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Use of non-invasive methods for the assessment of advancement of liver fibrosis in patients with chronic liver disease

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Abstract
Background: Chronic liver diseases (CLD) cause significant morbidity and mortality worldwide. Liver biopsy is the gold standard for assessment of liver fibrosis. There is a need to non-invasive methods for assessment of advancement in liver fibrosis.
Aims and Objectives: To compare the findings of fibroscan score with FIB-4 scores, APRI scores and AST/ALT Ratio.
Materials and Methods: Seventy six patients of CLD confirmed using abdominal ultrasound examination, biochemical and radiological parameters were studies at Dept. of Medicine, Gandhi Medical College/ Hamidia Hospital Bhopal from 2016 to 2018. Detailed demography including age and sex was obtained from each patient. Fibroscan examinations, serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST) and serum creatinine were measured. Estimation of AST/ALT ratio, APRI score and FIB-4 was also estimated for the study cohort.
Results: Male preponderance (84.2%) was observed with mean age of 44.51± 14.89 years. Mean Stiffness score was 42.70±20.86. Mean AST/ALT Ratio, APRI and FIB-4 Score was 1.84±2.62, 2.24±2.77 and 5.20±4.05 respectively. Majority of the patients had stage F4 of liver fibrosis (82.89%). Stiffness score, APRI and FIB-4 score was significantly higher in patients who were having liver fibrosis stage of >F2 as compared to patients who had stage of ≤F2 ($p<0.05$). Pearson correlation revealed that FIB-4 score ($r=0.422$, $p=0.022$), AST/ALT Ratio ($r=0.352$, $p=0.012$) and APRI ($r=0.519$, $p=0.026$) were positively correlated with the stiffness score.
Conclusion: The prevalence of advanced liver fibrosis is high. There is need of early diagnosis. Fibroscan along with serum markers including FIB-4 scores, APRI scores has been shown to be helpful for the diagnosis of advancement of fibrosis.

Keywords: chronic liver disease, stiffness score, liver fibrosis, fibroscan examinations

Introduction

In chronic liver disease (CLD) patients assessment of liver fibrosis advancement plays a very important role in predicting prognosis and outcome of the disease. Though liver biopsy is considered as the gold standard for the assessment of liver fibrosis in CLD patients, it has its limitations which also include the life-threatening complications [1, 2].

During the past decade, several advancement in the field of non-invasive and radiological testing has been evolved for the assessment of liver fibrosis in CLD patients. These non-invasive methods eliminate the limitation of liver biopsy [1, 2].

AST/ALT ratio, the AST platelet ratio index (APRI), and the Fibrosis 4 (FIB-4) score are important non-invasive methods for the assessment of assessment of liver fibrosis. Fibroscan which is an ultrasound technique is one of the most commonly used non-invasive methods for the assessment of assessment of liver fibrosis [3-5]. However fibroscane has limitation in obesity, as the diagnostic yield is limited. However this limitation has been overcome with the use of XL probe for patients with body mass indices (BMIs) of greater than 30 kg/m [2, 6, 7].

In present study we tried to compare the results of Fibroscan with FIB-4 scores, APRI scores, and AST/ALT ratios in CLD patients from one of the tertiary centre of central India.

Materials and Method

The present observational study was performed on 76 patients of chronic liver disease at Dept. of Medicine, Gandhi Medical College/ Hamidia Hospital Bhopal from 2016 to 2018 after getting approval from Madhya Pradesh Medical Science University Jabalpur, Ethical Committee.

Confirmation of chronic liver disease was done using abdominal ultrasound examination, biochemical and radiological parameters. Serum liver enzyme testing was also performed at the department.

Patients diagnosed with portal hypertension due to CLD of various etiologies by Clinical, biochemical and radiological parameters (ultrasound) having age between 15 - 80 years were included.

Patients with morbid Obesity, gross / tense Ascites, patient who are not giving consent or not willing for endoscopy/fibroscan and diagnosed cases of EHPVO and NCPF (Isolated Portal vein pathology) were excluded from the present study.

Demographic data on sex and age were obtained and recorded from each patient.

Included patients had undergone Fibroscan examinations within the study period. Estimation of serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST) and serum creatinine were measured as per the Akbar *et al.* study. (Akbar HO 2010)

Estimation of AST/ALT ratio was also done, and the APRI score was determined by using the following equation

$$APRI = \frac{\text{AST Level}/(/\text{ULN})}{\text{Platelet Counts (109/L)} \times 100}$$

FIB-4 was determined by using the following formula

$$\text{FIB} - 4 = \frac{\text{Age (y)} \times \text{AST (U/L)}}{\text{Platelet Count109/L} \times \sqrt{\text{ALT (U/L)}}}$$

All the data analysis was performed using IBM SPSS ver. 20 software. Frequency distribution was used to prepare the tables. Quantitative data is expressed as mean ± SD whereas categorical data is expressed as percentage. Student t test was used to compare the means. Correlation was obtained using pearson equation. P value of <0.05 is considered as significant.

