Role of Liver Stiffness Measurement in Prediction of Esophageal Varices in Chronic Hepatitis C Virus Infected Egyptian Patients

Fatma M. El-Senosy[*], **Walaa F. El-baz, Hatem H. Mohammed**

Departments of Internal Medicine, Faculty of Medicine (Girls) Al-Azhar University, Cairo, Egypt

Abstract   Background; Hepatitis C virus (HCV) infection is a public health problem worldwide. It is estimated more than 185 million people around the world have been infected with it according to the world health organization (WHO). The highest prevalence is in Egypt and constitute about 10-20% of the general population. Bleeding from esophago-gastric varices is the most important complication of cirrhosis. Fibro Scan is a non-invasive device that assesses stiffness of the liver via the technique of transient Elastography. Objective; to evaluate the role of fibro scan in prediction of esophageal varices in chronic HCV infected patients. Patients and methods; A cross sectional prospective study was conducted on 100 Egyptian patients with chronic HCV infection, Studied patients were subjected to full medical history, Routine laboratory investigations, Hepatitis markers including HBsAg, HCV antibody and HCV RNA by real time polymerase chain reaction (PCR), an Abdominal ultrasonography, upper gastrointestinal endoscopy and assessment of liver fibrosis by fibroscan which, was obtained using fibroscan device (Echosens, Paris, France) by an expert fibroscan operator who was not aware by patients data, abdominal ultrasound and upper gastrointestinal endoscopy results were done for all studied patients. Results: liver stiffness measurement revealed patients with values (2-33 kPa with mean ± SD of 8.40 ± 6.82) had no esophageal varices (EV) and patients with values of (11-68 kPa) had EV. And disturbed as the following; (11-54 kPa with mean ±SD of 26.071 ±15.606) for patients with grade I, (13-43 kPa with mean ±SD of 32.625 ±10.716) for patients with grade II, (32-64 kPa with mean ± SD of 43.188 ± 10.232) for patients with grade III and (22-68KPa with mean ±SD of 51.875 ±17.374) for patients with grade IV esophageal varices respectively ($P<0.001$). Also there was significant positive correlation between Fibro scan and each of serum ALT, AST, AST/PLT ratio, total bilirubin and INR. Conclusion; Liver stiffness measurement with Transient Elastography is a good alternative for liver biopsy and patients with values >21 kPa have an accuracy of presence of EV.

Keywords   HCV, Liver stiffness, Transient Elastography

1. Introduction

Hepatitis C virus (HCV) infection is a public health problem worldwide. It is estimated more than 185 million people around the world have been infected with it according to the world health organization (WHO) [1]. The highest prevalence is in Egypt and constitute about 10-20% of the general population [2].

Cirrhosis is a consequence of almost all progressive chronic liver diseases, approximately 10%-20% of patients with chronic hepatitis C virus infection have cirrhosis at first clinical   presentation, and as many as 20%-30% of those who don't have cirrhosis will eventually develop this condition and its complications within one or more decades [3].

Approximately half of patients with cirrhosis have esophageal varices (EV), and one-third of all patients with varices will develop variceal hemorrhage which is a major cause of morbidity and mortality in cirrhotic patients [4].

Esophago gastro duodenoscopy (EGD) is the gold standard for EV detection, but a generalized program of periodical EGD in patients with chronic liver disease might result in a heavy economic burden even for developed countries. Furthermore, repeated examinations when not performed under profound sedation are often poorly accepted by patients who may refuse further follow-up [5].

Transient Elastography (TE) is a noninvasive, ultrasound technique-based technology that assesses liver stiffness measurement (LSM). Established evidences indicated that TE has good sensitivity and specificity for fibrosis,

significant fibrosis, and cirrhosis, and it became popular over the last few years [6]. A good correlation between LSM and the presence of portal hypertension (PHT) and EV has been reported, suggesting that LSM could be an interesting tool for predicting the presence of large EV and selecting patients for endoscopic screening. [7]

Aim of the work; the aim of this study was to evaluate the role of fibro scan in prediction of esophageal avarices in chronic HCV infected patients and selection of patients for endoscopic screening.

