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COMPARISON BETWEEN FIB-4 INDEX AND APRI INDEX FOR PREDICTING THE SEVERITY OF LIVER DISEASE IN THE PATIENTS OF CHRONIC HEPATITIS C: A RETROSPECTIVE SINGLE-CENTRE STUDY

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Abstract

Hepatitis C virus (HCV) is a significant cause of chronic liver disease which may progress to liver fibrosis, liver cirrhosis and hepato-cellular carcinoma. According to the Pakistan Medical Association, the current prevalence of HCV in Pakistan is 7.5%, the highest recorded globally, equating to an estimated 9.8 million individuals living with the infection. In response to the global burden, the World Health Organization has set an ambitious target to eliminate hepatitis as a public health threat by the year 2030. This goal underscores the urgent need for accessible, cost-effective and non-invasive methods to assess the severity of liver disease in patients with HCV, particularly in rural and resource limited settings. Liver biopsy, though regarded as the gold standard, is invasive, necessitating specialized equipment and clinical expertise. Similarly, non-invasive modalities such as transient elastography and advanced imaging techniques remain expensive and operator dependent. The present study aimed to compare the diagnostic performance of the FIB-4 and APRI indices in predicting the severity of hepatic fibrosis or cirrhosis. A total of 159 medical records of patients diagnosed with HCV-related liver fibrosis were retrospectively analyzed. All patients underwent clinical examination, alongside laboratory investigations including complete blood count, liver function tests, serum albumin, prothrombin time, and abdominal ultrasonography. FIB-4 and APRI scores were subsequently calculated for each individual. Of the 159 patients, 39(24.53%) were found to have F4 fibrosis, while 120 (75.47%) had fibrosis graded between F0 and F3. Notably, patients with F4 fibrosis exhibited elevated FIB-4 scores (mean4.84±4.14) and APRI scores (mean 2.06 ± 3.22) compared to those with milder disease. Receiver operating characteristic (ROC) curve analysis demonstrated that the area under the curve (AUC) for the FIB-4 index was 0.855, compared to 0.767 for the APRI score. These results suggest that FIB-4 demonstrates marginally superior accuracy in identifying patients with advanced fibrosis or cirrhosis secondary to HCV infection.

INTRODUCTION

Hepatitis C virus (HCV) infection is a significant global health concern, capable of causing both acute and chronic hepatitis. The disease spectrum ranges from a self-limiting illness to chronic liver disease, which may progress to hepatic fibrosis, cirrhosis, and

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ultimately hepato-cellular carcinoma (HCC). In addition to hepatic involvement, HCV is associated with various extra-hepatic manifestations, including autoimmune phenomena and systemic conditions such as mixed cryoglobulinaemia, lichen planus, porphyria cutanea tarda, polyarteritis nodosa, and lymphoproliferative disorders. According to the World Health Organization (WHO), the estimated prevalence of HCV in Pakistan in 2025 was 4.3%. However, data from the Pakistan Medical Association indicate a significantly higher viraemic prevalence of 7.5%, the highest globally, equating to approximately 9.8 million individuals affected nationwide. The progression of chronic HCV infection leads to persistent hepatic inflammation, hepatocyte necrosis, and increased deposition of extracellular matrix, culminating in fibrotic changes and architectural distortion of the liver. Cirrhosis typically develops after 15 to 20 years of ongoing hepatic injury. Early detection and staging of liver fibrosis are essential for appropriate clinical management and prognosis. Liver biopsy remains the gold standard for assessing fibrosis; however, it is invasive, costly, and not routinely available in many healthcare settings, particularly in low-resource regions. Consequently, there has been growing interest in non-invasive alternatives, including imaging modalities and serum biomarkers. Among the most commonly used indices are the Fibrosis-4 (FIB-4) index and the Aspartate Aminotransferase to Platelet Ratio Index (APRI), both of which rely on routinely available laboratory parameters. These scoring systems are simple, cost-effective, and can be easily calculated in outpatient settings. The present study was undertaken to evaluate the utility of FIB-4 and APRI scores in predicting severe liver fibrosis or cirrhosis in patients with chronic HCV infection and to determine which of the two indices demonstrates greater diagnostic accuracy.

