

# APRI and FIB-4 performance to assess liver fibrosis against predefined Fibroscan values in chronic hepatitis C virus infection

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## ABSTRACT

**Backgrounds and Aims:** Chronic hepatitis C (CHC) infection can lead to chronic liver disease, fibrosis, then cirrhosis, and, finally, hepatocellular carcinoma (HCC); moreover, it is the most common indication for liver transplantation. Liver biopsy is still the gold standard method for the staging of liver fibrosis as it is an invasive procedure with complications. There are some noninvasive methods such as fibroscan that are now the investigation of choice; FIB-4 and aminotransferase to platelet ratio index (APRI) are other noninvasive tools to assess liver fibrosis by using aspartate aminotransferase (AST), alanine aminotransferase (ALT), platelet count, and age. This study aims to evaluate the efficacy and performance of FIB-4 and APRI against fibroscan in patients infected with the hepatitis C virus. **Method:** It is a cross-sectional study that was conducted in a tertiary health care center in Uttar Pradesh, India, from January 2017 to January 2020. Fibroscan was done for all patients. A blood sample was used to determine AST, ALT, and platelet count. FIB-4 and APRI were calculated from laboratory data. **Result:** 187 of the 487 patients in the study have F0-F1 fibrosis, 69 have F2, 53 have F3 fibrosis, and 178 have cirrhosis. Based on receiver operating characteristic (ROC) analysis, single optimum cut-offs for diagnosing significant fibrosis and cirrhosis were 1.2 for APRI and 2.25 for FIB-4. **Conclusions:** Compared with Fibroscan, APRI and FIB-4 showed good performance in detecting the patients without liver fibrosis as well as satisfactory performance in detecting significant fibrosis. These scores should be used in combination with other noninvasive scores for an accurate assessment of liver fibrosis.

**Keywords:** APRI, chronic hepatitis C (CHC), cirrhosis, FIB-4, fibrosis

## Introduction

Hepatitis C virus (HCV) was identified in 1989 as a major cause of parenterally transmitted hepatitis and was known as non-A non-B (NANB) hepatitis, later known as HCV. The

estimated global prevalence of HCV infection is 2%–3% and affects 122–185 million people worldwide.<sup>[1]</sup> It is characterized by varying degrees of inflammation and hepatic fibrosis. HCV infection causes injury to liver cells that can manifest as both acute and chronic hepatitis. Acute HCV infection is mostly asymptomatic with symptoms of mild viral illness for few weeks and occasionally jaundice. Chronic hepatitis C (CHC) infection can present as an incidental finding in laboratory investigations. After acute HCV infection, between 15% and 25% of the patients get spontaneous clearance of virus and the rest develop chronic infection. Chronic hepatitis C infection leads to liver

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Received: 08-04-2021

Revised: 08-07-2021

Accepted: 10-07-2021

Published: 29-11-2021

### Access this article online

#### Quick Response Code:



Website:  
www.jfmpc.com

DOI:  
10.4103/jfmpc.jfmpc\_666\_21

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**How to cite this article:** Rungta S, Kumari S, Deep A, Verma K, Swaroop S. APRI and FIB-4 performance to assess liver fibrosis against predefined Fibroscan values in chronic hepatitis C virus infection. J Family Med Prim Care 2021;10:4082-8.

fibrosis in about 20 to 25 years and then causes the accelerated progression of fibrosis to cirrhosis, decompensation, HCC, and death.<sup>[2]</sup> The management of chronic hepatitis C infection and its related complication is predominantly dependent upon the degree of liver fibrosis.

