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Original Article

The Predictive Value of Fibrosis-4 Score Index for Cirrhosis-Related Complications in a Libyan Patient Cohort

Abdelhakim M. Elbarsha[1,2] ، Sahar H.Summad[2] , Mabrouka M.Alshokri[2] , Sami A. Lawgaly[1,2] , Mussa G. Tuwati[1]

1. Department of Medicine, University of Benghazi, Benghazi, Libya

2. Department of Medicine, Benghazi Medical Center, Benghazi, Libya

Corresponding Author: Abdelhakim M.Elbarsha Email: abdelhakim.elbarsha@uob.edu.ly

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ABSTRACT

Background: Liver cirrhosis is the end stage of chronic liver disease, and it's considered a major cause of morbidity and mortality. Early detection of complications such as esophageal varices is critical for improving outcomes. There are non-invasive markers that can reduce the need for unnecessary invasive procedures. The Fibrosis-4 Index (FIB-4) has shown promise in assessing liver fibrosis and predicting the risk of varices and other complications. **Objectives:** This study aims to investigate the utility of the Fibrosis-4 Index score as a predictor for the presence of complications (current or past) in patients with established liver cirrhosis. **Methods:** A cross-sectional, observational study was conducted at the outpatient hepatology clinics of Benghazi Medical Center. A convenience sample of adult patients (aged 18 years and above) with an established diagnosis of liver cirrhosis was consecutively included in the study. The Fibrosis-4 (FIB-4) Index score was calculated for each patient. **Results:** The study included a total of 101 patients (48 (47.5%) males and 53 (52.5%) females), with liver cirrhosis. The FIB-4 Index score was evaluated in three categories: <1.45, 1.45–3.25, and >3.25. A statistically significant association was found between a FIB-4 Index score >3.25 and the overall frequency of complications (Pearson Chi-square = 7.509, $p = 0.006$). **Conclusions:** The study findings add to the existing evidence supporting the clinical utility of the FIB-4 index score (and platelet count) as a non-invasive marker of the presence of cirrhosis complications. It's particularly reliable in predicting the presence (cut-off value of 3.25) or absence of complications during the evaluation of liver cirrhosis patients, depending on the score value. Further work-up (e.g. endoscopy) can be restricted to patients with a high risk of having complications, thus avoiding unnecessary tests and reducing the costs.

Keywords: Fibrosis-4 index score, platelet count, cirrhosis complications, non-invasive fibrosis score

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INTRODUCTION:

Liver cirrhosis is the advanced stage of chronic liver disease. It's a major cause of morbidity and mortality worldwide. The liver architecture becomes distorted with the development of fibrosis and regenerative nodules. In addition, there is a progressive decrease in liver function.

Deaths due to liver cirrhosis are increasing. Over 1.32 million deaths worldwide were estimated in 2017, compared to 899,000 in 1990. Most of the deaths resulted from decompensated liver disease. [1,2] Diagnosis can be made at a late stage when complications of portal hypertension, such as variceal bleeding, ascites, or hepatocellular carcinoma (HCC), are evident. [3]Early identifications and risk stratification for these complications allows for appropriate prophylactic treatments and improve patients' outcomes. [3,4]

Esophageal varices (EV) and the risk of bleeding are major complications of cirrhosis and are a major cause of mortality. Endoscopic screening of cirrhotic patients is the standard method for detecting esophageal varices and assessing the risk of bleeding. The use of non-invasive markers with a reliable predictive value for the presence of varices and the risk of bleeding can reduce the need for unnecessary endoscopies. [4-6]Liver biopsy has been considered the gold standard for the assessment of liver fibrosis, but since it is not free of serious complications, the use of non-invasive tests for evaluating liver fibrosis has become increasingly validated. [6-9]Non-invasive tools include serum biomarkers, transient elastography, and a variety of scores that utilize simple and readily available clinical and laboratory data. [7,8]The Fibrosis-4 Index (FIB-4) score is a simple, widely used marker for assessing the degree of liver fibrosis in different chronic liver diseases. It's calculated using four simple parameters: age, aspartate aminotransferase (AST) level, alanine aminotransferase (ALT) level, and platelet count. [9,11-14] The FIB-4 index score was initially developed and validated in patients with chronic hepatitis C and HIV/HCV co-infection for predicting significant fibrosis and cirrhosis. [7,11,12]It has been then utilized in predicting fibrosis in other liver diseases, including non-alcoholic fatty liver disease (NAFLD), chronic hepatitis B, and alcoholic liver disease. [7,12-16]

