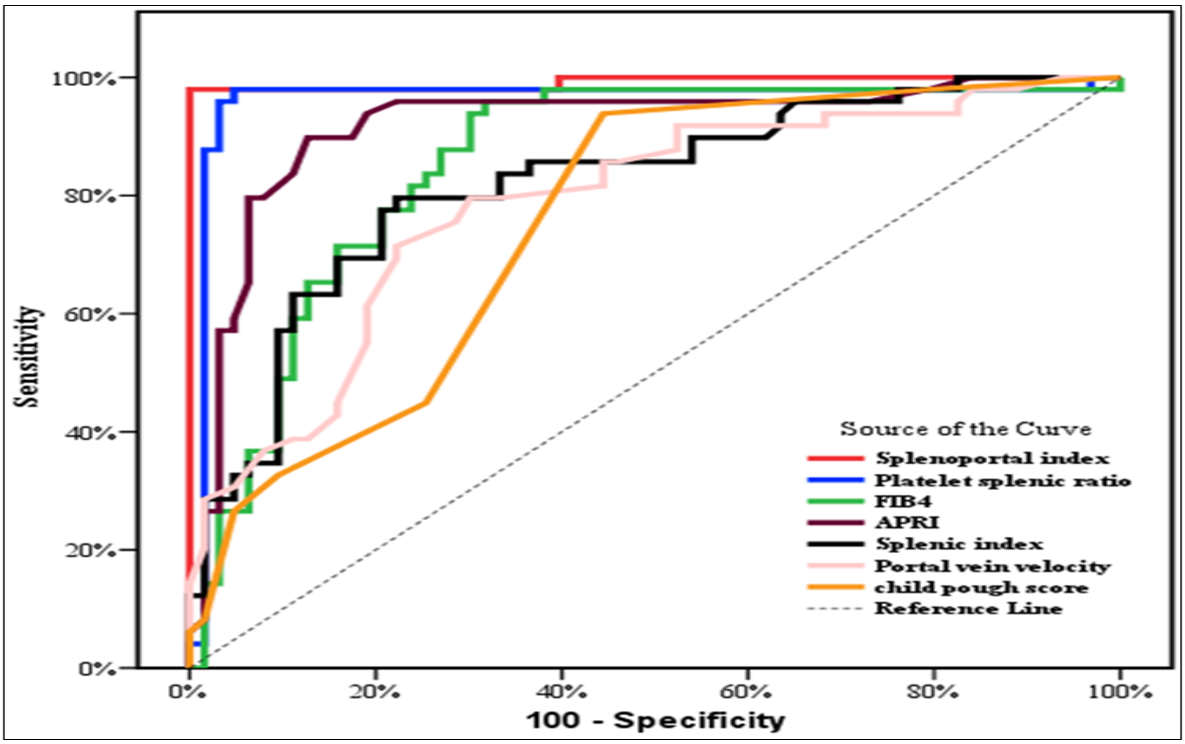

Fig 3 ROC Curve for Different Scores to Predict Large OV

Table 5 Prognostic Performance for Different Parameters to Discriminate Large EV (n = 49) from Small OV (n = 63)

	AUC	P	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV	Accuracy
Splenoportal index	0.992	<0.001*	0.976 – 1.0	>7.75	97.96	96.83	96.0	98.4	97.67
Platelet splenic ratio	0.963	<0.001*	0.916 – 1.0	≤514.08	97.96	95.24	94.1	98.4	97.27
FIB4	0.855	<0.001*	0.782 – 0.928	>7.66	87.76	73.02	71.7	88.5	84.03
APRI	0.919	<0.001*	0.861 – 0.977	>1.4	93.88	80.95	79.3	94.4	90.60
Splenic index	0.821	<0.001*	0.741 – 0.900	>122.4	79.59	77.78	73.6	83.1	79.13
Portal vein velocity (cm/s)	0.786	<0.001*	0.700 – 0.871	≤15	75.51	71.43	67.3	78.9	74.48
Child pough score	0.754	<0.001*	0.665 – 0.843	>6	93.68	55.56	62.2	92.1	72.24

ROC finds out the best CO of PC/ SD ratio, SPI, FIB4, APRI, SI, and PVV & detection of sensitivity & specificity at this point that discriminate Large OV (arm 3) from small (OV arm 2) in cirrhotic post-HCV after DAAs.

➢ *SPI:*

We found that the AUC was 0.992 with a significant value higher in the large variceal arm (arm 3) than small variceal arm (arm2), (P < 0.001) with the best cut of CO to be >7.75, The sensitivity was (97.96%), specificity (96.83%), PPV (96.0%), NPV (98.4%) and diagnostic Accuracy (97.67%).

➢ *(PCSDR) :*

We found that the AUC was 0.963 with a significant value higher in the large variceal arm (arm 3) than small variceal arm (arm 2), (P < 0.001) with the best CO to be ≤514.08, The sensitivity was (97.96%), specificity (95.24%), PPV (94.1%), NPV (98.4%) and diagnostic Accuracy (97.27%).

➢ *APRI:*

We found that the AUC was 0.919 with a significant value higher in the large variceal arm (arm 3) than small variceal arm (arm 2), (P < 0.001) with the best CO to be >1.4, The sensitivity was (93.88%), specificity (80.95%), PPV (79.3%), NPV (94.4%) and diagnostic Accuracy (90.60%).

➢ *FIB4:*

We found that the AUC was 0.855 with a significant value higher in large variceal arm (arm 3) than small variceal arm (arm 2), (P < 0.001) with the best CO to be >7.66 and diagnostic Accuracy (84.03%).

➢ *SI:*

We found that the AUC was 0.821 with a significant value higher in the large variceal arm (arm 3) than small variceal arm (arm 2), (P < 0.001) with the best CO to be >122.4, The sensitivity was (79.59 %), specificity (77.78 %), PPV (71.7%), NPV (83.1%) and diagnostic Accuracy (79.13%).

➢ *PVV:*

We found that the AUC was 0.786 with a significant value higher in the large variceal arm (arm 3) than small variceal arm (arm 2), (P < 0.001) with the best CO to be ≤15 and diagnostic Accuracy (74.48%).

