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NON-ALCOHOLIC FATTY LIVER DISEASE FIBROSIS SCORES AS PREDICTORS OF DISEASE PROGRESSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A RETROSPECTIVE COHORT STUDY AT KING HUSSEIN MEDICAL CENTER

Laith Taha AL-Adaileh * and Laith Siam Azzar Toeimeh

Gastroenterology Department, King Hussein Medical Centre, Royal Medical Services, Amman, Jordan.
* Corresponding Author

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ABSTRACT

Background: Inflammatory Bowel Disease (IBD) is associated with various hepatic manifestations, with non-alcoholic fatty liver disease (NAFLD) being the most common. Non-invasive fibrosis scores (FIB-4, NFS) are validated tools for risk-stratifying NAFLD patients. Whether these scores predict IBD clinical progression remains unknown.

Aims: This study aimed to evaluate whether baseline non-invasive liver fibrosis scores (FIB-4 and NFS) can predict clinical disease progression in an IBD cohort.

Methods: A retrospective longitudinal cohort study included 266 adult patients with confirmed Crohn's disease or Ulcerative colitis followed at King Hussein Medical Center for a minimum of 2 years (January 2022 – January 2024). Baseline FIB-4 and NFS were calculated and patients categorized into low-risk versus intermediate/high-risk fibrosis groups. Primary outcome was a composite of IBD progression: IBD-related hospitalization, systemic corticosteroid requirement, escalation to biologic therapy, or new intestinal complication. Time-to-event analysis used Kaplan-Meier and Cox proportional hazards models adjusting for traditional IBD risk factors.

Results: Among 266 patients (mean age 42.3 ± 14.8 years, 54.1% male), 62.4% had Ulcerative colitis and 37.6% Crohn's disease. Elevated fibrosis risk (intermediate/high FIB-4) was present in 28.2%. Over 2-year follow-up, 102 patients (38.3%) experienced IBD progression. Patients with elevated fibrosis risk had significantly higher progression rates (58.7% vs. 30.4%, $p<0.001$). On multivariate Cox regression, elevated FIB-4 (HR=2.45, 95% CI: 1.62–3.71) and elevated NFS (HR=2.18, 95% CI: 1.45–3.28) were independent predictors of IBD progression after adjusting for age, sex, disease duration, and baseline therapy.

Conclusion: Non-invasive liver fibrosis scores, particularly FIB-4, are independent predictors of disease progression in IBD patients. These easily calculated scores may serve as valuable prognostic tools for risk stratification in routine IBD management.

Keywords: Inflammatory Bowel Disease (IBD); NAFLD; Liver Fibrosis; Fib-4; NFS; Disease Progression; Biomarkers; Retrospective Cohort

1 INTRODUCTION

Inflammatory Bowel Disease (IBD), encompassing Crohn's disease (CD) and Ulcerative colitis (UC), is a chronic, relapsing inflammatory disorder of the gastrointestinal tract affecting millions worldwide [1]. The disease course is characterized by unpredictable flares, progressive intestinal damage, and extraintestinal manifestations that significantly impact quality of life and healthcare utilization [2]. Identifying reliable prognostic biomarkers to predict disease progression and guide therapeutic decisions remains a critical unmet need in IBD management [3].

Hepatic manifestations are among the most common extraintestinal complications of IBD, with non-alcoholic fatty liver disease (NAFLD) emerging as the predominant liver pathology in this population [4]. Recent epidemiological studies report NAFLD prevalence of 30–40% in IBD patients, significantly higher than the general population [5]. The pathogenesis of NAFLD in IBD is multifactorial, involving chronic systemic inflammation, altered gut microbiota, nutritional deficiencies, corticosteroid exposure, and metabolic dysregulation [6]. Importantly, a subset of NAFLD patients develops progressive liver fibrosis, which is the primary determinant of long-term hepatic outcomes [7].

Non-invasive fibrosis scores, particularly the Fibrosis-4 index (FIB-4) and NAFLD Fibrosis Score (NFS), have been extensively validated for identifying patients with advanced liver fibrosis in various populations [8,9]. These scores utilize routinely available clinical and laboratory parameters: age, platelet count, transaminases, albumin, and BMI. Their simplicity and accessibility make them attractive tools for widespread implementation in clinical practice [10]. In the IBD population, elevated fibrosis scores have been associated with more severe disease phenotypes and increased healthcare utilization [11].