Studies have shown that FIB-4 can accurately rule out advanced fibrosis using lower cut-off values and identify patients at high risk of advanced fibrosis using higher cut-off values. [7]

Repeated FIB-4 measurements over time improve the identification of patients at risk of severe liver disease. [1,4,9]

It has been shown that the FIB-4 cutoff of 2.78 had a high negative predictive value for high-risk varices, suggesting its potential to identify patients who could avoid initial screening endoscopy. [9]

It has also been demonstrated to be the most efficient non-invasive liver fibrosis marker for initial screening of esophageal varices despite its low diagnostic accuracy for predicting variceal bleeding. [4] This study aims to investigate the utility of the Fibrosis-4 Index score as a predictor for the presence of complications (current or past) in patients with established liver cirrhosis. It also aims to assess platelet count alone as a predictor of cirrhosis complications.

MATERIAL AND METHODS:

Study Design:

A cross-sectional, observational study conducted at the outpatient hepatology clinics of Benghazi Medical Center. A convenience sample of adult patients (aged 18 years and above) with an established diagnosis of liver cirrhosis was consecutively included in the study.

The diagnosis of liver cirrhosis was based on clinical, biochemical, and radiological findings. Patients were included regardless of the etiology of their cirrhosis. Patients with incomplete documentation for the presence or absence of cirrhosis complications were excluded.

Data Collection:

Data was collected over a period of 4 weeks. Relevant demographic data, clinical history, and laboratory findings were collected from outpatients, inpatients, and their files. These included age, gender, underlying etiology of liver cirrhosis, presence of comorbidities, and laboratory results (including aspartate aminotransferase (AST) level, alanine aminotransferase (ALT) level, and platelet count). The presence of liver cirrhosis-related complications (either current or past) was also recorded, specifically esophageal or gastric varices, portal hypertensive gastropathy, splenomegaly, ascites, upper gastrointestinal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis, and hepatocellular carcinoma.The Fibrosis-4 (FIB-4) Index score was calculated for each patient using the following formula:

FIB-4=Platelets(109/L)×ALT (U/L)
Age (years)×AST (U/L)

Patients were categorized into three groups based on their FIB-4 scores: <1.45, 1.45−3.25, and >3.25,

which correlate with the degree of fibrosis. Platelet counts were also categorized as <100×10³/µL, 100−150×10³/µL, and >150×10³/µL. (13)

Ethical Considerations:

The study protocol was approved by the Ethics Committee of Benghazi Medical Center.

Statistical Analysis:

Statistical analyses were performed using IBM SPSS Statistics version 25. Categorical variables were presented as frequencies and percentages. The Pearson Chi-square test was used to test for association. A *p-value* of <0.05 was considered statistically significant.

RESULTS:

The study included a total of 101 patients (48 (47.5%) males and 53 (52.5%) females) with liver cirrhosis. The mean age was 56.87 years (SD = 13.205), and the age range was 18 to 86 years. Among the participants, 83 patients (82.2%) had at least one complication secondary to liver cirrhosis. The most common complications (or complication-related signs) were esophageal or gastric varices (60.4%, n = 61), followed by gastropathy (42.6%, n = 43). Table 1

Table 1: Complications of Liver Cirrhosis

Complication	n (%)
Esophageal/Gastric Varices	61 (60.4)
Gastropathy	43 (42.6)
Splenomegaly	36 (35.6)
Ascites	35 (34.7)
Upper GIT Bleeding	23 (22.8)
Encephalopathy	12 (11.9)
Spontaneous Bacterial Peritonitis	5 (4.9)
Hepatocellular Carcinoma	3 (2.9)

