Measurement of Splenic Stiffness as a Predictor of Oesophageal Varices in Patients with Liver Cirrhosis in Zagazig University Hospitals

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Background and study aim: Portal hypertension (PH) is a frequent complication of cirrhosis, contributing to the development of ascites, esophageal varices (EV) and hepatic encephalopathy. The best available methodology for the assessment of PH is measurement of the hepatic vein pressure gradient (HVPG). However, the performance of HVPG is limited to highly specialized centers and requires extensive experience Predicting the presence, grading and follow up of esophageal varices by non-invasive means might increase compliance and would permit to restrict the performance of endoscopy to those patients with a high probability of having varices.

Patients and Methods: This study included 117 individuals divided into two groups. Group I: included 39 normal individuals as a control group for splenic stiffness measurement. Group II: included 78 cirrhotic patients. All patients of group II were subjected to upper GIT endoscopy and according to the results this group was subdivided into patients with no varices (IIa) and patients with esophageal varices (IIb). All patients underwent clinical assessment, routine laboratory evaluation, BMI, splenic and liver stiffness measurement, upper GIT endoscopy. Splenic stiffness measurement repeated for patients who had varices after 6 months of pharmaco medical treatment.

Results: Splenic stiffness was found to be higher in cirrhotic group than control group, splenic stiffness measurement was found to be higher in patients who had varices than no varices in cirrhotic patients, cut off of SSM for the presence of varices ≥39.5 kpa had AUROC 0.999, sensitivity 97.7%, specificity 96.9%, PPV 97.8% and NPV while LSM showed cut off value for presence of varices >22.5 kpa had AUROC 0.641 sensitivity 84.44%, specificity 60.61%, PPV 74.5% and NPV 74.1%. PSR showed cut of ≤657.7 had AUROC 0.855 sensitivity 95.56%, specificity 78.79%, PPV 86% and NPV 92.9%. APRI showed cut off >2.7 had AUROC 0.657 sensitivity 57.78, specificity 93.94%, PPV 92.9% and NPV 62%. There was highly significant difference in median SS in patients with large varices versus small varices (49.6vs 71.58 kpa with p<.0001)**.**SSM is not a useful tool for follow up of varices after pharmacological treatment with non selective beta-blockers (p=0.014).

Conclusion: Fibroscan is a sensitive and reliable method for detection of esophageal varices. Splenic stiffness showed the best performance on detection of eosophageal varices, when compared to other non invasive predictors, PSR came in the 2nd place. Splenic stiffness measurement can differentiate small and large varices

INTRODUCTION

Portal hypertension (PH) is a frequent complication of cirrhosis, contributing to the development of ascites, esophageal varices (EV) and hepatic encephalopathy.

The best available methodology for the assessment of PH is measurement

of the hepatic vein pressure gradient (HVPG). However, the performance of HVPG is limited to highly specialized centers and requires extensive experience and therefore is not used routinely **[1]**.

Accordingly, the introduction of noninvasive methods able to predict the stage of PH (i.e., not clinically significant, significant, and severe) could help to identify patients who are subjected to measurement of HVPG and, ultimately, optimize the diagnostic management of cirrhotic patients.

Several studies had shown that measurement of liver stiffness (LS) by transient elastography (TE) may represent a rapid and noninvasive method for predicting the presence of clinically significant (ie, HVPG ≥10 mm Hg) or severe (ie, HVPG ≥12 mm Hg) PH **[2]**. On the other hand, LS shows a poor correlation with HVPG values ≥12 mm Hg, because of the increased incidence of extrahepatic factors conditioning the progression of PH **[3]**.

Consequently, it is not surprising that LS is not an adequate method for prediction of the presence and grade of EV (and none of the thus far proposed noninvasive methods can be considered equivalent to measurement of HVPG or endoscopy in terms of overall accuracy **[4]**.

Splenomegaly plays an important role in the pathophysiology of PH by increasing splanchnic inflow **[5]**.

However, although splenomegaly represents a common finding in patients with cirrhosis and PH, the relationship between spleen size and PH grading or EV degree is controversial **[6]**.

The possibility of predicting the presence of EV by using clinical parameters related to splenomegaly was initially suggested by the use of the spleen diameter, assessed by ultrasonography (US), in the platelet count/spleen diameter ratio (Plt/Spl) **[7]**.