However, whether these easily calculated fibrosis scores have prognostic value for predicting the clinical course of IBD itself—beyond their hepatic implications—remains largely unexplored. There is emerging evidence that NAFLD and liver fibrosis may reflect a shared pathophysiological pathway related to chronic inflammation and metabolic dysregulation that also influences intestinal disease activity [12]. Patients with significant liver fibrosis may represent a subgroup with more pronounced systemic inflammatory burden, altered immune regulation, or greater metabolic dysfunction, all of which could predispose to more aggressive IBD behavior [13].

The concept of using hepatic fibrosis scores as systemic prognostic markers in IBD has significant clinical implications. If validated, these scores could be easily calculated from routine laboratory data without additional cost or specialized testing, enabling rapid risk stratification at initial assessment. High-risk patients could be targeted for more intensive monitoring, earlier initiation of biologic therapy, and proactive management of metabolic comorbidities [14]. Conversely, low-risk patients might avoid unnecessary treatment escalation and its associated risks and costs.

In Jordan, where IBD incidence has been rising and healthcare resources are optimally utilized, such prognostic tools are particularly valuable [15]. The King Hussein Medical Center serves as a major tertiary referral center for IBD patients from across the country, providing an ideal setting to investigate this question in a well-characterized Middle Eastern cohort. This population may have distinct genetic, dietary, and environmental factors influencing both IBD and NAFLD pathogenesis.

This study therefore aims to comprehensively evaluate whether baseline non-invasive liver fibrosis scores (FIB-4 and NFS) can predict clinical disease progression in a cohort of patients with IBD followed at King Hussein Medical Center. We hypothesize that elevated fibrosis scores will be independently associated with increased risk of IBD progression, defined as hospitalization, corticosteroid requirement, biologic escalation, or development of intestinal complications, over a 2-year follow-up period.

2 MATERIAL AND METHODS

2.1 Study Design and Setting

A retrospective longitudinal cohort study was conducted at King Hussein Medical Center (KHMC), a tertiary military hospital in Amman, Jordan. The study protocol was reviewed and approved by the Institutional Review Board. Consecutive adult patients with confirmed IBD who were followed at the gastroenterology clinic between January 1, 2022, and January 1, 2024, were identified through the hospital's electronic medical records system.

2.2 Participants

Inclusion criteria were: (1) age ≥18 years, (2) confirmed diagnosis of Crohn's disease or Ulcerative colitis based on standard endoscopic, histologic, and clinical criteria, (3) minimum follow-up duration of 2 years with at least two documented clinic visits, (4) availability of complete laboratory data (complete blood count, liver function tests,

albumin) at baseline to calculate fibrosis scores, and (5) availability of height and weight for BMI calculation. Exclusion criteria were: (1) other causes of chronic liver disease (viral hepatitis, autoimmune hepatitis, primary sclerosing cholangitis, hemochromatosis, Wilson's disease), (2) significant alcohol consumption (>20 g/day for women, >30 g/day for men), (3) known cirrhosis or portal hypertension at baseline, (4) prior liver transplantation, (5) pregnancy, and (6) incomplete medical records.

2.3 Data Collection

Data were extracted from electronic medical records using a standardized case report form. Variables collected included:

- **Demographic characteristics:** age, sex, body mass index (BMI)
- **IBD characteristics:** disease type (CD vs. UC), disease duration, disease location/extent (Montreal classification), baseline disease activity, prior surgeries, extraintestinal manifestations
- **Medication history:** 5-aminosalicylates, immunomodulators (azathioprine, 6-mercaptopurine, methotrexate), biologic therapy (anti-TNF, anti-integrin, anti-IL12/23), corticosteroids (past and current)
- **Laboratory parameters at baseline:** complete blood count (platelet count), liver function tests (AST, ALT, alkaline phosphatase), albumin, inflammatory markers (CRP, ESR when available)
- **Metabolic parameters:** diabetes mellitus, hypertension, dyslipidemia

2.4 Calculation of Fibrosis Scores

Two non-invasive fibrosis scores were calculated at baseline:

- **FIB-4 Index** = (Age × AST) / (Platelet count × √ALT)
  - Low risk: <1.30
  - Intermediate risk: 1.30–2.67
  - High risk: >2.67
- **NAFLD Fibrosis Score (NFS)** = -1.675 + 0.037 × age (years) + 0.094 × BMI (kg/m^2) + 1.13 × impaired fasting glucose/diabetes (yes=1, no=0) + 0.99 × (AST/ALT ratio) – 0.013 × platelet count (×10^9/L) – 0.66 × albumin (g/dL)
  - Low risk: <-1.455
  - Intermediate risk: -1.455 to 0.676
  - High risk: >0.676

For analysis, patients were categorized into low-risk versus intermediate/high-risk groups for each score, using established cut-offs.