➢ *Child-Pugh score:*

We found that the AUC was 0.754 with a significant value higher in the large variceal arm (arm 3) than in small (arm 2) (P < 0.001) with the best CO to be >6 ,The sensitivity was (93.68 %), specificity (55.56 %), PPV (62.2 %), NPV (92.1 %), and diagnostic Accuracy (72.24 %).Child–Pugh score came six in Discrimination of Large EV.

➢ *In Conclusion:*

The AUC and diagnostic Accuracy for SPI > Platelet/splenic ratio > APRI > FIB4 > SI > PVV >Child–Pugh score for Discrimination of Large EV (arm 3) from small (OV arm 2) in post-HCV liver cirrhotic patients after DAAs.

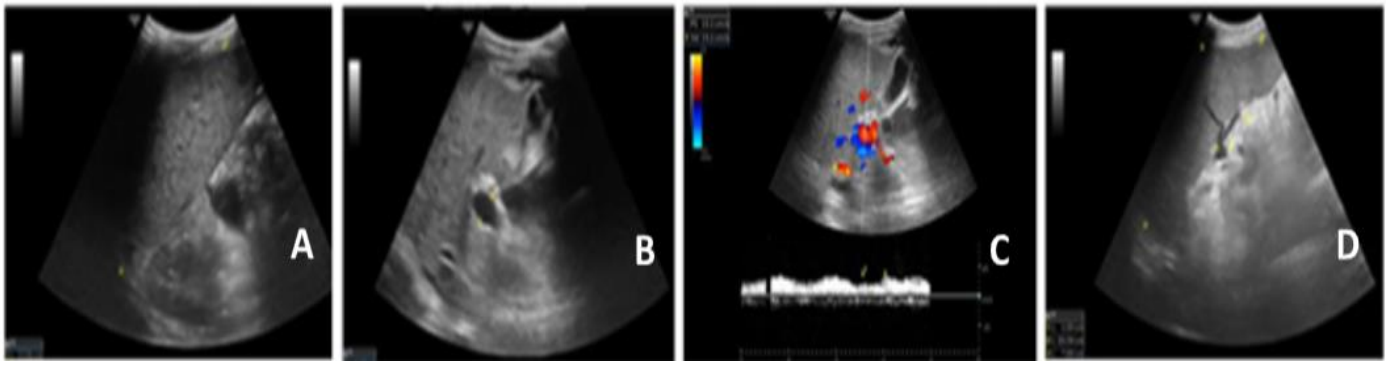

Fig 4 (A-D): A male patient 55 year old presented with grade III EV post DAAS therapy with platelet count 86000 n/ul.Abdominal ultrasonography reveals cirrhotic liver with liver span 13 cm (A),PV diameter 14.5mm (B), PVV 15.1cm/sec (C), longitudinal and transverse splenic diameters 20.39cm and 7.69cm. SI-20.39x7.69=156.79, SPI=156.79/15.1-10.38, PCSDR =86000/203.9=421.77

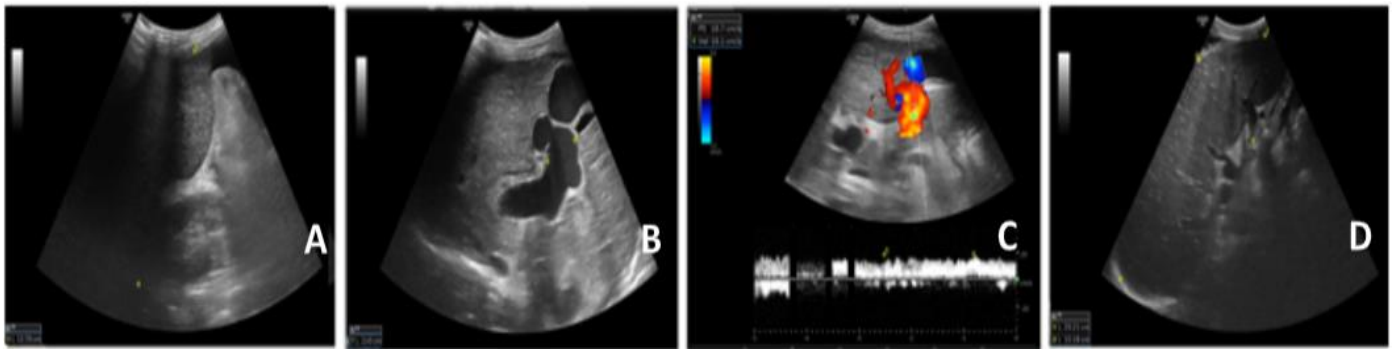

Fig 5 (A-D): A male patient 60 year old presented with grade IV EV post DAAS therapy with platelet count 63000 n/ul. Abdominal ultrasonography reveals cirrhotic liver with liver span 12.39cm (A), PV diameter 24.5mm (B), PVV 18.1cm/sec (C), longitudinal and transverse splenic diameters 29.21cm and 10.18cm. SI=29.21x10.18=297.35, SPI-297.35/18.1=16.42, PCSDR =63000/292.1=215.67

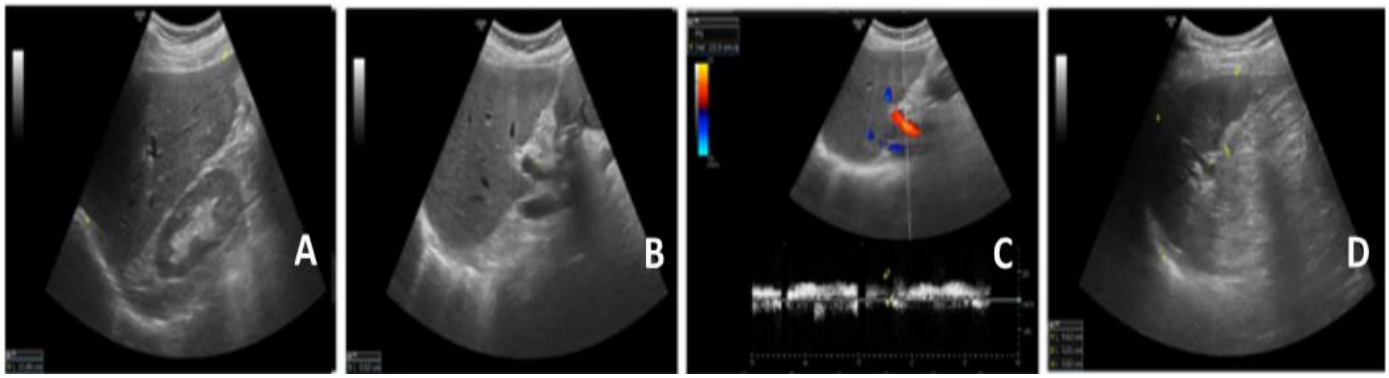

Fig 6 (A-D):A female patient 40 year old post DAAS therapy with no EV and platelet count 176000 n/ul. Abdominal ultrasonography reveals early cirrhotic liver with liver span 15.86cm (A),PV diameter 9.2mm (B), PVV 13.8cm/sec (C), longitudinal and transverse splenic diameters 9.62cm and 5.01cm. SI-9.62x5.01-48.19, SPI=48.19/13.8=3.49, PCSDR =176000/96.2=1829.5

