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Original Research Article

Role of Non-Invasive Fibrosis Markers in Predicting Liver Cirrhosis in Patients with Non-Alcoholic Fatty Liver Disease: A Prospective Observational Study

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Abstract:

Background: Non-alcoholic fatty liver disease (NAFLD) is one of the most common chronic liver disorders worldwide and is increasingly recognized as a leading cause of liver cirrhosis. Liver biopsy remains the gold standard for assessing hepatic fibrosis; however, its invasive nature, potential complications, and limited feasibility necessitate the use of reliable non-invasive alternatives. Various serum-based fibrosis markers and scoring systems have emerged as valuable tools for evaluating liver fibrosis and predicting cirrhosis in patients with NAFLD.

Objectives: To evaluate the diagnostic utility of non-invasive fibrosis markers in predicting liver cirrhosis among patients with NAFLD and to determine their correlation with clinical, biochemical, and radiological indicators of advanced liver disease.

Materials and Methods: This prospective observational study was conducted on 100 patients diagnosed with NAFLD attending the Department of Gastroenterology & Hepatology, Kalinga Institute of Medical Sciences, Bhubaneswar KIIT UNIVERSITY. And tertiary care teaching hospital over a period of 15 months. Detailed demographic, clinical, and laboratory data were collected. Non-invasive fibrosis markers including Fibrosis-4 Index (FIB-4), Aspartate Aminotransferase to Platelet Ratio Index (APRI), and NAFLD Fibrosis Score (NFS) were calculated for all participants. Ultrasonography and transient elastography were performed to assess liver fibrosis and cirrhosis. The predictive performance of these markers was analyzed using sensitivity, specificity, positive predictive value, negative predictive value, and receiver operating characteristic (ROC) curve analysis.

Results: Among the 100 NAFLD patients, 24% were found to have liver cirrhosis based on elastographic and radiological findings. Mean FIB-4, APRI, and NFS values were significantly higher in cirrhotic patients compared to non-cirrhotic patients ($p < 0.001$). FIB-4 demonstrated the highest diagnostic accuracy with an area under the ROC curve (AUROC) of 0.88, followed by NFS (0.85) and APRI (0.81). A significant positive correlation was observed between fibrosis marker scores and liver stiffness measurements. Combined use of FIB-4 and NFS improved the predictive accuracy for identifying cirrhosis.

Conclusion: Non-invasive fibrosis markers, particularly FIB-4 and NAFLD Fibrosis Score, are effective and practical tools for predicting liver cirrhosis in patients with NAFLD. These markers can serve as reliable screening methods to identify high-risk patients, reduce the need for liver biopsy, and facilitate early intervention and disease monitoring in routine clinical practice.

Keywords: Non-alcoholic fatty liver disease, NAFLD, liver cirrhosis, fibrosis markers, FIB-4, APRI, NAFLD fibrosis score, transient elastography, liver fibrosis.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is the most prevalent chronic liver disease worldwide and is closely associated with obesity, type 2 diabetes mellitus, dyslipidemia, and metabolic syndrome. It encompasses a spectrum of liver disorders ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), progressive fibrosis, cirrhosis, and hepatocellular carcinoma. The increasing prevalence of NAFLD has made it a major public health concern, particularly in

developing countries undergoing rapid lifestyle and dietary transitions. Liver fibrosis is the most important predictor of long-term outcomes in patients with NAFLD. Progressive fibrosis can eventually lead to liver cirrhosis, portal hypertension, liver failure, and liver-related mortality. Early identification of patients with advanced fibrosis or cirrhosis is therefore essential for timely intervention and improved prognosis. Traditionally, liver biopsy has been regarded as the gold standard for assessing the severity of fibrosis. However, its invasive nature, sampling variability, risk of complications, and high cost limit its routine use in clinical practice. To overcome these limitations, several non-invasive fibrosis markers and scoring systems have been developed and validated. These include the Fibrosis-4 Index (FIB-4), Aspartate Aminotransferase to Platelet Ratio Index (APRI), and NAFLD Fibrosis Score (NFS), which utilize readily available clinical and laboratory parameters. These markers provide a simple, cost-effective, and accessible means of assessing fibrosis severity and identifying patients at risk of cirrhosis. Recent studies have demonstrated the utility of these non-invasive markers in stratifying fibrosis risk and reducing the need for liver biopsy. However, their diagnostic performance may vary across different populations due to demographic, metabolic, and disease-related factors. Therefore, further evaluation of these markers in diverse clinical settings is warranted. The present prospective observational study was undertaken to assess the role of non-invasive fibrosis markers in predicting liver cirrhosis among patients with NAFLD and to determine their effectiveness as screening tools for identifying advanced liver disease.