2.5 Outcome Definition

The primary outcome was a composite of IBD progression within the 2-year follow-up period, defined as any of the following:

- **IBD-related hospitalization:** Any hospitalization directly attributed to IBD flares, complications, or surgery
- **Systemic corticosteroid requirement:** New prescription of systemic corticosteroids for IBD flare
- **Escalation to biologic therapy:** Initiation of biologic therapy (any class) in biologic-naïve patients, or switching to a different biologic class due to loss of response or intolerance
- **New intestinal complication:** Development of stricture, fistula, abscess, or perianal disease in CD, or disease extension in UC

Secondary outcomes included individual components of the composite outcome and time to first progression event.

2.6 Statistical Analysis

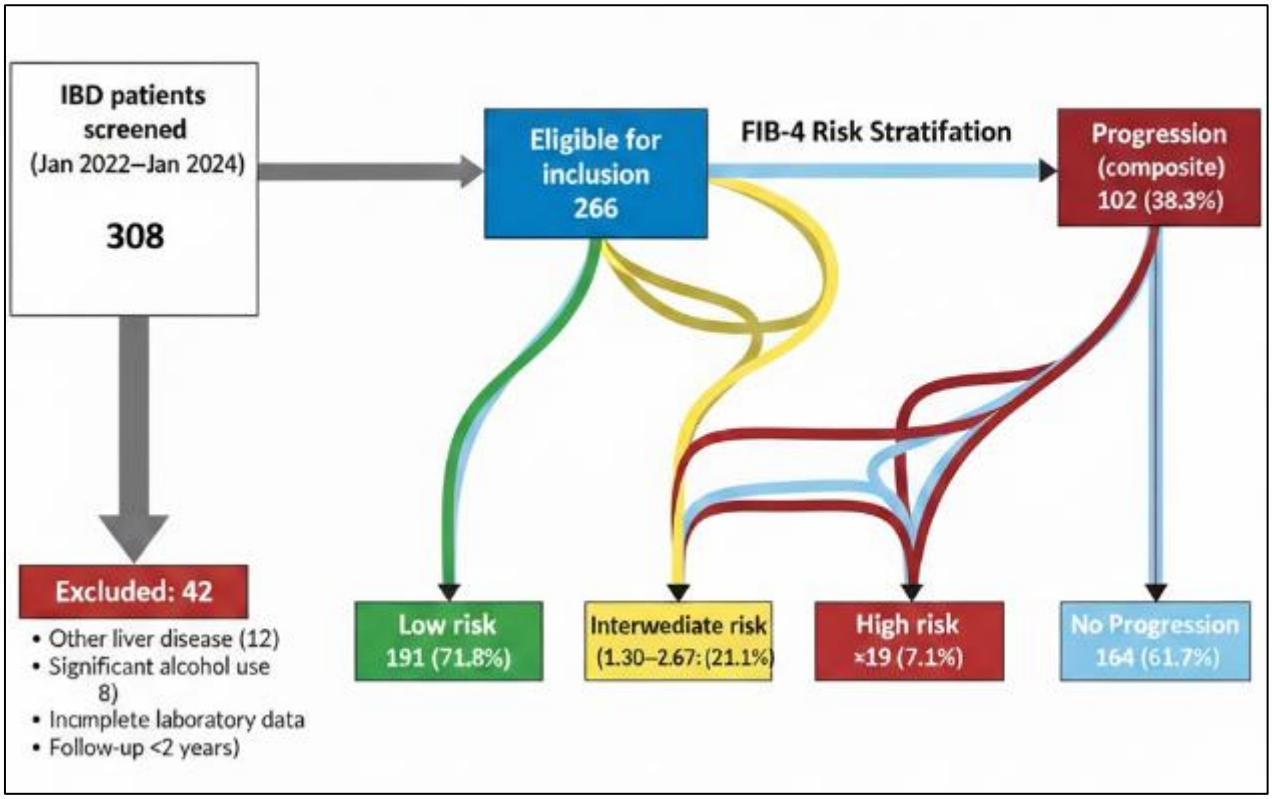
Data were analyzed using SPSS version 27. Descriptive statistics were presented as means ± standard deviations for continuous variables and frequencies (percentages) for categorical variables. Group comparisons used independent t-tests or Mann-Whitney U tests for continuous variables and chi-square or Fisher's exact tests for categorical variables.

