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COMPARISON OF APRI AND FIB-4 INDICES WITH ELASTOGRAPHY FOR NON INVASIVE ASSESSMENT OF LIVER INJURY IN CHRONIC HEPATITIS B: A COMPARATIVE RETROSPECTIVE STUDY IN A TERTIARY HEALTHCARE SETUP IN SOUTHERN ASSAM

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ABSTRACT

Background: Chronic hepatitis B is a global health problem with risk of progression to liver fibrosis, cirrhosis and hepatocellular carcinoma. Liver biopsy is the gold standard for the detection of liver fibrosis, but has limitations such as invasive procedure, high cost, risk of rare but potentially life-threatening complications. Non-invasive indices like aspartate transaminase to platelet ratio index (APRI) and fibrosis 4 (FIB-4) are increasingly used for identifying liver fibrosis and cirrhosis in patients with chronic hepatitis B virus (HBV)infection.
Objectives: To evaluate and compare the diagnostic performance of APRI and FIB 4 indices with elastography in assessment of liver fibrosis in patients with chronic hepatitis B(CHB).
Materials and methods: We conducted a comparative retrospective study on 87 patients with chronic hepatitis B at a tertiary care center in southern Assam.
Result and observation: In the present study, 87 patients were evaluated, with a predominance of males and a mean age of 40.72±13.73 years. Most patients had early stages of fibrosis on elastography, although nearly one third had significant fibrosis(>=F2). A significant association was observed between fibrosis stage and elastography categories (p=0.0001), confirming the reliability of elastography in staging liver fibrosis. Both APRI and FIB 4 showed a significant positive correlation with liver stiffness values (APRI r=0.311, p=0.003, FIB4r =0.307, p=0.004). ANOVA analysis also demonstrated significant differences in APRI and FIB-4 levels across fibrosis stages. ROC analysis showed moderate diagnostic performance of APRI and FIB -4 for detecting significant fibrosis, while both markers performed better in identifying advanced fibrosis. Agreement analysis revealed poor agreement between APRI and elastography, whereas FIB-4 showed fair agreement and a stronger association with elastography findings.
Conclusion: APRI and FIB 4 are useful noninvasive markers for assessment of liver fibrosis in chronic hepatitis B. Both scores correlate with elastography findings, but FIB 4 demonstrates better diagnostic performance and agreement with elastography making it a more reliable tool in clinical practice.

Keywords: *Chronic hepatitis B, APRI, FIB-4, elastography, liver fibrosis, non-invasive markers.*

INTRODUCTION

The World Health Organization estimated that the number of people exposed to the hepatitis B virus to be approximately 2 billion; 240 million of whom are chronic carriers worldwide (2). The spectrum of liver disease in people with chronic

hepatitis B ranges from minimal fibrosis to cirrhosis and hepatocellular carcinoma. The natural history of chronic hepatitis B has various phases and is dynamic, requiring lifelong monitoring and, potentially, antiviral treatment (1). Persistent viral replication leads to continuous necroinflammation and patients are at higher risk of cirrhosis, end-stage liver disease, hepatic decompensation, and hepatocellular carcinoma (HCC) (2). Complications of chronic liver damage from HBV include liver fibrosis, which can lead to cirrhosis, hepatic failure, and hepatocellular carcinoma (HCC). Fibrotic changes in the liver are part of functional and structural variations in chronic liver diseases (4). Antiviral treatment can suppress HBV replication and prevent progression of CHB to cirrhosis, HCC, and death. The indications for antiviral treatment mainly based on the combination of hepatitis B virus e antigen (HBeAg) status, HBV DNA levels, alanine transaminase (ALT) levels, and severity of liver histological changes. Liver biopsy is the gold standard for the detection of liver fibrosis, but has limitations such as invasive procedure, high cost, risk of rare but potentially life-threatening complications, and so on (3). Fibroscan, which measures liver stiffness, is increasingly being recognized as an excellent tool for the diagnosis of liver fibrosis because of its high diagnostic performance. However, the Fibroscan device is expensive (3). Among serum fibrosis models, aspartate transaminase-to-platelet ratio index (APRI) and fibrosis index based on four factors (FIB- 4) are commonly used for identifying liver fibrosis and cirrhosis in patients with chronic hepatitis B virus infection.