2. Patients and Methods

This a cross sectional prospective study was carried out on100 chronic HCV patients presented to the outpatient clinics at the internal medicine department, Al-Zahraa University hospital and Shebien Elkom Teaching Hospital during the period from June 2016 to Febreuary 2017.

All patients were diagnosed definitely to have a chronic HCV infection by HCV PCR testing as they were submitted to new antiviral therapy. Our Study included 100 patients (69 males and 31 females). Their age ranged from 18 to 70 years with a mean age of (41.58± 13.330) years.

Exclusion criteria:

Patients with BMI more than 35 kg/m^2, ascites, history of schistoniasis or alcohol intake co infection with HIV or hepatitis B virus (HBV), Patients with history or evidence of any malignancies, autoimmune diseases and Patients suffering from any organ failure, Diabetes mellitus. Haemolytic anaemia, Cytopeni, Age < 18 and >70 years were excluded from the study and History of upper GIT bleeding or hepatocellular carcinoma, and Patients with abdominal collaterals in abdominal ultrasound.

Methods:

All patients in this study were subjected to the following:

1. Full medical history and complete physical examination.
2. Measurement of body mass index (BMI): weight divided by the square of the height (Kg/m^2)
3. Laboratory investigations:

Sample collection and storage:

Five ml of venous blood were withdrawn under complete aseptic technique from the fasting patients in a sterile vacutainer tube 1ml for complete blood picture were taken on EDTA solution,3ml of the samples were taken in plain tube, left to clot, centrifuged at 2000×g for 10 minutes and sera were separated without delay.

Complete blood picture (CBC) were done on sysmex KN21, Fasting and post prandial blood sugar, Liver function tests (Serum albumin, bilirubin, alanine transaminases (ALT) and aspartate transaminase (AST), Kidney function tests including serum urea and creatinine All of them were done on cobas 311 clinical chemistry auto-analyzer from ROCH diagnostic company and Hepatitis markers including

(HBsAg), HCV antibody and HCV RNA by real time polymerase chain reaction (PCR) were done.

4. Esophago gastro duodenoscopy

EGD was done using Pentax EG-2990i Gastroscope (Pentax Medical, HOYA Corporation, Tokyo, Japan) by a single expert endoscopist blinded for the detailed clinical and laboratory data of the patients. EV was classified according to modified Thakeb classification as follow:

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

Grade II: Moderate-sized clubbed varices confined to the lower half of the esophagus, with well-defined areas of normal mucosa in-between.

Grade III: Gross varices extending into the upper half of the esophagus, with dilated capillaries in-between and normal mucosa might not be visible unless the esophagus is fully distended with air.

Grade IV: Gross varices extending into the upper half of the esophagus with dilated capillaries on top or in-between and encroaching on esophageal lumen [8-9].

5. Radiologic investigations:

A-Abdominal ultrasonography with special emphasis on:

Liver size, echo pattern and presence of focal lesion, splenic size and echo pattern, portal vein diameters, and presence or absence of ascites.

B-Fibro scan: Fibro Scan was obtained using fibroscan device (Echosens, Paris, Farance) by an expert fibroscan operator who was not aware by patients' data, US and EGD results. Liver hardness is evaluated by measuring the velocity of a vibration wave (also called a 'shear wave') generated on the skin. Shear wave velocity is determined by measuring the time the vibration wave takes to travel to a particular depth inside the liver [10].

Interpretation of results of Fibroscan:

1. Up to ten successful acquisitions were performed on each patient. Success rate was calculated as the ratio of the number of successful acquisitions over the total number of acquisitions.
2. The median value of successful measurements was kept as representative of the liver stiffness.
3. Only LSM obtained with 10 successful acquisitions and a success rate of at least 60% was considered reliable.

The **METAVAIR** scoring system is an algorithm for grading of activity in chronic hepatitis C;

The stage of fibrosis varied from 0 to 4 (F0 = no fibrosis; F1 = portal fibrosis without septa; F2 = portal fibrosis with few septa; F3 = septal fibrosis, without cirrhosis; F4 = cirrhosis [10].

In Hepatitis C:

2 to 7 kpa mean f0-f1 stage.

8 to 9 kpa mean f2 stage.

9 to 14 kpa mean f3 stage.