Table 2: Frequency of underlying etiology

Etiology	n	(%)
Hepatitis C virus	26	(25.7)
Alcohol Intake	10	(9.9)
Autoimmune Hepatitis	9	(8.9)
Hepatitis B virus	5	(5.0)
Alcohol	5	(5.0)
Bilharziasis	3	(3.0)
Primary Biliary Cholangitis	2	(2.0)
Budd-Chiari	2	(2.0)
Portal Vein Thrombosis	2	(2.0)
Hemochromatosis	2	(2.0)
Congestive Cardiac Failure	2	(2.0)
Non-Alcoholic Steatohepatitis	1	(1.0)
Methotrexate	1	(1.0)
Idiopathic	1	(1.0)
Not Investigated	1	(1.0)

Table 3 :Frequency of Comorbidities

Systemic Arterial Hypertension	19 (18.8%)
Diabetes Mellitus	12 (11.9%)
Hypothyroidism	8 (7.9%)
Coronary artery Disease	3 (3.0%)
Sjogren Syndrome	3 (3.0%)
Asthma	1 (1.0%)
Chronic Kidney Disease	1 (1.0%)
Dilated Cardiomyopathy	1 (1.0%)
Polycythemia	1 (1.0%)
Crohn's Disease	1 (1.0%)

Table 4 : Fibrosis-4 Index (FIB4-I) categories

Category	n (%)
FIB4-I < 1.45	12(11.90)
FIB4-I 1.45 - 3.25	28(27.70)
FIB4-I > 3.25	61(60.40)

Association Between Fibrosis-4 (FIB-4) Score and Complications

The FIB-4 Index score was evaluated in three categories: <1.45, 1.45–3.25, and >3.25. A statistically significant association was found between a FIB-4 Index score >3.25 and the overall frequency of complications (Pearson Chi-square = 7.509, *p = 0.006*). There was no association between FIB-4 Index score >3.25 with any of these complications (listed in table 1)) when tested separately (*p-values > 0.05*).

There were no significant associations between FIB-4 scores <1.45 (Pearson Chi-square = 3.533, p = 0.059) or 1.45–3.25 (Pearson Chi-square = 2.278, p = 0.131) and the overall frequency of complications.

Association Between Platelet Count and Complications

Fifty-one (50.5%) patients have a platelet count less than 100 x 10³/µL, 28 (27.7%) have a count of 100-150 x 10³/µL, and 22(21.8%) have a count more than 150 x 10³/µL. A statistically significant association was found between a platelet count <100 x 10³/µL and the presence of complications (Pearson Chi-square = 5.747, *p = 0.017*). In contrast, a platelet count >150 was significantly associated with a lower frequency of complications (Pearson Chi-square = 9.527, *p = 0.002*). However,

no significant association was observed for platelet counts between 100 and 150, and the complications (Pearson Chi-square = 0.340, *p = 0.560*).

DISCUSSION:

This study included 101 patients with liver cirrhosis and aimed to assess the predictive value of the FIB-4 score for the presence of cirrhosis complications. In 82.2% of patients, at least one cirrhosis-related complication was present. The most common complications were esophageal or gastric varices (60.4%), portal hypertensive gastropathy (42.6%), splenomegaly (35.6%), and ascites (34.7%). We attempted to study the benefit of the score to identify patients with a FIB-4 index score who likely developed complications related to portal hypertension and liver dysfunction. Most of the published studies assessed the diagnostic utility of the FIB-4 Index score for the presence of liver fibrosis in patients with chronic liver disease, such as non-alcoholic fatty liver disease and chronic viral (B and C) hepatitis. Patients who developed liver-related complications were more likely to have baseline high-risk FIB-4 scores. [14] The cutoff values of FIB-4 index scores used in different studies were variable. High cutoff values (2.67–3.25) were useful for diagnosing advanced fibrosis, while lower cutoff values (1.3–1.67) were found to be reliable for excluding advanced fibrosis. [11]

The FIB-4 index score was shown to identify patients with chronic hepatitis C who were at high risk of liver cirrhosis and HCC development. [12]