Recently, a direct correlation between splenic stiffness (SS), assessed by magnetic resonance elastography, and HVPG has been reported in a large animal model of PH **[8]**. Accordingly, the possibility of detecting the presence of EV by the measurement of SS by TE in cirrhotic patients has also been recently proposed **[9]**.

This possibility is truly intriguing because splenomegaly in cirrhosis is characterized by enlargement and hyper activation of the splenic lymphoid tissue, as well as increased angiogenesis and fibrogenesis, in addition to passive congestion due to PH **[10]**.

Regardless, a precise characterization of the relationship between SS and PH with relative complications, particularly the presence of EV, is still lacking.

This study aimed to determine efficacy of splenic stiffness measurement as a non-invasive tool in predicting the presence of esophageal varices in patients of liver cirrhosis evaluate validity of fibro scan of spleen in follow up degree of esophageal varices in patients of liver cirrhosis, Measure the ability of splenic stiffness measurement to determine grade of esophageal varices.

PATIENTS AND METHODS

This is a case control study which carried out in Gastroenterology and Hepatology Unit, Tropical Medicine Department, Faculty of Medicine, Zagazig University Hospitals, Egypt during the period from January 2015 to January 2017.This study included 117 individuals who were divided into two groups:

- **Group I:** included 39 normal individuals as a control group for splenic stiffness measurement.
- **Group II:** included 78 cirrhotic patients. Diagnosis of cirrhosis based on laboratory &imaging parameters. All patients of group II was subjected to upper GIT endoscopy and according to the results this group was subdivided into patients had no varices (IIa) and patients had esophageal varices (IIb).

Informed consent was taken from all participants before participating in the study.

Inclusion criteria:

- Patients were included after they had a diagnosis of cirrhosis
- Male and female patients above age of 18 years with liver cirrhosis Child A or B classification.
- BMI≤ 30 (kg/m2)

Exclusion criteria:

- Cirrhotic patients Child Pugh C (moderate to tense ascites)
- Cirrhotic patients with body mass index above 30
- Cirrhotic Pregnant females
- Cirrhotic patients with Hepatocellular carcinoma (HCC)
- Cirrhotic patients with portal vein thrombosis (PVT).

Methods:

All individuals were subjected to:

1- Thorough medical history

2- Clinical examination:

- General examination.
- Local examination (abdominal examination and other systems).

3- BMI calculated as weight in kg/square of body height in meter.

4- Routine investigations: (platelet count, international normalized ratio, prothrombin time, aspartate aminotransferase [AST], alanine aminotransferase [ALT], albumin, bilirubin).

5- Pelvi-Abdominal Ultrasonography examination to evaluate finding suggestive of cirrhosis, measure portal vein diameter, measure longitudinal (bipolar) diameter of spleen and size of right and left lobes of liver.

6- Upper Endoscopic Examination: A standard endoscopic examination was performed by the same operator .The endoscopic findings were recorded and graded as follows: small, varices were flattened by insufflation; large varices protruding in the lumen despite insufflation. The presence of red signs was also recorded in all patients. According to the criteria proposed at the Baveno V Consensus Conference **[11]**. Upper Endoscopic Examination was done only for group (II), Re endoscopy for patients after pharmaco-endoscopic therapy. Upper endoscopy was done by the same experienced endoscopist at single endoscopy unit using a flexible video gastroscope (Olympus or pentax).

7- Treatment of non risky Oesophageal varices (OV) by pharmacotherapy (non selective beta-blockers if not contraindicated for 6 months, risky and large varices were subjected to rubber band ligation and splenic stiffness measurement was done again after 6 months.

8- Measurement of Liver stiffness: LS values assessed using the FibroScan after at least 6 hours of fasting and after a complete abdominal US examination. As already stated, the examination was conducted by one operator experienced with both ultrasound and fibro scan. Patient was lying supine with the right arm placed behind the head to facilitate access to the right upper quadrant of the abdomen. The tip of the probe transducer was placed on the skin between the rib bones at the level of the right lobe of the liver. Results were expressed in KiloPascals (kPa) and corresponded to the median of 10 validated measurements .The examination was considered reliable if more than ≥ 10 valid measurements were acquired, the success rate (number of valid acquisitions divided by the number of attempts) was over 60%, and the ratio of the interquartile range to the median of 10 measurements (IQR/M) was less than or equal 0.3 **[12]**.

