https://doi.org/10.29309/TPMJ/2025.32.05.8915

The Professional Medical Journal
www.theprofesional.com
2025, Volume, 32 Issue, 05

ORIGINAL ARTICLE

APRI (AST to Platelet Ration Index) and (Fibrosis-4 Index) Performance to assess liver fibrosis against predefined fibroscan values in chronic Hepatitis C Virus Infection.

Rana Ahsan[1], Mansoor ul Haq[2]

Article Citation: Ahsan R, Mansoor ul Haq. APRI (AST to Platelet Ration Index) and (Fibrosis-4 Index) Performance to assess liver fibrosis against predefined fibroscan values in chronic Hepatitis C Virus Infection. Professional Med J 2025; 32(05):545-550. https://doi.org/10.29309/TPMJ/2025.32.05.8915

ABSTRACT… Objective: To compare the performance of Fibrosis-4 index (FIB-4), and the AST to platelet ratio index (APRI) versus Fibroscan in chronic hepatitis C virus (CHCV) infection. **Study Design:** Cross-sectional study. **Setting:** Department of Gastroenterology, Liaquat National Hospital and Medical College, Karachi, Pakistan. **Period:** July 2024 to December 2024. **Methods:** A total of 250 patients aged 20-70 years, and having CHCV were analyzed. APRI and FIB-4 scores were calculated according. The discriminative ability of APRI, and FIB-4 was evaluated drawing area under the curve (AUC) utilizing receiver operating characteristic (ROC) curve. Based on the optimal cut-off value, the sensitivity and specificity of both scoring systems were computed. **Results:** For a total of 250 patients, the median scores for APRI, FIB-4, and Fibroscan were 0.63 (0.39-1.05), 2.33 (1.13-3.60), and 9 (5.50-23.92), respectively. Fibrosis stages were noted as 98 (39.2%) F0-F1, 18 (7.2%) F2, 30 (12%) F3, and 104 (41.6%) F4. The AUC indicated that the FIB-4 score was a better predictor of chronic severity than the APRI score (AUC=0.994 vs AUC=0.866) among CHCV patients. The optimal cutoff for the FIB-4 score was 2.440 (sensitivity=92.5%, specificity=100%), 1.550 (sensitivity=100%, specificity=91.4%), and 2.565 (sensitivity=85.1%, specificity=100%). **Conclusion:** In the context of chronic HCV infection, FIB-4 was better than APRI at differentiating between individuals with and without severe fibrosis and cirrhosis.

Key words: APRI, FIB-4, Fibroscan, Hepatitis C, Liver, Platelet, Virus.

INTRODUCTION

Hepatitis C virus (HCV) infection is major public health concer worldwide.[1] HCV infection may lead to fibrosis, cirrhosis, and "hepatocellular carcinoma (HCC)".[2,3] Liver fibrosis (LF) generally occurs due to tissue damage caused in response to wound healing.[3] An estimated 20-30% untreated HCV patients develop LF in 20-30 years following the disease.[4]

The assessment of LF is important because it enables the tracking of lesion development and may guide therapy choices and screening for repercussions in liver disease patients. Liver tissue analysis done through transcutaneous biopsy is considered the gold standard for the determination of LF severity. Many experts have begun to support non-invasive methods for fibrosis stage determination.[5]

Fibroscan is known to be a novel yet non-invasive approach for evaluating liver stiffness in CHCV patients, depicting sensitivity, and specificity as 87%, and 91%, respectively.[6] Fibroscan is usually performed by "vibration-controlled transient elastography (VCTE)". "Fibrosis-4 index (FIB-4)", and "AST to platelet ratio index (APRI)" are well-researched LF evaluation tools in the context of CHCV infection.[7,8] FIB-4 has been found to be better than APRI in identifying severe fibrosis by some researchers. Patients without advanced liver disease may benefit greatly from FIB-4, particularly if alternative non-invasive techniques are not applicable.[7] Due to readily available, low-cost laboratory tests that use blood samples, these scores are accepted by many experts.[9,10]

1. MBBS, Post-graduate Resident Gastroenterology, Liaquat National Hospital, Karachi, Pakistan.
2. MBBS, FCPS (Medicine), FCPS (Gastroenterology), Head Gastroenterology, Liaquat National Hospital, Karachi, Pakistan

Correspondence Address:
Dr. Rana Ahsan
Department of Gastroenterology
Liaquat National Hospital, Karachi, Pakistan.
ranaahsan548@yahoo.com

Article received on: 05/12/2024
Accepted for publication: 14/02/2025

Advanced fibrosis is distinguished by APRI with an "area under curve (AUC)" of 0.835. With an AUC of 0.881 for advanced fibrosis, the results corresponding to the FIB-4 score are even better than with APRI.[10]

Assessment for LF is necessary to clinically manage CHCV patients.[11] It is crucial to find straightforward yet accurate diagnostic tools that may be applied at the primary healthcare level to facilitate the decentralization of hepatitis C management.[12] This study was planned to compare the performance of FIB-4, and APRI versus Fibroscan in the assessment of LF in CHCV patients.