Materials and Methods

This prospective observational study was conducted in the Department of Department of Gastroenterology & Hepatology, Kalinga Institute of Medical Sciences, Bhubaneswar KIIT UNIVERSITY. And tertiary care teaching hospital over a period of 15 months. The study included 100 consecutive patients diagnosed with Non-Alcoholic Fatty Liver Disease (NAFLD) based on clinical evaluation, biochemical investigations, and ultrasonographic evidence of fatty liver.

Study Population: A total of 100 adult patients aged 18 years and above with confirmed NAFLD. Patients with significant alcohol consumption, viral hepatitis (HBV or HCV), autoimmune liver disease, drug-induced liver injury, Wilson's disease, hemochromatosis, pregnancy, or known chronic liver diseases of other etiologies were excluded from the study.

Data Collection: A detailed history was obtained from all participants, including demographic characteristics, lifestyle factors, medical comorbidities, and medication history. Clinical examination was performed with special emphasis on signs suggestive of chronic liver disease and cirrhosis.

Laboratory Investigations

All patients underwent routine laboratory investigations including:

- Complete blood count (CBC)
- Liver function tests (AST, ALT, bilirubin, albumin)
- Renal function tests
- Fasting blood glucose
- Lipid profile
- Prothrombin time/INR

Based on these parameters, the following non-invasive fibrosis markers were calculated:

1. Fibrosis-4 Index (FIB-4)
2. Aspartate Aminotransferase to Platelet Ratio Index (APRI)
3. NAFLD Fibrosis Score (NFS)

Radiological Assessment: Abdominal ultrasonography was performed in all patients to assess the degree of hepatic steatosis and features suggestive of cirrhosis. Transient elastography (FibroScan) was used to measure liver stiffness and classify the severity of fibrosis. Patients were categorized as cirrhotic or non-cirrhotic based on elastographic findings and radiological evidence of advanced liver disease.

Outcome Measures: The primary outcome was the ability of non-invasive fibrosis markers to predict liver cirrhosis in patients with NAFLD. The correlation between fibrosis marker scores and liver stiffness measurements was also evaluated.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS software version 26.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. Comparisons between groups were performed using the Student's t-test and Chi-square test as appropriate. Receiver Operating Characteristic (ROC) curve analysis was used to determine the diagnostic performance of FIB-4, APRI, and NFS in predicting liver cirrhosis. A p-value of <0.05 was considered statistically significant.

Results

A total of 100 patients with confirmed Non-Alcoholic Fatty Liver Disease (NAFLD) were included in the study. The mean age of the study population was 48.6 ± 11.2 years, with a male predominance (62% males and 38% females). The most common associated comorbidities were

obesity (58%), type 2 diabetes mellitus (46%), hypertension (38%), and dyslipidemia (42%).

Table 1: Demographic and Clinical Characteristics of Study Participants (n = 100)

Characteristic	Value
Mean age (years)	48.6 ± 11.2
Male	62 (62%)
Female	38 (38%)
Obesity	58 (58%)
Type 2 Diabetes Mellitus	46 (46%)
Hypertension	38 (38%)
Dyslipidemia	42 (42%)

Prevalence of Liver Cirrhosis: Based on ultrasonography and transient elastography findings, 24 patients (24%) were diagnosed with liver cirrhosis, while 76 patients (76%) had no evidence of cirrhosis.

Table 2: Distribution of Patients According to Liver Status

Liver Status	Number (%)
Cirrhosis	24 (24%)
Non-cirrhosis	76 (76%)
Total	100 (100%)

Comparison of Non-Invasive Fibrosis Markers: Patients with cirrhosis had significantly higher fibrosis marker scores compared to non-cirrhotic patients.

Table 3: Comparison of Fibrosis Markers Between Cirrhotic and Non-Cirrhotic Patients

Parameter	Cirrhotic (n=24)	Non-Cirrhotic (n=76)	p-value
FIB-4 Score	4.12 ± 1.34	1.78 ± 0.82	<0.001
APRI Score	1.62 ± 0.56	0.72 ± 0.31	<0.001
NAFLD Fibrosis Score	1.21 ± 0.74	-0.84 ± 0.62	<0.001

Diagnostic Performance of Fibrosis Markers: Receiver Operating Characteristic (ROC) curve analysis demonstrated that FIB-4 had the highest diagnostic accuracy for predicting liver cirrhosis, followed by NFS and APRI.

Table 4: Diagnostic Accuracy of Non-Invasive Fibrosis Markers

Marker	AUROC	Sensitivity (%)	Specificity (%)
FIB-4	0.88	87.5	82.9
NFS	0.85	83.3	80.3
APRI	0.81	79.2	76.3

Correlation with Liver Stiffness: All fibrosis markers showed a significant positive correlation with liver stiffness measurements obtained by transient elastography. The strongest correlation was observed with FIB-4 ($r = 0.72$, $p < 0.001$), followed by NFS ($r = 0.68$, $p < 0.001$) and APRI ($r = 0.61$, $p < 0.001$).

