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Comparison of APRI, FIB-4 with Shear Wave Elastography in Assessment of Liver Fibrosis in Untreated Chronic Hepatitis C Patients

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Abstract

Background: Hepatitis C virus infection is one of the main causes of chronic liver disease worldwide. The high rates of progression of chronic hepatitis C to liver cirrhosis suggests an emergent need of effective tests to diagnose fibrosis in earlier stages. In this study we aim to compare the diagnostic accuracy of 2 non-invasive and easy to apply markers, i.e., APRI and FIB-4 with Shear Wave Elastography (which is taken as the reference) in detecting liver fibrosis in patients with chronic hepatitis C.

Material and methods: This hospital-based descriptive study was conducted on 70 untreated hepatitis C positive patients who came to outdoor or inpatient department in GGS Medical College and Hospital, Faridkot. All the patients underwent complete clinical evaluation and investigations including Shear wave Elastography (reference for liver fibrosis) and then APRI and FIB-4 Scores were calculated on all the patients.

Results: APRI and FIB-4 showed diagnostic accuracies of 84.29%, 81.43% (mild fibrosis), 78.95%, 92.11% (moderate fibrosis) and 73.68%, 73.68% (severe fibrosis), respectively in predicting fibrosis in untreated in chronic hepatitis C patients.

Conclusion: Both APRI and FIB-4 are simple and noninvasive for predicting mild, moderate, and severe fibrosis in untreated chronic hepatitis C patients in comparison to shear wave elastography. In case of moderate fibrosis, FIB-4 has a higher diagnostic accuracy as compared to APRI.

Key words: Hepatitis C virus, chronic hepatitis C APRI, FIB-4, Shear Wave Elastography.

Introduction

Hepatitis C virus (HCV) infection is one of the main causes of chronic liver disease worldwide[1]. There are approximately 130 to 150 million carriers of HCV, out of which 55 - 85% develop the chronic form of hepatitis C and 15 - 30% of these patients are at risk of developing cirrhosis within 20 years of their diagnosis[2]. Even India has a great burden of HCV with a population prevalence of 1 - 2.4%[3,4].

The natural course of HCV infection varies. Liver fibrosis and inflammation in chronic hepatitis C are dynamic processes. The progression of chronic hepatitis C (CHC) to liver fibrosis and then to liver cirrhosis correlates with an extensive accumulation of extracellular matrix (ECM), leading to the formation of large amounts of fibrotic tissue that facilitates the occurrence of cirrhosis and subsequently hepatocellular carcinoma. An early and prompt diagnosis and management of liver fibrosis can prevent complications and death[5].

Till date, liver biopsy has been the gold standard for diagnosing and staging fibrosis, but due to its limitations like invasiveness, associated morbidity (e.g., severe pain, GI bleeding, etc.)[6,7], sampling errors causing misclassification of stage of fibrosis and intra- and inter-observer variability in interpretation of histology, especially at lower stages of fibrosis, biopsy is no longer recommended[8].

The APRI is an indirect biochemical marker of fibrosis, which takes into account the serum level of aspartate aminotransferase (AST) and platelet count for staging liver fibrosis, with good accuracy[10].

The FIB-4 another score for liver fibrosis uses data routinely available in clinical practice, namely AST, ALT, platelet count and patient's age[11,12].

The Shear wave elastography can detect the presence and extent of fibrosis with fairly high accuracy and thus can replace liver biopsy for assessment of fibrosis. However, this diagnostic modality is not uniformly available at all centres imparting treatment to chronic hepatitis C patients. Thus, there arises an urgent need for other easily available, convenient, and non-invasive modalities for effective detection of fibrosis in patients with chronic hepatitis C infection. Hence, this study was undertaken to compare the diagnostic accuracy of 2 non-invasive and easy to apply

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markers, i.e., APRI and FIB-4 with Shear Wave Elastography (which is taken as the reference) in detecting liver fibrosis in patients with chronic hepatitis C.

Material and methods

This hospital-based observational study was conducted on 70 hepatitis C positive patients who came to outdoor or inpatient departments in GGS Medical College and Hospital, Faridkot. The study was carried-out from February 2018 to February 2019 after the approval from Institutional Ethics Committee, Guru Gobind Singh Medical College, Faridkot. Written informed consent was obtained from the patients.

