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Study of non-invasive parameter for detecting esophageal varices in patients of Chronic Liver Disease with special focus on Liver Stiffness Score and aspartate transaminase to platelets ratio index (APRI)

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Abstract

Background: Several investigators have devised non-invasive predictors for presence of esophageal varices (EV) in chronic liver disease (CLD) patients, thus avoiding unnecessary endoscopic screening. Liver stiffness and aspartate transaminase to platelets ratio index (APRI) measurements is good, but still limited tool to noninvasively assess complications and prognosis in patients with advanced liver disease.

Aims and Objective: To evaluate the relation between liver stiffness score and APRI measurement with the presence of EV in patient of portal hypertension in CLD.

Materials and Methods: Hundred and ten compensated CLD patients were studied at Gandhi Medical College and associated Hamidiya Hospital, Bhopal from August 2016 to January 2018. All the patients underwent a fibroscan examination and upper gastrointestinal endoscopy not more than 3 months apart. All patients were grouped based on Varies grades as Grade I (Small straight esophageal varices), Grade II (Enlarged tortuous EV <1/3 of Lumen), Grade III (Large coil shaped EV >1/3 of Lumen) and Grade IV (Cherry red spots with Impending Bleed or active Bleed). Liver stiffness score and APRI were evaluated for all the patients.

Results: Male preponderance (85.3%) was observed with mean of study cohort being 45.55± 12.89 years. Maximum patients had hepatitis B related CLD (43.2%) and belong to child pugh class B (68.2%). Splenomegaly (52.33%) was the most common USG finings. Maximum patients had Grade 3 (36.8%) followed by Grade 4 (28.4%) varices. Patients who had higher varices grading (3-4), more patients had APRI >1.5 (p=0.612). Liver stiffness was positively correlated with the varices grading (r=0.524, p<0.001), similarly APRI was positively correlated (r=529, p=0.012) with liver stiffness.

Conclusion: Present study has found a significant association between fibroscan score, APRI and severity of varices. That means fibroscan score and APRI are important tool for predicting the presence of varices.

Keywords: kPa, splenomegaly, hepatitis b, liver stiffness, ultrasonography, endoscopy, APRI

Introduction

Patients of chronic liver disease (CLD) are accompanied with progressive hepatic fibrosis followed by development cirrhosis. Approximately 10–20% of patients with chronic hepatitis C virus infection have cirrhosis at first clinical presentation, and as many 20–30% of those who do not have cirrhosis will eventually develop this condition and its complications within one or more decades [1]. These complications are liver failure, ascites, variceal bleeding, portal-systemic encephalopathy, and hepatocellular carcinoma [2].

Liver biopsy is the gold standard for assessing hepatic fibrosis. Nevertheless liver biopsy is an invasive and painful procedure and often accompanied with life threatening complications [3]. This has limited its acceptance and use in asymptomatic patients. Because of sampling error and inter observer variability, accuracy of liver biopsy can be questioned [4].

There is need of a non-invasive test that can accurately reflect the full spectrum of hepatic fibrosis, cirrhosis, and its severity in liver diseases. FibroScan is s a novel, rapid, and non-invasive technique which measures liver stiffness [5]. Recent reports have shown that liver stiffness measurement using FibroScan allowed accurate prediction of hepatic fibrosis in patients with chronic hepatitis C virus infection [6]. In patients with chronic hepatitis C liver stiffness measurements ranged from 2.4 to 75 kPa, with a median value of 7.4 kPa [7].

Aspartate transaminase to platelets ratio index (APRI) has an acceptable accuracy for the assessment of liver fibrosis in patients with CLD. Yilmaz *et al.* reported the usefulness of the APRI to assess liver fibrosis in patients with CLD. APRI is a simple and cheap method to ascertain the ratio between AST and platelets and is easy to use in clinical practice [8].

In present study we tried to evaluate the relation between liver stiffness measurement score and presence of EV in patient of portal hypertension in CLD.