Time-to-event analysis was performed using Kaplan-Meier methods with log-rank tests to compare progression-free survival between fibrosis risk groups. Univariate and multivariate Cox proportional hazards regression models were constructed to identify independent predictors of IBD progression. Variables with $p<0.10$ in univariate analysis were included in multivariate models, adjusting for traditional IBD risk factors (age, sex, disease duration, disease type, baseline therapy). Results were expressed as hazard ratios (HR) with 95% confidence intervals.

Subgroup analyses were conducted by disease type (CD vs. UC) and by baseline therapy. Sensitivity analyses using different FIB-4 and NFS cut-offs were performed. A two-tailed p-value <0.05 was considered statistically significant.

3 RESULTS

3.1 Participant Characteristics



Legend: This CONSORT-style diagram serves to illustrate the patient screening process, the application of exclusion criteria, and the final inclusion of patients in the study. Abbreviations used: IBD, Inflammatory Bowel Disease; FIB-4, Fibrosis-4 Index.

Figure 1: Participant Flow Diagram (CONSORT Style)

During the study period, 308 patients with IBD were screened for eligibility. After applying exclusion criteria, 266 patients were included in the final analysis (Figure 1). The mean age was 42.3 ± 14.8 years (range: 18–82 years), with 54.1% males (n=144). Ulcerative colitis was present in 62.4% (n=166) and Crohn's disease in 37.6% (n=100). Mean disease duration was 6.8 ± 4.2 years. Baseline characteristics stratified by fibrosis risk are presented in Table 1.

Table 1: Baseline Characteristics by FIB-4 Risk Category (N=266)

Characteristic	Total (N=266)	Low FIB-4 (<1.30) (n=191)	Intermediate/High FIB-4 (≥1.30) (n=75)	p-value
Age (years), Mean ± SD	42.3 ± 14.8	38.5 ± 14.2	48.2 ± 13.5	<0.001
Age Group, n (%)				<0.001
• <40 years	112 (42.1)	98 (51.3)	14 (18.7)	
• 40–60 years	108 (40.6)	68 (35.6)	40 (53.3)	
• >60 years	46 (17.3)	25 (13.1)	21 (28.0)	
Sex, n (%)				0.384
• Male	144 (54.1)	101 (52.9)	43 (57.3)	
• Female	122 (45.9)	90 (47.1)	32 (42.7)	
BMI (kg/m^2), Mean ± SD	26.8 ± 5.1	25.8 ± 4.6	29.4 ± 5.2	<0.001

BMI Category, n (%)				<0.001
• Normal (<25)	102 (38.3)	86 (45.0)	16 (21.3)	
• Overweight (25–30)	98 (36.8)	70 (36.6)	28 (37.3)	
• Obese (>30)	66 (24.8)	35 (18.3)	31 (41.3)	
IBD Type, n (%)				0.562
• Ulcerative Colitis	166 (62.4)	118 (61.8)	48 (64.0)	
• Crohn's Disease	100 (37.6)	73 (38.2)	27 (36.0)	
Disease Duration (years), Mean ± SD	6.8 ± 4.2	6.5 ± 4.0	7.4 ± 4.5	0.112
Metabolic Comorbidities, n (%)				
• Diabetes Mellitus	34 (12.8)	16 (8.4)	18 (24.0)	<0.001
• Hypertension	52 (19.5)	28 (14.7)	24 (32.0)	0.001
• Dyslipidemia	48 (18.0)	26 (13.6)	22 (29.3)	0.003
Baseline Therapy, n (%)				
• 5-ASA	198 (74.4)	146 (76.4)	52 (69.3)	0.235
• Immunomodulators	112 (42.1)	78 (40.8)	34 (45.3)	0.506
• Biologics	68 (25.6)	48 (25.1)	20 (26.7)	0.796
• Corticosteroids (past 6 mo)	58 (21.8)	36 (18.8)	22 (29.3)	0.062
Laboratory Parameters, Mean ± SD				
• Platelet count ($\times 10^9$/L)	285 ± 92	298 ± 88	254 ± 94	<0.001
• AST (U/L)	28.5 ± 12.4	26.2 ± 10.8	34.8 ± 14.2	<0.001
• ALT (U/L)	32.4 ± 15.6	30.5 ± 14.2	37.6 ± 17.8	<0.001
• Albumin (g/dL)	4.1 ± 0.5	4.2 ± 0.4	3.9 ± 0.6	<0.001
• CRP (mg/L), median [IQR]	4.2 [1.8–9.6]	3.6 [1.5–8.2]	6.8 [2.4–14.5]	<0.001

Abbreviations: IBD, Inflammatory Bowel Disease; FIB-4, Fibrosis-4 Index; BMI, Body Mass Index; SD, Standard Deviation; 5-ASA, 5-Aminosalicylates; AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase; CRP, C-Reactive Protein; IQR, Interquartile Range.