9- Measurement of SS: SS values were obtained using the FibroScan with the same probe used to perform LS after at least 6 hours of fasting and under US assistance. In the absence of guidelines for the measurement of SS by FibroScan, the same guidelines for the measurement of LS were applied (i.e., success rate, IQR, and IQR/M), with some adjustments due to individual spleen anatomic characteristics. In particular, with the patient in a supine position with maximal abduction of the left arm, the probe was positioned in an intercostal space where the spleen was correctly visualized by US. Measurement of SS at presentation and after 6 months of treatment for cirrhotic group.

10- Non-Invasive Predictive Scores for presence of oesophageal varices: The following non-invasive indices were determined in all patients; according to previously published formulas:

- Platelet count/spleen diameter ratio (PSR): as the ratio between platelet count (N/mm^3) and bipolar diameter of the spleen in millimeters **[13]**.
- AST-to-platelet ratio index (APRI) = [(AST/ULN) x 100]/ platelet count (109/L) (ULN = the upper limit of normal and was set at 40 IU/L) **[14]**.

Statistical analysis:

All data were collected, tabulated and statistically analyzed using SPSS 20.0 for windows. Quantitative data were expressed as the mean ± SD & median (range), and qualitative data were expressed as an absolute frequencies "number"& relative frequencies (percentage). Independent samples Student's t-test, Mann-Whitney U, Paired t-test and Wilcoxon signed ranks test were used when needed. Percent of categorical variables were compared using the Pearson's Chi-square test or Fisher's exact test when was appropriate.

(ROC) curve was constructed to permit selection of threshold values for test results and comparison of different testing strategies.

A larger area under a ROC curve (AUC) indicates superior test performance, with 1 representing 100% sensitivity and specificity and 0.5 representing no discriminatory utility.

All statistical comparisons were two tailed with significance Level of P-value ≤0.05 indicates significant, P<0.001 indicates highly significant difference while, P>0.05 indicates non-significant difference.

RESULTS

This study showed no statistically significant difference between demographic data in cirrhotic patients and apparently healthy control as shown in table (1).This study showed highly statistically significant difference regarding ALT, AST, Platelet count (PLT), Albumin, Total &Direct bilirubin, INR and PT between cirrhotic patients and apparently healthy control individuals in table (2). Table (3) showed highly statistically significant positive correlation between Liver Stiffness Measurement (LSM), Portal Vein Diameter (PVD), splenic bipolar diameter, ALT, AST, total and direct bilirubin, INR, PT, AST to platelet ratio index (APRI) and Splenic stiffness measurement (SSM), while there is highly statistically significant negative correlation between platelet count, albumin level and SSM in whole population. Table (4) and Figure (1) showed endoscopic findings in cirrhotic patients. Table (5) showed highly statistically significant difference regarding SSM, LSM, PSR and APRI between patients who had varices and who had no varices. Table (6) showed highly statistically significant difference regarding SSM values in cirrhotic patients regarding small, large varices and isolated gastric varices & oesophageal varices. The optimum cut off value of SSM for detection of varices >39.5 kpa, with 97.7% sensitivity and specificity 96.9, with AUC 0.999 p value <0.001 as shown in tables (7), (8) and figure (2) with comparison of these values regarding presence of cirrhosis, presence of varices and bleeding varices with LSM, APRI and PSR. On follow up of cirhhotic patients after six months of medical and endoscopic treatment of varices. There was no statistically significant difference of initial SSM and after 6 months of inderal treatment among cirrhotic patients with small varices while there was statistically significant difference of initial SSM and after 6 months cirrhotic patients with large and gastic varices after band ligation and gastric varices injection (Table 9).