The sample size was calculated considering the number of newly diagnosed treatment naïve hepatitis patients that present to GGSMCH, Faridkot each year.

Inclusion criteria

1. Patients of both gender above 20 and below 60 years of age who gave informed consent, and who fulfilled the following criteria:-

   HCV RNA positive by quantitative Polymerase Chain Reaction (PCR) assay, (with a limit of detection of > = 15 IU/ml), not treated for hepatitis-C previously, was included in the study.

Exclusion criteria

1. Patients with co-infection with hepatitis B virus or Human Immunodeficiency Virus (HIV) co-infection.
2. Patients with hepatocellular carcinoma (HCC).
3. Patients with significant alcohol abuse (> 80 grams/ day).
4. Patients with ALT flare [values five-fold the upper limit of normal (45 U/ml)].
5. Patients with failed or unreliable liver stiffness measurement.
6. Patients with co-infection with more than one HCV genotype.
7. Pregnancy.
8. NAFLD (Non-alcoholic fatty liver disease).

Study tools

1. The APRI[10] and FIB-4[11] are calculated using the following formulae, as originally reported:-
   - APRI = [AST/(ULN)/ platelet count (*10^9/L)] x 100.

APRI uses readily available laboratory tests to identify significant hepatic fibrosis and it is one of the simplest models proposed by Wai *et al*. It is based on the rationale that worsening of fibrosis and increasing portal pressures are associated with reduced production of thrombopoeitin by hepatocytes, increased platelet sequestration within the spleen and reduced clearance of AST[10].

   - FIB-4 = AST (IU/ml) x age (years)/platelet count (*10^9/L) x $ALT^{1/2}$ (IU/ml).

FIB-4 was originally developed to predict significant fibrosis and cirrhosis among human immunodeficiency virus (HIV)/ HCV co-infected patients in the APRICOT study[11]. Subsequently, it was validated for HCV mono-infected patients[30].

2. Shear Wave Elastography (SWE) (in kPa) is one of the extensively used non-invasive methods for liver stiffness assessment in recent past. It has attracted attention because it is a novel, rapid, objective, and quantitative method for measuring liver stiffness in patients with liver disease, including CHC liver disease[13]. It gauges liver stiffness by measuring the propagation velocity of mechanical shear waves generated in the liver tissuewith results expressed in kPa[9].

Methodology

After taking informed consent, a detailed history of each patient was taken. All of them underwent routine investigations and then APRI and FIB-4 scores were calculated for all the patients by single and same observer. On the same day, liver stiffness measurement was done by Shear Wave Elastography (SWE) using ultrasound machine Philips Affiniti 70. For each patient, the right lobe of liver was visualised through the optimal intercostal space with right arm in maximally abducted position while the patient was lying in supine position. Patient was instructed to hold their breath for 3 - 5 seconds for imaging. The visual depth of the system was fixed at 8 centimeters. The ROI (region of interest) was fixed at 1 - 2 centimeters beneath the right liver capsule (Glisson's capsule), away from intrahepatic vessels, bile duct, and gallbladder. The system was adjusted so that the sample volume depth will be 4 centimeter or less. The ultrasound beam is focused at a given location which creates plane shear waves, which propagate over a region of interest (ROI) of tissue. The particular segment of liver was shot 10 - 12 times and the result was considered reliable only when 10 successful shots and a measurement with success rate of > 80% was obtained. The machine automatically calculated the mean elastic modulus (in kPa) within the region of interest.

The proposed cut-offs for LSM values for HCV patients were as follows:-

Severity of fibrosis	METAVIR stages	LSM values (in kPa)
1. Normal	METAVIR F0-F1	3 - 7
2. Mild fibrosis	METAVIR F2	7.1 - 11
3. Moderate fibrosis	METAVIR F3	11.1 - 21
4. Severe fibrosis	METAVIR F4	> 21

Then, diagnostic accuracies of APRI and FIB-4 were compared with Shear wave elastography in assessing liver fibrosis by using appropriate statistical methods in SPSS version 21.0. A p value of < 0.05 was considered statistically significant and the diagnostic value was classified as low (Az = 0.50 - 0.70), moderate (Az = 0.70 - 0.90) and high (Az = 0.90 - 1.0).