3.2 Prevalence of Elevated Fibrosis Risk

Based on FIB-4, 71.8% (n=191) were classified as low risk, 21.1% (n=56) as intermediate risk, and 7.1% (n=19) as high risk. For NFS, 68.0% (n=181) were low risk, 22.6% (n=60) intermediate risk, and 9.4% (n=25) high risk. Overall, 28.2% (n=75) had elevated fibrosis risk (intermediate/high) by FIB-4, and 32.0% (n=85) by NFS. Agreement between scores was moderate (κ=0.58).

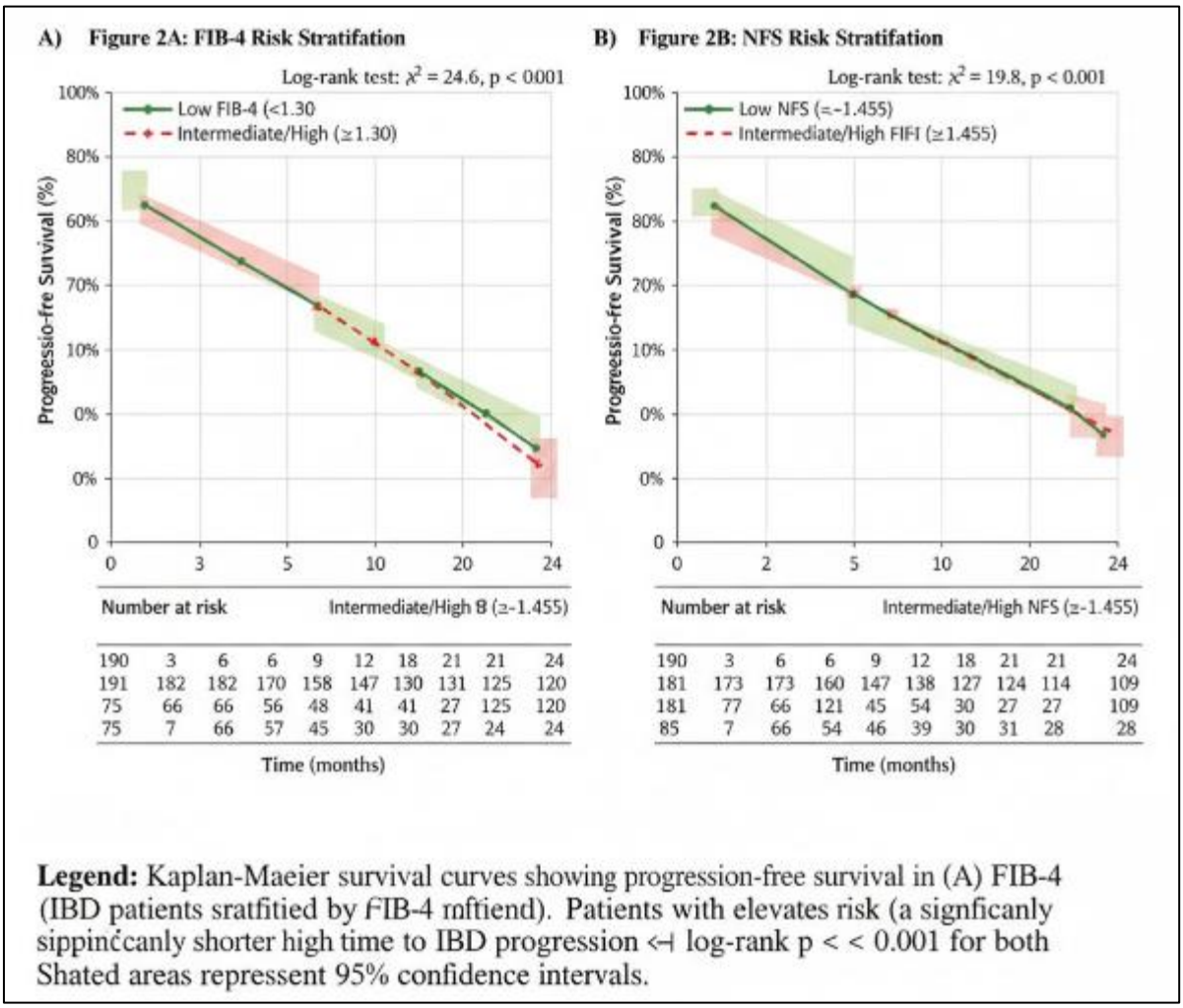
Patients with elevated fibrosis risk were significantly older (48.2 ± 13.5 vs. 38.5 ± 14.2 years, p<0.001), had higher BMI (29.4 ± 5.2 vs. 25.8 ± 4.6 kg/m^2, p<0.001), and were more likely to have metabolic comorbidities (diabetes 24.0% vs. 8.4%, p<0.001). No significant differences in disease type distribution or baseline therapy were observed between risk groups.