Table (1): Comparison between demographic data in cirrhotic patients and apparently healthy control

		Cirrhotic N=78	Control N=39	P value
Age (Years)		53.5 (40-70)	49.2 (32-65)	0.224
Sex	**Female**	32 (41.0%)	20 (51.3%)	0.392
	Male	46 (59.0%)	19 (48.7%)	

Table (2): Comparison between basal laboratory values in cirrhotic patients and apparently healthy control

	Cirrhotic N=78	Control N=39	P value
ALT, IU/L	65 (22-212)	38 (11-79)	<0.001
AST, IU/L	82 (17-218)	30 (9-56)	<0.001
PLT, X10^^{9}L	87 (46-167)	190 (158-310)	<0.001
Albumin, g/dL	3.5 (2.8-4.4)	4.2 (3.7-4.5)	<0.001
T. Bil, mg/dL	1.3 (0.1-2.9)	0.8 (0.2-1.2)	<0.001
D. Bil, mg/dL	0.8 (0.2-1.9)	0.1 (0-0.4)	<0.001
INR	1.3 (1-1.7)	1 (1-1.1)	<0.001
PT, Sec.	14 (12-18)	12 (11-13.5)	<0.001

Table (3): Correlations between certain studied parameters and SSM values in the whole population

Whole population	**SSM**		
	r	**p**	**Sig.**
Age, Years	0.78	0.135	NS
LSM	0.857	<0.001	HS
PVD (mm)	0.888	<0.001	HS
Splenic bipolar diameter (mm)	0.917	<0.001	HS
ALT, IU/L	0.363	<0.001	HS
AST, IU/L	0.737	<0.001	HS
PLT, X10^9L	-0.901	<0.001	HS
Albumin, g/dL	-0.826	<0.001	HS
T. Bil, mg/dL	0.755	<0.001	HS
D. Bil, mg/dL	0.837	<0.001	HS
INR	0.797	<0.001	HS
PT, Sec.	0.838	<0.001	HS
Platelet/Splenic D [PSR]	-0.865	<0.001	HS
APRI Score	0.332	<0.001	HS

Table (4): Endoscopic findings in cirrhotic patients (N=78)

Group (Cirrhotic)		**N (%)**
Attack	Yes	12 (15.4%)
	No	66 (84.6%)
Varices	Yes	45 (57.7%)
	No	33 (42.3%)
Variceal size	Non	33 (42.3%)
	Small-I	12 (15.4%)
	Small-II	8 (10.3%)
	Large-III	18 (23.1%)
	Large-IV	3 (3.8%)
	FV&OV-I	2 (2.6%)
	FV&OV-II	2 (2.6%)
Treatment	No	33 (42.3%)
	Ligated	24 (30.8%)
	Injected	4 (5.1%)
	Inderal	17 (21.8%)

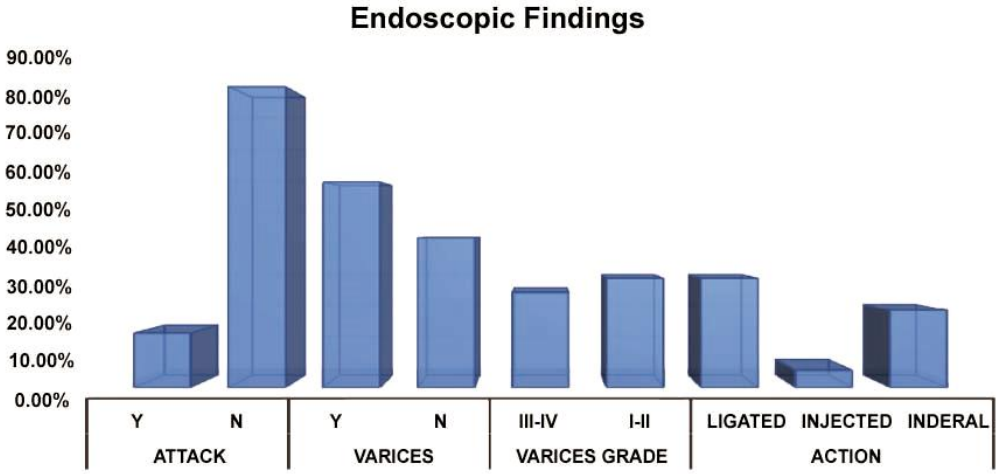

Figure 1:
Endoscopic findings in cirrhotic patients (N=78)

Table (5): Comparison between SSM, LSM, PSR and APRI Score values in cirrhotic patients reading presence of varices