Results

Table I: Frequency distribution of gender, occupation and area.

Demographic variables	Frequency	Per cent
Gender		
Male	55	78.57
Female	15	21.43
Total	70	100.0
Occupation		
Housewife	15	21.43
Labourer	10	14.29
Farmer	20	28.57
Driver	4	5.71
Business	13	18.57
Student	4	5.71
Service	4	5.71
Total	70	100.0
Area of residence		
Urban	18	25.71
Rural	52	74.29
Total	70	100.0

Table II: Table for age distribution

Age group	Frequency	Percentage
21 - 30	15	21.43%
31 - 40	19	27.14%
41 - 50	18	25.71%
51 - 60	18	25.71%
Total	70	100.00%

Table III: Frequency distribution of Shear Wave Elastography findings.

	Frequency (n)	Percentage (%)
Normal	32	45.71
Mild fibrosis	13	18.57
Moderate fibrosis	12	17.14
Severe fibrosis	13	18.57
Total	70	100.00

Table IV: Frequency distribution of severity of liver fibrosis.

	Frequency (n)	Percentage (%)
Mild fibrosis	13	34.21
Moderate fibrosis	12	31.58
Severe fibrosis	13	34.21
Total	38	100.00

Table V: Frequency distribution of modes of transmission of hepatitis C.

Risk Factors		Frequency (n)	Per cent (%)
Blood transfusion	No	67	95.71
	Yes	3	4.29
Unsafe injection use	No	54	77.14
	Yes	16	22.86
IVDU	No	56	80.0
	Yes	14	20.0
Unprotected sex	No	65	92.8
	Yes	5	7.14
Surgery	No	53	75.71
	Yes	17	24.29
Dental treatment	No	56	80.0
	Yes	14	20.0
Others	No	54	77.14
	Yes	16	22.86

Table VI: Association between risk factor and liver fibrosis.

		Liver fibrosis		Total	p-value
		No	Yes		
Age distribution	21 - 30	14 (93.33%)	1 (6.67%)	15 (100.00%)	0.0002*
	31 - 40	9 (47.37%)	10 (52.63%)	19 (100.00%)	
	41-50	4 (22.22%)	14 (77.78%)	18 (100.00%)	
	51-60	5 (27.78%)	13 (72.22%)	18 (100.00%)	
Total		32 (45.71%)	38 (54.29%)	70 (100.00%)	

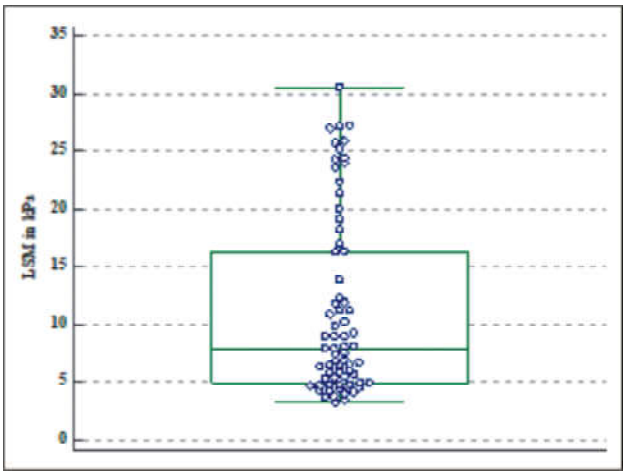

Fig. 1: *Box plot for swe LSM values.*

Table VII: Descriptive statistics and association between blood investigations parameters and fibrosis.

