ORIGINAL RESEARCH PAPER
Volume-8 | Issue-9 | September - 2019 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY OF HEPATIC FIBROSIS IN CHRONIC LIVER DISEASE PATIENTS USING NON-INVASIVE METHODS OF APRI SCORE AND TRANSIENT ELASTOGRAPHY

General Medicine

Dr Amar Patil

Dr Pradnya Diggikar* *Corresponding Author

Dr P K Satpathy

Dr Anuja Patil

Dr Shubham Mishra

ABSTRACT

Background: APRI and Transient elastography is recommended as the preferred non-invasive test to assess for the presence of cirrhosis (APRI score >2 in adults) in resource-limited settings. The present study was planned with an objective to study hepatic fibrosis in chronic liver disease patients using non-invasive methods of APRI score and transient elastography.

Methodology: The present study was a Cross-sectional Study conducted on cases with Chronic liver disease. The demographic details like age, gender, aetiology and duration of disease were recorded. Patients were assessed using APRI score and Transient Elastography. Stiffness is measured in terms of 'liver fibrosis index, and 'strain ratio'.

Results: It was seen that there was a positive correlation between APRI and LF index with correlation coefficient(r) of 0.30033 ($p<0.05$) and APRI and Strain index with correlation coefficient(r) of 0.2924 ($p<0.05$). While studying the diagnostic importance of APRI index, it was observed that it has a sensitivity of 87.50% while specificity of 35.29%.

Conclusion: Transient elastography and APRI score are promising non-invasive methods, complementary to each other and can be used to detect the presence and extent of fibrosis in chronic liver disease. APRI score is a sensitive but not a specific test to detect fibrosis in patients of chronic liver disease.

KEYWORDS

hepatic fibrosis, chronic liver disease, Transient elastography, APRI

INTRODUCTION

Cirrhosis is defined as a diffuse process characterised by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules. Its main characteristics by definition are not focal but rather involve most (if not all) of the diseased liver and include fibrous septa and parenchymal nodules.[1]

Liver biopsy is considered the gold standard method to stage liver disease and assess for the degree of fibrosis, but it is not widely used in resource-limited settings because of its high cost, invasiveness, patient discomfort, risk of complications, sampling error, as well as need for expert histological interpretation.[2] Several non-invasive fibrosis tests based on blood or serum indices (APRI, FIB-4) and imaging methods (MR elastography or transient elastography) are now available and increasingly used for evaluating and staging liver fibrosis, which reduces the need for liver biopsy in persons with an established cause of chronic liver disease.[3]

APRI (aspartate aminotransferase [AST]-to-platelet ratio index) is recommended as the preferred non-invasive test (NIT) to assess for the presence of cirrhosis (APRI score >2 in adults) in resource-limited settings. Transient elastography may be preferred NIT where they are available and cost is not a major constraint.[2] Transient Elastography is an ultrasound technique that can demonstrate increased stiffness in chronic liver diseases which correlates with the severity of fibrosis and are useful for noninvasively assessing the liver fibrosis.[4] The present study was planned with an objective to study hepatic fibrosis in chronic liver disease patients using non-invasive methods of APRI score and transient elastography.

MATERIALS AND METHODS

The present study was a Cross-sectional Study conducted in Dr.D.Y. Patil Medical College, Hospital and Research Centre, Pune between July 2015 to September 2017. The cases with Persistence of signs and symptoms of liver disease for more than six months duration, Alcoholic liver disease and Fibrosis due to viral hepatitis B and C were included in the study while cases with Non alcoholic fatty liver disease, Non alcoholic steato-hepatitis, Drug induced hepatic fibrosis, Idiopathic fibrosis, Hamochromatosis, Wilson,s disease, Alpha-1 anti-trypsin deficiency, Primary biliary cirrhosis, Obstructive liver disease and Congestive liver disease are excluded from the disease. The study was initiated after taking Institutional Ethical Clearance and participants were enrolled after taking informed written consent from them.

The demographic details like age, gender, aetiology and duration of disease were recorded on pre-designed questionnaire. Patients with chronic liver disease were identified on the basis of history and APRI score and Transient Elastography were performed in all 50 patients.

APRI score

APRI can be calculated as follows: (AST/ULN) * 100 / platelet count (10^9/L)

Where ULN signifies the upper limit for AST in the laboratory where these investigations will be undertaken. Value > 1.5 is significant for fibrosis whereas value >2 is consistent with presence of cirrhosis.