METHODS

This cross-sectional study was conducted at the Department of Gastroenterology, Liaquat National Hospital and Medical College, Karachi, Pakistan, from July 2024 to December 2024. This study was approved by the Research and Ethics Committee of Liaquat National Hospital (1065-2024-LNH-ERC-6/8/24). A sample size of 20 was calculated by taking the expected value of the AUC for APRI in diagnosis of fibrosis as 0.835[10], with 80% power of test, and 95% confidence level. Because of the large patient turnover in this hospital, a total of 250 patients were analyzed. Inclusion criteria were confirmed cases of CHCV (through enzyme-linked immunosorbent assay), age 20-70 years. Exclusion criteria were history of alcohol use, lipid-lowering agents, or hepatitis B, or with any other chronic liver disease (CLD) condition. For the purpose of recruitment, non-probability consecutive sampling technique was adopted. Written and informed consents were sought from all patients.

Demographical and clinial characteristics were noted, and relevant laboratory investigations were performed. The Fibroscan score was used to classify the stages of LF, and termed no or mild fibrosis (F0-F1) with < 7 kPa, moderate fibrosis (F2) as 7 to 8.99 kPa, severe fibrosis (F3) as 9 to 12.49 kPa, and cirrhosis (F4) ≥ 12.5 kPa. The stages were categorized into either mild fibrosis (F0-F2), or advanced fibrosis (F3-F4). APRI and FIB-4 scores were computed using the algorithm based on laboratory results. The APRI score was calculated as: "{AST (IU/L)/upper normal limit of AST (IU/L)}/platelet count (10^9/L)". The calculation of the FIB-4 score was based on the formula: "(Age (years)xAST (IU/L))/(Platelet count (10^9 /L)xALT (IU/L)$^{1/2}$)."

Data analysis were done using "IBM SPSS Statistics" version 26.0. The quantitative variables were expressed as mean and standard deviation, or median and inter-quartile range, where applicable. Qualitative variables were represented as frequencies and percentages. The predictive ability of scores was determined by plotting a "receiver operating characteristic (ROC)" curve. AUC was calculated, and applying the Youden index, optimal cut-off value of the scores was calculated. $P<0.05$ was taken as statistically significant.

RESULTS

Among the 250 patients in the current study, 160 (64.0%) were male. The median age was 60 (55-61) years with 191 (76.4%) patients aged above 50 years. The median height, weight, and BMI were 170 (150-170) cm, 72 (62-75) kg, and 27 (23-31) kg/m^2, respectively. Among 250 patients, 65 (25.2%) was obese. The median duration of disease was 24 (11-24) months with 47.6% having duration between 13-36 months. The median AST, ALT, and platelets were 39 (30-41) U/ml, 39 (35-45) U/ml, and 160 mm^3 (105-250) mm^3, respectively. The median APRI, FIB-4, and Fibroscan scores were 0.63 (0.39–1.05), 2.33 (1.13–3.60), and 9 (5.50–23.92), respectively. Fibroscan findings revealed 134(54%) patients with severe, and 116 (46%) with non severe CLD (Table-I).

The AUC indicates that the FIB-4 score (AUC=0.994, $p<0.001$) was a better predictor of CLD severity than the APRI score (AUC=0.866, $p<0.001$) among CHCV patients (Figure-1).

In terms of the detection severity of CLD among hepatitis C patients, the optimal cutoff for the APRI score was 0.541 (sensitivity=92.5%, specificity=83.6%), 0.599 (sensitivity=85.1%, specificity=83.6%), and 0.468 (sensitivity=92.5%, specificity=75.9%), while the optimal cutoff for

the FIB4 score was 2.440 (sensitivity=92.5%, specificity=100%), 1.550 (sensitivity=100%, specificity=91.4%), and 2.565 (sensitivity=85.1%, specificity=100%), as shown in Table-II.