ISSN No:-2456-2165

V. DISCUSSION

The non-endoscopic models that can predict the presence of high-risk varices are of significant interest. These studies have shown that the presence of EV can be accurately predicted using clinical, laboratory, and sonographic variables ***(Garcia-Tsao et al., 2006 & Ismail et al., 2008).***

The current study showed that EVs were more predominant in the male gender among three arms without a significant value. Several studies have found that males and females experience different rates of liver disease progression ***(Gu et al., 2013).***

In contrast to men, who make up between 55 to 70 percent of all cases, women have a much lower risk of developing chronic liver disease and are thought to have a better prognosis ***(Kim et al., 2002 & Ratib et al., 2015).***

Liver fibrosis caused by viral hepatitis or nonalcoholic steatohepatitis is less likely to progress in females. The lower rate of fibrosis progression in females is likely attributable to the protective effect of sex hormones ***(Yang et al., 2014)***.It has also been documented that women experience a lower incidence of hepatic decompensation than men ***(Rubin et al., 2020)***. It has been observed that the outcome of variceal bleeding varies by gender and country. According to a study of 266 patients in Norway, women with cirrhosis and variceal bleeding have a lower mortality risk than men ***(Haukeland et al., 2020).*** In accordance to our study ***(Fabian et al., 2019*** showed that females admitted to the hospital with variceal bleeding had a lower mortality rate than males ***(Fabian et al., 2019).***

All of these studies enrolled cirrhotic patients with different causes (viral, alcoholic, autoimmune, and mixed) and disease severity. However, in our study, all patients had liver cirrhosis post-C and after DAAS treatment.

Our study showed that age can provide a predictable factor for the large size of EV; there was a significant value directly proportional between the Size of EV and Age among the three arms and significantly greater in large EV (arm 3) than in Small EV (arm 2). These findings agree with the findings reported by ***Zhao et al. 2022 and Berger et al. 2021*** who found that the prevalence of high-risk varices increases significantly with age.

Our results of clinical findings showed that the large size of the spleen can provide a predictable factor for the presence of EV and directly proportion to the size of the spleen.

Ascites can provide predictable factors for the presence of large EVs.

Edema can provide a predictable factor for the prediction and determination of the size of EVs.

Several studies similar to our findings shown independent parameters like splenomegaly***, (Amarapurkar et al., 1994, Chalasani et al., 1999, Madhotra et al., 2002, Thomopoulos et al., 2003)*** ascites, ***(Pilette et al., 1999)*** Lower limb oedema ***(Elsherif et al., 2022)*** Child's grade, ***(Zaman et al., 2001)*** *as predictive factors for the presence of EV.*

The logistic regression analysis of the Biochemical analysis of three studied arms showed that high AST, AST/ALT ratio, and low Serum albumin, can provide information for predicting EV Presence between the cirrhotic variceal arm (arm 2& arm 3) and the cirrhotic nonvariceal arm (arm I). High serum Bilirubin, AST, ALT, AST/ ALT ratio, and low level of Albumin and prothrombin time concentration in arm 3 (Large variceal arm) than arm 1 (Non-variceal arm) and arm 2 (Small variceal arm) can provide information for discrimination of the size of EV.

Bilirubin mean level for three arms was: 0.78 for arm I, 1.23 for arm 2 and 2.94 for arm 3, and showed that Bilirubin can provide information for the presence and discrimination of the size of EV.

AST mean levels for three arms were: 38.82 for arm 1, 49.97 for arm 2 and 79.35 for arm 3. And showed that AST can provide information for the presence and discrimination of the size of EV.

ALT mean levels for three arms were: 29.74 for arm I, 33.14 for arm 2 and 43.31 for arm 3 showing that ALT can provide information for the presence of EV with a significant value higher between large variceal and non-variceal arms and ALT is higher in small variceal than non-variceal arms but without a significant value, and for the size of EV.

AST/ALT ratio mean level (The test of time = The De Ritis Ratio) for three arms was: 1.33 for arm I, 1.58 for arm 2 and 1.86 for arm 3 and showed that AST/ALT can provide information for the presence and discrimination the size of EV.

Botros & Sikaris 2013 Demonstrated that the ratio of AST to ALT represents the aggressiveness and rate of disease progression (36 h). A raised AST/ALT ratio is predictive of long-term complications such as fibrosis and cirrhosis in chronic viral diseases like chronic viral hepatitis and chronic alcoholism, as well as in non-alcoholic fatty liver disease.

The Albumin levels were: 3.89 for arm I, 3.35 for arm 2 and 3.05 for arm 3, and Albumin can provide information for the presence and discrimination of the size of EV.

The prothrombin time concentration mean level for the three arms was: 64.42 for arm I, 62.72 for arm 2 and 53.16 for arm 3 showing that Prothrombin time concentration can provide information for the presence and discrimination of the size of EV.

Consistent findings were also reported by**(*Camma. , Petta et al., 2009 and Nashaat et al., 2010.)*** Liver profile parameters and the presence of varices have been shown to have a strong correlation in other studies.***Pilette et al.,1999, Schepis et al., 2001, Bressler et al., 2005 ,Berzigotti et al., 2008.and Elsherif et al., 2022.***

Our findings regarding serum albumin were also consistent with those of ***Shehata et al., 2014***, Who evidenced that an albumin level of in the blood 3.8 indicated EV , studies of **Galal et al.2012**, Serum albumin could predict the presence of EV a cutoff of 3.2 or less, was reported. and the study by ***ELNaggar et al. 2012,*** Reported that at a CO of 3.3 or less serum albumin could predict the presence of EV.

