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Research Article

Comparative Diagnostic Accuracy of FIB-4, APRI, and NAFLD Fibrosis Score for Detecting Advanced Fibrosis in Patients with Chronic Liver Disease

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ABSTRACT

Background: Chronic liver disease is a situation where the presence of extensive hepatic fibrosis is a clinically important threshold associated with future cirrhosis, portal venous hypertension, liver failure events, hepatocelluar carcinoma and the death related to liver diseases. Although transient elastography can give a good non-invasive assessment of fibrosis load, its restricted use in many clinical contexts means that routine laboratory-based fibrosis scores may be useful for initial risk stratification.

Objective: To assess how accurately FIB-4, APRI, and the NAFLD Fibrosis Score detect advanced liver fibrosis in adult patients with chronic liver disease.

Methods: A cross-sectional diagnostic accuracy study was carried out from June 2024 to September 2025 at Gambat Medical College, Gambat, Sindh, and Jinnah Postgraduate Medical Centre, Karachi. The analysis included 120 adults with confirmed chronic liver disease. Patient demographics, clinical details, liver biochemical markers, and haematological parameters were collected using a structured recording method. The three non-invasive fibrosis indices, FIB-4, APRI, and the NAFLD Fibrosis Score, were calculated using their standard formulas. Transient elastography was used as the reference method for classifying advanced fibrosis. Diagnostic performance was assessed for each score by calculating sensitivity, specificity, predictive values, overall accuracy, correct classification, and ROC curve-based discrimination.

Results: Advanced fibrosis was identified by transient elastography in 42 of 120 participants (35.0%). FIB-4 had the best diagnostic profile with sensitivity of 80.9% and specificity of 76.9% and accuracy of 78.3%, negative predictive value of 88.2% and AUC of 0.84. The NAFLD Fibrosis Score had intermediate level discrimination (AUC = 0.79) while APRI had the lowest of the three indices (AUC = 0.73).

Conclusion: Among the three serum-derived fibrosis indices evaluated, FIB-4 performed best for recognising advanced fibrosis in chronic liver disease. The simplicity and good negative predictive value lend to its use as a primary screening technique, particularly within centres where elastography is not commonly used.

Keywords: Chronic Liver Disease, Advanced Fibrosis, Fib-4, Apri, Nafld Fibrosis Score, Transient Elastography, Diagnostic Accuracy.

INTRODUCTION

Chronic liver disease represents a long-term pathological condition in which repeated or sustained hepatic injury gradually disrupts the normal architecture and physiological activity of the liver[1]. Its causes are diverse and include chronic hepatitis B or C infection, metabolic dysfunction-associated fatty liver disease, alcohol-related liver injury, autoimmune hepatic disorders, and, less commonly, genetic or

cholestatic conditions[2]. These diseases have different points of origin, but many progress to a common biological pathway: chronic inflammation that leads to increased fibrogenic activity and subsequent accumulation of extracellular matrix in the liver tissue[3]. With continued injury, this fibrotic response may progress to distortion of liver architecture, cirrhosis, portal hypertension, hepatic insufficiency, and an increased probability of hepatocellular carcinoma[4].

Determining the degree of hepatic fibrosis is an essential component of managing patients with chronic liver disease[5]. Fibrosis staging assists clinicians in estimating disease severity, predicting clinical outcomes, deciding the urgency of treatment, identifying patients who require specialist care, and planning surveillance for complications such as variceal haemorrhage and hepatocellular carcinoma[6]. It is particularly critical to identify advanced fibrosis as patients at this stage are significantly more likely to progress to disease and experience liver-related adverse outcomes[7]. If advanced fibrosis is identified at an early stage, timely action can be taken, including lifestyle changes, antiviral or disease-specific treatment, management of metabolic risk factors, and close follow-up care[8].