Characteristics		Frequency (% age)
Gender	Male	160 (64.0%)
	Female	18 (7.2%)
Age (years)	≤ 35	41 (16.4%)
	36-50	191 (76.4%)
	>50	36 (14.4%)
Body mass index (kg/m^2)	Obese	63 (25.2%)
	Non-obese	187 (74.8%)
Disease duration (months)	≤12	111 (44.4%)
	13-36	119 (47.6%)
	>36	20 (8.0%)
Fibrosis stages (Fibroscan)	F0-F1	98 (39.2%)
	F2	18 (7.2%)
	F3	30 (12.0%)
	F4	104 (41.6%)
Chronic liver disease severity (Fibroscan)	Severe	134 (54.0)
	Non-severe	116 (46.0)

Table-I. Characteristics of patients (n=250)

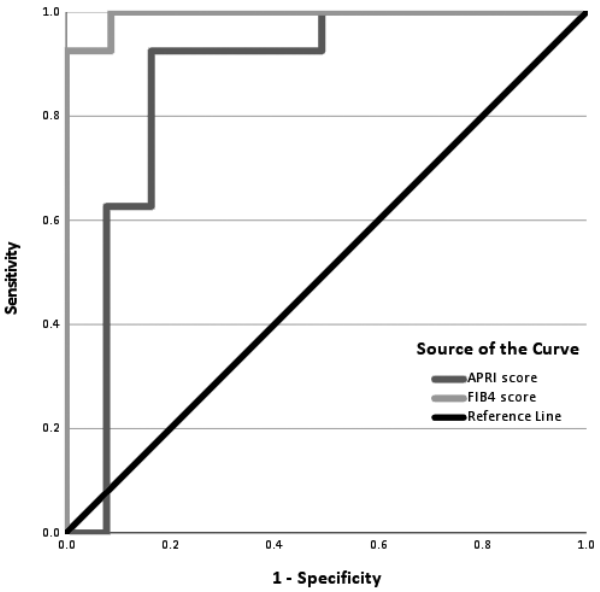

Figure-1. ROC analysis for APRI and FIB-4 score for prediction of CLD severity

DISCUSSION

The AUC indicated that the FIB-4 score was a better predictor of chronic severity than the APRI score (AUC=0.994 vs AUC=0.866) among hepatitis C patients. The optimal cutoff for the FIB-4 score was 2.440 (sensitivity=92.5%, specificity=100%), 1.550 (sensitivity=100%, specificity=91.4%), and 2.565 (sensitivity=85.1%, specificity=100%). The research conducted by Karic et al[13] reported that FIB-4 outperformed APRI in detecting individuals with cirrhosis or severe fibrosis in the context of CHCV infection (APRI's AUC of 0.861). A cut-off point of 1.08 was designated to determine individuals with cirrhosis, attaining a sensitivity of over 100%.[13] Similar findings have been shown by other investigators as well.[14-18] In one investigation carried out by Dramane et al, 83.3% score of APRI and 84.4% score of FIB-4 revealed higher non-significant fibrosis than Fibroscan (72.3%).[19] In a study from Senegal, it was discovered that non-significant fibrosis was present in 59.9% cases using Fibroscan.[20] An AUC over 0.8 indicates that the APRI and FIB-4 had high discriminatory capacity in identifying liver cirrhosis in CHCV.[12] The results of this study supported the capacity of both techniques to distinguish between cirrhotic and non-cirrhotic, and they were in line with the majority of earlier investigations.[21-25]

With an AUC of 0.84 and 0.83, for FIB-4, and APRI, respectively, both showed strong sensitivity as well as specificity performance in predicting cirrhosis in another study[11], supporting the findings of the present study. The findings of this study are comparable to a meta-analysis that used biopsy of liver as the standard for reference.[26] In a related study by Rungta et al, the advanced fibrosis group had lower platelets, hemoglobin, albumin levels, and ALT.

Tool	Score	Sensitivity	Specificity	Youden Index
AST to platelet ratio index	0.541	92.5%	83.6%	0.761
	0.599	85.1%	83.6%	0.687
	0.468	92.5%	75.9%	0.684
Fibrosis-4	2.440	92.5%	100%	0.925
	1.550	100%	91.4%	0.914
	2.565	85.1%	100%	0.851

Table-II. Optimal cut-off for the prediction of APRI score and FIB-4 score for detection of severe CLD

The results are expected as liver stiffness increases, which raises portal pressure and impairs the liver's synthetic functions. With 59.3% sensitivity, and 88.2% specificity, the cut-off of 1.5 suggested in an earlier research for moderate fibrosis also worked effectively.[27] In context of CHCV infection, the AUC of FIB-4 was 0.88 on ROC demonstrated better performance over the AUC of APRI (0.84) in identifying individuals with advanced fibrosis. The results of another investigation also support these findings.[28]

The findings of this study hold substantial clinical implications. These non-invasive indices offer cost-effective alternatives to Fibroscan. By providing a reliable method for monitoring LF progression over time, FIB-4 and APRI facilitate early identification of advanced liver disease stages, guiding timely intervention strategies and optimizing patient management. Clinically, these indices empower healthcare providers to make informed decisions regarding treatment initiation, follow-up frequency, and the need for further invasive assessments, thereby improving patient care outcomes and potentially reducing healthcare costs associated with liver disease management. This underscores their pivotal role in enhancing diagnostic accuracy and patient-centered care in the management of chronic HCV infection.