Results

Mean age of patients in study cohort was 44.51± 14.89 years which ranged from 12 to 76 years. Majority of the CLD patients were of 51-60 years (23.68%). Majority of the patients were male (84.2%).

In present study majority of the patients were suffering from hepatitis B related CLD (42.1%) followed by alcoholic liver disease (19.75) and hepatitis C related CLD (17.1%).

Mean Stiffness score was 42.70±20.86. Mean AST/ALT Ratio, APRI and FIB-4 Score was 1.84±2.62, 2.24±2.77 and 5.20±4.05 respectively.

Table 1: Distribution of Patients According to the Stage of Liver Fibrosis

Stage of Liver Fibrosis	Frequency	Percent
F0 (0-5.9)	4	5.26
F1 (6-6.9)	6	7.89
F2 (7-9)	2	2.6
F3 (9.1-10.3)	1	1.3
F4 (>10.4)	63	82.89
Total	76	100.0

Table 2: Showing means Laboratory Test values

Laboratory Test	Mean
AST (SGOT)	117.89±337.28
ALT (SGPT)	97.96±297.09

Table 3: Differences in Stiffness Scores, Aspartate Aminotransferase/Alanine Transaminase Ratio, Aspartate Aminotransferase to Platelet Ratio Index, and FIB-4 Scores between Patients with Mild to Moderate Fibrosis and Those with Advanced Fibrosis

Variables	>F2	≤F2	P value
Stiffness score	43.64±20.33	7.95±1.06	0.016
AST/ALT Ratio	1.86±2.65	0.91±0.007	0.616
APRI	2.68±2.42	0.74±0.38	0.021
FIB-4 score	5.30±4.06	1.34±0.75	0.002

Data is expressed as mean ± SD

Table 4: Showing Correlation between Fibrosis Scores on Fibroscan with FIB-4 score, AST/ALT Ratio and APRI

		FIB-4 Score	AST/ALT Ratio	APRI
Stiffness score	Pearson Correlation (r)	0.422	0.352	0.519
	P value	0.022	0.012	0.026
	No of patient	76	76	76

Discussion

In present study fibroscan examinations has revealed high prevalence of CLD with advanced stages of liver fibrosis. A strong positive correlation between stiffness score and AST/ALT ratio, APRI scores, and FIB-4 scores has provided further strength to this finding.

The present study finding of high prevalence of advanced stage of liver fibrosis in CLD patients is higher than the report of previous study [4, 5, 8] findings where previous authors have used fibroscan examinations to assess liver fibrosis. These higher rates are alarming for the Indian population where prevalence of diabetes population and metabolic syndrome is very high [9]. These higher rate of advanced fibrosis may be due to the fact that in present study majority of the patients had CLD.

In present study all CLD patients had undergone baseline abdominal ultrasound examinations that showed steatosis. However, the ultrasound alone is not efficient in the assessment of advancement of liver disease. A previous study by Razavizade *et al.* showed that using serum markers along with ultrasound examination has helped the author to categorize the NAFLD patients in to mild, moderate and severe NAFLD [10]. That means use of serum markers such as Mean AST/ALT Ratio, APRI and FIB-4 Score and stiffness score in addition to ultrasound provide assessment of NAFLD when more advanced methods are not available.

In present study advanced fibrosis was more common among the male patients who were in the fourth decade of their life. This may be due to the fact that male patients are more prone to chronic liver disease of most etiologies as reveled in the study done by Shimizu *et al.* and Miyagi *et al.* [11, 12] However Poordad *et al.* also explained the protective effect of female sex hormone on the progression of hepatic fibrosis [13] which again strengthen the male preponderance findings in advanced fibrosis in present study.

Out of four non invasive methods investigated in present study, AST/ALT ratio was has shown no difference in advancement of fibrosis that means AST/ALT ratio has failed to show any significant difference between mild to moderate and advanced fibrosis. Consequently Fibroscan examinations,

APRI scores, and FIB-4 score were proved to be useful in detecting advancement in CLD. However, previous studies have shown the usefulness of these non-invasive markers in the treatment of CLD [14, 15].

There were few limitations of the study; small sample and cross sectional nature were the main; a large clinical trial is needed to strengthen the present study findings.

Conclusion

The high prevalence of advanced fibrosis found is present study is the alarming signal. There is a need of national level program for the recognition of CLD in order to reduce the progression of liver disease. Our study has shown that all four non-invasive methods along with the ultrasound examination provide valuable information for the diagnosis of advancement of fibrosis in CLD patients. Non-invasive nature can also prevent the use of liver biopsy in those CLD patients where clear indication is present.

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