

## Intestinal Fatty Acid Binding Protein (I-FABP) in Patients with Inflammatory Bowel Diseases with and without MAFLD

Reda M. El-Badawy<sup>a</sup>, Magdy A. Gad<sup>a</sup>, Badawy A. Abd El Aziz<sup>a</sup>, Waled A. Abd Elhalem<sup>b</sup>, Ahmed I. Sakr<sup>a</sup>

<sup>a</sup> Hepatology, Gastroenterology and Infectious Diseases Department, Faculty of Medicine Benha University, Egypt.

<sup>b</sup> Clinical and Chemical Pathology Department, Faculty of Medicine Benha University, Egypt.

### Corresponding to:

Dr. Ahmed I. Sakr.  
Hepatology, Gastroenterology and Infectious Diseases Department, Faculty of Medicine Benha University, Egypt.

### Email:

hikmaclinic2019@gmail.com

**Received:** 3 November 2024

**Accepted:** 18 March 2025

### Abstract:

**Background:** Inflammatory bowel disease (IBD) consists of 2 well-established but not entirely discrete disease entities, Crohn disease (CD) and ulcerative colitis (UC). This study aimed to investigate the serum intestinal fatty acid-binding protein (I-FABP) as a possible biomarker for the diagnosis, monitoring activity and severity of IBD with & without MAFLD. **Methods:** This cross-sectional study included 50 patients with IBD who were admitted at the Hepatology and Gastroenterology Department of Benha University Hospital. Patients were selected and divided into two equal groups: group 1: (N= 50): patients with IBD, was subdivided according to association with MAFLD based on laboratory an abdominal ultrasound finding into: patients with IBD with MAFLD patients with IBD with no MAFLD. Group 2: (N= 25): patients admitted for colonoscopy for causes rather than UC as a control group. **Results:** Excellent predictive values of serum I-FABP levels were observed at cut off 526.0 and 430.5 in IBD with MAFLD and all IBD patients respectively ( $p<0.001$ ). **Conclusion:** Serum I-FABP is a promising biomarker for the diagnosis of inflammatory bowel disease in patients with IBD with & without MAFLD. **Keywords:** Intestinal Fatty Acid Binding Protein; Inflammatory Bowel Diseases; MAFLD

## Introduction

Inflammatory bowel disease (IBD) consists of 2 well-established but not entirely discrete disease entities, Crohn disease (CD) and ulcerative colitis (UC). They together are a group of closely related but heterogeneous disease processes <sup>(1)</sup>. Worldwide, UC is more common than Crohn's disease <sup>(2)</sup>.

The exact pathogenesis of IBD is unknown. A current hypothesis suggests that primary dysregulation of the mucosal immune system leads to an excessive immunologic response to normal micro flora. <sup>(3)</sup>

In patients with suspected ulcerative colitis, the most important laboratory studies are stool examinations for ova and parasites, stool culture and testing for *Clostridium difficile* toxin to help eliminate other causes of chronic diarrhea (Ford et al., 2013). Other tests, including fecal calprotectin or fecal lactoferrin, may be more sensitive and specific markers of intestinal inflammation <sup>(4)</sup>. However, none of these tests are specific for IBD, and results can be elevated with intestinal inflammation or infection of any cause. <sup>(5)</sup>

Despite success in practice, endoscopic and histopathological examinations are invasive, costly and have some complications in use <sup>(6)</sup>.

Fatty acid binding protein (FABP) is one of the intracellular proteins, with a low molecular weight of approximately 15 kDa, that plays important roles in the transportation and metabolism of long-chain fatty acids. <sup>(7)</sup> Intestinal fatty acid-binding protein (serum I-FABP) is specifically and abundantly present in epithelial cells of the mucosal layer of the intestinal tissue. Serum I-FABP is also considered to be rapidly released into the circulation just after intestinal mucosal tissue is injured. Based on this mechanism, many investigators have already reported the relationship between serum I-FABP concentration and small intestinal diseases from the early 1990s. Regarding these features, serum I-FABP has been reported

to have an association with small intestinal disease <sup>(8)</sup>.

Some studies indicate that MAFLD is more prevalent in patients with, IBD & so this study aimed to study the role of serum I-FABP as a possible biomarker of mucosal injury & MAFLD in patients with IBD

This study aimed to investigate the serum I-FABP as a possible biomarker for the diagnosis of inflammatory bowel disease in patients with IBD with & without MAFLD.