Regarding Prothrombin time concentration, several studies have reported that PT is related to EVs. At a cutoff greater than 17.05**,** With a sensitivity of 68.8 and a specificity of 81.8 percent, PT was found to be a predictor for EVs in cirrhotic patients by ***Zaman et al. (2011).*** At a CO greater than 15.1 seconds, Elatty et al. 2019 found a statistically significant distinction between the cirrhotic variceal and nonvariceal groups in the PT prediction of EV.

The logistic regression analysis of Complete Blood Picture (CBC) low level of HB, WBCs, and PLT of three studied arms showed that there was a significant value between arm 2 & arm 3 and arm 1 in the prediction of EV. And between arm 3 and arm 2 in prediction of the size of EV. The same findings were reported by ***Elsherif et al. 2022 and Gue et al. 2004.***

The cause of anemia in patients with EV: EV and gastric or portal hypertensive gastropathy may be associated with chronic slow blood loss. and development of chronic iron deficiency anemia, Chronic inflammation; liver disease associated with chronic inflammation, Lower Erythrobiotine level with more liver damage leading to a decrease in red cell production, Hypersplenism; the spleen breaks down red blood cells far more quickly than they are produced, Malnutrition & malabsorption; Nutrients like iron, vitamin B12, and Folate are important for red cell production and Medications; as interferon, ribavirin or azathioprine ***(Sethi et al., 2023).***

White Blood Cells (WBCs) can provide information for the prediction of the presence of EV, The Mean of WBCs for arm 1 were 6000.56, 5000.06 for arm 2 and 4000.79 for arm 3 with a significant value lower in the large variceal arm and small variceal arm (presence of EV) than a non-variceal arm. And large variceal arm is lower than the small variceal arm but with an insignificant value. Consistent with the findings of Gue et al. (2004), who discovered that if WBCSs were > 4000/ cubic mm, the diagnostic yield for varices grades 2 and 3 was 19.4 percent. Leucopenia and white blood cell (WBC) count can be used to stratify the risk of developing EV in cirrhotic patients (66.7 percent if total WBCs 3000-4000, and 94.8 percent if WBC count is 3000 cubic mm).

Platelets (PLT) can provide information for predicting the presence and size of (EVs.; The Mean value of PLT count for arm 1 (no variceal arm) was 178000.405, 110000.709 for arm 2 (small variceal arm), and 54000,609 for arm 3 (large Variceal arm) with a significant value lower in large variceal and small variceal arms than a non-variceal arm and Also between large and small variceal arm.

Chalasani et al., 1999 (346 patients) reported that a platelet count of 88.000/mm3 was an independent risk factor for the presence of large varices; this was later confirmed by Sarwar et al., 2005.

Patients without varices had a higher PLT count (mean PLTc, 128,500/mm3) than those with small varices (mean PLTc, 107,800/mm3), and a PLTc of 90,000/mm3 almost multiplied the risk of having a large E.V. by 2.5 times, as reported by Zaman et al., 2001. Low PLTc is an independent risk factor for the onset of varices (Garcia-Tsao et al., 1997; Pilette et al., 1999; Thomopoulos et al., 2003).

VI. THE NON-INVASIVE ULTRASOUND PARAMETERS:

The presence of varices was found to be significantly correlated with PV diameter, PVV, SI, SPI, and low PCSDR, as determined by logistic regression analyses of our sonographic parameters.

- *PortalVein Diameter(PVD):*

The mean diameter of the portal vein was 12.2mm in Arm 1, 13.27mm in Arm 2, and 12.98mm in Arm 3.

Our results showed that Portal vein diameter was a predictable factor for the presence from the absence of EV with a significant value higher between small variceal and non-variceal arms and mean Portal vein diameter higher for large variceal than non-variceal arms without a significant value, and for large variceal arm than small variceal arm but without a significant value as a discriminant predictor for the size of EV.

The presence of EV and PVD larger than 13 mm and inversion of flow within the portal system are both diagnostic of clinically significant PHT, as demonstrated by ***Berzigotti et al. (2013).***

Researchers have found that a PV diameter of 13 mm is an accurate predictor of EV in cirrhotic patients (Giannini et al., 2003; Gill et al., 2004). The optimum CO for a PV diameter of 13.5 mm was also reported by Nashaat et al., A PVD of >13 mm for small EVs and >14 mm for large EVs was confirmed by ***Cherian et al.*** (2011).

At a CO of 15.2 mm, Elatty et al. 2019 found a statistically significant distinction in PVD for EV prediction between the variceal and non-variceal groups.

The difference in the our results from other studies may be because this study was conducted on cases post hepatitis C liver cirrhosis after DAAS, unlike other studies that were conducted on patients suffering from active hepatitis C virus or other causes of cirrhosis.

➢ *Splenic Index:*

SI was a predictable factor for the presence of EVs and Also for Discrimination for the size of EVs.

Amarapurkar et al. (1994) reported that splenomegaly alone is a strong predictor of the emergence of large EVs.., According to these results, splenomegaly alone was a strong predictor of the emergence of large EVs. In a prospective study, splenomegaly was identified as a diagnostic sign of cirrhosis and PHT by Chalasani et al. (1999)., According to research by Sharma et al. (2007), splenomegaly is a reliable indicator of the presence of large varices, Independent predictors of large EV have been reported by Nashaat et al. (2010) and Cherian et al. (2011), who found that a best CO for the transverse splenic diameter >145 mm and a mean bipolar splenic dimension >160 mm were both significant.

➢ *Portal Vein Velocity(PVV):*

Both the presence of EVs and the ability to distinguish between EVs of different sizes could be predicted using PVV. Consistent with previous research showing a negative correlation between portal pressure and the presence of EVs (Korner 1996; Erdozain et al., 2000; Yin et al., 2001; Liu et al., 2008).