Blood Investigations	Min	Max	Mean ± SD	Median	Inter quartile range	p-value
Hb (gm/dl)	7.9	16.4	12.9 ± 1.9	12.95	11.6 - 14.3	0.149
TLC (cells/microliter)	3,800	10,600	7,067.14 ± 1,546.92	7,200	5,800 - 8,200	0.662
PLT (/µl)	57,000	4,86,000	2,12,642.9 ± 99,842.9	1,97,500	1,28,000 - 2,95,000	0.001*
AST/SGOT (IU/L)	21	252	95.99 ± 58.95	83	51 - 129	0.0001*
ALT/SGPT (IU/L)	17	224	108.4 ± 65.1	91.5	59 - 164	0.052
ALP (IU/L)	49	187	114.66 ± 30.46	106	92 - 135	0.313
TSP (gm/dl)	5.6	8.0	7.02 ± 0.47	7	6.8 - 7.2	0.204
Albumin (gm/dl)	2.0	4.9	3.64 ± 0.61	3.75	3.1 - 4.1	0.004*
INR	1.0	1.8	1.15 ± 0.17	1.1	1.08 - 1.20	0.046*
HCV viral load (log10 IU/L)	8,305	6,85,00,024	25,93,437.0 ± 85,46,022.5	5,67,000	1,99,000 - 12,77,642	0.203

Table VIII: Association between APRI, FIB-4 and liver fibrosis.

	Liver fibrosis		
	No	Yes	p-value
APRI			<.0001*
Sample size	32	38	
Mean ± SD	0.85 ± 0.77	2.24 ± 1.53	
Median	0.53	1.81	
Min - Max	0.1 - 3.28	0.26 - 8.98	
Inter quartile range	0.364 - 1.137	1.274 - 2.889	
FIB-4			<.0001*
Sample size	32	38	
Mean ± SD	1.26 ± 0.93	3.66 ± 2.4	
Median	0.89	2.96	
Min-Max	0.23 - 3.38	0.93 - 12	
Inter quartile range	0.597 - 1.995	1.790 - 5.090	

Table IX: Association between APRI and FIB-4 with levels of fibrosis.

	Severity of fibrosis			
	Mild	Moderate	Severe	p-value
APRI				0.004*
Sample size	13	12	13	
Mean ± SD	1.3 ± 0.55	2.35 ± 1.07	3.1 ± 2.03	
Median	1.34	2.53	2.5	
Min-Max	0.26 - 2.37	0.92 - 3.9	1.16 - 8.98	
Inter-quartile range	1.111 - 1.576	1.305 - 3.185	2.019 - 3.352	
FIB-4				0.0001*
Sample size	13	12	13	
Mean ± SD	1.82 ± 0.99	3.88 ± 1.71	5.3 ± 2.75	
Median	1.58	3.45	5.09	
Min-Max	0.93 - 4.68	1.37 - 6.97	2.76 - 12	
Inter-quartile range	1.140 - 2.221	2.878 - 4.694	2.871 - 6.504	

Table X: Correlation between variables and liver fibrosis.

	LSM (in kPa)		p-value
Age	Correlation co-efficient	0.451	0.0001*
	n	70	
Albumin	Correlation co-efficient	-0.399	0.0006*
	n	70	
ALP	Correlation co-efficient	0.164	0.1751
	n	70	
ALT/SGPT	Correlation co-efficient	0.14	0.2493
	n	70	
AST/SGOT	Correlation co-efficient	0.479	<0.0001*
	n	70	
BMI	Correlation co-efficient	0.112	0.3579
	n	70	
HGB	Correlation co-efficient	-0.164	0.174
	n	70	
INR	Correlation co-efficient	0.252	0.0355*
	n	70	
PLT	Correlation co-efficient	-0.398	0.0006*
	n	70	
TLC	Correlation co-efficient	0.023	0.8493
	n	70	
TSP	Correlation co-efficient	-0.1	0.41
	n	70	

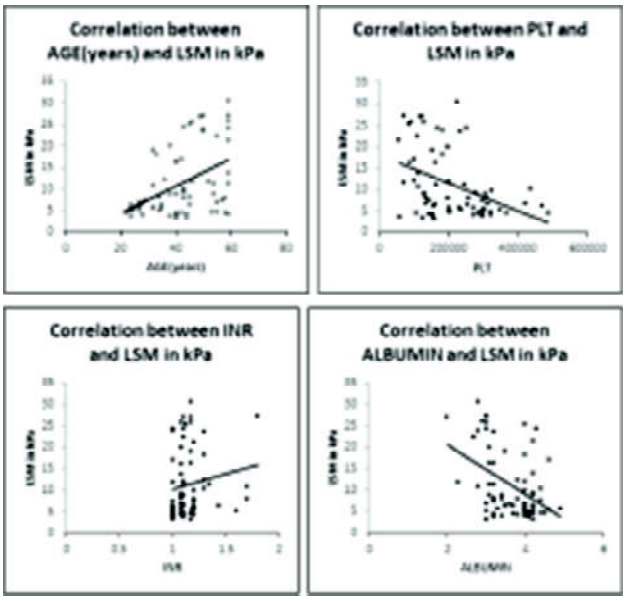

Fig. 2: *Correlation graphs for parameters and liver fibrosis.*

Table XI: Diagnosing mild fibrosis (f2).