This study had some limitations. The single center study setting marginalize the generalizability of present finings and warrants further multicentric studies involving larger population sets. Prospective trials can also be planned to evaluate the prognostic values of non-invasive methods for LF evaluation.

CONCLUSION

The study concluded that in the context of chronic HCV infection, FIB-4 was better than APRI at differentiating between individuals with and without severe fibrosis and cirrhosis. Since low-income nations lack access to transient elastography, FIB-4 may be highly helpful in identifying individuals who do not have advanced stage of liver disease so that a biopsy of liver may be postponed safely.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SOURCE OF FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Khatun M, Ray RB. **Mechanisms underlying Hepatitis C virus-associated hepatic fibrosis.** Cells. 2019; 8(10):1249. doi: 10.3390/cells8101249

2. Ekpanyapong S, Reddy KR. **Hepatitis C virus therapy in advanced liver disease: Outcomes and challenges.** United European Gastroenterol J. 2019; 7(5):642-650. doi: 10.1177/2050640619840149

3. Rockey DC, Friedman SL. **Fibrosis regression after eradication of Hepatitis C Virus: From bench to bedside.** Gastroenterology. 2021; 160(5):1502-1520. e1. doi: 10.1053/j.gastro.2020.09.065

4. Lee MH, Yang HI, Yuan Y, L'Italien G, Chen CJ. **Epidemiology and natural history of hepatitis C virus infection.** World J Gastroenterol. 2014; 20(28):9270-80. doi: 10.3748/wjg.v20.i28.9270

5. **European Association for the Study of the Liver. EASL Recommendations on Treatment of Hepatitis C 2016.** J Hepatol. 2017; 66(1):153-94. doi: 10.1016/j.jhep.2016.09.001

6. Lucidarme D, Foucher J, Le Bail B, Vergniol J, Castera L, Duburque C, et al. **Factors of accuracy of transient elastography (fibroscan) for the diagnosis of liver fibrosis in chronic hepatitis C.** Hepatology. 2009; 49(4):1083-89. doi: 10.1002/hep.22748

7. Karic U, Pesic-Pavlovic I, Stevanovic G, Korac M, Nikolic N, Radovanovic-Spurnic A, et al. **FIB-4 and APRI scores for predicting severe fibrosis in chronic hepatitis C - a developing country's perspective in DAA era.** J Infect Dev Ctries. 2018; 12(3):178-82. doi: 10.3855/jidc.10190

8. Dramane S, Florine G, Al-Vera VDM, Lah Bi R. **Performance of APRI and FIB-4 Scores Compared to Fibro Scan in the Assessment of Fibrosis in Chronic Viral Hepatitis in Cote D'Ivoire.** J Clin Gastroenterol Hepatol. 2022; 6(1):1-4

9. **European Association for the Study of the Liver; Clinical Practice Guideline Panel; Chair: EASL Governing Board representative: Panel members: EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis - 2021 update.** J Hepatol. 2021; 75(3):659-89. doi: 10.1016/j.jhep.2021.05.025

10. 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(11):4082-88. doi: 10.4103/jfmpc.jfmpc_666_21

11. Sripongpun P, Tangkijvanich P, Chotiyaputta W, Charatcharoenwitthaya P, Chaiteerakij R, Treeprasertsuk S, et al. **Evaluation of aspartate aminotransferase to platelet ratio index and fibrosis 4 scores for hepatic fibrosis assessment compared with transient elastography in chronic hepatitis C patients.** J Gastroenterol Hepatol Open. 2019; 4(1):69-74. doi: 10.1002/jgh3.12219

12. Suan MAM, Chan HK, Sem X, Shilton S, Hassan MRA. **Diagnostic performance of two non-invasive biomarkers used individually and in sequential combination for cirrhosis associated with hepatitis C virus infection.** Sci Rep. 2022; 12(1):20153. doi: 10.1038/s41598-022-24612-9

13. Karic U, Pesic-Pavlovic I, Stevanovic G, Korac M, Nikolic N, Radovanovic-Spurnic A, et al. **FIB-4 and APRI scores for predicting severe fibrosis in chronic hepatitis C - a developing country's perspective in DAA era.** J Infect Dev Ctries. 2018; 12(3):178-182. doi: 10.3855/jidc.10190