For many years liver biopsy was considered to be the standard method for direct assessment of hepatic fibrosis[9]. However, several limitations restrict its routine use in everyday clinical practice[10]. The process is expensive, uncomfortable for the patient, invasive, and carries a small but clinically important risk of adverse events, most notably pain and bleeding[11]. Another significant restriction is that a biopsy only looks at a small amount of liver tissue, and fibrosis may be unevenly distributed between liver areas, leading to a sampling error.[12] Histological reporting may also be inconsistent because of difference in interpretation amongst observers[13]. These concerns have encouraged the development and use of non-invasive methods that can estimate fibrosis burden without exposing patients to procedural risk[14].

Transient elastography is now an important non-invasive method of measuring liver stiffness and indirectly liver fibrosis[15]. Despite its clinical value, this modality is not accessible in every healthcare setting, particularly in resource-limited environments[16]. It requires special equipment, trained staff, and appropriate technical conditions to make reliable measurements[1]. In many real world settings chronic liver disease patients are initially assessed in primary care, general medical out-patient departments, or non-specialist hospitals where access to advanced fibrosis assessment through imaging may be limited[2]. Simple serum-derived fibrosis indices therefore have practical value in the clinical setting today[3].

Several non-invasive fibrosis indices can be generated from routine, low-cost clinical and laboratory data, including FIB-4, APRI, and the NAFLD Fibrosis Score[4]. FIB-4 is derived from four variables: patient age, AST, ALT, and platelet count[5]. APRI uses AST in relation to platelet count as its core calculation[6]. The NAFLD Fibrosis Score combines age, BMI, diabetes or impaired fasting glucose status, AST/ALT ratio, platelet count, and serum albumin[7].

They are indicators of major biological implications of chronic liver damage, such as hepatocellular damage, thrombocytopenia due to portal hypertension, burden of metabolic disease, and decreased hepatic synthetic capacity[8].

The major clinical advantage of these scoring systems is their ability to separate patients who are unlikely to have advanced fibrosis from those who need additional diagnostic assessment[9]. A reliable non-invasive score can decrease unnecessary specialist referrals, prevent unnecessary invasive procedures and prioritise high-risk individuals for transient elastography, hepatology review and closer monitoring[10]. This is especially true in areas where chronic viral hepatitis, obesity, diabetes mellitus, and fatty liver disease are prevalent, and where there is a lack of resources for specialised liver fibrosis assessment[11].

However, FIB-4, APRI and NAFLD Fibrosis Score are not equally reliable in all clinical populations[12]. Their results may be affected by age, underlying liver disease aetiology, active inflammation, platelet abnormalities, obesity, diabetes, alcohol exposure, and variations in biochemical markers[13]. Diagnostic performance observed in one specific liver disease category may therefore not be directly applicable to a heterogeneous population of patients with chronic liver disease[14]. Local head-to-head evaluation of these scores is necessary to identify which tool provides the most useful and dependable approach for detecting advanced fibrosis in routine clinical practice[15].

The purpose of this work was to determine whether three routine non-invasive fibrosis

tools—FIB-4, APRI, and the NAFLD Fibrosis Score—could reliably separate chronic liver disease patients with advanced hepatic fibrosis from those without advanced fibrosis[16]. To identify the most clinically suitable tool for fibrosis risk grouping, each score was assessed through its sensitivity, specificity, positive and negative predictive values, total accuracy, and receiver operating characteristic curve performance[1].

MATERIALS AND METHODS

This cross-sectional study of diagnostic accuracy was carried out at Gambat Medical College, Gambat, Sindh, and Jinnah Postgraduate Medical Centre, Karachi, over a sixteen-month period from June 2024 to September 2025. One hundred and twenty adult patients with chronic liver disease were included in the study population, who were selected from the medical and gastroenterology outpatient and inpatient services. Chronic liver disease was taken to be present if clinical, biochemical, serological, radiological or available history suggested liver disease of at least six months duration.