The association between high FIB-4 scores and the presence of complications in our cohort was also demonstrated in various studies that evaluated the non-invasive indices (including FIB-4 score) in predicting liver fibrosis and its complications. Our findings are consistent with these observations, supporting the evidence for the potential value of the FIB-4 score as a simple and accurate tool. Studies on patients with chronic hepatitis B and C showed that FIB-4 is not only useful for diagnosing advanced fibrosis (F3-F4), but also has a role in predicting complications such as esophageal varices and variceal bleeding, and predicts worse survival outcomes. In one study, serum liver fibrosis indexes (including the FIB-4 index score) were shown to have modest diagnostic accuracy in the detection of portal hypertension in cirrhotic patients. [1,4,15-17] Furthermore, research linked high FIB-4 index scores in HBV, HCV, NAFLD, and ALD with increased hepatocellular carcinoma (HCC) incidence. [16] FIB-4 index scores are also valuable for predicting extrahepatic cancers and major adverse cardiovascular events in patients with nonalcoholic fatty liver disease (NAFLD). [16]In addition to FIB-4, the platelet count was also shown to predict cirrhosis complications. FIB-4 score Index greater than 3.25 or low platelet count ($<100 \times 10^3/\mu L$) were significantly associated with the presence of complications. A platelet count above $150 \times 10^3/\mu L$ wasn't associated with either increased or decreased frequency of complications. A low platelet count, which is a sign of portal hypertension and hypersplenism, was strongly associated with the presence of complications in our patients' group, a finding that's comparable to other observations. A progressive decrease in platelet counts was associated with advanced liver fibrosis, as shown in other reports. The consistency of these findings suggests that FIB-4 predictive accuracy can be further increased when combined with platelet counts. [18,19]This study demonstrated significant associations between overall complications and both high FIB-4 scores and low platelet counts. There is no significant association between these indices and any of the complications separately. Similar conclusions were also published in other studies, although one study showed that an FIB-4 index score < 2.78 significantly excludes the presence of varices, and endoscopy could be safely avoided. [5,9,19] The lack of significant association between the FIB-4 score and the presence of a specific cirrhosis complication can be explained by the difference in mechanisms by which these complications develop. It can be due to other factors, specifically the underlying etiology, patients' comorbidities, and sample size. Therefore, when the FIB-4 score (and platelet count) is used, it should be taken into consideration that the presence of cirrhosis complications in general is tested, rather than a specific complication.FIB-4 score is a reliable tool, particularly in resource-limited settings, where other non-invasive and invasive procedures (e.g., transient elastography and liver biopsy) are not easily accessible. The advantages are cost-effectiveness, simplicity, and repeatability. Combining FIB-4 with transient elastography or biopsy improves accuracy. [16] Studies demonstrated that repeated measurements could improve risk prediction. This allows monitoring of disease progression and potentially initiates earlier interventions. [7] The use of the FIB-4 index score in clinical practice can facilitate the early identification of patients at risk for liver cirrhosis-related complications. In addition to the FIB-4 index score, there are other non-invasive scores with similar accuracy and can be a supplementary non-invasive tool to FIB-4. The enhanced liver fibrosis (ELF) scores have been shown to correlate

strongly with short-term cirrhosis-related outcomes. [10,20]Similarly, studies in non-alcoholic fatty liver disease (NAFLD) have shown that high FIB-4 scores are not only associated with advanced fibrosis but also with an increased risk of hepatocellular carcinoma (HCC) and overall mortality. These findings suggest that non-invasive scores have both diagnostic and prognostic utility. [11,12,19,21]AST to platelet ratio index (APRI), another non-invasive score, was shown to be comparable to the FIB-4 index score. Gamma-glutamyl transpeptidase to platelet ratio (GPR) index, on the other hand, could rule out more patients without cirrhosis compared to the APRI and FIB-4 index scores [22,23].FIB-4 index score was superior to both GPR and APRI in predicting HCC, according to. It was also found superior to APRI in the identification of significant fibrosis and advanced fibrosis in HBV patients. [12,24] Despite the results, our study has several limitations, particularly the small sample size. This may explain the lack of significant associations between the FIB-4 index score and specific complications. Since the FIB-4 index score depends on parameters that are also affected by many other conditions, its accuracy might be affected by the different etiologies of liver disease and other comorbidities. The impact of these factors on the FIB-4 index score wasn't taken into consideration in our analysis. [25,26]

CONCLUSION:

Our findings add to the existing evidence supporting the clinical utility of the FIB-4 index score (and platelet count) as a non-invasive marker. It's particularly reliable in predicting the presence (cut-off value of 3.25) or absence of complications during the evaluation of liver cirrhosis patients, depending on the score value. Further work-up (e.g., endoscopy) can be restricted to patients with a high risk of having complications, thus avoiding unnecessary tests and reducing the costs.