14 or higher kpa means f4 stage

Statistical Analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 20. Qualitative data were presented as number and percentages while quantitative data were presented as mean, standard deviations and ranges when parametric. The comparison between two groups with qualitative data were done by using Chi-square test and/or Fisher exact test was used instead of Chi-square test when the expected count in any cell was found less than 5.The comparison between two groups regarding quantitative data with parametric distribution was done by using Independent t-test..Spearman correlation coefficients were used to assess the correlation between two quantitative parameters in the same group. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P > 0.05: Non significant. P < 0.05: Significant. P < 0.01: Highly significant. ROC-curve: Receiver Operating Characteristic curve analysis.

Sensitivity: Probability that the test results will be positive when the disease is present (true positive rate, expressed as a percentage).

Specificity: Probability that the test results will be negative when the disease is present (true negative rate, expressed as a percentage).

PPV: Positive Predictive value (probability that the disease is present when the test is positive).

NPV: Negative Predictive value (probability that the disease is present when the test is negative).

Accuracy: the ratio of the true positive and true negative on all patients.

3. Results

Demographic data of studied patients showed;

This study was conducted on 100 chronic HCV Egyptian patients, 69 (69%) males and 31 (31%) females. Their ages ranged between 18-70 years with a mean ± SD of (41.58± 13.330) years and BMI ranged from (19-25) with mean± SD of (22.89±1.6).

Al patients were examined by upper gastrointestinal endoscopy with full special emphasis on presence or absence of esophageal or gastric varices and quantification of liver fibrosis by Fibro scan.

The Main clinical presentations of the HCV patients as regard easy fatigability, abdominal pain, headache, jaundice, ascites and Hematemesis are shown in (table 1).

Laboratory investigation of the patients showed that mean ± SD of ALT, AST, Total bilirubin were (38.520 ± 13.653), (46.130 ± 18.070) and (1.164 ± 0.776) respectively. The INR values ranged from 1- 2.2 with mean ± SD (1.259 ± 0.268). The mean± SD of the serum Albumin level, Hemoglobin and platelet count were (3.827± 0.789), (11.610 ± 1.723) and (198.000 ± 86.952) respectively. (Table 2)

Endoscopic examination of 100 HCV patients showed that 61 (61%) patients had no esophageal varices, 7 (7%) patients

had grade1 varices, 8(8%) patients had grade II varices, 16(16%) patients had grade III varices, and 8 (8%) patients had grade 1v esophageal varices. (figure 1)

Fibro scan examination revealed that; 21(21%) patients were (F0), 11(11%) patients were (F1), 4(4%) patients were (F2), 17(17%) patients were (F3) and 47(47%) patients were (F4). (Table 3)

The relation between endoscopic finding and stages of fibrosis assessed by fibro scan revealed that; The patients with Fibrosis index (F0, F1 and F2) had no esophageal varices while patients with Fibrosis index F3-F4 had esophageal avarices and disturbed as the following; (2 patients with F3 and 5 patients with F4 showed grade I EV) and the reaming patients with F4 showed; 8 patients had grade II EV, 16 patients had grade III EV, and 8 patients had grade IV EV. (P< 0.001) So decompensated patients had increased incidence of EV. (Table 4).

The relation between liver stiffness measurement in Kpa and grades of esophageal varices revealed that;

Patients with values (2-33 kPa with mean ± SD of 8.40 ± 6.82) had no EV and patients with values of (11-68) kPa had EV. And disturbed as the following; (11-54 KPa with mean ± SD of 26.071 ± 15.606) for patients with grade I, (13 -43 Kpa with mean ± SD of 32.625 ± 10.716) for patients with grade II, (32-64 Kpa with mean ± SD of 43.188 ± 10.232) for patients with grade and (22-68KPa with mean ± SD of 51.875 ± 17.374) for patients with grade IV esophageal avarices respectively. Thus liver stiffness measurement by fibroscan was significantly higher in patients with grade 111 and grade 1V esophageal varices (P<0.001). (Table 5)

We tried to establish the value of liver stiffness which predict the presence of varices. For a cut–off value of 21 kPa, liver stiffness measurement by fibroscan had 87.1% sensitivity and 95.0% specificity with 91.9% PPV and 92.1% NPV (Table 6).