According to the European Association for the Study of the Liver guideline, staging of hepatic fibrosis is done by meta-analysis of histological data in viral hepatitis through METAVIR scoring system for which liver biopsy is required while histological staging is observer-dependent analysis.<sup>[3]</sup> Liver biopsy is still the gold standard but procedure-related complications, contraindications, small sample size, and observer dependency makes it less popular.<sup>[4]</sup>

Fibroscan has emerged as a new tool for liver stiffness assessment. It is a noninvasive method based on vibration-controlled transient elastography (VCTE) technique and has sensitivity and specificity of 87% and 91% respectively for detecting liver cirrhosis in CHC infection; however, it has some flaws, e.g. it cannot assess liver stiffness accurately in presence of ascites, high intra-abdominal fat (BMI >30 kg/m<sup>2</sup>), acute hepatitis (SGPT >200 U/L), etc.<sup>[5]</sup>

Due to its high cost and non-availability at primary and community health centers in India, many scholars reevaluate some existing fibrosis scores to categorize liver fibrosis. Fibrosis-4 index (FIB-4) and aspartate aminotransferase (AST) to platelet ratio index (APRI) are the most studied and extensively used fibrosis scores, which are calculated using relatively inexpensive and easily available laboratory tests using blood samples. The cut-off values of FIB-4 and APRI for significant fibrosis and cirrhosis were studied and defined against the METAVIR scoring system [Table 1].<sup>[6]</sup> The present study has aimed to evaluate the effectiveness of FIB-4 and APRI to differentiate stages of liver fibrosis against fibroscan-based staging of liver stiffness in chronic hepatitis C infection.

## Materials and Methods

This is a cross-sectional study performed from January 2017 to January 2020 in the Department of Medical Gastroenterology, King George Medical University, Lucknow, Uttar Pradesh, India. During the study period, 487 patients (aged of maximum 71 years) with a confirmed diagnosis of HCV infection, diagnosed by detecting anti-HCV antibodies by enzyme-linked immunosorbent assay (ELISA), were enrolled. Hepatitis C infection was further evaluated for quantitative HCV RNA by RT-PCR assay.

All patients were asked about their exposure to risk factors (i.e. drug addiction, blood transfusion, major or minor surgeries, etc.), presence of ascites, jaundice, hematemesis, melena, pedal edema, easy bruising, bleeding gums, and recent use of any alternative medicine or alcohol.

Patient's history, physical examination, hematological and biochemical investigations (e.g. hemogram), liver function tests,

**Table 1: Demographic and laboratory characteristics of the study population**

Character	Value
Females	265 (54.41%)
Males	222 (45.58%)
Age (Mean±SD) in years	42.41±14.46
AST (IU/L)	54.96±23.33
ALT (IU/L)	55.18±22.67
Platelets (10 <sup>9</sup> /L)	173.25±111.27
Protein (g/dl)	7.79±0.81
Albumin (g/dl)	4.02±0.67
Fibroscan value (kPa)	16.12±10.43
Stages of liver fibrosis as per fibroscan, n (%)	
F0-F1 (<7 kPa)	187 (38.39%)
F2 (7-8.99 kPa)	69 (14.16%)
F3 (9-12.49 kPa)	53 (10.88%)
F4 (≥12.5 kPa)	178 (36.55%)
APRI score (Median)	1.10 (0.09-27.86)
FIB-4 score (Median)	2.26 (0.18-40.06)
Fibroscan score (Median)	8.50 (2.6-75)

ALT: alanine aminotransferase, AST: aspartate aminotransferase, APRI: aspartate aminotransferase-to-platelet ratio Index, FIB-4: fibrosis index based on four factors.

serum protein and albumin tests, ultrasonography (USG), and transient elastography (TE) were done in all the patients. Patients with the presence of other causes of liver disease, HCC, prior interferon therapy, human immunodeficiency virus (HIV) and co-infected with HBV, and liver transplantation were excluded from the study.

## Laboratory methods

Hematological and biochemical parameters were determined using commercially available assays. All patients' samples were tested for HBsAg by using commercial ELISA kits, and anti-HCV by a third-generation ELISA kit (Abbott HCV EIA, Abbott laboratories, Chicago, IL, USA). Anti-HCV-positive subjects were further investigated for quantitative HCV RNA by reverse transcription-polymerase chain reaction (RT-PCR), and PCR product was subjected to nucleotide sequencing to identify the HCV genotype (Applied Biosystems, CA, USA).