Materials and Methods

Present cross-sectional study was performed on 110 patients who had compensated chronic liver disease of any etiology at Gandhi Medical College and associated Hamidiya Hospital, Bhopal from August 2016 to January 2018.

A written informed consent from each patient and Ethical Committee approval of Madhya Pradesh Medical Science University Jabalpur was obtained before starting the study.

Patients who had compensated chronic liver disease of any etiology without a previous history of variceal bleeding and had agreed to undergo both fibroscan examination and a screening of upper gastrointestinal endoscopy, not more than 3 months apart during the study period were identified from the hepatology and endoscopy unit.

Patients diagnosed with Portal Hypertension due to Chronic Liver Disease (Various etiologies) by clinical, biochemical and radiological parameters (ultrasound) having age between 15 - 80 years were included whereas patients with morbid obesity, gross / tense ascites, who are not giving consent or not willing for endoscopy/fribroscan and diagnosed cases of EHPVO and NCPF (Isolated Portal vein pathology) were excluded from the present study.

All the patients were divided based on Japanese classification of UGI grading of varices in to Grade I (Small straight esophageal varices), Grade II (Enlarged tortuous EV <1/3 of Lumen), Grade III (Large coil shaped EV >1/3 of Lumen) and Grade IV (Cherry red spots with Impending Bleed or active Bleed). All the patients had undergone endoscopy by two senior expert gastroenterologist hepatologists. We categorized the endoscopic findings as no varices, small grade 1 and 2 varices, large grade 3 and 4 varices, PHG, gastric varices and both varices.

All the data analysis was performed using IBM SPSS ver. 20 software. Student's t test and one-way ANOVA was used to compare the mean stiffness scores and different variables. The Chi square test for the relation between the stiffness score and the presence of varices.

Results

Mean age of study cohort was 45.55± 12.89 years. Maximum patients belong to age group of 51-60 years (24.76%). Maximum patients were male [64 (85.3%)].

Table 1: Baseline parameters of study cohort (n=110)

Parameters	Mean	SD
Total Bilirubin	2.68	1.70
Direct bilirubin	1.24	0.42
AST	123.91	15.20
ALT	98.15	16.15
Cholesterol	148.56	34.80
HDL	36.21	5.62
VLDL	24.24	6.14
LDL	84.65	8.52
TG	74.21	13.72
Alkaline phosphatase	168.21	23.24
Albumin	2.82	0.42
Globulin	2.42	0.56
PT	22.34	6.98
INR	1.56	0.42
Hb	8.35	1.21
TWBC	7186.94	3542.87
Platelet count	124156.64	54356.33
Na	131.15	3.13
K	3.99	0.34
Urea	39.13	21.69
Creatinine	1.14	0.76
APRI	2.31	1.45
kPA	41.68	18.16
Child Pugh score	8.30	1.54
Varices grading	2.82	0.76

AST; aspartate aminotransferase, ALT; alanine aminotranferease, HDL; high density lipoprotein, VLDL; very low density lipoprotein, LDL; low density lipoprotein, TG; triglyceride, PT; prothrombin time, INR; international normalized ratio, Hb; hemoglobin, Na; sodium concentration, K; potassium concentration

Maximum patients had hepatitis B related CLD (43.2%) and belong to child pugh class B (68.2%). Splenomegaly (52.33%) followed by altered echotexture of liver (24.88%) were the most common USG finings. Maximum patients had Grade 3 (36.8%) followed by Grade 4 (28.4%) varices. Patients who had higher varices grading (3-4), more patients had APRI >1.5 (p=0.612)

Table 2: Comparing KPA cut off of 25 with varices grading

Parameter		KPA		Total	Pearson Chi-Square	P value
		≤25	>25			
Grading of Varices	1	4	6	10	9.076	0.002
	2	8	15	23		
	3	6	37	43		
	4	5	29	34		
Total		23	87	110		