➢ *Spleno Portal Index(SPI):*

SPI was a predictor of the presence of EVs, as well as the discrimination of large EVs. When portal resistance increases in cirrhosis, stagnant portal blood flow causes an increase in the resistance of splenic venous outflow, resulting in congestive splenomegaly. Splenomegaly, brought on by increased blood flow to the spleen, also makes PHTN worse. Extracellular vesicle formation is stimulated and splenomegaly is made worse by elevated portal pressure. ***(Iwao et al; 1997).*** Previous research also demonstrated a correlation between the decrease in mean PVV the severity of PHTN and the risk of EV bleeding. ***(Iwao et al; 1997).*** This non-invasive index demonstrated correct diagnoses with a sensitivity of 79.4 percent and a specificity of 72 percent when set to 3.5 cm/s.***(Wadhwa, et al 2014).***

In line with what was discovered by Liu et al (2008), who found that SPI has a stronger correlation with varices than SI and mean PVV. Furthermore, SPI's diagnostic accuracy (AUC) in our series was similar to that reported by Liu et al (2008). (0.93)

➢ *Platltes Count Splenic Diameter Ratio(PCSDR):*

The PCSDR ratio was useful for both detecting the presence of EVs and differentiating between comparatively small and large EVs. The presence of EV has been linked to PC/D in a number of studies. According to a 2002 study by Malhotra et al., thrombocytopenia is a common complication of liver cirrhosis, affecting up to 76% of patients**.**, 50,000 uL to 75,000 uL) occurs in approximately 13% of cirrhotic patients. Multiple factors contribute to the development of thrombocytopenia in these patients. Splenic sequestration may be caused by either of two potential mechanisms... One is crucial, involving myelosuppression as a result of hepatitis viruses or myelotoxicity as a result of excessive alcohol consumption., Second, antibodies that attack platelets are present in the body. Furthermore, it is condition and cause-specific. ***(Watanabi et al 2000).*** Splenomegaly is common, particularly in patients with non-alcoholic cirrhosis, due primarily to congestion of the red pulp of the spleen caused by PHTN. Local and Western studies demonstrated greater sensitivity and specificity for PCSDR with a CO of 909.

Giannini et al. 2003, and Agha et al. (2009) showed that the PC/SDR ratio had 100% sensitivity, 97% specificity, and 100% positive predictive value for detecting the presence of EV at a CO of 909. ***Sheta et al. (2018)*** discovered a significant relationship between the presence and grade of EV (P0.001) at a CO 570, with a sensitivity of 77.19% and a specificity of 93.02%. and With an 81% sensitivity and an 81% specificity, the CO of the PC/SD ratio (750) was found to be optimal for predicting EV by El Hady et al., 2016.

The AUC for Platelet/splenic ratio was > SPI and more accurate in predicting the presence of EV while that The AUC for SPI > PC/SDR was more accurate for discriminating Large EVs.

When evaluating the sensitivity, specificity, and diagnostic accuracy of non-invasive parameters for detecting EVs in our population, we found that both PCSDR and SPI performed very well. However, CO was greater when compared to ***Giannini et al;2003***. This discrepancy may be best explained by the fact that the majority of patients in our study had cirrhosis caused by HCV and not active after treatment by DAAS, whereas the most common causes of cirrhosis in the West are non-viral, including alcoholic cirrhosis, metabolic cirrhosis, primary biliary cirrhosis, primary sclerosing cholangitis, viral, and mixed cirrhosis. Patients of varying cirrhosis and liver disease etiology can have their SPI measured at routine biannual US screening for HCC in the outpatient clinic.

➢ *Non-Invasive Laboratory Parameters Comparison between the Studied Arms*

- *APRI:*

The presence of EVs as well as the size distribution of EVs could be anticipated using APRI. The presence of EV could be predicted with a sensitivity of 68.8 percent and a specificity of 65 percent using APRI with a CO greater than 1.14, as shown by El attya et al. in 2019**.** agrees with research from Mattos et al. 2013 showing that APRI at a CO of 1.3 can predict the presence of EV with a sensitivity of 64.70 percent and a specificity of 72.70 percent.

Shehata et al. (2014) demonstrated that an APRI with a CO greater than 1.26 can predict the presence of EV with a sensitivity of 72.4% and a specificity of 61.9%.

Our results were in accordance with ***Badawi et al. 2020*** who situated that the AUCs of APRI for determining the presence of varices were 0.73 with CO value > 0.6 with a specificity of 60% and sensitivity was 80%. It is possible that this result is due to the fact that this study was conducted on cases that were treated for the DAAS virus, and the C virus was no longer active in these patients. As for the other studies, most of them were done on cases due to active C virus or for other reasons of fibrosis.

Our study showed that APRI was a predictable factor for the presence of large EV and showed that the AUC was 0.919 with a significant value higher in the large variceal arm than the small variceal arm, ($P < 0.001$) with the best CO to be >1.4, The sensitivity was (93.88%), specificity (80.95%), PPV (79.3%), NPV (94.4%).

- *FIB4:*

FIB4 was a predictor for the presence of EVs as well as for the differentiation of large EVs. ***Ishida et al. 2020*** demonstrated that patients with cirrhosis and a FIB-4 2.78 are less likely to have high-risk varices and should undergo FIB-4 reassessment every 6–12 months; this study is consistent with our study of the presence or absence of EV**.**

Ishida et al. 2020 demonstrated that those with a FIB-4 2.78 should undergo endoscopic variceal screening**.**

Our study determined the CO of FIB4 for large varices 7.6. This result can be explained because this study was conducted on post-HCV patients after DAAS, unlike other studies that were conducted on patients suffering from active hepatitis C virus or from other causes of cirrhosis.

- *Child–Pugh score:*

The mean of Child–Pugh score in arm 1 was 6.0 (5.0–6.0) while in arm 2 was 6.0 (6.0–7.50) and in arm 3 was 7.0 (7.0–10.0) with a significant value among three arms in prediction of the presence of EV and significant in prediction of large varices with advanced score.

Non-variceal arm (arm1) showed that Thirty Tree (86.8 %) had Child's class A liver disease, 5 (13.2%) had Child's class B disease while no patient had Child's class C disease Small variceal arm (arm2) showed 35 (55.6%) had Child's class A liver disease, 25 (25%) had Child's class B disease while 3 (4.8%) patient had Child's class C disease. Large Variceal arm (arm3) showed 3(55.6 %) had Child's class A liver disease, 33(67.3%) had Child's class B disease, and 13 (26.5%) patients had Child's class C disease.