14. Schmid P, Bregenzer A, Huber M, Rauch A, Jochum W, Müllhaupt B, et al. **Progression of Liver Fibrosis in HIV/HCV Co-Infection: A Comparison between Non-Invasive Assessment Methods and Liver Biopsy.** PLoS One. 2015; 10(9):e0138838. doi: 10.1371/journal.pone.0138838

15. Merli M, Galli L, Castagna A, Salpietro S, Gianotti N, Messina E, et al. **Diagnostic accuracy of APRI, FIB-4 and Forns for the detection of liver cirrhosis in HIV/HCV-coinfected patients.** New Microbiol. 2016; 39(2):110-113.

16. Ragazzo TG, Paranagua-Vezozzo D, Lima FR, Mazo DFDC, Pessoa MG, et al. **Accuracy of transient elastography-FibroScan®, acoustic radiation force impulse (ARFI) imaging, the enhanced liver fibrosis (ELF) test, APRI, and the FIB-4 index compared with liver biopsy in patients with chronic hepatitis C.** Clinics (Sao Paulo). 2017; 72(9):516-25. doi: 10.6061/clinics/2017(09)01

17. Puigvehí M, Hernández J, Broquetas T, Coll S, Garcia-Retortillo M, Cañete N, et al. **Diagnostic Accuracy of the Enhanced Liver Fibrosis (ELF®) Score Using HCV-Infected Serum Samples Cryopreserved for up to 25 Years.** PLoS One. 2016; 11(12):e0164883. doi: 10.1371/journal.pone.0164883

18. Pradat P, Voirin N, Tillmann HL, Chevallier M, Trépo C. **Progression to cirrhosis in hepatitis C patients: an age-dependent process.** Liver Int. 2007; 27(3):335-339. doi:10.1111/j.1478-3231.2006.01430.x

19. Dramane S, Florine G, Al-Vera VDM, Lah Bi R. **Performance of APRI and FIB-4 Scores Compared to Fibro Scan in the Assessment of Fibrosis in Chronic Viral Hepatitis in Cote D'Ivoire.** J Clin Gastroenterol Hepatol. 2022; 6(1):2 (Repeat)

20. Toure PS, Berthe A, Diop MM, Diarra AS, Lo G. **Non-invasive markers in the evaluation of hepatic fibrosis in Senegalese chronic carriers of the hepatitis B virus: About 404 cases.** Afrn J of Int Med. 2017; 4(2):30-4.

21. 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 Fam Med Prim Care. 2021; 10:4082-88. (Repeat)

22. Vallet-Pichard A, Mallet V, Nalpas B, Verkarre V, Nalpas A, Dhalluin-Venieret V, al. **FIB-4: An inexpensive and accurate marker of fibrosis in HCV infection. Comparison with liver biopsy and fibrotest.** Hepatology. 2007; 46(1):32-36. doi: 10.1002/hep.21669

23. Lin ZH. **Performance of the aspartate aminotransferase-to-platelet ratio index for the staging of hepatitis C-related fibrosis: An updated meta-analysis.** Hepatol Baltim Md. 2011; 53:726-36.

24. Joo SK. **Prospective comparison of noninvasive fibrosis assessment to predict advanced fibrosis or cirrhosis in Asian patients with hepatitis C.** J Clin Gastroenterol. 2015; 49:697-704.

25. Holmberg SD. **Noninvasive serum fibrosis markers for screening and staging chronic hepatitis C virus patients in a large US cohort.** Clin Infect Dis. 2013; 57:240-46.

26. Chou R, Wasson N. **Blood tests to diagnose fibrosis or cirrhosis in patients with chronic hepatitis C virus infection: A systematic review.** Ann Intern Med. 2013; 158:807-20.

27. Borsoi Viana MS, Takei K, Collarile Yamaguti DC, Guz B, Strauss E. **Use of AST platelet ratio index (APRI Score) as an alternative to liver biopsy for treatment indication in chronic hepatitis C.** Ann Hepatol. 2009; 8:26-31.

28. Papadopoulos N, Vasileiadi S, Papavdi M, Sveroni E, Antonakaki P, Dellaporta E, et al. **Liver fibrosis staging with combination of APRI and FIB-4 scoring systems in chronic hepatitis C as an alternative to transient elastography.** Ann Gastroenterol. 2019; 32:498-503.

AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Rana Ahsan:** Data collection, drafting, proof reading, responsible for data's integrity.
2	**Mansoor ul Haq:** Conception and designed, proof reading, critical revisions.