## Liver stiffness evaluation

All patients included in this study underwent fibroscan (transient elastography) examination (equipment: Fibroscan, 402 with VCTE technology).

## Liver fibrosis stages were categorized based on the fibroscan score as follows:

Stage F0–F1 (No or Mild fibrosis) (<7 kPa), Stage F2 (Moderate fibrosis) (7–8.99 kPa), Stage F3 (Severe fibrosis) (9–12.49 kPa), and Stage F4 (cirrhosis) (≥12.5 kPa).

## Quantification of liver fibrosis

Based on laboratory findings, FIB-4 and APRI scores were calculated for each patient and the values were rounded to two decimal places. Based on the available data from the scientific

literature, the lower and upper cut-off values of 1.45 and 3.25, respectively, for FIB-4 and 0.5 and 1.5, respectively, for APRI were used to predict patients with significant fibrosis. However, 1.0 and 2.0 are the lower and upper cut-off values, respectively, of APRI to detect cirrhosis, while for FIB-4, no cut-off value was found to be satisfactory to detect cirrhosis.<sup>[6,7]</sup>

APRI AND FIB-4 formula:

The scores were calculated by the following formulas:

FIB-4 score = Age (years) \* AST (IU/L)/Platelet count ( $10^9/L$ ) \* ALT (IU/L)<sup>1/2</sup> [Soderberg C 2010]<sup>[8]</sup>

APRI =  $\{ \{ \text{AST (IU/L)} / \text{Upper normal limit of AST (IU/L)} \} / \text{Platelet count (} 10^9/L \text{)} \}$  [Chalasani N. 2012]<sup>[9]</sup>

### Patient categorization according to fibrosis stages

As liver cirrhosis is the driving factor in CHC infection to determine treatment regimen, duration, and follow-up strategy, the test should be able to differentiate the maximum number of cirrhotic (F4) and advanced fibrosis (F3) from normal or early staged (F1 and F2) fibrotic patients. So, patients were categorized into two groups based on fibrosis stages of the fibroscan score.

The first group, named mild fibrosis, included patients with normal fibroscan and mild fibrosis (F0–F1, F2 fibrosis), and the second group, named significant fibrosis, included patients with advanced fibrosis and cirrhosis (F3 and F4 fibrosis).

A single cut-off for both APRI and FIB-4 is sought, at which sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) are at their highest. Both of the procedures used in the study were compliant with the Helsinki Declaration of 1975, as updated in 2008, and the ethical guidelines of the responsible committees on human experimentation (institutional and national). The information was processed anonymously.

### Statistical analysis

IBM's SPSS Statistics version 24.0 Software was utilized to conduct statistical analysis and to graph the data. For descriptive analysis, median and interquartile range (IQR) were obtained for non-parametric continuous variables, and percentages and numbers were obtained for categorical variables. The statistical significance of the difference between the variables was computed using a *t*-test. The *t*-test was used to compare the age distribution between the two subgroups formed to assess the performance of tests. Diagnostic performance of APRI and FIB-4 score was measured by area under the receiver operating characteristic (ROC) curve. The balance between sensitivity (Se) and specificity (Sp) for a particular value of the test to rule out or rule in the patients of interest was obtained from the coordinates

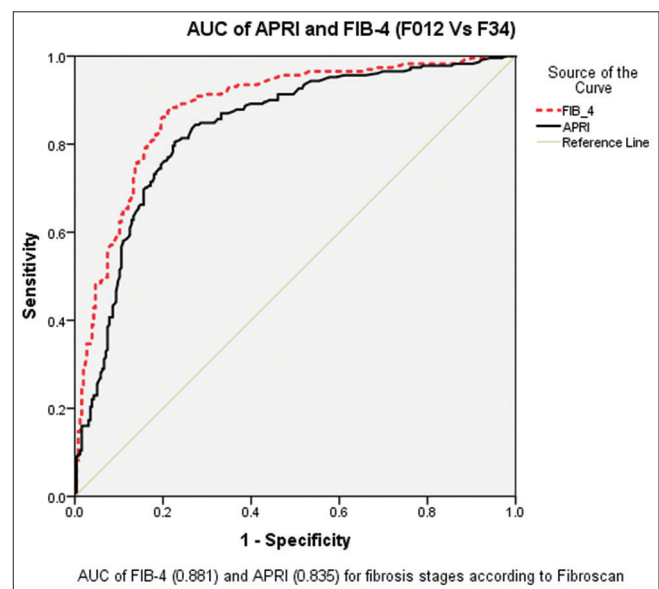
of the curve. Positive predictive values (PPV) and negative predictive values (NPV) were also obtained for the cut-off value of the test. Statistical significance was defined as  $P < 0.05$ .