A number of studies have also described that APRI and FIB4 are suitable markers for detecting significant fibrosis and ci rrhosis in Chronic Hepatitis B patients (3). Recent WHO HBV guidelines recommend APRI as the preferred non-invasive test to assess for the presence of cirrhosis in resource-limited settings (3). The diagnostic performances and cut-offs of APRI and FIB-4 for the diagnosis of significant fibrosis and cirrhosis were controversial, although they have been recommended by the recent WHO HBV guidelines (3). Evaluation of Liver Fibrosis stages have been improved by the fibrosis-4 (FIB-4) index, transient elastography ultrasound (Fibroscan), and platelet to aspartate aminotransferase ratio index (APRI). APRI and FIB-4 are recommended as non-invasive methods to designate the Liver Fibrosis stages in countries with limited resources by the WHO and several guidelines (4).

AIMS AND OBJECTIVES

1. To study APRI, FIB-4 and elastography results in Chronic Hepatitis B patients.
2. To compare APRI, FIB-4 indices with elastography results in Chronic Hepatitis B patients.

MATERIALS AND METHODS

Study Setting:

The study was conducted in the Department of Medicine, Silchar Medical College and Hospital, Silchar, Assam. Located in the district of Cachar, in the southwestern part of Assam, it is the only tertiary care hospital in the Barak Valley, catering to the health care of not only the patients of this valley but also patients from the neighbouring states of Tripura, Mizoram, Manipur and Meghalaya.

PERIOD OF STUDY:

The present study was for a period of one year.

SAMPLE SIZE: The sample size was 87.

STUDY DESIGN: The study is a hospital based comparative retrospective study.

Method of collection of data :- All the patients attending the outdoor and indoor of the Department of Medicine of Silchar Medical College & Hospital with features suggestive of Chronic Hepatits B Virus Infection were included. Data including age, sex was recorded. Diabetes melllitus was recorded from documentation in medical chart or blood values of fasting glucose more than 126 mg/dl or HbA1c more than 6.5%.

Blood level of liver enzymes (AST, ALT), Platelet, Haemoglobin, WBC, Bilirubin, Albumin, serum creatinine, APRI, FIB 4 SCORE, USG W/A, PT -INR was recorded. FIB 4 and APRI Score indices were compared with elastography results in Chronic Hepatits B patients.

INCLUSION CRITERIA

1.Chronic Hepatitis B Patients.
2.Age more than 18years.

EXCLUSION CRITERIA

1.Malignancies
2.Coinfection with other viruses
3.Organ failure

Statistical analysis : Data was entered using Microsoft Excel and exported to SPSS version 26.0. Analysis of data was done based on descriptive statistics.

RESULT AND OBSERVATION

A total 87 patients were included in the study. There was male predominance with male to female ratio of 71: 16. The mean age was 40.72±13.73 years. AST (185±398 IU/L) and ALT (169±291 IU/L) show very high standard deviations. Platelet count (26.8±29.2×10-3/ µl) is markedly low with wide variability, supporting portal hypertension/ advanced fibrosis in a subset. Mean liver stiffness (kPa) is 5.34±2.67, but distribution shows clustering in low fibrosis with a tail toward advanced fibrosis. Mean APRI and FIB-4 scores were 1.63±2.97 and 17.25±138.88, respectively.

Table 1: Baseline characteristics

		Mean	SD
Sex (M:F)	71:16		
AGE		40.72	13.73
AST		185.38	397.85
ALT		169.06	291.23
PLATELET_COUNT (/10^3)		26.77	29.23
kPa		5.34	2.67
APRI		1.63	2.97
FIB4		17.25	138.88

Table 2: Distribution of fibrosis stage by elastography

Elastography	Frequency	Percent
Low (<7)	70	80.5
Borderline (7-9.5)	9	10.3
High (9.5-12.5)	4	4.6
Extremely high (>12.5)	4	4.6
Total	87	100

F	Frequency	Percent
F0-F1	32	36.8
F1-F2	27	31
F2-F3	23	26.4
F3-F4	5	5.7
Total	87	100

Most patients have early fibrosis and nearly one third have have significant fibrosis (≥F2).

Table 3: Association between fibrosis stage and elastography

	Elastography					Chi-Square Tests
F	Low (<7)	Borderline (7-9.5)	High (9.5-12.5)	Extremely high (>12.5)	Total	P value
F0-F1	32	0	0	0	32	0.0001
F1-F2	27	0	0	0	27	
F2-F3	10	9	4	0	23	
F3-F4	1	0	0	4	5	
Total	70	9	4	4	87	

Table 4: Correlation of APRI and FIB-4 with elastography values

Correlations Pearson		
	kPa	P value**
APRI	0.311	0.003
FIB4	0.307	0.004

Correlation is significant at the 0.01 level (2-tailed).