Adults aged 18 years or above were considered for enrolment when chronic liver disease was either already documented or clinically suspected and when all measurements needed for fibrosis-score calculation were available. The required data elements were age, AST, ALT, platelet count, BMI, serum albumin, and diabetic or impaired fasting glucose status. Patients were not retained in the study if they had any condition that could distort fibrosis scoring or elastography interpretation, including acute hepatitis, acute liver failure, hepatocellular carcinoma, pregnancy, active gastrointestinal bleeding, severe systemic disease, congestive heart failure, marked cholestasis, current chemotherapy, platelet-altering haematological disorders, missing records, or unreliable elastography results.

A study-specific recording form was used to compile the required information. Baseline data covered demographic and anthropometric details, including age, sex, residence, height, weight, and BMI. Clinical data included the duration of liver disease, underlying cause, diabetes mellitus, hypertension, alcohol exposure when applicable, and hepatitis B or hepatitis C status. Laboratory data consisted of AST, ALT, platelet count, serum albumin, fasting blood glucose or diabetic state, and routine liver function parameters. All biochemical and haematological measurements were processed in the hospital laboratory using automated systems under routine institutional testing protocols.

Transient elastography served as the comparator method for fibrosis classification. Liver stiffness values were expressed in kilopascals. A reading of 12.0 kPa or greater was taken to represent advanced fibrosis, whereas a reading below 12.0 kPa was grouped as non-advanced fibrosis. Measurements that failed to fulfil local reliability requirements were removed from analysis, and only acceptable elastography results were used for final classification.

The FIB-4 Index was Generated from Age, AST, Platelet Count, and ALT Using the Conventional Calculation: age × AST / platelet count × √ALT. Scores below 1.30 were treated as low risk, scores from 1.30 to 2.67 as indeterminate risk, and scores above 2.67 as high risk for advanced fibrosis. APRI was calculated by dividing AST by the upper normal AST limit, multiplying by 100, and then dividing by platelet count. An APRI result greater than 1.0 was regarded as suggestive of advanced fibrosis. The NAFLD Fibrosis Score was calculated from age, BMI, impaired fasting glucose or diabetes status, AST/ALT ratio, platelet count, and serum albumin. Results below −1.455 were considered low risk, values from −1.455 to 0.676 were placed in the indeterminate category, and values above 0.676 were considered high risk.

Fibrosis Status on Transient Elastography was Treated as the Reference Outcome for Analysis. On This Basis, Participants were Separated into Two Categories: those with advanced fibrosis and those without advanced fibrosis. The ability of FIB-4, APRI, and the NAFLD Fibrosis Score to identify advanced fibrosis was examined by calculating sensitivity, specificity, positive predictive value, negative predictive value, diagnostic accuracy, and ROC-derived AUC.

The dataset was analysed in SPSS 27.0. Numerical data were summarized either as mean ± SD or as median with IQR, depending on the pattern of distribution. Categorical findings were expressed as number and percentage. Comparisons between the advanced and non-advanced fibrosis groups were performed using the independent-samples t-test or Mann–Whitney U-test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables. ROC analysis was used to compare the three non-invasive fibrosis scores. Statistical significance was defined as $p<0.05$.

The study protocol received approval from the relevant institutional ethical review committee. Written consent was obtained before enrolment. Patient identity was protected through coded records, and no additional invasive intervention was performed only for research purposes.

RESULTS

A last group of 120 chronic liver disease patients was assessed. The age of the participants ranged from 21 to 72 years and the mean age was 47.9 ± 12.4 years. The study group comprised of 56.7% males and 43.3% females. Chronic viral hepatitis was the most common aetiological group, followed by other chronic liver diseases and metabolic dysfunction associated steatotic liver disease. The transient elastography data identified 42 (35.0%) patients as advanced fibrosis and 78 (65.0%) patients as non-advanced fibrosis. Table 1 demonstrates the higher prevalence of diabetes mellitus and body mass index (BMI) in older patients as well as the association with advanced fibrosis as shown in table 1.