Transient Elastography

Transient elastography was performed using AERITTA 60 (HITACHI ALOKA JAPAN) high-end ultrasound colour Doppler machine with elastography. Stiffness is measured in terms of 'liver fibrosis index' and 'strain ratio'. At least 6 valid measurements should be taken. A single measurement takes no more than 15 seconds. A final reading is derived from the median of the individual readings, in order to exclude outlying measurements.

For estimating validity of APRI and Transient Elastography, sensitivity, specificity, positive predictive value and negative predictive value with 95% confidence interval was calculated using biopsy as gold standard. For assessing agreement between APRI and Transient Elastography, Cohen Kappa coefficient was used.

RESULTS

Table 1: Distribution of study participants according to age, gender, aetiology and duration of disease

Age group	No. (%)
31-40	8 (16)
41-50	18 (36)
51-60	18 (36)

61-70	6 (12)
Gender	
Male	43 (86)
Female	7 (14)
Aetiology	
ALD	30 (60)
Hep B	12 (24)
Hep C	8 (16)
Duration of disease	
≤ 6months	2 (4)
>6mth-1yr	18 (36)
1yr-5yr	22 (44)
5-10yr	5 (10)
>10yr	3 (6)

It was observed that the mean haemoglobin, TLC count and platelet count was 10 ± 2.09 gm/dl, 7450±2634.02 and 97520±46734.14 per ml respectively. The mean serum AST, total bilirubin and direct bilirubin was 59.36±18.33 units/L, 1.92±2.28 mg/dL and 1.274±2.02 respectively.

Table 2: Distribution of cases according to LF index and strain index

LF index	No. (%)
F0	16 (32)
F1	18 (36)
F2	8 (16)
F3	1 (2)
F4	7 (14)
Strain index	
F1	29 (58)
F2	10 (20)
F3	8 (16)
F4	3 (6)

It was seen that 32% patients were having LF index F0, 36% were having LF index F1. It was observed that majority of the patients (58%) were having F1 strain index, followed by F2 strain index (20%), F3 strain index (16%) and F4 strain index (6%).

Table 3: Distribution according to Ultrasonoghraphy findings

Ultrasonography findings	No. (%)
Hepatomegaly	2 (4)
liver parenchymal disease	22 (44)
normal size with coarse echotexture	16 (32)
shrunken liver with coarse echotexture	9 (18)
shrunken with nodular surface	1 (2)

It was seen that on ultrasonography 44% patients were diagnosed to be of liver parenchymal disease followed by normal size with coarse echotexture was observed in 32% and shrunken liver with coarse echotexture was seen in 18% patients.

Table 4: Comparison of APRI index with duration of illness

Duration of disease	APRI	
	<1.5	≥1.5
≤ 6months	0	2 (5.56%)
>6mth-1yr	7 (50.00%)	11 (30.56%)
1yr-5yr	5 (35.71%)	17 (47.22%)
5-10yr	1 (7.14%)	4 (11.11%)
>10yr	1 (7.14%)	2 (5.56%)
Total	14 (100%)	36 (100%)

It was observed that majority of the patients with APRI score less than 1.5 was having duration of disease less than one year. However patients with APRI score≥1.5 were having duration of disease more than one year.

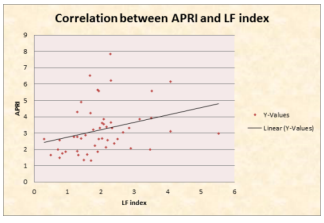

Figure 1: Correlation between APRI and LF index

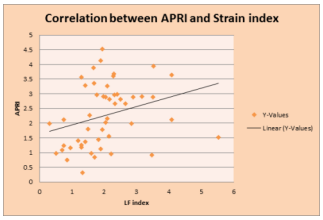

Figure 2: Correlation between APRI and Strain index

It was seen that there was a positive correlation between APRI and LF index with correlation coefficient® of 0.30033 ($p<0.05$) and APRI and Strain index with correlation coefficient(r) of 0.2924 ($p<0.05$).

Table 5: Sensitivity, Specificity, Positive predictive value and Negative predictive value

Statistic	Value	95% CI
Sensitivity	87.50	61.65 to 98.45
Specificity	35.29	19.75 to 53.51
Positive Likelihood Ratio	1.35	0.99 to 1.84
Negative Likelihood Ratio	0.35	0.09 to 1.40
Disease prevalence	32.00	19.52 to 46.70
Positive Predictive Value	38.89	31.83 to 46.45
Negative Predictive Value	85.71	60.29 to 95.95

DISCUSSION

The mean age of study population in the present study was 50.16±8.86years. In a study conducted by Krishna C. Sajja et al[5] out of 2017 patients, 219 (11%) were under the age of 40 and 1,798 (89%) were above the age of 40. The average age of all patients was 52±11 years. In another study by Xing wang et al [6], the average age of the patients was found to be 50.5±13 years. Thus the mean age of patients in this study was similar to other studies. In the study conducted by Xing wang et al [6], of the 8080 patients with liver cirrhosis in this study, 6719 (83.2%) were male, 1361 (16.8%) were female. Our findings are similar to other studies.