AUTHORSHIP

All authors actively contributed to the work, including analysis and interpretation of data for the work, drafting and revising, and final approval to be published.

CONFLICT OF INTERESTS

There is no conflict of interest

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REFERENCES

1. Kumar S, Kumar V, Giri R, Agarwal S, Gautam SK. Prediction of esophageal varices and risk of bleeding in liver cirrhosis by aspartate aminotransferase to-platelet ratio index and fibrosis-4 index. Int J Adv Med. 2023 Apr 26;10(5):382–7.
2. Sepanlou SG, Safiri S, Bisignano C, Ikuta KS, Merat S, Saberifiroozi M, et al. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol. 2020 Mar;5(3):245–66.
3. Gotlieb N, Schwartz N, Zelber-Sagi S, Chodick G, Shalev V, Shibolet O. Longitudinal decrease in platelet counts as a surrogate marker of liver fibrosis. World J Gastroenterol. 2020 Oct 14;26(38):5849–62.
4. Kraja B, Mone I, Akshija I, Koçollari A, Prifti S, Burazeri G. Predictors of esophageal varices and first variceal bleeding in liver cirrhosis patients. World J Gastroenterol. 2017 Jul 14;23(26):4806–14.
5. Cifci S, Ekmen N. Evaluation of Non-invasive Fibrosis Markers in Predicting Esophageal Variceal Bleeding. Clin Endosc. 2021 Nov 30;54(6):857–63.
6. Yu JH, Lee HA, Kim SU. Noninvasive imaging biomarkers for liver fibrosis in nonalcoholic fatty liver disease: current and future. Clin Mol Hepatol. 2023 Feb 28;29(Suppl):S136–49.
7. Hagström H, Talbäck M, Andreasson A, Walldius G, Hammar N. Repeated FIB-4 measurements can help identify individuals at risk of severe liver disease. J Hepatol. 2020 Nov;73(5):1023–9.
8. Mózes FE, Lee JA, Selvaraj EA, Jayaswal ANA, Trauner M, Boursier J, et al.