Summary of Findings: The prevalence of liver cirrhosis among NAFLD patients was 24%. Non-invasive fibrosis markers were significantly elevated in cirrhotic patients. FIB-4 demonstrated the highest diagnostic performance and strongest correlation with liver stiffness measurements, suggesting its usefulness as a reliable screening tool for identifying NAFLD patients at risk of cirrhosis.

Discussion

Non-Alcoholic Fatty Liver Disease (NAFLD) has emerged as one of the leading causes of chronic liver disease worldwide, with an increasing burden of advanced fibrosis and cirrhosis. Early identification of patients at risk of progression to cirrhosis is essential for timely intervention and prevention of liver-related complications. In the present study, the role of non-invasive fibrosis markers in predicting liver cirrhosis among patients with NAFLD was evaluated. Among the 100 patients included in the study, 24% were found to have liver cirrhosis based on ultrasonographic and transient elastography findings. This prevalence is comparable to previous studies that have reported advanced fibrosis or cirrhosis in approximately 15–30% of NAFLD patients, particularly among those with metabolic risk factors such as obesity and diabetes mellitus.

The present study demonstrated significantly higher FIB-4, APRI, and NAFLD Fibrosis Score (NFS) values in cirrhotic patients compared to non-cirrhotic patients. These findings indicate that increasing fibrosis marker scores are associated with progressive liver damage and worsening hepatic fibrosis. Similar observations have been reported by Angulo et al., McPherson et al., and Shah et al., who found that non-invasive fibrosis scores effectively identify patients with advanced fibrosis and cirrhosis.

Among the markers evaluated, FIB-4 showed the highest diagnostic accuracy with an AUROC of 0.88, followed by NFS (0.85) and APRI (0.81). The superior performance of FIB-4 may be attributed to its incorporation of age, aminotransferase levels, and platelet count, which are closely associated with the progression of hepatic fibrosis. These results are consistent with previous studies that have identified FIB-4 as a reliable and widely applicable tool for fibrosis risk stratification in NAFLD patients. The study also demonstrated a significant positive correlation between fibrosis marker scores and liver stiffness measurements obtained through transient elastography. This finding supports the validity of these markers as surrogate indicators of hepatic fibrosis. The strongest correlation was observed with FIB-4, suggesting its potential utility as a first-line screening tool in routine clinical practice. One of the major advantages of non-invasive fibrosis markers is their simplicity, low cost, and easy availability. Unlike liver biopsy, they do not expose patients to procedural risks and can be repeatedly performed for disease monitoring. Their use can help reduce unnecessary referrals for invasive investigations while ensuring that high-risk patients receive further evaluation and management. However, certain limitations should be acknowledged. The study was conducted at a single tertiary care center with a relatively small sample size of 100 patients, which may limit the generalizability of the findings. Additionally, liver biopsy was not performed in all patients for histopathological confirmation of fibrosis stage. Larger multicentric studies incorporating histological assessment would further strengthen the evidence regarding the predictive value of these markers. Overall, the findings of the present study support the use of non-invasive fibrosis markers, particularly FIB-4 and NFS, as effective tools for predicting liver cirrhosis in patients with NAFLD. Their incorporation into routine clinical assessment may facilitate early diagnosis, risk stratification, and appropriate management of patients with advanced liver disease.

Conclusion

The present prospective observational study demonstrates that non-invasive fibrosis markers are valuable tools for predicting liver cirrhosis in patients with Non-Alcoholic Fatty Liver Disease (NAFLD). Among the markers evaluated, the Fibrosis-4 Index (FIB-4) showed the highest diagnostic accuracy, followed by the NAFLD Fibrosis Score (NFS) and Aspartate Aminotransferase to Platelet Ratio Index (APRI). All three markers were significantly elevated in patients with cirrhosis and showed a positive correlation with liver stiffness measurements obtained by transient elastography. These findings suggest that non-invasive fibrosis markers can effectively identify NAFLD patients at high risk of advanced fibrosis and cirrhosis, thereby reducing the dependence on invasive liver biopsy. Their simplicity, affordability, and widespread availability make them suitable for routine clinical practice, especially in resource-limited settings. Early application of these markers can facilitate timely diagnosis, risk stratification, closer monitoring, and appropriate therapeutic interventions, ultimately improving patient outcomes and reducing the burden of liver-related complications. Further large-scale multicentric studies are recommended to validate these findings and establish standardized cut-off values for different populations.

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