Test result variable(s)	Area	Std. error[a]	P-value	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
APRI	0.842	0.05	< 0.0001*	0.735	0.918
FIB-4	0.874	0.0408	< 0.0001*	0.773	0.941

Table XII: Diagnosing moderate fibrosis (≥ f3).

Test result variable(s)	Area	Std. error[a]	p-value	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
APRI	0.818	0.0683	<0.0001*	0.660	0.924
FIB-4	0.926	0.0511	<0.0001*	0.793	0.986

Table XIII: Diagnosing severe fibrosis (f4).

Test result variable(s)	Area	Std. error[a]	p-value	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
APRI	0.735	0.0886	0.0066*	0.567	0.865
FIB-4	0.809	0.07	<0.0001*	0.649	0.918

Table XIV: Comparision of diagnostic accuracies of APRI and FIB-4 for all stages of fibrosis.

	Mild fibrosis	Moderate fibrosis	Severe fibrosis
Difference between areas	0.0321	0.108	0.0738
Standard Error	0.0284	0.0672	0.0639
95% Confidence Interval	-0.0237 to 0.0878	-0.0240 to 0.239	-0.0514 to 0.199
z statistic	1.127	1.602	1.156
p-value	0.2596	0.109	0.248

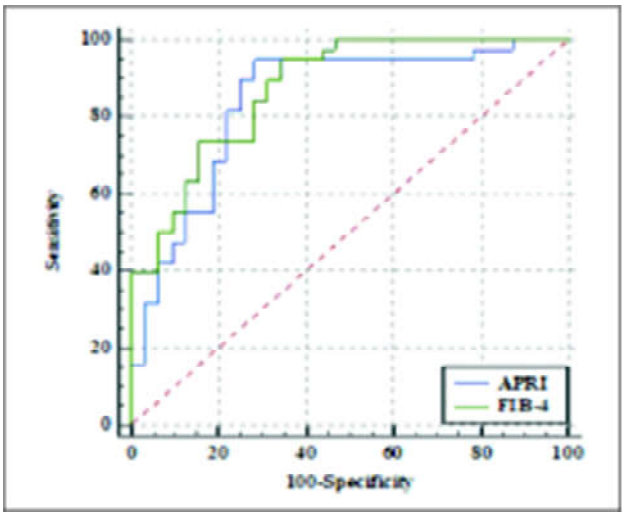

Fig. 3: *ROC curves for comparison of diagnostic accuracies of APRI and FIB-4 for diagnosing mild fibrosis.*

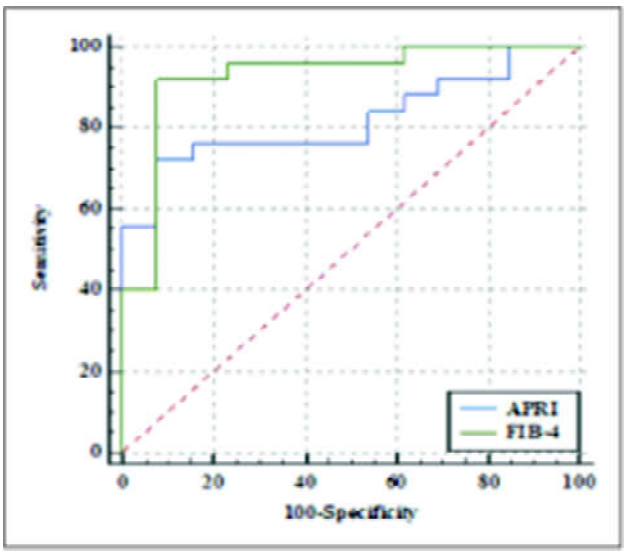

Fig. 4: *ROC curves for comparison of diagnostic accuracies of APRI and FIB-4 for diagnosing moderate fibrosis.*

Discussion

Chronic hepatitis C affects approximately 70 million people worldwide, representing one of the leading causes of liver-related death, hepatocellular carcinoma and liver transplantation. In the present study of 70 newly diagnosed untreated hepatitis C patients, majority belonged to older age groups of 41 - 50 (25.71%), 51 - 60 (25.71%). The study conducted by Jeong *et al* and other studies also had included majority of elderly population[19,20,22].