The prevalence of varices was found to be significantly higher in Child B and Child C patients compared to Child A patients, in Elatty et al. 2019 and Yosry et al.2009 studies. Large varices, fundal varices, congestive gastropathy, and signs of impending rupture of varices were significantly more prevalent in Child B and C patients than in Child A patients. These findings suggested that patients with Child B and C cirrhosis have a greater risk of developing varices and a greater risk of bleeding ***(Sheta ET al, 2016).***

Similar to other reports from Western countries, our study revealed a significant correlation between variceal size and the severity of liver disease. In a meta-analysis, the values recorded in this study were greater than those reported by the North Italian Endoscopic Club for the study and treatment of EV. (NICE 1998). These findings were consistent with Said et al. (2010) and Tafarel et al. (2011), who reported that the size of EV increased as the Child's score increased. In addition, the Child score and the presence of EV were found to have a strong positive correlation. Child-Pugh scores of B and C were significantly correlated with EV, as determined by Kim et al. (2011).

VII. CONCLUSIONS AND RECOMMENDATIONS

The AUC and diagnostic Accuracy for Platelet/splenic ratio was > SPI > FIB4> APRI > PVV > SI >Child–Pugh score for prediction EV in post-HCV liver cirrhotic patients after direct-acting antiviral drugs (DAAs).

The AUC and diagnostic Accuracy for SPI > Platelet/splenic ratio > APRI > FIB4 > SI > PVV >Child–Pugh score for Discrimination Large OV from in post-HCV liver cirrhotic patients after direct-acting antiviral drugs (DAAs).

Conflicts of interest: There are no conflicts of interest.

Ethics statement: The Helsinki Declaration on Human and Animal Rights, 1975 served as the basis for the research., as amended in 2000 and 2008, and the authors obeyed the policy regarding Informed Consent.

REFERENCES

[1]. Abdelaal Em, Amer km, oda aa, and elsakhawy mm.the platelet/spleen diameter ratio; represent an acceptable surrogate parameter for the scope of all strategy for the detection of esophageal varices in patients with liver cirrhosis. asian journal of science and Technology December 2015; Vol.06, Issue, 12, pp.2133-2138.

[2]. Agha A, Anwar E, Bashir K, Savarino V, Giannini EG. External validation of the platelet count/spleen diameter ratio for the diagnosis of esophageal varices in hepatitis C virus-related cirrhosis. Dig Dis Sci 2009; 54:654–660

[3]. Amarapurkar DN, Parikh SS, Shankaran K, Chopra K, Dhawan P, Kalro RH, et al. Correlation between splenomegaly and oesophageal varices in patients with liver cirrhosis. Endoscopy 1994; 26:563.

[4]. Amico GD, Morabito A. Noninvasive markers of esophageal varices: Another round, not the last. Hepatology 2004;39:30-4.

[5]. Badawi R,Elsaid Wasfy E, ElKassas G, Elnawasany S, Elkasrawy K, Soliman S, Samah A Elshweikh S A, Abd-Elsalam S,* A Novel Non-invasive Score Precisely Predicts Development of Esophageal Varices in Patients with Chronic Viral Hepatitis C. Govaresh/ Vol.25/ No.1/ Spring 2020, 56-64.
[6]. Berger A, Ravaioli F, Farcau O, Festi D, Stefanescu H, Buisson F, et al. Including ratio of platelets to liver stiffness improves accuracy of screening for esophageal varices that require treatment. Clin Gastroenterol Hepatol 2021;19(4):777–787.e17
[7]. Berzigotti A, Seijo S, Reverter E, Bosch J. Assessing portal hypertension in liver diseases. Expert Rev Gastroenterol Hepatol 2013; 7:141–155.
[8]. Botros M & Sikaris KA.The De Ritis Ratio: the test of time.Clin Biochemical Rev 2013 Dec;34(3);117-130.
[9]. Bressler B, Pinto R, El-Ashry D, Heathcote EJ. Which patients with primary biliary cirrhosis or primary sclerosing cholangitis should undergo endoscopic screening for oesophageal varices detection? Gut 2005; 54:407-10.
[10]. Camma` C, Petta S, Vito Di Marco, Fabrizio Bronte, Stefania Ciminnisi, Giusalba Licata, Sergio Peralta, Fabio Simone, Giulio Marchesini, and Antonio Crax. Insulin Resistance Is a Risk Factor for Esophageal Varices in Hepatitis C Virus Cirrhosis. Hepatology 2009; 49:195- 203.
[11]. Chalasani N, Imperiale TF, Ismail A, Sood G, Carey M, Wilcox CM, et al. Predictors of large esophageal varices in patients with cirrhosis. Am J Gastroenterol 1999; 94:3285-91.
[12]. Chalasani N, Imperiale TF, Ismail A, Sood G, Carey M, Wilcox CM, et al. Predictors of large esophageal varices in patients with cirrhosis. Am J Gastroenterol 1999; 94:3285-91
[13]. Cherian JV, Deepak N, Ponnusamy RP, Somasundaram A, Jayanthi V. Noninvasive predictors of esophageal varices. Saudi J Gastroenterol 2011; 17:64-8.
[14]. Cooke GS, Andrieux-Meyer I, Applegate TL, et al. Accelerat- ing the elimination of viral hepatitis: a Lancet Gastroenterology & Hepatology commission. Lancet Gastroenterol Hepatol 2019; 4:135-84.
[15]. Crisan D, Radu C, Lupsor M, Sparchez Z, Grigorescu MD, Grigo- rescu M. Two or more synchronous combination of noninvasive tests to increase accuracy of liver fibrosis assessement in chronic hepatitis C; results from a cohort of 446 patients. Hepat Mon 2012; 12: 177-184 [PMID: 22550525 DOI: 10.5812/hepatmon.853]
[16]. D'Amico G, De Franchis R. Upper digestive bleeding in cirrhosis: Post-therapeutic outcome and prognostic indicators. Hepatology 2003; 38:599-612.
[17]. De Franchis R,Boesch J,Gracia-Tsao G, Reiberger T, Ripll C, On behalf of the Baveno VII Faculty; Journal of Hepatology 2022; 76: 959– 974.
[18]. El attya E AA, Elshayeba EI , Badra MH, Mousab WAE , El Mansory MF. Noninvasive parameters for assessment of esophageal varices. The Egyptian Journal of Internal Medicine. Vol. 31 No. 4, October-December 2019. 31:536–543
[19]. El hady HA, Hammam AA, Elnimr SA, Osha A. Evaluation of some non invasive predictors for presence of esophageal varices in patients with compensated HCV positive cirrhosis. Int J Sci Res 2016; 5:461–469.
[20]. El Naggar AA, GomaaMS,Fawzy MM. Non endoscopicpredictors of large esophageal varices. Egypt J Intern Med 2012; 24:97–99.
[21]. El Sheif Mohamed Saad El Din, Afify Shimaa and Berengy Mohamed S Clinical charcterstic variceal bleeding among patients with HCV induced liver cirrhosis : An observational compative study ; Polos one 2022; 17(10) e0275373 october
[22]. Erdozain Sosa JC, Martin Hervas C, Morena Blanco MA, Zapata Aparicio I, Herrera Abian A, Conde Gacho P, et al. Color duplex Doppler ultrasonography in the evaluation of the risk of esophageal varices bleeding in cirrhotic patients. Gastroenterol Hepatol 2000; 23 (10):466- 9 [Abstr].
[23]. Fabbian F, Fedeli U, De Giorgi A, et al. Sex and acute oesophageal variceal bleeding-related in-hospital mortality: a 15-year retrospective study. Eur Rev Med Pharmacol Sci. 2019;23(2):811–817. Jan
[24]. Galal G, Ghweil A, Muhammad EM, Yousef LM. Clinical utility of simple fibrosis markers in prediction of oesophageal varices in chronic hepatitis C patients with advanced cirrhosis. Med J Cairo Univ 2012; 80:85–93. 17 El Naggar AA, Gomaa MS, Fawzy MM. Non endoscopic predictors of large esophageal varices. Egypt J Intern Med 2012; 24:97–99.
[25]. Giannini E, BoĴ a F, Borro P, Risso D, Romagnoli P, Fasoli A, et al. Platelet count/spleen diameter ratio: Proposal and validation of noninvasive parameter to predict the presence of oesophageal varices in patients with liver cirrhosis. Gut 2003;52:1200-5.
[26]. Gill ML, Atiq M, Sattar S, Khokhar N. Non-endoscopic parameters for the identification of esophageal varices in patients with chronic Hepatitis. J Pak Med Assoc 2004; 54: 575-7.
[27]. Grace ND. Diagnosis and treatment of gastro-intestinal bleeding secondary to portal hypertension. American College of Gastroenterology Practice Parameter Committee. Am J Gastroenterol Arm 1997; 92:1081-91.
[28]. Gue C S,Yap C K&NG H Sthe correlation between cytopenia and Esophgeal varices in patients with liver cirrhosis. Med J Malaysia 2004 ;59(5) :604-608 december
[29]. Guerra J, Garenne M, Mohamed MK, Fontanet A. HCV burden of infection in Egypt: results from a nationwide survey. J Viral Hepat 2012; 19: 560-567 [PMID: 22762140 DOI: 10.1111/j.1365- 2893. 2011. 01576.x]
[30]. Guy J, Peters MG. Liver disease in women: the influence of gender on epidemiology, natural history, and patient outcomes. Gastroenterol Hepatol (N Y). 2013;9(10):633–639.