According to the degree of liver Fibrosis **METAVAIR** scoring system our patients were divided into two groups compensated (group A) and de compensated (group B).

(group A) included 32 (32%) patients with grades (F0 and F1). they were 19 males and 13 females and(group B) included 68 (68%) patients with grades (F2, F3 and F4) they were 50 males and 18 females.

Comparison between group A (compensated cirrhosis stage F0 and F1) and group B (de compensated cirrhosis stage F2, F3, and F4).

There were highly significant increase in the Mean ± SD of serum bilirubin, AST, ALT and INR in group B when compared to group A while there were highly significant decrease in the Mean ± SD of hem globulin level, platelets count, serum albumin and AST/PLT ratio in group B in comparison with group A. (table 7)

There was significant positive correlation between Fibro scan in kPa and each of ALT, AST, AST/PLT ratio, total bilirubin and INR. However, there were significant negative correlation between Fibro scan in kPa and each of hemoglobin level, platelet count and serum albumin. (Table 8).

Table 1. The main clinical data among the patients group

Clinical data	Number of patients (60)	Percentage (%)
Asymptomic	60	(60%)
Easy fatigability	10	(10%)
Vague abdominal pain	8	(8%)
Headache	3	(3%)
Jaundice	8	(8%)
Ascites	4	(4%)
Hematemesis	7	(7%)

Table 3. Fibro scan study of 100 HCV patients

Fibrosis index		
Stage	N	%
F0	21	21.00
F1	11	11.00
F2	4	4.00
F3	17	17.00
F4	47	47.00
Total	100	100.00

Table 2. Laboratory investigation of 100 HCV patients

Descriptive Statistics		
parameter	Range	Mean±SD
ALT U/L	16-90	38.520±13.653
AST U/L	18-113	46.130±18.070
Creatinine mg/dL	0.5-1.5	0.988±0.427
HB g/dL	8.5-15.2	11.610±1.723
PLT(X109/L) (cell/cml)	52-360	198.000±86.952
AST/PLT	0.06-1.85	0.329±0.307
Bilirubin mg/dL	0.3-2.3	1.164±0.776
INR	1-2.2	1.259±0.268
Albumin (g/dL)	2.4-5	3.827±0.789

Where: ALT: alanine transaminase enzyme AST: aspartate transaminase enzyme
HB: Hemoglobulin level. PLT(X109/L: platelets count INR: international normalized ratio.

Table 4. Endoscopic findings of HCV patients with different degree of fibrosis index

E.V. Grade	Fibrosis index												Chi-Square	
	F0		F1		F2		F3		F4		Total			
	N	%	N	%	N	%	N	%	N	%	N	%	X2	P-value
No	21	100	11	100	4	100	15	88.24	10	21.28	61	61		
Grade I	0	0	0	0	0	0	2	11.76	5	10.64	7	7		
Grade II	0	0	0	0	0	0	0	0	8	17.02	8	8	63.247	<0.001*
Grade III	0	0	0	0	0	0	0	0	16	34.04	16	16		
Grade IV	0	0	0	0	0	0	0	0	8	17.02	8	8		
Total	21	100	11	100	4	100	17	100	47	100	100	100		

Where:
Grade I: Small straight cords of varices confined to the lower third of esophagus.
Grade II: Moderate-sized clubbed varices confined to the lower half of the esophagus, with well-defined areas of normal mucosa in-between.
Grade III: Gross varices extending into the upper half of the esophagus, with dilated capillaries in-between and normal mucosa might not be visible unless the esophagus is fully distended with air.
Grade IV: Gross varices extending into the upper half of the esophagus with dilated capillaries on top or in-between and encroaching on esophageal lumen. [9-10].