In the study conducted by Romanas Zykus et al [7] the sensitivity and specificity was found to be 84.6% and 87.2% respectively. The p value in this study was found to be 0.08. Wai et al.[8] found the APRI score showed sensitivity of 41.2% and APRI > 1.5 showed specificity of 95%. They also accomplished a better coefficient ($r = 0.60$; $P<0.01$).

A study done by Gabriella Pár et al [9] found that APRI score has sensitivity of 91% and specificity of 47% while an APRI >1.5 suggests *F*2 or more fibrosis with PPV 88% and NPV 64%. A study by L.C. Mendes et al[10] found sensitivity and specificity of 26% and 95% respectively. Positive predictive value was found to be 85% and negative predictive value was 56%. The results for sensitivity and specificity in our study were not found to be similar, but the correlation coefficient was similar and correlation was statistically found to be significant.

CONCLUSION

The extent of fibrosis in Chronic liver disease related to the duration of disease. More the duration, greater is the degree of fibrosis in a patient. The incidence of cirrhosis is highest when the duration of disease is more than 1 year.

Transient elastography and APRI score are promising non-invasive methods, complementary to each other and can be used to detect the presence and extent of fibrosis in chronic liver disease. APRI score is a sensitive but not a specific test to detect fibrosis in patients of chronic liver disease.

REFERENCES

1. Maurizio Soresi, Lydia Giannitrapani, Melchiorre Cervello, Anna Licata, and Giuseppe Montalto. Non invasive tools for the diagnosis of liver cirrhosis. World J Gastroenterol. 2014 Dec 28; 20(48): 18131–18150.
2. Guidelines for the Prevention, Care and Treatment of Persons with Chronic Hepatitis B Infection. Geneva: World Health Organization; 2015 Mar. 4, Recommendations: Non-invasive assessment of liver disease stage at baseline and during follow up. Available from: https://www.ncbi.nlm.nih.gov/books/NBK305554/ assessed on 10/02/2018.
3. Yoav Lurie, Muriel Webb, Ruth Cytter-Kuint, Shimon Shteingart, and Gerardo Z Lederkremer. Non-invasive diagnosis of liver fibrosis and cirrhosis. World J Gastroenterol. 2015 Nov 7; 21(41): 11567–11583.
4. Julius Wilder, Keyur Patel. The clinical utility of FibroScan as a noninvasive diagnostic test for liver disease. Med Devices (Auckl). 2014; 7: 107–114.
5. Sajja K C, Mohan D P, andRockey D C : Age and Ethnicity in Cirrhosis. J Investig Med. 2014 October ; 62(7): 920–926.
6. Xing Wang, Shang-Xiong Lin, Jin Tao et al. Study of liver cirrhosis over ten consecutive

years in Southern China. World J Gastroenterol2014 October 7; 20(37): 13546-13555.
7. Romanas Zykus1, 3,Laimas Jonaitis1,Vitalija Petrenkienė et al. Combination of transient elastography with serum-based non-invasive tests improves prediction of liver fibrosis in patients with chronic hepatitis C: a prospective cohort study. ACTA MEDICA LITUANICA. 2015. Vol. 22. No. 2. P. 77–84.
8. Wai, C. T., Greenson, J. K., Fontana, R. J., Kalbfleisch, J. D., Marrero, J. A., Conjeeevaram, H.S., Lok, AS-F.: A simple non-invasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitisC. Hepatology, 2003, 38, 518–526.
9. Gabriella Pár, ÁronVincze, TimeaBerki et al. Serum Fibrosis Markers (Procollagen-III-Peptide, Hyaluronic Acid, Transforming Growth Factor -1), Aspartate-Aminotransferase to Platelet Ratio Index (APRI), and Transient Elastography (FibroScan) in Patients with Chronic HCV Infection. CEMED.2005. vol 11. 101-118.
10. Mendes L.C, P.A. Ferreira P. A., Miotto N. et al : Transient elastography and APRI score:looking at false positives and false negatives.Diagnostic performance and association to fibrosisstaging in chronic hepatitis C. Brazilian Journal of Medical and Biological Research 2016. 49(9).