Materials and Methods

This retrospective, single-centre study was conducted after obtaining formal approval from the District Health Authority, Rawalpindi, Punjab, Pakistan. The research adhered to the ethical principles outlined in the Declaration of Helsinki (1975). Medical records of 159 patients diagnosed with HCV-related liver disease were reviewed. The age of the patients ranged from 30 to 60 years.

Diagnosis of liver fibrosis or cirrhosis was based on a combination of clinical evaluation, laboratory investigations and abdominal ultrasonography. Patients were excluded if they had chronic liver disease due to causes other than hepatitis C, co-infection with hepatitis B or HIV/AIDS, decompensated liver cirrhosis or hepato-cellular carcinoma (HCC).

All included patients had undergone thorough assessment, which encompassed medical history, physical examination, complete blood count (CBC), liver function tests (LFTs), serum albumin, prothrombin time and abdominal ultrasonography. Based on disease severity, the cohort was categorized into two groups: those with F4 fibrosis and those with non-F4fibrosis (F0–F3).

FIB-4 and APRI scores were calculated for each patient using standard formulae. Cut-off values derived from existing literature were applied: A FIB-4 score of ≥3.25 and an APRI score≥ of 2.0 were considered indicative of cirrhosis.

Statistical Analysis

Continuous variables were expressed as means with standard deviations (SD), while categorical variables were reported as frequencies and percentages. Pearson's correlation coefficient was used to assess the relationship between quantitative variables. Comparisons between groups were conducted using the independent sample st-test for continuous variables and the chi-squared (χ^2) test for categorical variables.

Diagnostic performance of the FIB-4 and APRI indices in detecting cirrhosis was evaluated using receiver operating characteristic (ROC) curve analysis. The area under the ROC curve (AUC) was calculated for both indices, with values ranging from 0.50 (no discriminatory ability) to 1.00 (perfect discrimination).

All statistical analyses were performed using SPSS-21. A p-value of less than 0.05 was considered statistically significant.

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Results

Out of the 159 patients included in the study, 39(24.53%) were found to have F4 fibrosis, while the remaining 120 (75.47%) had fibrosis ranging from F0 to F3. Among the non-F4 group, 73 patients (45.91%) were classified as having F0–F1 fibrosis, 27 patients (16.98%) had F2 fibrosis and 20 patients (12.58%) had F3 fibrosis.

Table-1 presents the demographic characteristics and laboratory findings of the total cohort as well as the subgroups, along with the statistical comparisons between the patients with F4 fibrosis and those with non-F4 fibrosis. Significant differences were observed across several parameters ($p<0.05$). Specifically, patients with F4 fibrosis had significantly lower platelet counts ($p<0.001$) and higher levels of AST ($p=0.01$), FIB-4 index ($p=0.006$) and APRI index ($p=0.044$) as compared to the non-F4 group.

Sr #	Variable	Study Population	F4 Fibrosis Group	Non-F4 Fibrosis Group	*p*-value
1	**Number of Males**	83 (52.21 %)	15	68	-
2	**Number of Females**	76 (47.79 %)	24	52	-
3	**Age (years)**	51.24 ± 10.36	59.5 ± 18.16	55.35 ± 15.63	0.156
4	**Platelets (10^9/l)**	179.52 ± 71.57	132.50 ± 40.50	205.40 ± 60.02	< 0.001
5	**S. Total Bilirubin (mg/dl)**	0.83 ± 0.33	0.83 ± 0.33	0.83 ± 0.33	0.544
5	**S. Total Bilirubin (mg/dl)**	0.83 ± 0.33	0.83 ± 0.33	0.83 ± 0.33	0.544
6	**ALT (IU/l)**	64.99 ± 58.88	88.46 + 70.81	57.36 + 53.01	0.010
7	**AST (IU/l)**	55.1 ± 33.74	79.08 + 51.59	47.33 + 21.97	0.063
8	**S. Albumin (g/dl)**	4.15 ± 0.51	3.52 + 1.12	4.20 + 0.57	0.350
9	**FIB-4 Index**	2.91 ± 3.41	4.84 + 4.14	2.29 + 2.90	0.006
10	**APRI Index**	1.01 ± 1.78	2.06 + 3.22	0.68 + 0.76	0.044