A Chi-square test showed a significant association between fibrosis stage and elastography categories(p=0.0001), indicating non random distribution across stages. Pearson correlation showed a significant positive correlation between liver stiffness (kPa) and APRI (r=0.311,p=0.003) and FIB-4(r=0.307,p=0.004)

Table 5: ANOVA Marker levels across fibrosis stages.

	APRI		FIB4	
F	Mean	SD	Mean	SD
F0-F1	0.64	1.00	1.37	0.80
F1-F2	1.71	4.18	1.98	1.50
F2-F3	2.32	2.54	3.64	2.92
F3-F4	4.42	3.52	263.92	577.82

ANOVA F value	3.337		6.687	
P value	0.023		0.0001	

ANOVA demonstrated a significant difference in APRI values across fibrosis stages (F=3.337, p=0.023) and a highly significant difference in FIB-4 values (F=6.687, p=0.0001)

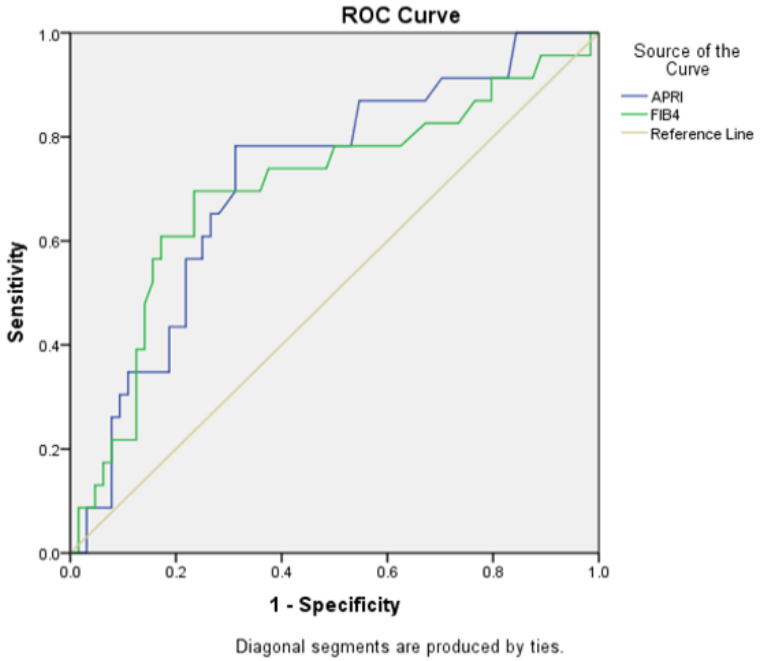

FIGURE 1:

ROC curve analysis for detection of significant fibrosis (F2-F3) showed an AUC of 0.718(p=0.002) for APRI and 0.701 (p=0.004) for FIB-4. At a cutoff of 0.215, APRI demonstrated a sensitivity of 91% and specificity of 17%. FIB-4 at cutoff0.34, showed sensitivity of 96% and specificity of 98%.