Diagnostic accuracy of non-invasive tests for advanced fibrosis in patients with NAFLD: an individual patient data meta-analysis. Gut. 2022 May;71(5):1006–19.
9. Ishida K, Namisaki T, Murata K, Fujimoto Y, Takeda S, Enomoto M, et al. Accuracy of Fibrosis-4 Index in Identification of Patients with Cirrhosis Who Could Potentially Avoid Variceal Screening Endoscopy. J Clin Med. 2020 Oct 29;9(11):3510.
10. Blanco-Grau A, Gabriel-Medina P, Rodriguez-Algarra F, Villena Y, Lopez-Martínez R, Augustín S, et al. Assessing Liver Fibrosis Using the FIB4 Index in the Community Setting. Diagnostics. 2021 Nov 29;11(12):2236.
11. Han JW, Kim HY, Yu JH, Kim MN, Chon YE, An JH, et al. Diagnostic accuracy of the Fibrosis-4 index for advanced liver fibrosis in nonalcoholic fatty liver disease with type 2 diabetes: A systematic review and meta-analysis. Clin Mol Hepatol. 2024 Sep 30;30(Suppl):S147–58.
12. Li X, Xu H, Gao P. Fibrosis Index Based on 4 Factors (FIB-4) Predicts Liver Cirrhosis and Hepatocellular Carcinoma in Chronic Hepatitis C Virus (HCV) Patients. Med Sci Monit. 2019 Sep 27;25:7243–50.
13. Sterling RK, Lissen E, Clumeck N, Sola R, Correa MC, Montaner J, et al. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection†‡. Hepatology. 2006 Jun;43(6):1317–25.
14. Johnson AL, Hayward KL, Patel P, Horsfall LU, Cheah AEZ, Irvine KM, et al. Predicting Liver-Related Outcomes in People With Nonalcoholic Fatty Liver Disease: The Prognostic Value of Noninvasive Fibrosis Tests. Hepatol Commun. 2022 Apr;6(4):728–39.
15. 15. Wang HW, Peng CY, Lai HC, Su WP, Lin CH, Chuang PH, et al. New noninvasive index for predicting liver fibrosis in Asian patients with chronic viral hepatitis. Sci Rep. 2017 Jun 12;7(1):3259.
16. 16. Xu X lan, Jiang L shun, Wu C si, Pan L ya, Lou Z qi, Peng C ting, et al. The role of fibrosis index FIB-4 in predicting liver fibrosis stage and clinical prognosis: A diagnostic or screening tool? J Formos Med Assoc. 2022 Feb;121(2):454–66.
17. Wang L, Feng Y, Ma X, Wang G, Wu H, Xie X, et al. Diagnostic efficacy of noninvasive liver fibrosis indexes in predicting portal hypertension in patients with cirrhosis. Yu ML, editor. PLOS ONE. 2017 Aug 18;12(8):e0182969.
18. Zijlstra MK, Gampa A, Joseph N, Sonnenberg A, Fimmel CJ. Progressive changes in platelet counts and Fib-4 scores precede the diagnosis of advanced fibrosis in NASH patients. World J Hepatol. 2023 Feb 27;15(2):225–36.
19. Younes R, Caviglia GP, Govaere O, Rosso C, Armandi A, Sanavia T, et al. Long-term outcomes and predictive ability of non-invasive scoring systems in patients with non-alcoholic fatty liver disease. J Hepatol. 2021 Oct;75(4):786–94.
20. Are VS, Vuppalanchi R, Vilar-Gomez E, Chalasani N. Enhanced Liver Fibrosis Score Can Be Used to Predict Liver-Related Events in Patients With Nonalcoholic Steatohepatitis and Compensated Cirrhosis. Clin Gastroenterol Hepatol. 2021 Jun;19(6):1292-1293.e3.
21. Vieira Barbosa J, Milligan S, Frick A, Broestl J, Younossi Z, Afdhal NH, et al. Fibrosis-4 Index as an Independent Predictor of Mortality and Liver-Related Outcomes in NAFLD. Hepatol Commun. 2022 Apr;6(4):765–79.
22. Maev IV, Kuznetsova EI, Andreev DN, Dicheva DT. Diagnostic accuracy of predictive indexes of liver fibrosis in patients with chronic hepatitis C. Ter Arkh. 2020 Feb 27;92(2):24–8.
23. Liu X, Li H, Wei L, Tang Q, Hu P. Optimized cutoffs of gamma-glutamyl transpeptidase-to-platelet ratio, aspartate aminotransferase-to-platelet ratio index, and fibrosis-4 scoring systems for exclusion of cirrhosis in patients with chronic hepatitis B. Hepatol Commun. 2022 Jul;6(7):1664–72.
24. Xiao G, Yang J, Yan L. Comparison of diagnostic accuracy of aspartate aminotransferase to platelet ratio index and fibrosis-4 index for detecting liver fibrosis in adult patients with chronic hepatitis B virus infection: A systemic review and meta-analysis. Hepatology. 2015 Jan;61(1):292–302.
25. Cheng CH, Chu CY, Chen HL, Lin IT, Wu CH, Lee YK, et al. Subgroup analysis of the predictive ability of aspartate aminotransferase to platelet ratio index (APRI) and fibrosis-4 (FIB-4) for assessing

hepatic fibrosis among patients with chronic hepatitis C. J Microbiol Immunol Infect. 2020 Aug;53(4):542–9.

26. Li Y, Chen Y, Zhao Y. The Diagnostic Value of the FIB-4 Index for Staging Hepatitis B-Related Fibrosis: A Meta-Analysis. Schmidt RLane, editor. PLoS ONE. 2014 Aug 28;9(8):e105728.