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A Comparison of Aspartate Aminotransaminase to Platelet Ratio Index (APRI) and Fibrosis-4 (FIB-4) Score with Transient Elastography in Patients of Chronic Hepatitis C

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Abstract

Background: To establish a non-invasive scoring system in evaluation of chronic hepatitis C infection. **Material and Methods:** 30 Hepatitis C virus positive patients were evaluated by ultrasonography (USG) abdomen and transient elastography (TE). Liver stiffness measurement (LSM) values were measured, recorded and correlated in all patients based on TE, and APRI with FIB4 score with grading of fibrosis and cirrhosis. **Results:** Out of 30 study subjects 53.3% were male and 46.7% were females. Based on fibroscan, 40% of subjects were having F1 and F4 grade each and 13.7% subjects were seen in F3 grade and 6.7% subjects were seen in F2 grade. Based on APRI scoring, fibrosis was seen in 43.3% of subjects, advanced fibrosis was seen in 20% of subjects and cirrhosis was seen in 36.7% of subjects. Based on FIB4 scoring, fibrosis was seen in 26.7% of subjects, advanced fibrosis was seen in 33.3% of subjects and cirrhosis was seen in 40% of subjects. APRI revealed advanced fibrosis in 6 whereas on fibroscan it was 2 advanced fibrosis, 2 cirrhosis and 2 fibrosis. Out of 11 cases of cirrhosis, on fibroscan, 8 found to be cirrhosis, 1 advanced fibrosis and 2 fibrosis. Out of 13 cases of fibrosis on APRI, 8 found to be fibrosis, 4 advanced fibrosis and 1 cirrhosis on fibroscan. **Conclusion:** Hepatitis C virus is notorious in its ability to persist in human liver following acute infection resulting in chronic hepatitis. Over years it leads to hepatic structural abnormalities resulting in fibrosis. When severe, it leads to cirrhosis which may be a precursor of HCC in CHC patients. Liver/hepatic biopsy, the mainstay for the detection of hepatic fibrosis and diagnosis of cirrhosis is not only invasive but is also traumatic and has chances of sampling errors.

Keywords: Hepatitis C virus, cirrhosis.

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Introduction

Chronic contamination with hepatitis C virus (HCV) is among the significant global public health trouble which is ever-increasing numbers and currently extra than 71.1 million sufferers worldwide. India, harbors nearly 12-18million HCV-inflamed human beings with an envisioned prevalence of 0.5-1.5%.[2] Hepatitis C, resulting from HCV can produce both acute & chronic ailment through a couple of routes of dissemination in particular from transfusions of blood, mother to fetus, hospital needle injuries, sexual act and drug abuse through intravenous. Chronic hepatitis C (CHC) leads to progressive hepatic failure with 20-30% of patients who are not treated develop cirrhosis with an average time ranging from 20-30years.[4] There is simultaneous increased risk of hepatic failure with subsequent need for hepatic transplantation; hepatocellular carcinoma and even death.[5]

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Hepatitis C accounts for huge share of chronic liver ailment patients (approximately 40%) and is the commonest indication for hepatic transplantation.[6]

Liver biopsy remains the gold standard procedure for diagnosis but currently many non-invasive gear have been developed viz. Transient elastography- TE for measuring liver stifness and biochemical markers & scoring systems (viz. APRI; Aspartate Amino transaminase to Platelet Ratio Index) rating and FIB 4 ;Fibrosis-four rating, which are taken into consideration as surrogate markers of hepatic fibrosis.[7,8]

To determine the fibrosis of liver, this noninvasive ultrasound procedure is used. To evaluate the firmness, they made this noninvasive tool extremely desirable. The mechanism "Vibration Controlled Transient Elastography" (VCTE) used by fibroscans to create error-free computable dimensions of key liver variables. Hardness of the liver is deduced by estimating the pace of a vibration produced over skin. Calculating the amount of time took by means of wave to reach particular volume. Hence, our present study aims to set up a scoring system (noninvasive) in assessment of chronic hepatitis C as those are not considerably evaluated in our country. Our present study additionally aims to create data on patterns of liver stiffness in our region.