Table 5. Relation between liver stiffness values in Kpa and grades of esophageal varices

E.V. Grade	N of cases	Fibroscan (kPa)		ANOVA	
		Range	Mean ± SD	F	P-value
No	61	2-33	8.403±6.824		
Grade I	7	11-54	26.071±15.606		
Grade II	8	13-43	32.625±10.716	71.46	<0.001
Grade III	16	32-64	43.188±10.232		
Grade IV	8	22-68	51.875±17.374		

Table 6. Cut off value for the presence of EV

ROC curve between Yes E.V. Grade and No E.V. Grade					
Cut-off	Sens.	Spec.	PPV	NPV	Accuracy
>21	87.18	95.08	91.9	92.1	97%

Table 7. Comparison between group A and group B as regard: ALT, AST, serum bilirubin, serum albumin, INR, HB level, PLT and AST/PLT ratio

Parameter	Group A	Group B	P value	Sig
Bilirubin mg/dL	0.579±0.194	1.440±0.794	< 0.001	HS
AST U/L	32.563±8.640	52.515±17.85	< 0.001	HS
ALT U/L	29.969±7.994	42.554±13.95	< 0.001	HS
INR	1.072±0.144	1.347±0.268	< 0.001	HS
Serum albumin g/ dL	4.566±0.447	3.479±0.667	< 0.001	HS
HB level g/dL	13.016±1.761	10.949±1.252	< 0.001	HS
Platelets count (X109/L) (cell/ cmL)	299.969±34.7	150.015±57.5	0.001	HS
AST/PLT	0.110±0.035	0.431±0.325	0.001	HS

Table 8. Correlation between Fibro scan results in kPa and all studied parameters as regard: ALT, AST, serum bilirubin, serum albumin, INR, HB level, PLT and AST/PLT ratio in all patients

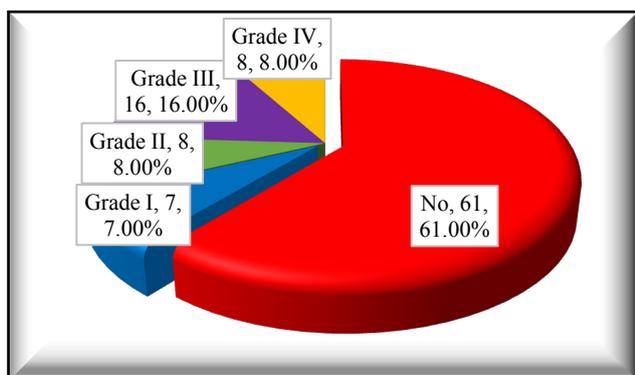| Correlations		
parameter	Fibro scan (kPa)	
	R	P-value
ALT U/L	0.576	<0.001
AST U/L	0.599	<0.001
Bilirubin mg/dL	0.692	<0.001
INR	0.635	<0.001
Albumin g/dL	-0.742	<0.001
HB g/dL	-0.638	<0.001
PLT(X109/L) (cell/cmL)	-0.796	<0.001
AST/PLT	0.759	<0.001

Figure 1. Endoscopic examination of 100 HCV patients

4. Discussion

Portal hypertension is the hemodynamic abnormality associated with the most severe complications of cirrhosis, including ascites, hepatic encephalopathy, and bleeding from gastroesophageal varices [11].

Bleeding from esophago-gastric varices is the most important complication of cirrhosis [12]. The first crucial step in prevention is to identify the patients at risk for bleeding by endoscopic screening, in order to select them for prophylactic treatment [13].

Several studies in the past have shown independent parameters like splenomegaly or ascites [14].

Spider naevi [15], Child's grade [16], prothrombin time/activity or portal vein diameter [17], platelet count/ spleen diameter ratio [18] as significant predictors for the presence of esophageal varices.

Liver stiffness (LS) measured by Transient Elastography has been reported to be well correlated with histologically assessed liver fibrosis stage [19].

Our study was carried to evaluate the role of fibro scan in prediction of esophageal varices in chronic HCV infected Egyptian patients and selection of patients for endoscopic screening.

Our results revealed that patients with values (2-33 kPa with mean ± SD of 8.40 ± 6.82) had no EV and patients with values of (11-68) kPa had EV. And disturbed as the following; (11-54 KPa with mean ± SD of 26.071 ± 15.606) for patients with grade I, (13-43 Kpa with mean ± SD of 32.625 ± 10.716) for patients with grade II, (32-64 Kpa with mean ± SD of 43.188 ± 10.232) for patients with grade III and (22-68KPa with mean ± SD of 51.875 ± 17.374) for patients with grade IV esophageal varices respectively. Thus only patients with 11 kPa or above should be screened for EV. (P<0.001)

And patients with values less than 11kPa should be ruled out from endoscopic screening for E.V and a cut –off value of ≥21 KP had 87.1% sensitivity and 95% specificity for presence of esophageal varices.