Most of the subjects included in this study were males (78.6%) and 21% were females similar to other studies (71.9%, 64.3%)[15,22]. In our study, most of the patients resided in rural area (74.3%) while 25.7% resided in urban area.

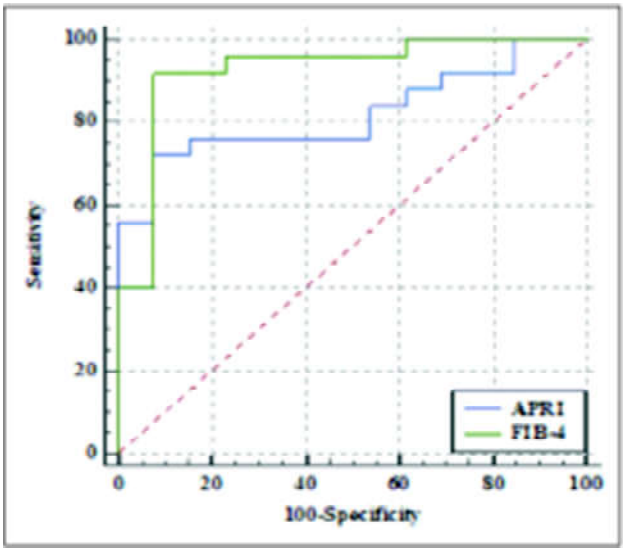

Fig. 5: *ROC curves for comparision of diagnostic accuracies of APRI and FIB-4 for diagnosing severe fibrosis.*

This could be because of the location of this hospital which caters mostly to rural patients.

In the present study, majority of subjects were farmers (28.6%) followed by housewives (21.4%), owned business (18.6%), labourers (14.3%), drivers (5.7%), students (5.7%) and in-service (5.7%). This could be because the main source of income in this area is agriculture.

The mean BMI in the present study was 25.50 ± 3.47 kg/m^2. According to the WHO and Asia Pacific Obesity classification, most of the patients belonged to overweight class. But, the remarkable feature of SWE is that it can show viscoelastic properties in all areas in the ROI with a colour look-up table. Thus, it overcomes the limitations of Transient Elastography (TE) by which liver stiffness cannot be measured accurately in patients with severe obesity, thick subcutaneous fat or ascites as it was seen in the study by Tada *et al*[18].

In the present study, it was observed that 46% (n = 32) of the patients showed no fibrosis, 19% (n = 13) had mild fibrosis, 17% (n = 12) had moderate fibrosis and only 19% (n = 13) had severe fibrosis.

In this study, we included only the untreated hepatitis C patients because the APRI and FIB-4 values differ as the liver fibrosis reversal occurs with treatment. Tada T *et al* had similar exclusion criteria as seen in our study, except that they excluded chronic hepatitis C (CHC) patients with severe fibrosis (F4)[18].

The present study highlights surgeries to be the most common modes of transmission of hepatitis C (24.3%, n = 17). The other less common modes observed in our study were unsafe injection use (22.9%, n = 16), others (22.9%, n = 16), IVDU (20%, n = 14), dental treatment (20%, n = 14), unprotected sex (7.1%, n = 5) and blood transfusion being the least common of all (4.3%, n = 3). Others included risk factors like haemodialysis. Unsafe injection use included sharing of needles, tattooing and needle stick injuries. While in the study by Wai *et al*, in 30% patients HCV was transmitted by intravenous drug use, 13% by transfusions of blood or blood products and 26% belonged to others and unknown category[10]. While in other study, the most frequent modes were parenteral drug use (47%), transfusions (22%), and unknown in the remaining patients (31%)[26]. The present study highlights dental treatment, IVDU and unsafe injection use as other important sources of transmission, viz a viz other studies. These are issue of concern and can be attributed to improper sterilisation of surgical and dental equipments. The lack of awareness regarding possible hazards of needle sharing, tattooing and ear piercing from unauthorised professionals may be another contributing factor.