Methodology

This prospectively, hospital-based, observational study was performed on thirty patients which includes both out & indoor in the department of medicine over a length of 18 months, diagnosed with chronic Hepatitis-C following. Inclusion criteria was all patients of chronic Hepatitis C >=18 years of age. Exclusion criteria was chronic hepatitis B co-infection, HIV co-contamination, known case of malignancy and alcoholic liver disease.

In addition to demographic information of all patients diagnosed with chronic hepatitis C (patients with anti-HCV RNA high-quality), detailed clinical history, past records, family history and treatment history if any, was also recorded. Blood tests like blood count and liver function tests were done in every patient. All the patients additionally were evaluated through ultrasonography (USG) stomach and transient elastography (TE). Liver stiffness measurement (LSM) values have been measured, recorded and correlated in all patients primarily based on TE, and APRI with FIB4 score with grading of fibrosis and cirrhosis. The clinical data was recorded systematically in predesigned proforma and statistically evaluated using appropriate tests and tools. Following formulae had been used for the diagnosis of fibrosis and cirrhosis:

- APRI score will be calculated using the proposed formula:

$$\text{APRI} = \frac{\frac{\text{(AST level)}}{\text{ULN}}}{\text{Platelet count } (10^9/\text{L})} \times 100$$

*ULN, AST upper level of normal (or 40 IU/L)

- The FIB-4 score will be determined using the following for

$$\text{FIB-4} = \frac{[\text{age} \times \text{AST}]}{\text{Platelet count } (10^9/\text{L})} \times \sqrt{\text{ALT}}]$$

Methods	Parameters	Advanced fibrosis	Cirrhosis
APRI	AST, Platelet Count	>1	>1.5
FIB-4	ALT and AST, Platelet Count and age of pateint	>1.45	>3.25
Transient Elastography	Measures shear wave speed generated by vibration through liver tissue	>7.3kPa	>15kPa

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In year 2003 Echosens (Paris, France) developed fibro scan. Liver elasticity was measured in kilopascals (kPa) with range of 2.5-75 kPa.[9] Data that obtained were then subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table 1: Distribution of patients

Total- 30		
Gender	**Male**	**Female**
	14	16

Out of 30 study subjects 53.3% were male and 46.7% were females.

Table 2: Distribution of cases based on occupation

Occupation	**Frequency**	**Percent**
Farmer	5	16.7
Housewife	13	43.3
Landlord	1	3.3
Shopkeeper	4	13.3
Social worker	2	6.7
Student	4	13.3
Teacher	1	3.3
Total	30	100.0

The majority of subjects esp. females were housewives (43.3%) followed by 16.7% farmers, and 13.35 each were shopkeepers & students.

Table 3: Statistical values of cases based on clinical/biochemical/score values

Parameter	**Minimum**	**Maximum**	**Mean**	**SD**
BP/ systolic	90.00	180.00	127.40	23.25
BP / diastolic	60.00	100.00	76.67	12.95
Pulse	63.00	119.00	85.30	13.27
Spo2 %@RA	90.00	100.00	97.07	2.13
HB	4.10	14.60	10.66	2.45
TLC	2900.00	15000.00	8032.67	3016.63
PLT	5500.00	517000.00	147750.00	114973.07
Bilirubin (T)	0.20	5.20	1.21	1.08
SGOT	16.00	196.00	52.19	32.89
SGPT	13.00	170.00	50.34	33.09
Fibroscan: LSM (kPa)	2.30	73.50	15.32	15.97
APRI score	0.10	3.80	1.28	0.97
FIB-4 score	0.62	15.08	3.79	3.49

The above table shows mean values with range of all the biochemical, laboratory and clinical parameters.

Table 4: Distribution of cases based on fibroscan grade

Fibroscan Grading cut-off value	**Frequency (n=30)**	**Percentage (%)**
F1	12	40.0
F2	2	6.7
F3	4	13.3
F4	12	40.0
Total	30	100.0

Based on fibroscan, 40% of subjects were having F1 and F4 grade each and 13.7% subjects were seen in F3 grade and 6.7% subjects were seen in F2 grade.