Also our results showed there was significant positive correlation between Fibro scan in kPa and each of ALT, AST, AST/PLT ratio, total bilirubin and INR. However, there were significant negative correlation between Fibro scan in kPa and each of hemoglobin level, platelet count and serum albumin.

In agreement with our results A study was done by Beom

Kyung Kim, (2017) [20] suggested that TE adequately reflects the findings of hepatic venous pressure gradient (HVPG), indicating that it is a useful modality for evaluating portal hypertension and cirrhotic complications. They found that TE value<13 kPa reliably excludes any increase in HVPG, while values >21 kPa have an accuracy equal to that of HVPG ≥10 mmHg.

In previous study was done by Sporea et al., (2011) [21] who studied value of Transient Elastography as a predictor for Variceal bleeding, they established a value of 31 kPa for the presence of EV and 50.7 kPa as a value for bleeding EV.

In consistent with our study another previous study done by Sebastian Mueller et al., (2010) [22] suggested that LS highly correlates with portal pressure, and esophageal varices are likely at values >20 kPa.

In A study done by Romanas Zykus et al., (2015) [23] both Liver and spleen transient Elastography were used to predicts Portal hypertension. The study suggested that Liver and spleen stiffness correlate with HVPG and could be used to predict clinically significant portal hypertension (CSPH) or severe (SPH). Spleen Elastography was not superior to liver Elastography in predicting portal hypertension.

Also Kumar A and his colleagues (2017) [24] studied the diagnostic accuracy of TE for detecting clinically significant portal hypertension (CSPH) in Indian patients with cirrhotic portal hypertension. The study was conducted on 326 patients with liver cirrhosis and reported that TE has a fair positive correlation with HVPG thus; TE can be used as a non-invasive modality to assess the degree of portal hypertension. A cut-off TE value of 21.6 kPa identifies CSPH with a positive predictive value of 93%.

Another study was done In South Korean by Hong WK et al., (2013) [25] LS measurement with transient Elastography in 59 cirrhotic patients who underwent hemodynamic heptic venous pressure gradient (HVPG) measurement. Their results suggested that LS measurement exhibited a significant correlation with HVPG in patients with cirrhosis with a cutoff value 24.25 kPa with 82.9% sensitivity and 70.8% specificity.

Also in agreement with our results Yasmin et al. (2013), [10] who reported that liver stiffness measurement was significantly higher in patients with esophageal varices and at the best cut off value 29.7 Kpa, LSM sensitivity was 95% and 67% specificity.

In a similar Egyptian study was done by Tag-aden et al, (2017) [26] who studied Liver stiffness measurement in 123 egyptian patients with chronic HCV and revealed that LSM cut off ≥ 17 Kpa was a good predictor for the presence of esophageal varices with 93.6% sensitivity and 95% specificity.

Moreover, studies carried out by Vizzutti et al., (2007) [27] a cut-off value for prediction of esophageal varices was 17.6 kPa, these cut off values are lower than we obtained this can be explained by the different demographics and patients characteristics as well as the type of fibroscan machines were used . In contrary to our study Castera L et al., (2009) [28] showed that Transient Elastography could be a valuable tool in diagnosis of cirrhosis but cannot replace endoscopy for variceal screening.

The main limitation of our study was the inclusion of a small number of patients with the same etiology for liver disease (CHC). Also, despite TE was accurate for detecting clinically significant PHT with a mean area under the receiver-operating curve (AUROC) of 0.93 in a meta-analysis, [29] it has certain limitations in ascetic and obese patients. [30] However, newer methods like point shear-wave elastography, 2-dimensional real-time shearwave elastography, and magnetic resonance elastography show promising results [31-33] and could represent future research.

5. Conclusions

Liver stiffness measurement with Transient Elastography is a good alternative for liver biopsy and could be used in clinical practice as a non invasive tool for prediction of esophageal varices and patients with values >21 kPa have an accuracy of presence of EV.