	Varices		P value
	Yes N=45	**No N=33**	
SSM	64.5 (39.5-75)	30.1 (22.5-39.6)	<0.001
LSM	29.8 (19-48)	21.8 (15.3-36.4)	<0.001
Platelet/Splenic D [PSR]	431.3 (297.1-1000)	850 (287.5-1284.6)	<0.001
APRI Score	3 (0.9-7.8)	1.5 (0.3-6.8)	<0.001

SSM : spleen stiffness measurement, LSM : Liver stiffness measurement, PSR : platelet count/spleen diameter ratio, APRI : AST-to-platelet ratio index,

Table (6): Comparison between SSM, LSM, PSR and APRI Score values in cirrhotic patients regarding small and large varices

	Varices			P value
	Small N=20	**Large N=21**	**IGV & small OV N=4**	
SSM	49.6 (39.5-67.6)	71.58 (50.5-75)	55.4 (46.9-67.7)	<.00001
LSM	26.7 (25.8-30.8	33.4 (19-48)	29.6 (20-41.4)	0.628
Platelet/Splenic D [PSR]	370.8 (344.4-388.9)	400 (297.1-651.6)	478.7 (351.9-1000)	0.133
APRI Score	2.4 (1.4-4.8)	3.1 (1.2-5.7)	2.9 (0.9-7.8)	0.768

SSM : spleen stiffness measurement, LSM : Liver stiffness measurement, PSR : platelet count/spleen diameter ratio, APRI : AST-to-platelet ratio index,

Table (7): Area under the ROC curve of SSM as a predictor for detection of presence of Cirrhosis, and development of attack, and varices, in Cirrhotic patients

Predictor	Predicted outcome	(AUC)	SE	95% CI	P value
SSM	Cirrhosis	0.991	0.005	0.952 to 1.000	<0.001
	Attack	0.862	0.044	0.766 to 0.930	<0.001
	Varices	0.999	0.001	0.952 to 1.000	<0.001
LSM	Cirrhosis	1	0	0.969 to 1.000	<0.001
	Attack	0.777	0.0532	0.669 to 0.864	<0.001
	Varices	0.641	0.0707	0.525 to 0.747	0.0455
APRI	Cirrhosis	0.985	0.00898	0.943 to 0.999	<0.001
	Attack	0.793	0.0523	0.686 to 0.876	<0.001
	Varices	0.657	0.0767	0.540 to 0.760	0.0411
PSR	Cirrhosis	1	0	0.969 to 1.000	<0.001
	Attack	0.913	0.0374	0.827 to 0.965	<0.001
	Varices	0.855	0.0472	0.757 to 0.925	<0.001

SSM : spleen stiffness measurement, LSM : Liver stiffness measurement, PSR : platelet count/spleen diameter ratio, APRI : AST-to-platelet ratio index,

Table (8): Validity of SSM as a predictor for detection of presence of Cirrhosis, and development of attack, varices, OV Grade 3-4 and OV Grade 1-2 in Cirrhotic patients

Predictor	Predicted outcome	Cut-off	Sensitivity %	95% CI	Specificity %	95% CI	PPV %	95% CI	NPV %	95% CI
SSM	**Cirrhosis**	>10	100	95.4 - 100.0	100	91.0 - 100.0	100	95.4 - 100.0	100	91.0 - 100.0
	Varices	>39.5	97.7	88.2 - 99.9	96.9	84.2 - 99.9	97.8	88.2 - 99.9	97	84.2 - 99.9
	Attack	>66	83.3	51.6 - 97.9	83.3	72.1 - 91.4	47.6	25.7 - 70.2	96.5	87.9 - 99.6
LSM	**Cirrhosis**	>10	100	95.4 – 100.0	100	91.0 – 100.0	100	95.4 – 100.0	100	91.0 – 100.0
	Varices	>22.5	84.44	70.5 - 93.5	60.61	42.1 - 77.1	74.5	60.4 - 85.7	74.1	53.7 - 88.9
	Attack	>23.4	91.67	61.5 - 99.8	45.45	33.1 - 58.2	23.4	12.3 - 38.0	96.8	83.3 - 99.9
APRI	**Cirrhosis**	>0.7	93.59	85.7 - 97.9	100	91.0 - 100.0	100	95.1 - 100.0	88.6	75.4 - 96.2
	Varices	>2.7	57.78	42.2 - 72.3	93.94	79.8 - 99.3	92.9	76.5 - 99.1	62	47.2 - 75.3
	Attack	>2.2	75	42.8 - 94.5	54.55	41.8 - 66.9	23.1	11.1 - 39.3	92.3	79.1 - 98.4
PSR	**Cirrhosis**	≤1284.6	100	95.4 - 100.0	100	91.0 - 100.0	100	95.4 - 100.0	100	91.0 - 100.0
	Varices	≤657.7	95.56	84.9 - 99.5	78.79	61.1 - 91.0	86	73.3 - 94.2	92.9	76.5 - 99.1
	Attack	≤468.6	91.67	61.5 - 99.8	74.24	62.0 - 84.2	39.3	21.5 - 59.4	98	89.4 - 99.9