## Patients and methods

This cross-sectional study included 50 patients with Inflammatory bowel disease (IBD) who were admitted at the Hepatology and Gastroenterology Department of Benha University Hospital in the duration from September 2022 to September 2024

An informed written consent was obtained from the patients. Every patient received an explanation of the purpose of the study and had a secret code number. The study was done after being approved by the Research Ethics Committee, Faculty of Medicine, Benha University.

**Inclusion criteria** were patients Age: more than 18 years, both sexes and Patients diagnosed as IBD diagnosis was based on standard clinical, radiological, endoscopic, and histological criteria of ulcerative colitis (UC) or Chron's disease.

**Exclusion criteria** were patients with auto-immune disease, chronic renal or liver disease, history of bowel resection or cardiovascular surgery, intestinal ischemia, sepsis, tuberculosis infection or vasculitis, recent bacterial, viral, or parasitic infection, malignancy, pregnancy, organ transplant patients, HBV, HCV infection, Wilson, Hemochromatosis,  $\alpha$  1 AT, AIH, unwillingness of the patient to participate the study, alcohol intake, infectious colitis and patients taking systemic drugs.

**Grouping:** Patients were selected and divided into two equal groups: **Group 1:** (N= 50): patients with IBD, was

subdivided according to association with MAFLD based on laboratory and abdominal ultrasound finding into: patients with IBD with MAFLD patients with no MAFLD.

**Group 2:** (N= 25): patients admitted for colonoscopy for causes rather than ulcerative colitis as a control group.

**All studied cases were subjected to the following: thorough history taking including** [age, sex habits, residency, marital status, and occupation]. **History taking including** [family history of IBD, history of previous appendectomy, present history including age at diagnosis, duration of disease and disease extension).

**Complete clinical examination: included** [general and local examination (body mass index (BMI) and abdominal examination of (Areas of localized tenderness, intestinal sounds and abdominal distension)]. **Laboratory investigations: included** Complete blood count (CBC), liver function test, kidney function test, glycated hemoglobin (HbA1c), erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), fecal Calprotectin and intestinal Fatty Acid Binding Protein (serum I-FABP).

NAFLD score was calculated with the following formula (NAFLD fibrosis score =  $-1.675 + 0.037 \times \text{age (year)} + 0.094 \times \text{BMI (kg/m}^2) + 1.13 \times \text{IFG/diabetes (yes = 1, no = 0)} + 0.99 \times \text{AST/ALT ratio} - 0.013 \times \text{platelet count (}\times 10^9/\text{L)} - 0.66 \times \text{albumin (g/dL)}$ ). NAFLD patients with a score less than -1.5 were classified as “low probability of advanced liver fibrosis,” and those patients with a score of at least -1.5 were classified as “intermediate or high probability of advanced liver fibrosis”<sup>(9)</sup>.

Venous blood was drawn in the morning after an overnight fast. Serum creatinine was analyzed according to the kinetic Jaffé method on a SYNCHRON CX System analyzer (SYNCHRON, Los Angeles, CA) using reagents from Beckman (Beckman Coulter Diagnostic, Los Angeles, CA). Serum albumin, glucose, and white blood cell (WBC) count were determined using standard commercial methods on a

parallel-multichannel analyzer (SYNCHRON, Los Angeles, CA), hemoglobin A1c (HbA1c) was measured using high performance liquid chromatography. Serum alanine aminotransferase (ALT) was measured following the International Federation of Clinical Chemistry methods. Serum concentration of I-FABP was measured using a commercially available ELISA kit (EIAab, Wuhan, China) according to the manufacturer's instruction.

#### **Intestinal fatty acid binding protein (serum I-FABP):**

The ELISA kit uses the Sandwich-ELISA principle. The micro-ELISA plate provided in this kit has been pre-coated with an antibody specific to Human IFABP/FABP2. Standards or samples are added to the micro-ELISA plate wells and combined with the specific antibody. Then a biotinylated detection antibody specific to Human IFABP/FABP2 and Avidin-Horseradish Peroxidase (HRP) conjugate are added successively to each micro plate well and incubated. Free components are washed away. The substrate solution is added to each well. Only those wells that contain Human IFABP/FABP2, biotinylated detection antibody and Avidin-HRP conjugate will appear blue in color. The enzyme-substrate reaction is terminated by the addition of stop solution and the color turns yellow. The optical density (OD) is measured spectrophotometrically at a wavelength of  $450 \text{ nm} \pm 2 \text{ nm}$ .