## Results

Four hundred eighty-seven patients with CHC had undergone liver stiffness testing by fibroscan during the study period. Females were more than males (54% vs. 45%) in the study population, and the mean age of the population was 42 years. The mean fibroscan score was  $16.12 \pm 10.43$  kPa, the median APRI score was 1.10 with 95% CI (0.09–27.86), and the median FIB-4 score was 2.26 with 95% CI (0.18–31.4). Patients with different stages of liver fibrosis were found as follows: 187 (38.39%) patients in stage F0–F1, 69 (14.16%) patients in stage F2, 53 (10.88%) patients in stage F3, and 187 (36.55%) patients in stage F4 [Table 1].

For study purposes, we divide the study population into two groups based on liver stiffness stages, i.e. mild fibrosis and advanced fibrosis. The area under the curve (AUC) was obtained for each group through the receiver operating curve (ROC) analysis that was found statistically significant.

APRI differentiated advanced fibrosis ( $P < 0.0001$ ) with AUC mean (95% CI) 0.835 (0.798–0.871) [Table 2, Figure 1]. The values corresponding to FIB-4 score are even better than APRI evaluation, with AUC mean (95% CI) 0.881 (0.850–0.912) ( $P < 0.0001$ ) for advanced fibrosis. [Table 2, Figure 1]. Both the tests have proven good to diagnose fibrosis, but FIB-4 has more AUC than APRI in each set; therefore, FIB-4 is better than APRI [Table 2, Figure 1].



**Figure 1:** Performance of FIB-4 and APRI on receiver operating curve for liver fibrosis stages based on fibroscan with (b) group mild fibrosis vs. advanced fibrosis, AUC; area under the curve, APRI: aspartate aminotransferase-to-platelet ratio Index, FIB-4: fibrosis index based on four factors

Sensitivity and specificity at upper and lower cut-offs for mild and advanced fibrosis for both APRI and FIB-4 were calculated for the study population and compared with the cut-off values proposed by the WHO HBV guidelines [Table 3]. We calculated the single optimum cut-off value to detect advanced fibrosis as 1.2 with more than 75% sensitivity and NPV for APRI and 2.25 for FIB-4 with more than 84% sensitivity and NPV in this study [Table 4].

Demographic data and laboratory parameters were also calculated for the advanced fibrosis group. Patients in the group were older than those in the mild fibrosis group (48.23 vs. 37.16 years, respectively;  $P < 0.0001$ ), and the advanced fibrosis group had a higher AST level (62.7 vs. 47.98 IU/L) and less hemoglobin, platelets, albumin, and ALT levels than mild fibrosis group, which is an expected trend of these parameters when fibrosis stage increases [Table 5]. The sensitivity, specificity, PPV, and NPV for the same cut-offs of both APRI and FIB-4 were studied to differentiate the advanced fibrosis group [Table 4]. An optimum value was found (1.2 for APRI and 2.25 for FIB-4) for both the test at which all sensitivity, specificity, PPV, and NPV are in the balanced state, but 2.25 for FIB-4 has better performance than 1.2 for APRI (sensitivity: 84.0 vs. 76.2%, specificity: 80.5 vs. 79.7, PPV: 79.5 vs. 77.2%, and NPV: 84.8 vs. 78.8%, respectively) [Table 4].