Figures 2 and 3 illustrate the distribution of FIB-4 and APRI indices across fibrosis stages as determined by abdominal ultrasonography. Both indices were significantly elevated in patients with F4 fibrosis relative to those with milder stages.

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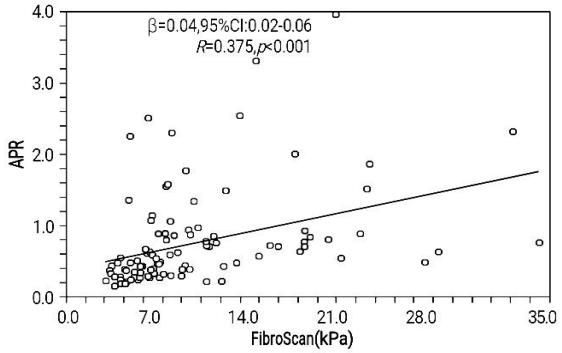


Fig.2. Association of aspartate aminotransferase-to-platelet-ratio index (APRI) and FibroScan .kPa—kilopascals

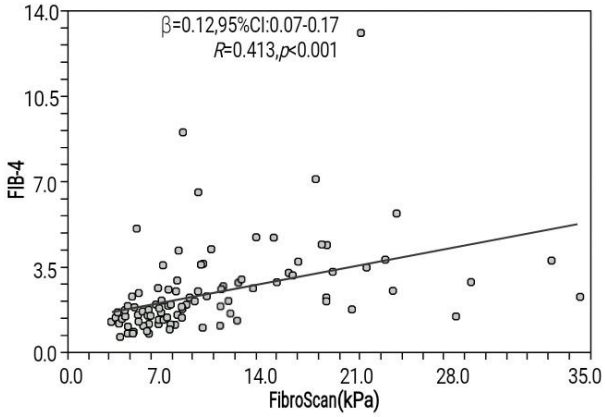
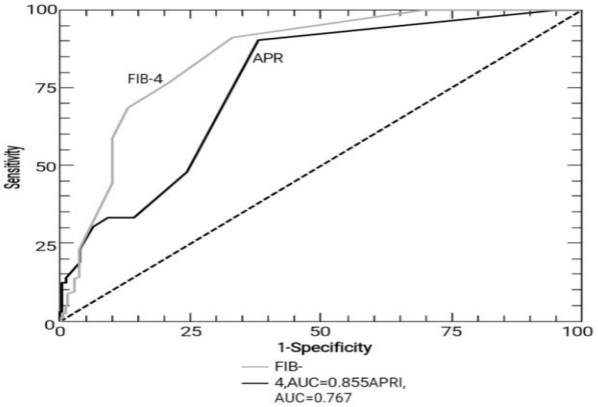


Fig.3. Association of fibrosis index based on fou rfactors (FIB-4) and FibroScan. kPa —kilopascals

Receiver operating characteristic (ROC) curve analysis was performed to assess the diagnostic accuracy of FIB-4 and APRI in predicting cirrhosis. The area under the curve (AUC) for the FIB-4 index was 0.855, while the AUC for the APRI index was 0.767. These findings indicate that although both indices demonstrated acceptable discriminatory ability, the FIB-4 index exhibited superior performance in identifying patients with cirrhosis. Predictors of cirrhosis revealed that the FIB-4 had an area under the curve (AUC) of 0.855 (CI: 0.813 - 0.936) while the APRI score had an AUC of 0.767 (CI: 0.79 - 0.932). The ROC analysis demonstrated that the FIB-4 and APRI scores were indeed able to predict cirrhosis satisfactorily (AUC = 0.875, p < 0.001for FIB-4 and AUC = 0.076, p <0.001 for APRI) (Fig.4).