#### **Abdominal ultrasonography:**

It was performed on using machine SonoscapeS11, the participants were examined while fasting for 6 hours at least; survey scanning was done through several projections visualizing different organs in deep suspended inspiration, examination of the liver: size, surface, echogenicity, focal lesions, hepatic veins and the portal vein. A prominent gastroenterologist reviewed the images, Abdominal ultrasonography, with stress on hepatic steatosis that will be graded based on

echogenicity of the liver tissue compared to the kidney and the loss of echoes from the walls of the portal system and diaphragm.

Steatosis is graded as follows: Absent (score 0) when the echotexture of the liver is normal; mild (score 1), when there is a slight and diffuse increase of liver echogenicity with normal visualization of the diaphragm and of the portal vein wall; moderate (score 2), in case of a moderate increase of liver echogenicity with slightly impaired appearance of the portal vein wall and the diaphragm; severe (score 3), in case of marked increase of liver echogenicity with poor or no visualization of portal vein wall, diaphragm, and posterior part of the right liver lobe <sup>(10)</sup>.

#### **Endoscopic examination:**

Included the status of the clinical activity of patients with UC was assessed according the criteria of Montreal classification of extent and severity of ulcerative colitis (UC) <sup>(11)</sup>. Disease severity was categorized according to the endoscopic Mayo Score / Disease Activity Index (DAI) for Ulcerative Colitis. Mayo's DAI for UC consists of four evaluated items: stool frequency, rectal bleeding, colonoscopic mucosal appearance and physician and rating of disease activity. Each item was graded on 0-3 scale for a total Mayo score of  $\geq 11$  indicates severe disease activity, 6-10 indicates moderate disease activity and score of  $< 6$  indicates mild disease activity <sup>(12)</sup>.

#### **Approval Code: MD 24-9-2022**

#### **Statistical analysis**

Statistical analysis was done by SPSS v28 (IBM Inc., Armonk, NY, USA). Quantitative variables were presented as mean and standard deviation (SD). Qualitative variables were presented as frequency and percentage (%). Logistic regression is also used to estimate the relationship between a dependent variable

and one (univariate) or more (multivariate) independent variables. A two tailed P value  $< 0.05$  was considered statistically significant.

#### **Results**

No significant difference among all studied groups regarding age, sex, family history of disease or waist-hip ratio, while BMI and prevalence of smokers, waist-circumference were significantly higher among IBD cases with MAFLD than cases without MAFLD and control group. The three groups under the study were matched for age and sex. There was a significant difference observed between IBD with MAFLD and IBD without MAFLD groups regarding BMI ( $p=0.032$ ), similarly, a significant higher BMI in IBD with MAFLD compared with controls ( $p<0.001$ ). Also, a significant difference was observed between IBD with MAFLD and IBD without MAFLD groups, and between IBD with MAFLD and controls ( $p<0.05$ ). IBD patient groups did not show any significant difference regarding disease characteristics. Abdominal pain was the most common complaint among both groups. Ulcerative colitis showed predominance in the study (96.0, and 92.0) in both groups. A severe Mayo score was found in 12% of IBD without MAFLD compared with 4.0% only in IBD with MAFLD; however, this difference was not enough to be significant. **Table 1**

A statistically significant increase of ALT, AST, FPG and CRP among IBD cases with MAFLD than other 2 groups. Hb level was significantly the highest among control group serum FABP levels were significantly elevated in studied IBD cases ( $751.8 \pm 104.3$  pg/mL in MAFLD and  $471.5 \pm 73.2$  pg/mL among cases without MAFLD) compared to control group  $383.1 \pm 102.7$  pg/mL ( $p<0.001$ ). **Table 2**

**Table 1:** Basic and disease characteristics of the studied groups (IBD with MAFLD , IBD without MAFLD, and control group)