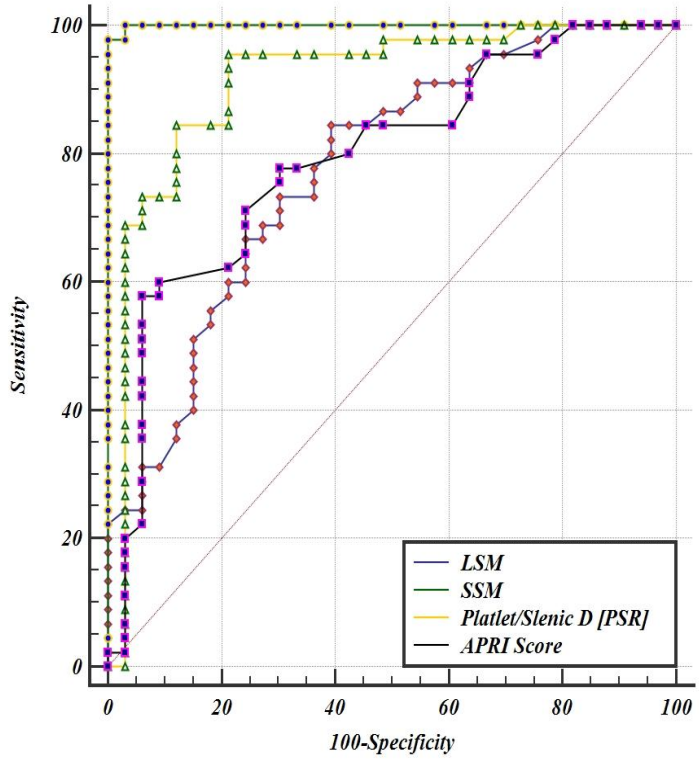

Figure 2:
ROC curve of SSM:(spleen stiffness measurement) , LSM (: Liver stiffness measurement) , APRI (AST-to-platelet ratio index) and PSR (platelet count/spleen diameter ratio) to detect developmentof varices in cirrhotic patients

Table (9): Comparison between Initial SSM values in cirrhotic patients with small oesophageal varices and large oesophageal & gastric varices and on follow up after 6 Months

SSM	Initial SSM(median-range)	SSM after 6 Ms (median-range)	P value
Small varices	49.6 (39.5-67.6)	48.3 (36.4-62.7)	0.014
Large varices and gastric varices	69.03 (46.9-75)	73.42 (64.3-75)	<0.01

SSM (spleen stiffness measurement)

DISCUSSION

Development of esophageal varices (EV) is a common complication of liver cirrhosis, therefore endoscopic screening for EV in cirrhotic patients is recommended by clinical guidelines **[11]**. Because of the impact of upper gastric bleeding caused by EV in prognosis of cirrhotic patients, Baveno IV 2005 consensus work shop **[15]**, and the American Association for the study of liver disease (AASLD) had determined that every patient diagnosed with cirrhosis should be investigated for presence of EV regardless child class and the cause. The splenomegaly developing in the context of liver cirrhosis is commonly ascribed to blood congestion, but older studies demonstrated that it cannot be considered only as a consequence of increased portal pressure and augmented resistance to splenic vein outflow **[16]**. Surprisingly, no relationship could be found between the spleen size and the degree of esophageal varices **[17]**. Multiple studies demonstrated pooling of blood in the red pulp, intraparenchymal arterial aneurysms, and other multiple histopathologic

changes, which evolve towards diffuse fibrosis of the spleen **[18]**. So, in this study, it is only logical to presume that the increase in size should determine changes in the spleen's density as well, which is a physical parameter that may be quantified by elastography.