REFERENCES

[1]   Mohamed A, Afifi E, El-Awady R, et al. (2015): Correlation between serum levels of TNFR and IL6 with treatment response to pegylated interferon and ribavirin therapy in chronic hepatitis C Egyptian patients. Virol J Curr Res; 1: 6–10.

[2]   Mohamed A, El-Toukhy N, Reyad E et al. (2017): Serum Interleukin-6 Concentration Associated with Response to Therapy for Chronic Hepatitis C Patient HGJ: Vol 6, No 4.

[3]   Ikeda K, Saitoh S, Suzuki Y, Kobayashi M, Tsubota A, Koida I, et al. (1998): Disease progression and hepatocellular carcinogenesis in patients with chronic viral hepatitis: a prospective observation of 2215 patients. J Hepatol.; 28: 930–8.

[4]   Garcia-Tsao G, Sanyal AJ, Grace ND, et al (2007): Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology; 46: 922–38.

[5]   Shahinul Alamr, Ahmed Lutful Moben AKM, Khorshed AIam. et al (2013): Prediction of esophageal varices in cirrhotic patients by measuring liver stiffness by fibroscan. BSMMU J; 6: 85–9.

[6]   Vignier N, Esmat G, Elsharkawy A, et al (2011): Reproducibility of liver stiffness measurements in hepatitis C virus (HCV)-infected patients in Egypt. J Viral Hepat; 18: e358–65.

[7]   Esmat G, Elsharkawy A, El Akel W, et al. (2013): Fibroscan of chronic HCV patients coinfected with schistosomiasis. Arab J Gastroenterol; 14: 109–12.

[8]   Thakeb F, Zakaria S, Hunter M. Thakeb F, Zakaria S, et al. (1988): editors. A study of the esophagus by endoscopy and radiology after sclerotherapy. Gastrointestinal Endoscopy: An Egyptian View. Egypt: El-Sona El-Mohamadia;. 51.

[9] Yasmin Saad, Mohamed Said, Mohamed O, et al. (2013): Liver stiffness measurement by fibroscan predicts the presence and size of esophageal varices in Egyptian patients with HCV related liver cirrhosis. J Clin Diagn Res; 7: 2253–7.

[10] Bedossa P and Poynard T (1996): An algorithm for the grading of activity in chronic hepatitis C. The METAVIR Cooperative Study Group. Hepatology 24: 289-293.

[11] de Franchis R (2015):. Expanding consensus in portal hypertension Report of the Baveno VI Consensus Workshop: stratifying risk and individualizing care for portal hypertension. J Hepatol; 63: 743–52.

[12] D'Amico G, Garcia-Pagan JC, Luca Aand Bosch J. (2006): "Hepatic vein pressure gradient reduction and prevention of variceal bleeding in cirrhosis: a systematic review"; Gastroenterology.; 131(5): 1611–24.

[13] Garcia-Tsao G, Sanyal AJ, Grace ND and Carey WD. (2007): Practice Guidelines Committee of American Association for Study of Liver Diseases; Practice Parameters Committee of American College of Gastroenterology. Prevention and management of gastroesophagealvarices and variceal hemorrhage in cirrhosis. Am J Gastroenterol.; 102: 2086–2102.

[14] Thomopoulos KC, Labropoulou-Karatza C, Mimidis KP, Katsakoulis EC, et al (2003): Non-invasive predictors of the presence of large oesophageal varices in patients with cirrhosis Dig Liver Dis.; 35(7): 473-8.

[15] C. Pilette, F. Oberti, C. Aubé et al., (1999): "Non-invasive diagnosis of esophageal varices in chronic liver diseases," Journal of Hepatology, 31(5). 867–873.

[16] A. Zaman, R. Hapke, K. Flora, H. R. Rosen, and K. Benner, (1999): "Factors predicting the presence of esophageal or gastric varices in patients with advanced liver disease," American Journal of Gastroenterology, 94(11) 3292–3296.

[17] Schepis F, Cammà C, Niceforo D, Magnano A, Pallio S, Cinquegrani M, D'amico G, Pasta L, (2001): "Which patients with cirrhosis should undergo endoscopic screening for esophageal varices detection?" Journal of Hepatology; 33(2): 333-338.