Table 5: Distribution of cases based on fibrosis grade as per APRI

APRI Grading	**Frequency (n=30)**	**Percentage (%)**
Advanced Fibrosis	6	20.0
Cirrhosis	11	36.7
Fibrosis	13	43.3

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Based on APRI scoring, fibrosis was seen in 43.3% of subjects, advanced fibrosis was seen in 20% of subjects and cirrhosis was seen in 36.7% of subjects.

Table 6: Distribution of Cases based on Fibrosis Grade as Per FIB-4

FIB4 Grading	Frequency (n=30)	Percentage (%)
Advanced Fibrosis	10	33.3
Cirrhosis	12	40.0
Fibrosis	8	26.7

Based on FIB4 scoring, fibrosis was seen in 26.7% of subjects, advanced fibrosis was seen in 33.3% of subjects and cirrhosis was seen in 40% of subjects.

Table 7: Comparison of Cases based on Fibrosis Grade as Per APRI vs Fibroscan

APRI	Fibroscan			Total
	Advanced Fibrosis	Cirrhosis	Fibrosis	
Advanced Fibrosis	2	2	2	6
Cirrhosis	1	8	2	11
Fibrosis	4	1	8	13
Total	7	11	12	30

Table shows comparative distribution between fibroscan and APRI scoring. APRI revealed advanced fibrosis in 6 whereas on fibroscan it was 2 advanced fibrosis, 2 cirrhosis and 2 fibrosis. Out of 11 cases of cirrhosis, on fibroscan, 8 found to be cirrhosis, 1 advanced fibrosis and 2 fibrosis. Out of 13 cases of fibrosis on APRI, 8 found to be fibrosis, 4 advanced fibrosis and 1 cirrhosis on fibroscan.

Table 8: Comparison of Cases based on Fibrosis Grade as Per FIB-4 vs Fibroscan

FIB4	Fibroscan			Total
	Advanced Fibrosis	Cirrhosis	Fibrosis	
Advanced Fibrosis	5	1	4	10
Cirrhosis	1	10	1	12
Fibrosis	1	0	7	8
Total	7	11	12	30

The above table shows comparative distribution between fibroscan and FIB4 scoring.

Table 9: Statistical Parameters based on Fibrosis Grade as Per APRI vs Fibroscan

APRI	Cirrhosis	Advanced Fibrosis	Fibrosis
Sensitivity	72.7	28.6	66.7
Specificity	84.2	82.6	72.2
PPV	72.7	33.3	61.5
NPV	84.2	79.2	76.5
Accuracy	80.0	70.0	70.0

Table 10: Statistical Parameters based on Fibrosis Grade as Per FIB-4 vs Fibroscan

FIB4	Cirrhosis	Advanced Fibrosis	Fibrosis
Sensitivity	90.9	71.4	58.3
Specificity	89.5	78.3	94.4
PPV	83.3	50.0	87.5
NPV	94.4	90.0	77.3
Accuracy	90.0	76.7	80.0

The above table shows sensitivity, specificity, positive predictive value, negative predictive value and accuracy of APRI in comparison to fibroscan with respect to diagnosis of fibrosis, advanced fibrosis and cirrhosis.

DISCUSSION

The evaluation of staging hepatic fibrosisis required for control of disease in patients with chronic liver diseases of numerous aetiologies. for instance, the determination F4 by METAVIR staging in the settings of cirrhosis, helps in treatment of cirrhosis care, which include portal hypertension hepatocellular carcinoma survillence .In many guidelines prior

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to the initiation of antiviral treatment in chronic hepatitis C significant fibrosis (SF) (≥F2 by METAVIR staging) need to be present; and it has been also proved to be an important surrogate marker for the many liver diseases like NAFLD and Chronic hepatitis B. according to who elimination target of Hcv with prior SF (≥F2 fibrosis through METAVIR score) and it remains to be the mainstay of resource allocation in countries with low and middle income group. The present study was carried out to examine aspartate aminotransaminase to platelet ratio index (APRI) and fibrosis-4 (FIB-4) score with transient elastography in patients of chronic hepatitis C.