[31]. Haukeland JW, Småstuen MC, Pålsdatter PP, et al. Effect of gender on mortality and causes of death in cirrhotic patients with gastroesophageal varices. A retrospective study in Norway. PLoS One. 2020;15(3):e0230263. Published 2020 Mar 12.
[32]. Ishida K,Namisaki T,* Murata K, Fujimoto Y, Takeda S, Enomoto M, Ogawa H, Takagi H,Tsuji Y, Daisuke Kaya D,et al. Accuracy of Fibrosis-4 Index in Identification of Patients with Cirrhosis Who Could Potentially Avoid Variceal Screening Endoscopy. J Clin Med. 2020 Nov; 9(11): 3510.
[33]. Iwao T, Toyonaga A, Oho K, Tayama C, Masumoto H, Sakai T, et al. Value of Doppler ultrasound parameters of portal vein and hepatic artery in the diagnosis of cirrhosis and portal hypertension. Am J Gastroenterol.1997; 92:1012-17.
[34]. Kim BK, Kim DY, Hank H, Kim BK, Kim DY, Han KH, et al. Risk assessment of esophageal variceal bleeding in B viral liver cirrhosis by a liver stiffness measurement based model. J Gastroenterol Sep 2011; 106:1654–1730.
[35]. Kim WR, Brown RS, Terrault NA, et al. Burden of liver disease in the United States: summary of a workshop. Hepatology. 2002;36(1)In :227–242.
[36]. Koda M, Matunaga Y, Kawakami M, Kishimoto Y, Suou T, Murawaki Y. FibroIndex, a practical index for predicting significant fibrosis in patients with chronic hepatitis C. Hepatology 2007; 45: 297-306 [PMID: 17256741 DOI: 10.1002/hep.21520]
[37]. Korner T. Portal duplex sonography in liver cirrhosis. A useful supplement to endoscopic evaluation of bleeding risk of esophageal varices? Scand J Gastroenterol 1996; 31(5):495-9
[38]. Liu C-H, Shih-Jer Hsu,Cheng-Chao Liang, Feng-Chiao Tsai, et al. Esophageal Varices: Noninvasive Diagnosis with Duplex Doppler US in Patients with Compensated Cirrhosis Radiology: Volume 248: Number 1—July 2008; 132-139
[39]. Madhotra R, Mlcahy H, Willner I, Reuben A. Prediction of esophageal varices in patients with cirrhosis. J Clin Gastroenterol 2002; 34:81–85
[40]. Mattos AZ, de Mattos AA, Daros LF, Musskopf AI. Aspartate aminotransferase-to-platelet ratio index (APRI) for the non-invasive prediction of esophageal varices. Ann Hepatol 2013; 12:810–814.
[41]. Merli M, Nicolini G, Angeloni S, Rinaldi V, Incidence and natural history of small esophageal varices in cirrhotic patients. J Hepatol 2003;38:266-72.
[42]. Mohammad KT, Mohammad HS, Farhang S, Jalilvand M. Portal hemodynamics as predictors of high risk esophageal varices in cirrhotic patients. World J Gastroenterol 2008; 14:1898–1912.
[43]. Nashaat E H, Hossam Abd-Elaziz , Manal Sabry&Ahmed Aly Ibrahim. NonEndoscopic Predictors of Esophageal Varices and Portal Hypertensive Gastropathy. Nature and Science 2010;8(6):43-50.
[44]. Paquet KJ. Prophylactic endoscopic sclerosing treatment of esophageal wall in varices: A prospective controlled trial. Endoscopy 1982; 14:4-5.
[45]. Pilette C, Oberti F, Aube C, Rousselet MC, Bedossa P, Gallois Y. Non-invasive diagnosis of esophageal varices in chronic liver diseases. J Hepatol 1999; 31:867-73.
[46]. Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol 2017;2:161-76.
[47]. Ratib S, West J, Crooks CJ, et al. Diagnosis of liver cirrhosis in England, a cohort study, 1998–2009: a comparison with cancer. Am J Gastroenterol. 2014;109(2):190–198.
[48]. Rubin JB, Sundaram V, Lai JC. Gender differences among patients hospitalized with cirrhosis in the United States. J Clin Gastroenterol. 2020; Jan54(1):83–89.
[49]. Said HE, Elsayed EY, Ameen A, Abd Elal H. Cytopenia as a predictor of oesophageal varices in patients with liver cirrhosis. Rep Opin 2010; 2:35–41
[50]. Sarangapani A, Shanmugam C, Kayanasundaram M, Rangachari B, Thangavelu P, Subbarayan JK. Noninvasive prediction of large esophageal varices in chronic liver disease patients. Saudi J Gastroenterol 2010;16:38-42.
[51]. Sarwar S, Khan AA, Butt AK, Shafqat F, Malik K, Ahmad I, et al. Non-endoscopic prediction of esophageal varices in cirrhosis. J Coll Physicians Surg Pak 2005;15:528-31.
[52]. Schepis F, Camma 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; 33:333-8.
[53]. SethiSaurabh what"s the Relationship between Liver Cirrhosis and AnemiaMPH- by San ferquson on April 2023
[54]. Shehata M, AboAlia LA, El-Shafey K, El-Hossary M. A comparative study of Duplex Doppler ultrasound and blood indices as noninvasive predictors of oesophageal varices in cirrhotic patients. Tanta Med J 2014; 42:83–91.
[55]. Sheta EA, Yosef M, Abd Elsalam M, Mohammed RE, Ismail A, EL-Kalla F, et al. Non invasive diagnosis of esophageal varices: can it replace screening endoscopy? Int J Curr Microbiol
[56]. Tafarel JR, Tolentino LH, Correa LM, Bonilha DR, Piauilino P, Martins FP, et al. Prediction of esophageal varices in hepatic cirrhosis by noninvasive markers. Eur J Gastroenterol Hepatol 2011; 23:754–758.
[57]. Talwalkar JA, Kamath PS. screening for esophageal varices among patients with cirrhosis of the liver. Am J Gastroenterol 2001; 96: 3039-3040 [PMID: 11693352 DOI: 10.1111/j.1572-0241. 2001.04692.x]
[58]. 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.
[59]. Thomopoulos KC, Mimidis KP, Katsakonlis EC. Non-invasive predictors of the presence of large esophageal varices in patients with cirrhosis. Dig Liver Dis 2003; 35:473-8.