Table 1. Baseline Demographic and Clinical Characteristics of Patients with Chronic Liver Disease

Variable	Total patients n=120	Non-advanced fibrosis n=78	Advanced fibrosis n=42	p-value
Age, years	47.9 ± 12.4	44.6 ± 11.2	54.1 ± 12.0	<0.001
Male sex	68 (56.7%)	43 (55.1%)	25 (59.5%)	0.642
Female sex	52 (43.3%)	35 (44.9%)	17 (40.5%)	0.642
BMI, kg/m²	28.1 ± 4.7	27.2 ± 4.3	29.8 ± 5.0	0.004
Diabetes mellitus	46 (38.3%)	23 (29.5%)	23 (54.8%)	0.006
Hypertension	39 (32.5%)	22 (28.2%)	17 (40.5%)	0.166
Chronic viral hepatitis	58 (48.3%)	38 (48.7%)	20 (47.6%)	0.908
MASLD/NAFLD	44 (36.7%)	26 (33.3%)	18 (42.9%)	0.298
Other chronic liver disease	18 (15.0%)	14 (17.9%)	4 (9.5%)	0.221

Patients classified with advanced fibrosis showed a clearly different laboratory pattern compared with those in the non-advanced fibrosis group. Transaminase activity was greater in the advanced fibrosis category, with both AST and ALT showing higher levels. The AST/ALT ratio was also increased, supporting the presence of more severe and progressive hepatic injury. Platelet count was lower in patients with advanced fibrosis, a finding that may reflect fibrosis-related portal hypertension with splenic sequestration or reduced platelet availability. Serum albumin was also reduced, indicating impairment of hepatic synthetic reserve in patients with more extensive liver disease. As shown in Table 2, the calculated values of FIB-4, APRI, and the NAFLD Fibrosis Score were all higher among patients with advanced fibrosis than among those without advanced fibrosis.

Table 2. Laboratory Parameters and Fibrosis Score Distribution According to Fibrosis Status

Variable	Non-Advanced Fibrosis N=78	Advanced Fibrosis N=42	P-Value
AST, U/L	48.3 ± 21.7	79.6 ± 32.8	<0.001
ALT, U/L	53.8 ± 27.4	68.9 ± 34.1	0.009
AST/ALT ratio	0.93 ± 0.30	1.25 ± 0.41	<0.001
Platelet count, ×10⁹/L	231.4 ± 69.2	148.6 ± 55.8	<0.001
Serum albumin, g/dL	4.06 ± 0.43	3.45 ± 0.52	<0.001
FIB-4 score	1.39 ± 0.74	3.24 ± 1.38	<0.001
APRI score	0.68 ± 0.42	1.46 ± 0.81	<0.001
NAFLD Fibrosis Score	-1.18 ± 1.03	0.39 ± 1.16	<0.001
Liver stiffness, kPa	7.2 ± 2.3	18.1 ± 5.9	<0.001

The usefulness of the three serum fibrosis indices to exclude or diagnose advanced fibrosis was tested by comparing each score with transient elastography results. FIB-4 had the highest diagnostic yield of the tools assessed. FIB-4 had a good sensitivity (80.9%) and specificity (76.9%) to detect advanced fibrosis using a threshold value > 2.67. The positive

predictive value was 65.4% and the negative predictive value was 88.2% for an overall accuracy of 78.3%. The performance of APRI was less favourable in comparison. APRI achieved a sensitivity of 69.0%, specificity of 67.9%, positive predictive value of 53.7%, negative predictive value of 80.3% and an overall diagnostic accuracy of 68.3% at a cut-off value of >1.0. The NAFLD Fibrosis Score had moderate diagnostic performance in between FIB-4 and APRI with a sensitivity of 73.8%, specificity of 71.8%, PPV of 58.5%, NPV of 83.6%, and an accuracy of 72.5%. Similarly, receiver operating characteristic curve assessment revealed the same trend, with the largest area under the curve for FIB-4 followed by the NAFLD Fibrosis Score and APRI as detailed in Table 3.