Parameters			IBD with MAFLD n=25	IBD without MAFLD n=25	Control group n=25	p-value
Age (years)		Mean $\pm$ SD	40.3 $\pm$ 9.1	37.0 $\pm$ 11.4	37.8 $\pm$ 12.3	0.453 <sup>+</sup>
Sex	Male	Range	28-55	21-55	20-60	0.613 <sup>++</sup>
	Female	n (%)	13 (52.0)	10 (40.0)	13 (52.0)	
DM		n (%)	12 (48.0)	15 (60.0)	12 (48.00)	<b>0.009</b> <sup>++</sup>
Smoking		n (%)	5 (20.0)	13 (52.0)	4 (16.0)	<b>0.001*</b> <sup>++</sup>
Family history		n (%)	20 (80.0)	10 (40.0)	8 (32.0)	1.0 <sup>+++</sup>
BMI		Mean $\pm$ SD	5 (20.0)	4 (16.0)	5 (20.0)	<b>0.002*</b> <sup>+</sup>
		Range	31.0 $\pm$ 5.0	27.8 $\pm$ 3.6	25.9 $\pm$ 4.2	
Pairwise comparisons of groups			19.1-40.0	20.0-32.8	20.0-32.0	
Waist-circumference		Mean $\pm$ SD	P1= 0.032*, p2= <0.001*, p3= 0.264			<b>0.008*</b> <sup>+</sup>
		Range	94.2 $\pm$ 14.9	82.0 $\pm$ 15.8	82.2 $\pm$ 17.5	
Pairwise comparisons of groups			54-113	50.0-103.0	50.0-104.0	
Waist-hip ratio		Mean $\pm$ SD	P1= 0.024*, p2= 0.027*, p3= 0.999			0.722 <sup>+</sup>
		Range	0.8 $\pm$ 0.1	0.8 $\pm$ 0.1	0.8 $\pm$ 0.1	
Disease characteristics			0.7-0.9	0.7-0.9	0.6-0.9	
Complaint	Abdominal pain	no (%)	20 (80.0)	17 (68.0)		0.748 <sup>+</sup>
	Diarrhea	no (%)	2 (8.0)	3 (12.0)		
	Tenesmus	no (%)	1 (4.0)	2 (8.0)		
Type	Constipation	no (%)	2 (8.0)	3 (12.0)		1.0 <sup>+</sup>
	Ulcerative colitis	no (%)	24 (96.0)	23 (92.0)		
	Crohn`s disease	no (%)	1 (4.0)	2 (8.0)		
Extent	E1	no (%)	10 (40.0)	8 (32.0)		0.801 <sup>++</sup>
	E2	no (%)	8 (32.0)	10 (40.0)		
	E3	no (%)	7 (28.0)	7 (28.0)		
Mayo Score	Normal	no (%)	4 (16.0)	5 (20.0)		0.631 <sup>+</sup>
	Mild	no (%)	12 (48.0)	12 (48.0)		
	Moderate	no (%)	8 (32.0)	5 (20.0)		
	Severe	no (%)	1 (4.0)	3 (12.0)		

\*Indicates significant p-value, <sup>+</sup>Kruskal-wallis test, <sup>++</sup>Chi-square test, <sup>+++</sup>Fisher exact test. Significant Kruskal tests were followed by Tukey correction for multiple tests to calculate the adjusted P value, \*indicates significant p value

**Table 2:** Comparison between different groups regarding laboratory data and Comparison between studied groups regarding plasma FABP level