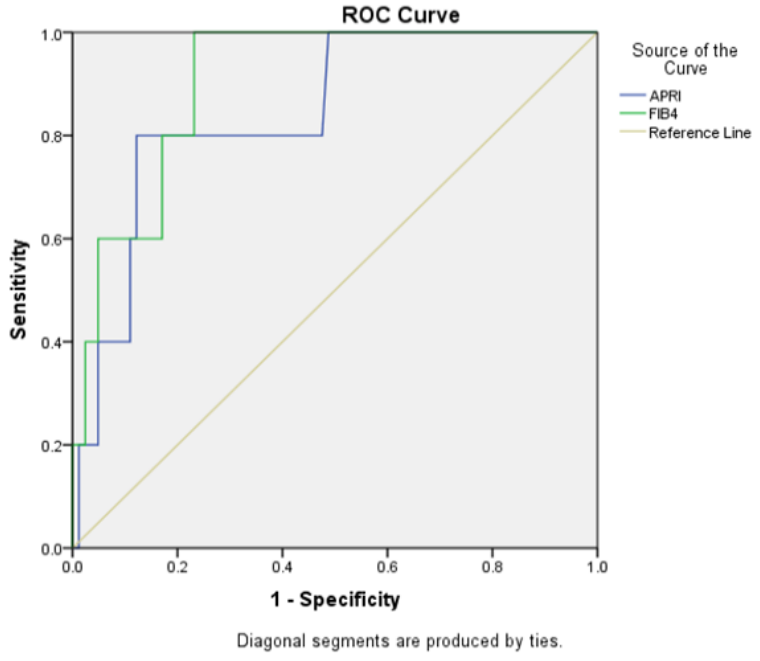

Figure : 2

ROC analysis for detection of advanced fibrosis (F3-F4) showed an AUC of 0.845 (p=0.01) for APRI and 0.905 (p=0.002) for FIB-4. Both scores demonstrated 80% sensitivity, with higher specificity for FIB-4 (77%).

Table 6: Agreement between APRI and elastography

	Elastography					Chi-Square Tests
APRI_score	Low (<7)	Borderline (7-9.5)	High (9.5-12.5)	Extremely high (>12.5)	Total	P value
Low	56	6	2	1	65	0.082
Borderline	2	1	0	0	3	
High	12	2	2	3	19	
Total	70	9	4	4	87	

Measure of Agreement	Value	SD	Approx. T	Approx. P value	
Kappa	0.165	0.082	2.484	0.013	

Table 7: Agreement between FIB-4 and elastography

	Elastography					Chi-Square Tests
FIB4_score	Low (<7)	Borderline (7-9.5)	High (9.5-12.5)	Extremely high (>12.5)	Total	P value
Low	54	7	0	0	61	0.0001
Borderline	5	1	0	1	7	
High	11	1	4	3	19	
Total	70	9	4	4	87	

Measure of Agreement	Value	Asymp. Std. Error	Approx. T	Approx. P value
Kappa	0.229	0.084	3.417	0.001

Chi-square analysis showed no significant association between APRI categories and elastography (p=0.082). Agreement analysis revealed poor but statistically significant agreement (k=0.165, p=0.013). A significant association was observed between FIB-4 categories and elastography (p=0.0001). Kappa analysis showed fair agreement (k=0.229, p=0.001)

DISCUSSION

Assessment of liver fibrosis is important in patients with chronic hepatitis B for disease monitoring and treatment decisions. In the present study, 87 patients were evaluated, with a predominance of males and a mean age of 40.72±13.73 years. Most patients had early stages of fibrosis on elastography, although nearly one third had significant fibrosis (>= F2).

A significant association was observed between fibrosis stage and elastography categories (p=0.0001), confirming the reliability of elastography in staging liver fibrosis. Both APRI and FIB 4 showed a significant positive correlation with liver stiffness values (APRI r=0.311, p=0.003, FIB4 r=0.307, p=0.004). ANOVA analysis also demonstrated significant differences in APRI and FIB-4 levels across fibrosis stages.

ROC analysis showed moderate diagnostic performance of APRI and FIB -4 for detecting significant fibrosis, while both markers performed better in identifying advanced fibrosis. Agreement analysis revealed poor agreement between APRI and elastography, whereas FIB-4 showed fair agreement and a stronger association with elastography findings.

CONCLUSION

APRI and FIB-4 are useful noninvasive markers for assessment of liver fibrosis in chronic hepatitis B. Both the scores correlate with elastography findings, but FIB 4 demonstrated better diagnostic performance and agreement with elastography. Therefore, FIB-4 may serve as a more reliable and practical tool for identifying significant and advanced fibrosis in clinical practice.

STUDY LIMITATIONS

1. Small sample size- the study included a relatively small number of patients (n=87), which may limit the generalizability of the findings to the broader population of patients with chronic hepatitis B
2. Single centre study – As the study was conducted at a single centre, the results may not fully represent patients from different geographic or clinical settings
3. Absence of liver biopsy – Liver biopsy, the gold standard for fibrosis assessment, was not performed. Elastography was used as the reference method, which may introduce some degree of measurement variability.
4. Cross sectional design- The study evaluated patients at a single point in time, so progression of fibrosis and long term predictive value of APRI and FIB -4 could not be assessed.
5. Biochemical variability – wide variability in AST, ALT and platelet count may have influenced the calculated APRI and FIB- 4 scores, potentially affecting their diagnostic accuracy.

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