Discussion

Liver fibrosis, if left undetected and untreated, can progress to cirrhosis and hepato-cellular carcinoma, leading to significant morbidity and mortality. Early diagnosis is therefore critical to delay or halt the progression of liver disease. Although liver biopsy remains the gold standard for diagnosing fibrosis due to its histo-pathological accuracy, it is not feasible for routine use owing to its invasiveness, cost, and associated complications.

In recent years, non-invasive alternatives such as transient elastography have gained attention. However, this modality is limited by several factors, including high cost, the need for trained personnel, and reduced accuracy in patients with obesity, ascites, narrow intercostal spaces, acute hepatitis, or extra-hepatic cholestasis. Consequently, serum-based biomarkers such as the FIB-4 and APRI indices, which rely on routine laboratory parameters, have emerged as valuable tools in the assessment of hepatic fibrosis.

In this study, using cut-off values of 3.25 for

FIB-4 and 2.0 for APRI to predict cirrhosis, both indices showed significantly higher values in patients with F4 fibrosis compared to those with milder stages (F0–F3). ROC curve analysis demonstrated that the FIB-4 index had an AUC of 0.855, indicating excellent discriminative ability, whereas the APRI index had a slightly lower AUC of 0.767. Both results were statistically significant ($p < 0.001$), affirming the diagnostic utility of these indices.

PThe superior performance of FIB-4 over APRI may be attributed to the broader range of parameters it

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incorporates. In addition to AST and platelet count, FIB-4 includes age and ALT—variables that potentially enhance diagnostic precision. However, in our study, neither ALT (p=0.063) nor age (p=0.156) showed statistically significant differences between the fibrosis groups, which may have slightly influenced the FIB-4's performance.

Conversely, APRI is based solely on AST and platelet count. In our cohort, AST levels were significantly elevated in the F4 fibrosis group compared to the non-F4 group (74.08±56.59 IU/ mL vs. 42.33±26.97 IU/ mL; p=0.01), while platelet counts were markedly reduced in the F4 group (p<0.001). These findings support the relevance of these two parameters in identifying advanced fibrosis.

Overall, both FIB-4 and APRI proved to be reliable, accessible and cost-effective non-invasive tools for assessing liver fibrosis and reducing the reliance on more sophisticated modalities like transient elastography.

Limitations

The principal limitations of this study include its retrospective design and relatively small sample size. Future research should aim to validate these findings through prospective studies with larger patient cohorts to further strengthen the evidence base for the routine use of these indices in clinical practice.

Conclusions

This study confirms that both FIB-4 and APRI

indices are effective non-invasive tools for predicting severe hepatic fibrosis and cirrhosis in patients with chronic Hepatitis C virus (HCV) infection. Among the two, the FIB-4 index demonstrated superior diagnostic performance in distinguishing patients with cirrhosis from those without cirrhosis. These findings suggest that FIB-4 index may serve as a more valuable screening tool to identify patients, in whom liver biopsy could be safely deferred, thereby reducing the need for invasive procedures in routine clinical practice.