[18] Giannini EG, Zaman A, Kreil A, et al. (2006): Platelet count/spleen diameter ratio for the noninvasive diagnosis of esophageal varices: Results of a multicenter, prospective, validation study. Am J Gastroenterol.; 101: 2520–2.

[19] Cardoso AC, Carvalho-Filho RJ and Marcellin. (2011): "Transient Elastography in chronic viral hepatitis: a critical appraisal". Gut 2011; 60: 759-764.

[20] Beom Kyung Kim (2017): "Transient elastography can be integrated into routine clinical practice for the evaluation of portal hypertension?" Clin Mol Hepatol.; 23(1): 27–30.

[21] Sporea I, Ratiu I, Sirli R, Popescu A, Bota S. (2011): Value of transient elastography for the prediction of variceal bleeding. World J Gastroenterol., 7; 17(17): 2206–10. [PMC free article]

[22] Sebastian Mueller and Laurent Sandrin. (2010): "Liver stiffness: a novel parameter for the diagnosis of liver disease". Hepat Med. 2010; 2: 49–67.

[23] Romanas Zykus, Laimas Jonaitis, Vitalija Petrenkienė, Andrius Pranculis, and Limas Kupčinskas: (2015): "Liver and spleen transient elastography predicts portal hypertension in patients with chronic liver disease: a prospective cohort study"; BMC Gastroenterol.; 15: 183.

[24] Ashish Kumar, NoorMuhammad Khan, Shrihari Anil Anikhindi and Praveen Sharmaand Naresh Bansal, (2017): "Correlation of transient elastography with hepatic venous pressure gradient in patients with cirrhotic portal hypertension: A study of 326 patients from India"; World J Gastroenterol. 2017; 28; 23(4): 687–696.

[25] Hong, W.K., Kim, M.Y., Baik, S.K., Shin, S.Y., Kim, J.M., Kang, Y.S. et al. (2013): "The usefulness of non-invasive liver stiffness measurements in predicting clinically significant portal hypertension in cirrhotic patients: Korean data Clin Mol Hepatol.; 19: 370–375.

[26] Mohammed Tag-Adeen, Mohamed Alsenbesy, Ali Abdelrahman Ghweil, M. Ali Hussein Abd Elrazek, Elsayed A. Elgohary et al, (2017): "Liver stiffness measurement and spleen diameter as predictors for the presence of esophageal varices in chronic hepatitis C patients"; Medicine (Baltimore).; 96(46): e8621.

[27] Vizzutti F, Arena U, Romanelli RG, Rega L, Foschi M, Colagrande S, et al. (2007): Liver stiffness measurement predicts severe portal hypertension in patients with HCV-related cirrhosis. Hepatology. 2007; 45:1290–97.

[28] Castera L, Vergniol J, Foucher J, Le Bail B, Chanteloup E, Haaser M, et al. (2009): Early detection in routine clinical practice of cirrhosis and oesophageal varices in chronic hepatitis C: comparison of transient elastography (FibroScan) with standard laboratory tests and non-invasive scores. J Hepato; 50: 59–68.

[29] Shi KQ, Fan YC, Pan ZZ, et al. (2013): Transient elastography: a meta-analysis of diagnostic accuracy in evaluation of portal hypertension in chronic liver disease. Liver Int; 33:62–71.

[30] Tag-Adeen M, Sabra AM, Akazawa Y, et al. (2017): Impact of hepatitis C virus genotype-4 eradication followin g antivirals on liver stiffness measurement. Hepat Med; 9:45–53.

[31] Takuma Y, Nouso K, Morimoto Y, et al. (2013): Measurement of spleen stiffness by acoustic radiation force impulse imaging identifies cirrhotic patients with esophageal varices. Gastroenterology; 144:92–101.

[32] Elkrief L, Rautou PE, Ronot M., et al. (2015): Prospective comparison of spleen and liver stiffness by using shear-wave and transient elastography for detection of portal hypertension in cirrhosis. Radiology; 275: 589–98.

[33] Asrani SK, Talwalkar JA, Kamath PS, et al. (2014): Role of magnetic resonance elastography in compensated and decompensated liver disease. J Hepatol; 60: 934–9.