Out of 30 study subjects, 53.3% had been male and 46.7% have been girls. The majority of subjects, especially females have been housewives (43.3%) followed by 16.7% farmers and 13.35% had been shopkeepers & college students. Aurora Loaeza – del - Castillo et al assessed the role of APRI in detection of liver fibrosis in 164 CHC patients. The authors discovered an AUC of 0.776/0.803 for significant fibrosis/advanced fibrosis respectively. The authors in the end that APRI is a beneficial tool for assessing fibrosis and cirrhosis in CHC patients.[10]

We found that primarily based on fibroscan, forty% of topics were having F1 and F4 grade each and thirteen.7% topics had been seen in F3 grade and six.7% subjects have been visible in F2 grade. Based totally on APRI scoring, fibrosis was seen in 43.3% of subjects, advanced fibrosis was visible in 20% of subjects and cirrhosis was seen in 36.7% of subjects.

Vallet- Pichard et al,[11] conducted a study on 847 biopsy proven cases CHC with an aim to validate FIB-4 (combined benefits of multiple standard biochemical values - platelets, ALT, AST) and age along with its comparison with Fibro Tests in 592 CHC patients. The authors observed that FIB-4 index accurately identified severe fibrosis (F3-F4)/cirrhosis with an AUROC of 0.85/0.91 respectively. FIB-4 index <1.45 had NPV of 94.7% for excluding severe fibrosis with 74.3% sensitivity while FIB-4 index >3.25 had PPV/specificity of 82.1%/98.2% for significant fibrosis (F3-F4). Using the above ranges, FIB-4 had an accuracy of 72.8%. Based on FIB4 scoring, fibrosis was seen in 26.7% of subjects, advanced fibrosis was seen in 33.3% of subjects and cirrhosis was seen in 40% of subjects. APRI revealed advanced fibrosis in 6 whereas on fibroscan it was 2 advanced fibrosis, 2 cirrhosis and 2 fibrosis. Out of 11 cases of cirrhosis, on fibroscan, 8 found to be cirrhosis, 1 advanced fibrosis and 2 fibrosis. Out of 13 cases of fibrosis on APRI, 8 found to be fibrosis, 4 advanced fibrosis and 1 cirrhosis on fibroscan. Shaheen et al[12] in their systematic review & meta-analysis study evaluated APRI in detection of cirrhosis in CHC patients. The authors observed a sensitivity/specificity of 76%/71% for cirrhosis. The authors finally concluded that major strength of APRI was exclusion of fibrosis.

Ziol et al,[13] evaluated TE-LS in 327 CHC patients for detection of hepatic fibrosis. The authors observed optimal LSM cut-off values of 8.7kPa & 14.5 kPa for F>2 & F4 respectively. The authors opined that significant fibrosis or cirrhosis could be detected in CHC patients by TE-LS with a reliable accuracy.

CONCLUSION

Hepatitis C virus is notorious in its ability to persist in human liver following acute infection resulting in chronic hepatitis. Over years it leads to hepatic structural abnormalities resulting in fibrosis. When severe, it leads to cirrhosis which may be a precursor of HCC in CHC patients. Liver/hepatic biopsy, the mainstay for the detection of hepatic fibrosis and diagnosis of cirrhosis is not only invasive but is also traumatic and has chances of sampling errors. The quest for non-invasive tests for replacing the more invasive liver biopsy over last two decades for detection of advanced fibrosis/cirrhosis in CHC patients has led to development of transient elastography, APRI and FIB-4 scores. These non-invasive tests have been validated in multiple studies including ours for moderate to high sensitivity and moderate specificity &

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accuracy for detecting hepatic fibrosis. Frequent use of these simple to use and inexpensive test may completely obviate the need of hepatic biopsy in future for monitoring the progression of disease in CHC patients.

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