Table 3: Correlation of APRI, Grading, Platelet count, KPA

	Grading of Varices	KPA	Platelet count

KPA	Pearson Correlation	.514**		.001
	Sig. (2-tailed)	<0.001		.996
	N	76		76
APRI	Pearson Correlation	.162	.609	-.457**
	Sig. (2-tailed)	.162	0.02	<0.001
	N	76	76	76

Pearson correlation has revealed that APRI was insignificantly positively correlated with varices grading(r=0.266, p=0.156). Liver stiffness was significantly positively correlated with the varices grading (r=0.524, p<0.001) which means as the liver stiffness increases varices grading also increases. APRI was also significantly positively correlated (r=529, p=0.012) with liver stiffness that mean as the APRI increases liver stiffness also increases.

Discussion

Esophago-gastric varices bleeding is one of the severe complication of CLD [9]. To prevent the bleeding it is very important to fist indentify the patients who are at risk using endoscopic screening in order to initiate prophylactic treatment. [10] Studies have shown that many of the patients with CLD will not have varices; hence screening all the patients using upper GI endoscopy will result in unnecessary endoscopies. This will increase the workload of endoscopy units [11]. Anticipation of presence of EV using non -invasive means will restrict the use of endoscopy in all the patients with CLD [12].

Results of present study have revealed that fibroscan score has shown a significant correlation with the EV grading in endoscopic screening. In agreement to present study findings several authors using different cut off of fibroscan score have also suggested a significant correlation of fibroscan score with EV grading in patients of CLD [13-15]. Castera *et al.* [15] studied 298 consecutive chronic hepatitis C patients and concluded that FibroScan is the most accurate non-invasive method for early detection of cirrhosis. Castera *et al.* used a cut off of 21.5 kPa for the prediction of grade 2-3 varices. Saad *et al.* [14] studied 32 patients to predict EV presence using fibroscan score and reported that using a cutoff of 29.7 on multivariate analysis fibroscan (OR 1.113; p=0.005) was the positive predictors of EV presence. For the detection of large varices Saad *et al.* [14] used a cut off of 38.2 kPa. Results of the Saad *et al.* [14] and Castera *et al.* [15] are in agreement with the present study results where fibroscan score was positively correlated with the varices grading. Kazemi *et al.* [16] studied 165 patients with cirrhosis to find out the relation between the presence of EV assessed by endoscopy, and liver stiffness measurement by Fibroscan and reported that liver stiffness measurement was highly correlated to the grade of EV (r = 0.6, p < 0.0001). Kazemi *et al.* also reported that liver stiffness measurement value < 19 kPa was highly predictive of the absence of EV grade > or = II, which is in agreement to the present study where fibroscan score was positively correlated with the varices grading. In agreement to present study findings Foucher *et al.* studied 711 patients with CLD and reported that stiffness was significantly correlated with fibrosis stage (r = 0.73, p,0.0001) [16]. However all these reports did not show any definite cut off fibroscan score that can be used to predict EV with a great level of surety.

In present study APRI was insignificantly positively correlated with varices grading. Similar reports were depicted by others studies. (Kazemi F 2006, Saad Y 2013, Castera L 2009) Indeed, in Yilmaz *et al*..'s study APRI was significantly associated with fibrosis scores in subjects with chronic hepatitis C (p = 0.0059) but not in those with chronic hepatitis B (p = 0.1495). Similar reports were reveled in present study most of the patients were of chronic hepatitis B. Yilmaz *et al.* also reported that APRI may be a useful asset in clinical practice to identify the natural course of NAFLD as it approaches the advanced stages [8].

The present study had few limitation of being less in sample size; a large randomized clinical trial is needed to strengthen the present study findings. Cross sectional nature was another limitation which restricts the use of present study findings to large population.

Conclusion

Present study results have shown that fibroscan score can has significant role in predicting the presence of EV in patients with CLD. Though insignificant but APRI may be a useful asset in clinical practice for assessing varices grading. Present study has also found a significant association between fibroscan score and severity of varices.

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