In the present study, all patients who consumed alcohol more than 80 grams per day were not included since, it itself is a major cause of liver fibrosis and all such causes have been excluded. Moreover, the SWE cut-off criteria are different for different aetiologies of chronic liver disease. But, one-third of the total hepatitis C patients in the study (31.4%, n = 22) consumed alcohol occasionally. And, there was no difference among patients with occasional alcohol consumption (i.e., < 30 grams/day) and the non-alcoholics in terms of presence of liver fibrosis ($P > 0.05$). While, in another study done in PGI Chandigarh, it was reported that there was significantly higher fibrosis in CHC patients even with alcohol consumption of more than 30 grams per day[17].

In the present study, there were statistically significant differences between patients with and without fibrosis when age, platelet count, albumin level and INR were taken into consideration, showing that these were associated with liver fibrosis (i.e., the patients with higher age seemed to have liver fibrosis than patients with younger age. The patients with liver fibrosis had lower platelet counts, albumin levels, and higher INR levels). Also, there was statistically significant difference seen in APRI and FIB-4 scores between patients with and without fibrosis (i.e., the patients with liver fibrosis seemed to have higher levels of APRI and FIB-4 values). Also, we observed statistically significant association between liver fibrosis progression and platelet count, albumin level, APRI and FIB-4. Similar associations were reported in the study by Tada *et al* between platelet level, ALT ($p = 0.003$, $p < 0.001$) and grades of fibrosis. But, age was not associated with liver fibrosis unlike in our study. Also, Tamaki and colleagues found similar association when compared age and platelet counts with grades of fibrosis (mild and severe) ($p < 0.001$, $p < 0.001$). Both the above two studies compared the serum markers with SWE[18,20]. One of the earliest studies validating the use of APRI and FIB-4 along with another study by Wang

et al had similar associations between patients' age, platelet count, ALT and liver fibrosis, but in these studies liver biopsy was taken as standard[10,12,16].

In this study, significant correlation was observed between patient's development of liver fibrosis in chronic hepatitis C patients and levels of platelet, albumin, and INR. There was statistically significant correlation between fibrosis and platelet count (p = 0.0006) and albumin levels (p = 0.0006) (i.e., the presence of fibrosis, was correlated negatively with platelet count and albumin levels). While, there was a positive correlation between fibrosis and age (p = 0.0001) and INR (p = 0.0355). It seems that growing age plays an important role in the progression of fibrosis. Our observations regarding correlation were similar to various other studies done previously[10,12,22,23,28].

In the systematic review by Parks and co-workers, the various studies assessed by Quality Assessment of Diagnostic Accuracy Studies (QADAS) were taken into consideration. It showed that the predictive values of serum markers and various indices for liver fibrosis assessment were affected by disease prevalence, causing a lack of generalisability to individual practice. Therefore, knowledge of fibrosis prevalence is important to determine aptness of a test in a particular persons' clinical practice. It also inferred that it was possible that some tests performed better in low or high prevalence populations (e.g., test with a high sensitivity across lower test scores, will perform best in low prevalence populations as the NPV will be higher and the test is applicable to a significant part of the study population; and the converse applies in high prevalence populations)[14].

In our study, AUROC of APRI and FIB-4 were 0.842 and 0.874 with the cut-off for APRI and FIB-4 to predict patients with mild fibrosis being > 0.70 and > 1.12 respectively in comparison to SWE taken as reference. Both APRI and FIB-4 scores showed moderate diagnostic accuracy of 84.29% and 81.43% respectively for mild fibrosis. Similar results were reported in earlier study for predicting significant fibrosis, which concluded that APRI and FIB-4 showed moderate diagnostic accuracy similar to the present study, although cirrhosis patients were excluded from one of the studies unlike the present study (0.88); (n = 55, Az = 0.88, 0.86); (0.809, 0.803); (0.77, 0.76); (0.88, 0.85)[10,18,19,21,29]. While, contrasting results were obtained in study by Jeong and co-workers showing APRI (0.691) to have low diagnostic accuracy in comparision to SWE[22].