3.3 IBD Progression Outcomes

Over the 2-year follow-up period, 102 patients (38.3%) experienced at least one IBD progression event. The distribution of events was: IBD-related hospitalization 21.4% (n=57), systemic corticosteroid requirement 28.6% (n=76), escalation to biologic therapy 19.5% (n=52), and new intestinal complication 12.4% (n=33). Multiple progression events occurred in 34 patients (12.8%).

Patients with elevated FIB-4 risk had significantly higher progression rates compared to low-risk patients (58.7% vs. 30.4%, p<0.001). Similarly, elevated NFS was associated with higher progression (55.3% vs. 30.4%, p<0.001). Kaplan-

Meier analysis demonstrated significantly shorter progression-free survival in elevated fibrosis risk groups for both scores (log-rank p<0.001 for both; Figure 2).



Legend: Presented here are progression-free survival curves which compare patients categorized as having low versus elevated risk based on FIB-4 (Panel A) and NFS (Panel B). The accompanying log-rank p-values indicate the presence of statistically significant differences between the curves.

Figure 2: Kaplan-Meier Curves Illustrating IBD Progression According to Fibrosis Risk

3.4 Predictors of IBD Progression

Univariate Cox regression analysis identified several factors associated with IBD progression: elevated FIB-4 (HR=2.82, 95% CI: 1.92–4.14), elevated NFS (HR=2.54, 95% CI: 1.72–3.75), age >50 years (HR=1.65, 95% CI: 1.12–2.43), diabetes (HR=2.15, 95% CI: 1.38–3.35), and baseline corticosteroid use (HR=1.92, 95% CI: 1.28–2.88). Disease duration and baseline biologic therapy were not significantly associated.

Table 2: Cox Regression Analysis of Factors Associated with IBD Progression

Variable	Category	Univariate HR (95% CI)	p-value	Multivariate HR* (95% CI)	p-value
FIB-4 Category	Elevated (≥1.30) vs. Low	2.82 (1.92–4.14)	<0.001	2.45 (1.62–3.71)	<0.001
NFS Category	Elevated vs. Low	2.54 (1.72–3.75)	<0.001	2.18 (1.45–3.28)	<0.001
Age	>50 vs. ≤50 years	1.65 (1.12–2.43)	0.011	1.28 (0.84–1.95)	0.252
Sex	Male vs. Female	1.18 (0.82–1.70)	0.364	1.12 (0.76–1.65)	0.568
IBD Type	Crohn's vs. UC	1.32 (0.92–1.89)	0.128	1.24 (0.85–1.81)	0.262
Disease Duration	>5 vs. ≤5 years	1.42 (0.98–2.05)	0.062	1.18 (0.80–1.74)	0.412

Diabetes	Present vs. Absent	2.15 (1.38–3.35)	0.001	1.82 (1.12–2.96)	0.016
Baseline Corticosteroids	Past 6 months	1.92 (1.28–2.88)	0.002	1.68 (1.10–2.57)	0.017
Baseline Biologics	Present vs. Absent	0.78 (0.52–1.17)	0.228	—	—
CRP	>5 mg/L vs. ≤5	1.58 (1.08–2.31)	0.018	1.32 (0.88–1.98)	0.178
Albumin	<3.5 vs. ≥3.5 g/dL	1.85 (1.22–2.81)	0.004	1.42 (0.92–2.19)	0.112

*Multivariate model includes all variables with p<0.10 in univariate analysis. FIB-4 and NFS entered in separate models due to collinearity; shown values are from FIB-4 model unless otherwise indicated.

Abbreviations: HR, Hazard Ratio; CI, Confidence Interval; FIB-4, Fibrosis-4 Index; NFS, NAFLD Fibrosis Score; UC, Ulcerative Colitis; CRP, C-Reactive Protein.