REFERENCES

1. Goto K, Roca Suarez AA, Wrensch F, et al. Hepatitis C virus and hepatocellular carcinoma: when the host loses its grip. Int J Mol Sci 2020; 21: E3057.
2. Kchir H, Kaffel D, Cherif D, et al. Rheumatologic manifestations during chronic viral hepatitis C. Tunis Med 2019; 97: 1251-1257.
3. Gill K, Ghazinian H, Manch R, et al. Hepatitis C virus as a sys-temic disease: reaching beyond the liver. Hepatol Int 2016; 10: 415-423.
4. WHO. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Geneva, Switzerland 2018.
5. Flisiak R, Zarębska-Michaluk D. Perspectives of hepatitis C virus (HCV) elimination in Poland. Clin Exp Hepatol 2019; 5:210-214.
6. Roehlen N, Crouchet E, Baumert TF. Liver fibrosis: mechanistic concepts and therapeutic perspectives. Cells 2020; 9: 875.
7. Böttcher K, Pinzani M. Pathophysiology of liver fibrosis and the methodological barriers to the development of anti-fibrogenic agents. Adv Drug Deliv Rev 2017; 121: 3-8.
8. Sebastiani G, Gkouvatsos K, Pantopoulos K. Chronic hepatitis C and liver fibrosis. World J Gastroenterol 2014; 20: 11033-11053.
9. Gudowska M, Wrona A, Gruszewska E, et al. Simple non-invasive markers for early diagnosis and determination of the severity of liver diseases. Clin Exp Hepatol 2016; 2: 149-154.
10. Catanzaro R, Sapienza C, Milazzo M, et al. Liver fibrosis: evaluation with diffusion-weighted magnetic resonance imaging in patients with chronic liver disease. Minerva Gastroenterol Dietol 2013; 59: 313-320.
11. Catanzaro R, Milazzo M, Arona S, et al. Diagnostic accuracy of enhanced liver fibrosis test to assess live fibrosis in patients with chronic hepatitis C. Hepatobiliary Pancreat Dis Int 2013;12: 500-507.fibrosis in patients with chronic hepatitis C.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Hepatobiliary Pancreat Dis Int 2013;12: 500-507.

12. Baranova A, Lal P, Birerdinc A, et al. Non-invasive markers for hepatic fibrosis. BMC Gastroenterol 2011; 11: 91.
13. Wai CT, Greenson JK, Fontana RJ, et al. A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. Hepatology 2003; 38: 518-526.
14. WHO Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection.(July 2018) Available at: https://www.who.int/publications/i/item/guide-care-treat-persons-diagnosed-chronic-hepatitis-c-978-92-4-155034-5
15. Zeybel M, İdilman R. Serum biomarkers for the evaluation of liver fibrosis: the need for better tests. Turk J Gastroenterol 2018; 29: 377-378.
16. Sebastiani G, Alberti A. How far is noninvasive assessment of liver fibrosis from replacing liver biopsy in hepatitis C? J Viral Hepat 2012; 19: 18-32.
17. Millonig G, Reimann FM, Friedrich S, et al. Extrahepatic cholestasis increases liver stiffness (FFibroscan irrespective of fibrosis. Hepatology 2008; 48: 1718-1723.
18. Lurie Y, Webb M, Cytter-Kuint R, et al. Non-invasive diagnosis of liver fibrosis and cirrhosis. World J Gastroenterol 2015; 21: 11567-11583.
19. Sterling RK, Lissen E, Clumeck N, et al. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. Hepatology 2006; 43: 1317-1325.
20. Vallet-Pichard A, Mallet V, Nalpas B, et al. FIB-4: an inexpensive and accurate

    marker of fibrosis in HCV infection, comparison with liver biopsy and fibrotest. Hepatology 2007; 46: 32-36.
21. Güzelbulut F, Akkan Çetınkaya Z, Sezikli M, et al. AST-platelet Ratio Index, Forns Index and FIB-4 in the prediction of significant fibrosis and cirrhosis in patients with chronic hepatitis C. Turk J Gastroenterol 2011; 22: 279-285.
22. Yen YH, Kuo FY, Kee KM, et al. APRI and FIB-4 in the evaluation of liver fibrosis in chronic hepatitis C patients stratified by AST level. PLoS One 2018; 13: e0199760.
23. Yunihastuti E, Wicaksana B, Wiraguna A, et al. Diagnostic performance of APRI and FIB-4 for confirming cirrhosis in Indonesian HIV/HCV co-infected patients. BMC Infect Dis 2020;20: 372.
24. Papaluca T, Craigie A, McDonald L, et al. Non-invasive fibrosis algorithms are clinically useful for excluding cirrhosis in prisoners living with hepatitis C. PLoS One 2020; 15: e0242101.