### Discussion

Chronic liver disease (CLD) is a considerable public health issue, mainly responsible for significant morbidity, mortality. Prognosis and management of CLD mainly depend on the stage of liver fibrosis and its progression toward liver cirrhosis. Precise measurement of the liver fibrosis stage is crucial for therapeutic decision-making and follow-up. Liver biopsy is the gold standard test for the evaluation of liver fibrosis and its staging; however, because of its invasive nature, complications, contraindications, and inter and intra-observer variability in histopathological examination, it is almost replaced by noninvasive methods to assess liver fibrosis stages in CHC.<sup>[3,4]</sup>

Fibroscan is based on the principle of TE wherein the extension velocity of a wave through a homogeneous tissue is proportional to its elasticity, which is correlated with the amount of fibrosis in the liver.<sup>[10]</sup> Fibroscan is the most reliable noninvasive tool for the assessment of liver fibrosis, but because of its high cost and non-availability in small cities, the use of this tool is limited.<sup>[5]</sup>

APRI and FIB-4 scores are the other noninvasive methods that can diagnose advanced fibrosis and cirrhosis with high accuracy in CHC patients compared to liver biopsy.<sup>[7,11]</sup>

Diagnostic accuracy and the optimum cut-off value of both APRI and FIB-4 are not yet very well established in comparison with fibroscan in chronic hepatitis C patients. Presently, with the help of direct-acting antivirals (DAAs), treatment of chronic hepatitis C patients is possible. Determining the advanced fibrosis and cirrhosis is a deciding factor not only for treatment duration but also to decide further evaluation after the successful sustained viral response mainly for decompensation and surveillance of hepatocellular carcinoma (HCC).<sup>[3]</sup>

The mean age of the advanced fibrosis group is higher in the most analyzed cohort of chronic hepatitis C.<sup>[12-16]</sup> A similar finding of 48.23 for advanced fibrosis stages vs. 37.16 years, mild fibrosis stages was found in this study respectively. The hemoglobin, platelets, ALT, and albumin levels in the present study are lower in the advanced fibrosis group (11.55 vs. 12.62 gm./dl, 133 vs. 208 × 10<sup>9</sup>/L, 55.73 vs. 57.36 IU/L and 3.73 vs. 4.27 gm/dl, respectively), and these findings are expected as liver stiffness increase, leading to a rise in portal pressure and impairment in synthetic functions of the liver. The difference in mean values of hemoglobin, platelets, and albumin are significantly different except for ALT, while the mean value of AST is significantly higher (62.70) in the advanced fibrosis group; it is expected with the increase in fibrosis leading to the reversal of the AST/ALT ratio. These findings are almost similar to the findings of other studies.<sup>[6,11,15]</sup> It is evident with the above findings that the advanced fibrosis group has higher FIB-4 (5.53) and APRI (2.56), and this is congruent with the findings of other studies by Karic U *et al.*<sup>[15]</sup> and Daniela *et al.*<sup>[16]</sup>

Wai *et al.*<sup>[17]</sup> in 2003 developed a formula called APRI that used platelet and AST levels to determine liver fibrosis. Several studies compared APRI diagnostic output to the METAVIR scoring system, with different findings depending on the sample population and cut-off points. Hence, the AUC for significant

**Table 2: AUC and 95% CI of APRI and FIB-4 for liver fibrosis according to fibroscan**

	Advanced fibrosis (95% CI)	P
APRI	0.835 (0.798-0.871)	<0.0001
FIB-4	0.881 (0.850-0.912)	<0.0001

APRI: Aspartate aminotransferase-to-platelet ratio Index, FIB-4: Fibrosis index based on four factors

**Table 3: Performance of APRI and FIB-4 against METAVIR score for different cut-off values proposed by the WHO HBV guidelines**