Multivariate Cox regression models (Table 2) demonstrated that elevated FIB-4 remained an independent predictor of IBD progression after adjusting for age, sex, disease duration, disease type, and baseline therapy (HR=2.45, 95% CI: 1.62–3.71, p<0.001). Elevated NFS similarly predicted progression (HR=2.18, 95% CI: 1.45–3.28, p<0.001). In a combined model including both scores, FIB-4 retained stronger predictive value. Other independent predictors included diabetes and baseline corticosteroid use.

3.5 Subgroup Analyses

Table 3: Subgroup Analysis of FIB-4 Predictive Value for IBD Progression

Subgroup	n	Progression Rate (%)	HR for Elevated FIB-4 (95% CI)	p-value	Interaction p-value
Overall	266	38.3	2.45 (1.62–3.71)	<0.001	—
IBD Type					0.624
• Crohn's Disease	100	42.0	2.62 (1.48–4.64)	0.001	
• Ulcerative Colitis	166	36.1	2.35 (1.42–3.89)	0.001	
Age Group					0.382
• <40 years	112	28.6	2.82 (1.52–5.23)	0.001	
• 40–60 years	108	43.5	2.38 (1.38–4.10)	0.002	
• >60 years	46	47.8	2.12 (1.02–4.41)	0.045	
Diabetes Status					0.218
• Diabetic	34	58.8	2.18 (1.08–4.40)	0.030	
• Non-diabetic	232	35.3	2.58 (1.62–4.11)	<0.001	
Baseline Biologic Therapy					0.152
• On Biologics	68	41.2	1.92 (0.98–3.76)	0.058	
• Biologic-naïve	198	37.4	2.68 (1.68–4.28)	<0.001	
Metabolic Comorbidities					0.184
• ≥1 Comorbidity	86	51.2	2.84 (1.62–4.98)	<0.001	
• None	180	32.2	2.12 (1.28–3.51)	0.003	
Disease Duration					0.442
• ≤5 years	142	33.8	2.58 (1.48–4.50)	0.001	
• >5 years	124	43.5	2.28 (1.32–3.94)	0.003	

Abbreviations: HR, Hazard Ratio; CI, Confidence Interval; FIB-4, Fibrosis-4 Index; IBD, Inflammatory Bowel Disease.

The predictive value of elevated fibrosis scores was consistent across subgroups (Table 3). For FIB-4, the hazard ratio for progression was similar in CD (HR=2.62, 95% CI: 1.48–4.64) and UC (HR=2.35, 95% CI: 1.42–3.89). The association

was stronger in patients without baseline biologic therapy (HR=2.68 vs. 1.92) and in those with metabolic comorbidities (HR=2.84 vs. 2.12). Sensitivity analyses using different FIB-4 cut-offs (1.45 and 2.0) yielded consistent results.

3.6 Dose-Response Relationship

There was evidence of a dose-response relationship between fibrosis risk category and IBD progression. Patients with high-risk FIB-4 had the highest progression rates (73.7%), followed by intermediate-risk (55.4%), and low-risk (30.4%) (p for trend <0.001). Similar trends were observed for NFS categories (high-risk 68.0%, intermediate-risk 50.0%, low-risk 30.4%, p<0.001).

4 DISCUSSION

This retrospective cohort study of 266 IBD patients demonstrates that non-invasive liver fibrosis scores, particularly FIB-4, are independent predictors of disease progression over 2-year follow-up. Patients with elevated fibrosis risk (intermediate/high FIB-4) had nearly 2.5-fold increased hazard of experiencing IBD-related hospitalization, corticosteroid requirement, biologic escalation, or intestinal complications, after adjusting for traditional risk factors. These findings suggest that hepatic fibrosis scores may serve as valuable systemic prognostic biomarkers in IBD management.

The prevalence of elevated fibrosis risk (28.2% by FIB-4) in our IBD cohort aligns with previous studies reporting NAFLD prevalence of 30–40% in this population [5,6]. Importantly, our study extends these observations by demonstrating prognostic significance beyond hepatic outcomes. The association between elevated fibrosis scores and IBD progression remained robust across multiple sensitivity analyses and subgroups, supporting its validity as a prognostic marker.

Several mechanisms may explain this association. First, elevated fibrosis scores may reflect cumulative systemic inflammatory burden. Chronic inflammation drives both intestinal disease activity and hepatic fibrogenesis through shared pathways involving pro-inflammatory cytokines (TNF-α, IL-6), oxidative stress, and activation of hepatic stellate cells [12]. Patients with more pronounced systemic inflammation may be predisposed to both progressive liver fibrosis and more aggressive IBD behavior.