This study showed significant increase in liver and splenic stiffness values in cirrhotic patients as compared with controls which are consistent with Bureau et al. **[19]** and Stefanescu et al. **[20]**. In this study among cirrhotic group 33 patients (42.3%) had no varices, 45 patients (57.7%) had varices.

This study revealed highly significant increase in portal vein diameter, splenic bipolar diameter, total and direct bilirubin, INR and prothrombin time in patients who had oesophageal varices (EV) between cirrhotic patients with and without varices respectively and these results was in accordance with Schepis et al. **[21]** who showed that high portal vein diameter serve as a predictor for presence of EV and with Sharma et al. **[22]** who concluded that increase splenic bipolar diameter in patients with EV. Also there is highly significant decrease in platelet count and albumin in patients who had EV compared to patients who had no varices in cirrhotic group and this is consistent with **[23]**.

Non invasive methods of liver fibrosis detection as liver stiffness measurement (LSM), Splenic stiffness measurement (SSM), Platelet count/spleen diameter ratio (PSR) and AST to platelet ratio index (APRI) and its relation to portal hypertension and so oesophageal varices prediction was studied by many authors as Saad et al. **[24]**, Calvaruso et al. **[25]**, Mohsen et al. **[26]**, Sharma et al.**[22]**.

In this study there is a highly significant difference between patients with EV and those without regarding the spleen diameter, Platelet count/spleen diameter ratio (PSR) AST to platelet ratio index, (APRI), Liver stiffness measurement (LSM) and Splenic stiffness measurement(SSM). These results are consistent with Saad et al. **[24]**. Also, SSM and LSM were evaluated by Calvaruso et al. **[25]**. This study concluded a highly significant difference in mean SSM values between patients with EV and those without (64.5 versus 24.6 kPa respectively; P<0.001).

In this study SSM had a cut of ≥39.5 kpa for the presence of EV, with 97.7%,96.9% sensitivity and specificity respectively and PPV 97.8% , NPV 97%, and AUROC 0.999, while LSM had lower sensitivity and specificity 84.44%,60.61% respectively and low PPV and NPV 74.5%, 74.1%, respectively and AUROC 0.641.So SSM is more sensitive and specific than LSM in the prediction of EV, these results are in agreement with Mohsen et al. **[26]**, Liu et al. **[27]**, Sharma et al. **[22]** and Fraquelli et al. **[28]**.

At the same time PSR had a low specificity 78.79% at cut of ≤657.7 and reasonable sensitivity 95.56%, for EV prediction with AUROC0.855. While APRI had the reverse of PSR as it had high specificity 93.9% and low sensitivity 57.78% at a cut of value ≤657.7 with PPV74.5% and NPV 74.1%, these results are in agreement with Mohsen et al. **[26],** who showed that SSM had better performance than LSM. A cut-off value ≥16.5 kPa for LSM had AUROC 0.895, sensitivity 94.4%, specificity 72.7%, PPV 73.9% and NPV 94.1%. While a cut-off value ≥29 kPa for SSM had AUROC 0.934, sensitivity 94.4%, specificity 86.4%, PPV 85% and NPV 95%.

Also, Colecchia et al. **[29]** concluded that SSM and LSM were more accurate than other non-invasive parameters in identifying patients with EV. In their study, LSM could predict EV with cut-off ≥25 with sensitivity 56% and specificity 97%, while SSM could predict EV with cut-off value ≥55 with sensitivity 71% and specificity 95%. According to our study SSM showed better performance than LSM, Also SSM was the most sensitive parameter when compared with APRI, PSR and LSM as regards EV detection, PSR came in the 2nd place similarly.

Giannini et al. **[30]** proposed PSR of ≤909, as an accurate non-invasive marker for the presence of EV.

The result of this study are the same results of *Cherian et al.* **[31]** and González-Ojeda et al. **[32]** who found that PSR was significantly lower in patients with EV than in those without. Mangone et al. **[33]** concluded that PSR is not a useful parameter to avoid unnecessary upper endoscopy in cirrhotic patients. Using the ROC curves, they found that PSR <936.4 for the prediction of presence of EV showed sensitivity 64.5%, specificity 64.3%, PPV 50% and NPV 76.6% (accuracy 0.671). Chawla et al. **[34]** supported these data in their meta-analysis where they concluded that PSR cut-off level of 909 may not be adequate to completely replace upper GI endoscopy as a non-invasive screening tool for EV.