Cut-off values suggested by most of the authors	≥F2		Cirrhosis (F4)	
	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
APRI Lower cut-off (0.5 for ≥ F2 and 1 for F4)	82% (77-86)	57% (49-65)	77% (73-81)	78% (74-81)
APRI Higher Cut-off (1.5 for ≥ F2 and 2 for F4)	39% (32-47)	92% (89-94)	48% (41-56)	94%(91-95)
FIB-4 Lower cut-off (1.45 for ≥ F2)	89% (79-95)	42% (25-61)	-	-
FIB-4 Higher cut-off (3.25 ≥ F2)	59% (43-73)	74% (56-87)	-	-

APRI: aspartate aminotransferase-to-platelet ratio Index, FIB-4: fibrosis index based on four factors

**Table 4: Upper and lower cut-offs of APRI and FIB-4 to detect fibrosis against fibroscan in the study population**

	APRI				
	Advanced fibrosis			Cirrhosis (F4)	
Cut-off	0.5	1.5	1.2*	1.0	2.0
Sensitivity	95.2%	69.3%	76.2%	88.8%	51.7%
Specificity	41.4%	84.4%	79.7%	67.6%	88.3%
PPV	59.5%	80.0%	77.2%	61.2%	71.9%
NPV	90.6%	75.3%	78.8%	91.3%	76.0%

	FIB-4		
	Advanced fibrosis		
Cut-off	1.45	3.25	2.25*
Sensitivity	91.3%	62.3%	84.1%
Specificity	68.8%	89.8%	80.5%
PPV	72.5%	84.7%	79.5%
NPV	89.8%	72.6%	84.8%

APRI: aspartate aminotransferase-to-platelet ratio Index, FIB-4: fibrosis index based on four factors; PPV: Positive Predictive Value, NPV: Negative Predictive Value; \*Single Best optimum value for advanced fibrosis

**Table 5: Characteristics of both groups (mild fibrosis vs. advanced fibrosis) and the significance of the difference**

Characteristics	Mild fibrosis (n=256) Mean±SD	Advanced fibrosis (n=231) Mean±SD	Significance
Age (Years)	37.16±14.27	48.23±12.31	P<0.0001
Hemoglobin (g/dl)	12.62±2.17	11.55±2.4	P<0.0001
Platelets (109/L)	208±118.61	133±87.14	P<0.0001
ALT (IU/L)	57.36±24.3	55.73±23.59	P=0.45
AST (IU/L)	47.98±21.0	62.70±23.4	P<0.0001
Albumin (g/dl)	4.27±0.53	3.73±0.70	P<0.0001
Fibroscan (kPa)	6.07±1.53	27.44±18.42	P<0.0001
FIB-4	1.67±2.80 (Median=1.09)	5.53±5.20 (Median=3.70)	P<0.0001
APRI	0.94±1.2 (Median=0.6)	2.56±2.7 (Median=1.95)	P<0.0001

fibrosis ranged from 0.7 to 0.95, and for cirrhosis, it ranged from 0.72 to 0.94.<sup>[18-20]</sup>

The literature-validated cut-offs for significant fibrosis were 0.5 with 77%–86% sensitivity and 49%–65% specificity, and 1.5 with 32%–47% sensitivity and 89%–94% specificity, indicating that APRI may be a valuable tool for fibrosis evaluation without the need for a liver biopsy. [WHO Guideline].

In this study, it was found that at 1.2 cut-offs to differentiated mild versus advanced fibrosis had sensitivity, specificity, PPV, and NPV all are >75%; therefore, APRI may be a reliable method for detecting patients without advanced liver fibrosis, in which different treatment and follow-up strategy may be used. However, the cut-off of 1.5 as proposed in other studies<sup>[21]</sup> for this discrimination of mild fibrosis also perform satisfactorily in our study, with 89% PPV, 59.3% sensitivity, and 88.2% specificity. Although APRI is a satisfactory, simple, and rapid method to determine the stage of liver fibrosis, it must be used with caution, especially when we want to differentiate between cirrhosis and no

cirrhosis. APRI may overestimate liver fibrosis because AST is not only correlated with fibrosis but also with necroinflammatory activity in the liver too.<sup>[12]</sup>