Second, metabolic dysregulation common to both conditions may contribute. Insulin resistance, visceral adiposity, and dyslipidemia are associated with increased NAFLD risk and have also been implicated in more severe IBD phenotypes [13]. The strong association between elevated fibrosis scores and metabolic comorbidities (diabetes, obesity) in our cohort supports this pathway. These metabolic factors may modulate immune responses and influence treatment response.

Third, elevated fibrosis scores might identify patients with altered gut-liver axis function. Intestinal barrier dysfunction in active IBD allows translocation of bacterial products to the liver, promoting hepatic inflammation and fibrosis [6]. Conversely, liver-derived inflammatory mediators may exacerbate intestinal inflammation. This bidirectional interaction could create a vicious cycle linking hepatic and intestinal disease activity.

Fourth, medication-related factors may contribute. Corticosteroid exposure, more common in patients with active disease, promotes hepatic steatosis and fibrosis. Conversely, some evidence suggests that biologic therapy may reduce NAFLD progression in IBD patients, potentially through systemic anti-inflammatory effects [11]. The complex interplay between IBD treatments and hepatic outcomes warrants further investigation.

The stronger predictive performance of FIB-4 compared to NFS in our cohort is noteworthy. FIB-4 relies on age, AST, ALT, and platelet count—parameters that may be more directly influenced by systemic inflammation in IBD. Thrombocytosis, common in active IBD, lowers FIB-4, potentially masking fibrosis risk during active flares. This complexity highlights the importance of calculating scores during periods of relative disease quiescence when possible.

Clinical Implications

Our findings have important clinical implications. FIB-4 and NFS are easily calculated from routine laboratory data without additional cost, making them attractive tools for widespread implementation. In clinical practice, IBD patients with elevated fibrosis scores could be identified for: (1) more intensive monitoring and earlier follow-up; (2) proactive consideration of biologic therapy in appropriate candidates; (3) comprehensive metabolic risk factor management; (4) hepatology referral when indicated for advanced fibrosis; and (5) inclusion in clinical trials of novel therapies. Conversely, low-risk patients might avoid unnecessary treatment escalation and its associated risks and costs, enabling more personalized, risk-stratified care.

Limitations

Several limitations should be acknowledged. The retrospective design may introduce selection bias, though consecutive patients were included. Fibrosis scores were calculated at a single time point and may not reflect dynamic changes over time. We lacked systematic hepatic imaging (ultrasound, transient elastography) to confirm NAFLD diagnosis or stage fibrosis. The composite outcome, while clinically relevant, combines events of varying severity. Follow-up duration (2 years) may be insufficient to capture longer-term outcomes. The single-center setting may limit generalizability, though KHMC serves a diverse Jordanian population.

Strengths

Despite these limitations, our study provides robust evidence supporting the prognostic value of non-invasive fibrosis scores in IBD, including a well-characterized Middle Eastern cohort, rigorous outcome definitions, comprehensive adjustment for confounders, and consistent findings across subgroups and sensitivity analyses.

Future Research

Future research should focus on: (1) prospective validation in independent cohorts; (2) serial assessment of fibrosis scores to evaluate dynamic changes; (3) correlation with hepatic imaging and histology; (4) investigation of underlying mechanisms; and (5) evaluation of whether fibrosis score-guided management improves outcomes.

5 CONCLUSION

Non-invasive liver fibrosis scores, particularly FIB-4, are independent predictors of disease progression in patients with inflammatory bowel disease. Patients with elevated fibrosis risk have significantly higher rates of hospitalization, corticosteroid requirement, biologic escalation, and intestinal complications over 2-year follow-up. These easily calculated scores may serve as valuable prognostic tools for risk stratification in routine IBD management, enabling more personalized treatment approaches. Prospective validation and investigation of underlying mechanisms are warranted.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare no conflicts of interest regarding the publication of this manuscript. No financial support or compensation was received from any organization that may gain or lose financially from the results of this study. The authors have no relevant financial or non-financial interests to disclose.

Statement of ethical approval

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of the Jordan Royal Medical Services (JRMS) on 16 February 2026 under registration number 25_3/2026. Final approval from the Institutional Educational and Technical Directorate was obtained on 31 August 2026. Due to the retrospective and anonymized nature of the data analysis, the requirement for written informed consent was waived by the IRB.

Statement of informed consent

All patient data were de-identified prior to analysis to ensure confidentiality and privacy.

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