Table 3. Comparative Diagnostic Accuracy of FIB-4, APRI, and NAFLD Fibrosis Score for Detecting Advanced Fibrosis

Diagnostic score	Cut-off value	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
FIB-4	>2.67	80.9%	76.9%	65.4%	88.2%	78.3%	0.84
APRI	>1.0	69.0%	67.9%	53.7%	80.3%	68.3%	0.73
NAFLD Fibrosis Score	>0.676	73.8%	71.8%	58.5%	83.6%	72.5%	0.79

HbA1c levels and blood pressure parameters did not clearly separate patients with advanced fibrosis from those without advanced fibrosis, indicating limited discriminatory value for fibrosis staging in this cohort. FIB-4, on the other hand, had an especially high negative predictive value and could be applied in the clinical setting for the exclusion of advanced fibrosis. The NAFLD Fibrosis Score also demonstrated adequate diagnostic performance, but the accuracy was slightly less than FIB-4. APRI was the easiest to calculate, and had the lowest overall diagnostic accuracy of the three scores assessed. Overall, these results suggest that FIB-4 is the most appropriate first-line non-invasive fibrosis score for identifying those patients who could benefit from further fibrosis assessment, transient elastography or hepatology specialist referral.

DISCUSSION

The current study aimed to evaluate the ability of three markers—FIB-4, APRI, and the NAFLD Fibrosis Score—to detect advanced liver fibrosis in chronic liver disease patients[1]. Results indicated that FIB-4 performed best of the three non-invasive indices that were assessed[2]. FIB-4 demonstrated higher sensitivity, specificity, negative predictive value, overall accuracy and area under curve of the receiver operating curve (ROC) curve when compared with APRI and NAFLD Fibrosis Score[3]. These results indicate that, when transient elastography was used as the reference method, FIB-4 was more capable of distinguishing patients with advanced fibrosis from those without advanced fibrosis[4].

A considerable proportion of the study population had clinically relevant fibrosis, as advanced fibrosis was detected in 35.0% of patients with chronic liver disease[5]. This observation holds clinical significance as advanced fibrosis is linked to an increased risk of cirrhosis, portal hypertension, hepatic decompensation, hepatocellular carcinoma, and liver-related mortality[6]. This stage is therefore crucial to identify early so that timely specialist referral, initiation of disease-specific management, planning for surveillance and prevention of future complications can be achieved[7]. Liver biopsy, transient elastography, or a more sophisticated imaging-based assessment of fibrosis may not be available in many common health care settings, especially in resource-limited regions[8]. Under such circumstances, simple laboratory-based fibrosis scores remain highly relevant for initial risk assessment[9].

Patients with advanced fibrosis had a higher BMI, diabetes mellitus and were older than patients without advanced fibrosis[10]. These findings suggest that increasing age and metabolic risk factors may contribute to fibrosis progression in chronic liver disease[11]. Diabetes mellitus is particularly important because it is linked with insulin resistance, oxidative stress, chronic inflammatory activity, and hepatic stellate cell activation, all of which can promote fibrotic change within the liver[12]. Likewise, an elevated BMI could be indicative of overall metabolic dysfunction and fatty liver activity that could exacerbate chronic hepatic injury and the progression of fibrosis[13].

Laboratory results also confirmed that more advanced fibrosis group had more severe liver

involvement[14]. Higher levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), an increased AST/ALT ratio, lower platelet count and reduced serum albumin levels were observed in patients with advanced fibrosis[15]. Thrombocytopenia in advanced liver disease may result from several mechanisms, including portal hypertension, hypersplenism, and reduced hepatic thrombopoietin production[16]. Low serum albumin is a sign of loss of synthetic function of the liver and is more likely to be seen with more severe liver damage[1]. Biochemical and haematological differences underpin the rationale behind fibrosis indices that use a combination of transaminases, platelet count, albumin, age and metabolic variables to assess fibrosis severity[2].