In the present study, AUROC of APRI and FIB-4 were 0.818 and 0.926 with the cut-off for APRI and FIB-4 to detect moderate fibrosis being > 1.758 and > 2.46 respectively. APRI showed moderate diagnostic accuracy of 78.95% and FIB-4 showed high diagnostic accuracy of 92.11% for predicting moderate fibrosis. Other studies also reported similar results of AUROC and moderate diagnostic accuracy for APRI and FIB-4 in predicting moderate liver fibrosis (FIB-4 AUROC = 0.85; p < 0.001, < 0.001, Az = 0.819, 0.836; summary AUROC of APRI = 0.77)[12,19,21].

In this study, AUROC of APRI and FIB-4 were 0.735 and 0.809 with the cut-off for APRI and FIB-4 to detect severe fibrosis being > 1.76 and > 2.72 respectively. Both APRI and FIB-4 showed moderate diagnostic accuracy of 73.68% and 73.68% for detecting severe fibrosis. Previous studies reported similar results with AUROCs of 0.815, 0.852 and 0.83, 0.82, respectively indicating moderate diagnostic accuracy for both APRI and FIB-4 tests[19,21]. Holmberg and co-workers in their large US cohort of HCV-infected patients, found that FIB-4 exhibited significantly higher diagnostic accuracy than APRI for differentiating severe fibrosis (stages F3 - F4) from mild-to-moderate fibrosis (stages F0 - F2) (AUROC = 0.83 versus 0.80)[25]. When compared with the earliest studies done using APRI and FIB-4, the present study reported a comparatively lower reliability in diagnosing severe fibrosis (0.94; 0.91)[10,12]. While, other studies reported contrasting results of low diagnostic accuracy of APRI for severe fibrosis (0.683)[22].

Thus, in this study both APRI and FIB-4 diagnosed mild fibrosis from patients with no fibrosis with moderate accuracy and showed least accuracy in differentiating patients of severe fibrosis, while FIB-4 alone showed high reliability in predicting moderate grades of fibrosis in patients with hepatitis C. While several studies concluded opposite results indicating that APRI and FIB-4 exhibit high reliability for predicting liver fibrosis in CHC[12,15,24].

But, the present study finally compared the AUROCs of APRI and FIB-4 in predicting mild, moderate and severe fibrosis and it was observed that both the scores can be used as equally reliable diagnostic tools in predicting various levels of fibrosis in untreated hepatitis C patients. While contrasting findings with statistically significant difference between area under the ROC curves were reported in other studies between SWE and APRI for mild, moderate and severe fibrosis (p = 0.003, 0.032, 0.002)[22].

Strength of the study

The strengths of this study is that we considered necroinflammatory activity grades and did not include the patients with ALT flare (i.e., values higher than five-fold upper limit of normal). In several studies, influence of necroinflammatory activity, jaundice and/or congestion are present in liver[16,27]. Also, very few studies from India have focused on analysis of diagnostic accuracy of simple, non-invasive, inexpensive markers like APRI and FIB-4 for assessment of liver fibrosis in untreated chronic hepatitis C patients. The diagnostic accuracy of these markers was validated in comparison to Shear Wave Elastography which is a valid reference for assessment of liver fibrosis. These

markers can be useful for early detection of liver fibrosis in untreated chronic hepatitis C patients where Shear Wave Elastography is not available or not affordable.

Limitations of the study

The limitations were single-centered study with a small sample size. Further studies with a larger number of patients are warranted.

Conclusion

In conclusion, both APRI and FIB-4 are viable alternatives for predicting mild, moderate, and severe fibrosis in untreated chronic hepatitis C patients in comparison to Shear Wave Elastography. In case of moderate fibrosis, FIB-4 has a higher diagnostic accuracy as compared to APRI.

APRI and FIB-4 can be used as simple, non-invasive tools for assessing liver fibrosis in the majority of chronic hepatitis C patients and can be supplemented with shear wave elastography, where higher degree of fibrosis is suspected.

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