Parameters		IBD with MAFLD n=25	IBD without MAFLD n=25	Control group n=25	p-value
Hb (mg/dl)	Mean ±SD Range	9.5 ± 1.4 6.8-12.0	9.8 ± 0.8 8.9-11.3	11.0±1.4 7.8-13.6	<0.001* <sub>†</sub>
Pairwise comparisons WBCs (10 <sup>9</sup> /L.)	Mean ±SD Range	5.7 ± 1.7 3.0-9.6	6.4 ± 1.8 3.2-10.0	6.1±1.7 3.8-10.0	0.399 <sub>†</sub>
PLT (10 <sup>9</sup> /L.)	Mean ±SD Range	293.2 ± 52.2 221.0-390.0	306.1 ± 72.1 133.0-435.0	289.6±68.6 133.0-400.0	0.611 <sub>†</sub>
ALT (U/L.)	Mean ±SD Range	41.7 ± 7.9 20.0-57.0	36.2 ± 8.2 22.0-55.0	30.0±9.3 12.0-55.0	<0.001* <sub>†</sub>
Pairwise comparisons AST (U/L.)	p1=0.059, p2=<0.001*, p3=0.031* Mean ±SD Range	33.2 ± 6.7 21.0-51.0	27.8 ± 5.8 19.0-41.0	25.0±6.9 10.0-36.0	<0.001* <sub>†</sub>
Pairwise comparisons Albumin (g/dL)	p1=0.014*, p2=<0.001*, p3=0.286 Mean ±SD Range	4.2 ± 0.5 3.0-4.9	4.4 ± 0.4 3.6-5.0	4.3±0.4 3.6-5.4	0.379 <sub>†</sub>
Bilirubin	Mean ±SD Range	0.5 ± 0.2 0.2-0.8	0.7 ± 0.2 0.4-0.9	0.6±0.2 0.4-0.9	0.008* <sub>†</sub>
Pairwise comparisons Creatinine	p1=0.005*, p2=0.243, p3=0.254 Mean ±SD Range	0.6 ± 0.2 0.4-1.0	0.7 ± 0.3 0.3-1.3	0.7±0.3 0.3-1.3	0.871 <sub>†</sub>
FPG	Mean ±SD Range	105.2 ± 12.4 80.9-123.0	83.8 ± 22.5 11.2-114.0	87.9±20.1 51.4-123.0	0.001* <sub>†</sub>
Pairwise comparisons CRP	p1=<0.001*, p2=0.005*, p3=0.724 Mean ±SD Range	3.9 ± 2.4 1.0-11.3	2.4 ± 1.6 0.9-6.0	2.6±1.7 1.0-6.0	0.005* <sub>†</sub>
Pairwise comparisons ESR	p1=0.011*, p2=0.025, p3=0.953 Mean ±SD Range	11.5 ± 4.5 6.0-30.0	11.5 ± 2.0 8.0-18.0	11.8±2.3 8.0-18.0	0.139 <sub>†</sub>
HbA1C	Mean ±SD Range	6.4±0.6 5.4-7.8	6.0±0.4 5.3-6.9	5.8±0.6 4.2-6.9	0.006* <sub>†</sub>
Pairwise comparisons Fecal calprotectin (µg/mg)	p1=0.027*, p2=<0.001*, p3=0.494 Mean ±SD Range	482.2±163.4 223.0-748.0	452.3±180.9 229.0-765.0	31.4±10.4 15.0-57.0	<0.001* <sub>†</sub>
Pairwise comparisons	p1=0.734, p2=<0.001*, p3=<0.001*				

†Kruskal-Wallis test, † †One-way ANOVA, \*indicates significant p-value Significant Kruskal tests were followed by Tukey correction for multiple tests to calculate the adjusted P value, \*indicates significant p value

NAFLD scores were significantly different between the 3 group. The proportion of patients with intermediate or high probability of advanced liver fibrosis was higher in IBD patients with MAFLD (20.0) compared to the other 2 groups (4.0%), however the difference was not enough to make it significant. There was a significant difference observed between

IBD with MAFLD and IBD without MAFLD groups regarding NAFLD score (p=0.005), similarly, a significant difference between IBD with MAFLD compared with controls (p=0.033). **Table 3**

I-FABP levels were significantly elevated in studied IBD cases (751.8 ± 104.3 pg/mL in MAFLD and 471.5 ± 73.2 pg/mL

among cases without MAFLD) compared to control group  $383.1 \pm 102.7$  pg/mL ( $p < 0.001$ ). **Table 4**

Figure 1 (a) represents ROC analysis of predictive ability of serum I-FABP in identifying IBD with MAFLD from control group, while Figure 1 (b) represents ROC analysis of predictive ability of serum I-FABP in identifying IBD from control group. Excellent

predictive values of serum I-FABP levels were observed at cut off 526.0 and 430.5 in IBD with MAFLD and all IBD patients respectively ( $p < 0.001$ ). The AUC, sensitivity, and specificity of serum I-FABP levels were in IBD with MAFLD (0.966, 96.0% and 92.0%), and all IBD patients (0.914, 92.0% and 80.0%), respectively. **Figure 1**