Fibrosis index based on four factors (FIB-4 score), i.e. AST, ALT, platelets, and age of the patient, was first developed to assess liver fibrosis in HIV-HCV co-infected patients.<sup>[13,19]</sup> As four factors are being used in the equation, it can produce more accurate findings than APRI.<sup>[22]</sup>

The results were confirmed by comparing the FIB-4 score to the METAVIR rating system of liver fibrosis in HCV-infected patients only. The findings of various studies showed that patients without fibrosis had an AUC of about 0.8 with NPV 94.7%, 74.3% sensitivity, and 80% specificity for cut-off value 1.45; however, the upper cut-off value of 3.25 to diagnose significant fibrosis had a sensitivity of 59% and a specificity of 74%.<sup>[6,13,19,22,23]</sup>

With 89.8% NPV and 91.3% sensitivity, we found our findings alarming in this analysis using the cut-off of 1.45; however, the cut-off for diagnosing advanced fibrosis was set at 3.25, with a higher PPV (84.7%) with high specificity (89.8%).

Further analysis revealed that the test has an NPV of 89.8% and a sensitivity of 91.3% at a cut-off point of 1.45, allowing it to rule out nearly 90% of patients with advanced fibrosis. In total, 85% of patients with advanced fibrosis are correctly classified using the upper cut-off value of 3.25. This result is superior to that in previous studies. Based on the findings that 25% of patients are in the gray zone and need more investigation, we determined a single optimum cut-off value of 2.25 for advanced fibrosis, which was found to be quite useful with sensitivity, NPV of nearly 85%, and PPV of around 80%.

We also compared our study population between cirrhotic and non-cirrhotic at lower cut-off 1.0 and upper cut-off 2.0 as described by the WHO guideline against the METAVIR scoring system and found that sensitivity for lower cut-off (88.8% vs. 77%), i.e. higher than WHO results, while specificity for lower cut-off (67.6% vs. 78%), while sensitivity and specificity for upper cut-off (51.7% vs. 48% and 88.3% vs. 94%), i.e. lower than the WHO guideline [Table 4]. It is appropriate to distinguish between patients with advanced fibrosis and those with mild fibrosis based on the above findings. As F3 fibrosis patients are more likely to be cirrhotic and decompensate over time, the treatment plan and follow-up protocol should be similar to that of cirrhotic patients.

In this study, the AUC of FIB-4 (0.881) on ROC showed superiority over the AUC for APRI (0.835) to recognize the patients of advanced fibrosis in the setting of chronic hepatitis C infection. This also supports the findings of studies by other researchers.<sup>[24]</sup>

As both APRI and FIB4 can be calculated with the help of inexpensive serum biomarkers, it is a cheaper option over fibroscan, and primary-care physicians can stage liver fibrosis

in the absence of fibroscan. Primary-care physicians should take caution where APRI and FIB4 scores are in the gray zone. FIB4 should be preferred over APRI to diagnose significant liver fibrosis.

## Conclusions

As liver cirrhosis is the driving factor in chronic hepatitis C infection to determine treatment regimen, duration, and follow-up strategy, the test should be able to differentiate the maximum number of cirrhotic (F4) and significant fibrosis (F3) from normal or early stages of fibrosis (F1 and F2). APRI and FIB-4 scores also showed good performance in detecting the patients without liver fibrosis compared with fibroscan. FIB-4 is a more reliable test to differentiate advanced fibrosis with a cut-off of 1.75 and to decide future management. Both the tests are not reliable for differentiating the intermediate stages of fibrosis. Thus, the use of these scores alone in patients with evidence of fibrosis should be made with caution moreover the use of a different combination of the noninvasive score for a most accurate assessment of liver fibrosis is recommended.

## Acknowledgments

The authors are thankful to the Vice-Chancellor of King George's Medical University Lucknow. Special thanks to the patients enrolled in this study.

## Author's contribution

Kamlendra Verma, Amar Deep, and Sumit Rungta had roles in the designing and writing of the manuscript with the help of Shweta Kumari, and the article is critically reviewed by Suchit Swaroop.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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