On the contrary, Abu El Makarem et al. **[35]** found that PSR had a better diagnostic performance. In their study, PSR in patients with EV was significantly lower than in those without. In an analysis of the receiver operating characteristic curves (ROCs), an optimal cutoff value of 939.7 for this ratio, gave sensitivity 100%, specificity 86.3%, PPV 95.6%, NPV100% and AUROC of 0.94, 96.6% accuracy.

Regarding APRI, our results agreed with Zambam de Mattos et al. **[36]**, that APRI was not a good index for the prediction of EV, because its sensitivity, specificity and predictive values were insufficient. In their cross-sectional study, APRI with a cutoff point of 1.3 demonstrated a sensitivity 64.7%, specificity 72.7%, PPV 86.5% and NPV 43.2%.

Regarding large EV detection, in this study among 45 cirrhotic patients had varices, 20 of them had small varices, 21 of them had large varices and 4 patients had both fundal varix and small varices. There was highly significant difference in median SS in patients with large varices versus small varices (49.6vs 71.58 kpa with P<.00001) respectively. However there is no significant difference in median LSM 26.7 VS 33.4 kpa with p 0.929. Also there is no significant difference in median APRI in patients with large varices versus small varices (2.4 vs 3.1 with p 0.768), Also there is no statistically significant difference in median PSR between both groups.

The results of this study agreed with Sharma et al. **[22]** who concluded that SS measurement can differentiate between small and large varices (56 kPa vs. 49 kPa, P=0.001), also these results agreed with Hua et al. [37] reported who that LSM couldn't assess EV accurately with no significant difference in LSM value between patients with large EV and those having small EV (31 kPa versus 28.18 kPa).

On contrary to this study Mohsen et al. **[26]** showed APRI was the best for detecting large varices median 1.38, followed by SS measurement median 72.1kpa for large varices.

As regards bleeding varices, 12 Patients among 45 patients presented with attack of haematemesis and melena, this study showed SSM had moderate performance with cut-off ≥66 with sensitivity and specificity 83.3% and 83.3 % respectively, PPV and NPV47.6% 96.5% respectively, which is consistent with Sharma et al. **[22]** who showed that SS measurement useful to differentiate bleeding vs non bleeding with cut off value 58 kpa.

PSR showed the best performance regarding bleeding varices with cut off value ≤468.6 had AUROC 0.913 sensitivity and specificity 91.67% and 74.24% respectively, PPV 39.3 % and NPV 98%.which is consistent with Sharma et al. **[38]** showed that PSR useful to differentiate bleeding vs non bleeding with cut off value ≤ 777.

LSM showed cut off value >23.4 kpa had AUROC 0.777 sensitivity, specificity91.67% and 45.45% respectively, PPV 23.4% and NPV 96.8 %.while APRI showed cut off value >2.2 had AUROC 0.793 sensitivity 75 %, specificity 54.55 %, PPV 23.1 % and NPV 92.3%.

So this study showed moderate performance of SS and superiority of PSR which may be explained by hemodynamic changes at time of attack may affect platelet count, also SS not measured at the same time.

In this study all patients with small oesophageal varices underwent pharmacological treatment and follow up of splenic stiffness after 6 months. There was no statistically significant difference between initial SSM measurement and SSM after 6 months with p value 0.004, This may be attributed to short period of follow up, to be evaluated by further studies. While patients with large EV and gastric varices who underwent endoscopic band ligation and endoscopic injection respectively there was statistically significant increase of SSM after 6 months with p value <0.001 which may be explained by closure of collateral channels in the form of oesophageal and gastric varices and this reflected as increased splenic congestion and fibrosis and so increased SSM.

From this study and its results we concluded that Spleen stiffness measurement by Fibroscan is a sensitive and reliable method for detection of esophageal varices.

Splenic stiffness showed the best performance on detection of oesophageal varices, when compared to other non invasive predictors, PSR came in the 2nd place.

Splenic stiffness measurement can differentiate small and large varices.

Splenic stiffness measurement can not be used as a tool for follow up of patients with oesophageal varices, who under went either pharmacological or endoscopic treatment.

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