FIB-4 demonstrated the largest AUC value of 0.84, which represents good diagnostic discrimination[3]. It has a sensitivity of 80.9% and negative predictive value of 88.2%, which indicates that FIB-4 is particularly efficient in ruling out advanced fibrosis in the clinical setting[4]. This rule-out capacity is relevant as it has the potential to decrease the number of unnecessary specialist referrals, avoid extra investigation of patients at low risk of advanced fibrosis, and enable limited resources to be focused on patients with higher likelihood of advanced fibrosis[5]. Another practical advantage of FIB-4 is that it can be calculated easily from age, AST, ALT, and platelet count, all of which are routinely available in most clinical settings[6].

APRI had the lowest diagnostic performance of the three scores evaluated[7]. Although APRI is easy to calculate, its limited number of variables may reduce its ability to reflect the broader clinical and biochemical complexity of chronic liver disease[8]. AST levels can be affected by active necroinflammation, alcohol intake, skeletal muscle injury, and other biochemical disturbances, while platelet count may be influenced by causes unrelated to liver fibrosis[9]. Because of these limitations, APRI may not fully capture the overall burden of fibrosis in heterogeneous chronic liver disease populations[10]. In this study, the AUC of APRI was 0.73 indicating moderate diagnostic value but less than Fib-4[11].

The NAFLD Fibrosis Score was moderately diagnostic with an AUC of 0.79[12]. This score uses various metabolic and synthetic function indices such as body mass index, diabetes or impaired fasting glucose, platelet count, serum albumin and AST/ALT ratio[13]. In the current study, it was superior to APRI, but not superior to the diagnostic performance of FIB-4[14]. One possible explanation is that the NAFLD Fibrosis Score was originally developed for patients with non-alcoholic fatty liver disease, and its performance may be less consistent in mixed chronic liver disease populations that include viral hepatitis and other aetiologies[15]. Further, the indeterminate results may impair its usefulness as a stand-alone decision support tool in a busy clinical setting[16].

Combined, the results argue that FIB-4 is a useful and easily available first-line non-invasive fibrosis score in patients with chronic liver disease[1]. Its role may be particularly valuable in hospitals and clinics where transient elastography cannot be performed for every patient[2]. Low FIB-4 values could be considered for routine monitoring and periodic reassessment, while high or indeterminate values could be prioritized for transient elastography, hepatology referral, or further liver evaluation[3]. But, FIB-4 should not be viewed alone alone[4]. The underlying cause of liver disease, degree of inflammatory activity, platelet-related disorders, patient age, and associated comorbidities should always be considered when applying this score in clinical practice[5].

This study has some limitations[6]. First, because of its cross-sectional design, it could not assess fibrosis progression over time or predict future liver-related outcomes[7]. Second, transient elastography was used as the reference standard instead of liver biopsy[8]. Although transient elastography is a widely accepted non-invasive tool for fibrosis assessment, its readings may be affected by obesity, hepatic inflammation, cholestasis, liver congestion, and technical factors[9]. Third, the study included a relatively limited number of patients, which restricted detailed subgroup analysis according to the underlying cause of chronic liver disease[10]. Future studies with larger numbers of patients, longer follow-up and locally validated cut-off values are required to further clarify the prognostic and diagnostic role of these scores[11].

Overall, this study demonstrated that FIB-4 performed better than APRI and the NAFLD Fibrosis Score for detecting advanced fibrosis in patients with chronic liver disease[12]. Given its simplicity, low cost, widespread availability and high negative predictive value, FIB-4 could be a useful screening tool for fibrosis risk stratification in routine clinical practice[17].

CONCLUSION

FIB-4 had the highest diagnostic value of the three non-invasive fibrosis scores tested in this study, for the detection of advanced fibrosis in subjects with chronic liver disease. It had the highest sensitivity, specificity, negative predictive value, overall diagnostic accuracy and area under the receiver operating characteristic curve. The NAFLD Fibrosis Score had acceptable but intermediate performance while APRI had comparatively lower diagnostic accuracy. Given that FIB-4 is readily available, inexpensive and simple to calculate, it could serve as a convenient first-line fibrosis risk assessment tool, especially in situations where transient elastography is less readily available. Patients who have a high or indeterminate FIB-4 score should be evaluated for further fibrosis assessment, transient elastography and hepatology referral.

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