[60]. Wadhwa RK, Abbas Z, Hasan SM, Luck NH, Younus M , Anis S , Mubarak M. Platelet count to splenic diameter ratio and splenoportal index as non-invasive screening tools in predicting esophageal varices in patients with liver cirrhosis. JOURNAL OF TRANSLATIONAL INTERNAL MEDICINE ; JUL-SEP 2014; VOL 2; ISSUE 3:127-131.
[61]. Wai CT, Greenson JK, Fontana RJ, Kalbfleisch JD, Marrero JA, Conjeevaram HS, Lok AS. A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. Hepatology 2003; 38: 518-526 [PMID: 12883497 DOI: 10.1053/jhep.2003.50346]
[62]. Waked I, Gamal Esmat, Aisha Elsharkawy, Magdy El-Serafy, et al. Screening and Treatment Program to Eliminate Hepatitis C in Egypt. n engl j med March 2020;19:1166-1174.
[63]. Watanabe S, Hosomi N, Kitade Y, Kurokohchi K, Arima K, Kawabata H, et al. Assessment of the presence and severity of esophagogastric varices by splenic index in patients with liver cirrhosis. J Comput Assist Tomogr 2000;24:788-9
[64]. Yang JD, Abdelmalek MF, Pang H, et al. Gender and menopause impact severity of fibrosis among patients with nonalcoholic steatohepatitis. Hepatology. 2014;59(4):1406–1414.
[65]. Yin XY, Lu MD, Huang JF, Xie Xy, Liang LJ. Color Doppler velocity profile assessment of portal hemodynamics in cirrhotic patients with portal hypertension: correlation with esophageal variceal bleeding. J Clin Ultrasound 2001; 29(1):7- 13.
[66]. Yosry A, Fouad R, Abdel Bary M, Hamdy S, Mahmoud M, Khairy M. Non invasive prediction of varices in egyptian cirrhotic patients. Med J Cairo Univ 2009; 77:343–349.
[67]. 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 2011; 161:2564–2570. 38 Hong WD, Dong L, Jiang Z, Zhu Q, Jin S. Prediction of large esophageal varices in cirrhotic patients using classification and regression tree analysis. Clinics 2011; 66:119–124.
[68]. 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.
[69]. Zhang W, Wang L, Wang L, Li G, Huang A, Yin P, Yang Z, Ling C, Wang L. Liver stiffness measurement, better than APRI, Fibroindex, Fib-4, and NBI gastroscopy, predicts portal hypertension in patients with cirrhosis. Cell Biochem Biophys 2015; 71: 865-873 [PMID: 25417057 DOI: 10.1007/s12013-014-0275-z]
[70]. Zhao Lili,Wang Ting,Guo Chunxia, Zhuo Li Han Ping, Wang Chunyan,Ma Ying, Wang Jing,Gao Min&Li Jia modified andalternative Baveno VI crieteria based on age for ruling out high risk varicesin patients with compensated cirrhosis;Hepatology International2022; 16 936-943.