**Table 3:** Comparison between studied groups regarding plasma FABP level

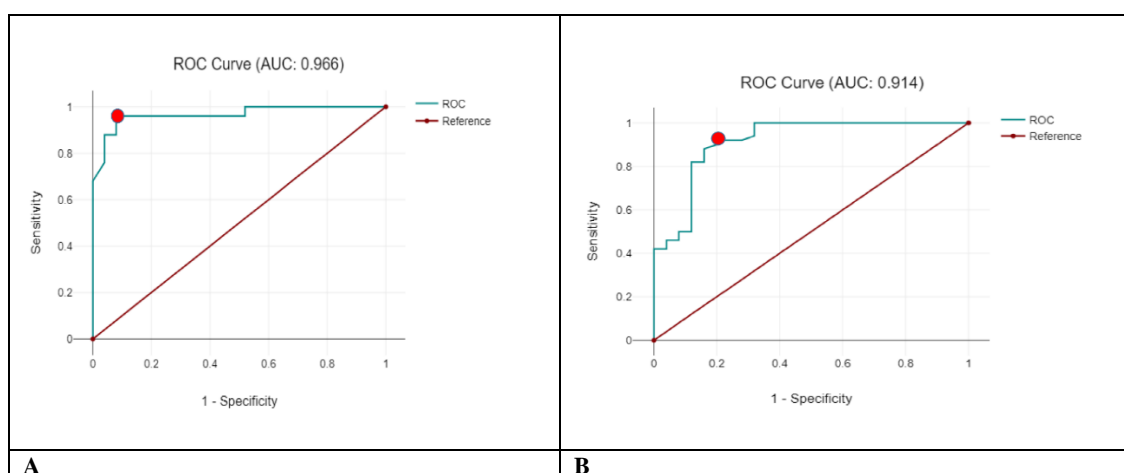
Parameter		IBD with MAFLD N=25	IBD without MAFLD N=25	Control group N=25	P
NAFLD score	Mean $\pm$ SD	$-2.4 \pm 1.2$	$-3.6 \pm 1.3$	$-3.3 \pm 1.1$	<b>0.004*</b> <sup>†</sup>
	Range	-4.8/-0.6	-6.2/-0.4	-5.5/-1.1	
Probability of advanced liver fibrosis	Low	no 20 (80.0)	24 (96.0)	24 (96.0)	0.112
	Intermediate	no 5 (20.0)	1 (4.0)	1 (4.0)	
	or high	(%)	(%)	(%)	
Pairwise comparisons		p1=0.005*, p2=0.033*, p3=0.765			

<sup>†</sup>One-way ANOVA test, \*Chi-square test, \*indicates significant p value

**Table 4:** Comparison between studied groups regarding I-FABP level

Parameter		IBD with MAFLD N=25	IBD without MAFLD N=25	Control group N=25	P
Serum I-FABP level (pg/ml)	Mean	$751.8 \pm 104.3$	$471.5 \pm 73.2$	$383.1 \pm 102.7$	<b>&lt;0.001*</b> <sup>†</sup>
	$\pm$ SD				
	Range	450.0-840.0	407.0-760.0	220.0-670.0	

<sup>†</sup>Kruskal wallis test, \*indicates significant p value



**Figure 1:** (A) Receiver Operating characteristics curve ROC analysis of plasma FABP as a predictor of IBD with MAFLD, (B) ROC analysis of plasma FABP as a predictor of IBD

## Discussion

To our knowledge, no previous studies had the same aim and study grouping as our study, but other previous studies evaluated serum I-FABP in different diseases with different grouping.

In this current study, BMI, waist circumference and prevalence of smoking were significantly higher among IBD cases with MAFLD than cases without MAFLD and control group. The BMI in IBD with MAFLD and IBD without MAFLD were  $31.0 \pm 5.0$  and  $27.8 \pm 3.6$  respectively.

In the same line of this study, <sup>(13)</sup> stated that the BMI among the IBD patients was  $26.2 \pm 4.9$ , which was non-significantly different from controls whose BMI was  $26.3 \pm 4.8$ .

On contrary, <sup>(14)</sup> found that NAFLD in patients with CD correlates more with BMI in the underweight range than in UC. They explained that NAFLD is associated with malnutrition because of more severe disease activity in CD.

This current study identified that the most common type of IBD was UC (94.0%).

An Egyptian study reported nearly similar finding to this current study <sup>(15)</sup>. Esmat reported that the most common type of IBD in his study was UC (86%)

A study conducted by <sup>(16)</sup> reported a different finding to our current study. Sartini et al., (2018) found that CD was more common than UC. CD was reported in 53.8% of studied patients compared with UC (46.2%).

We found no significant difference between both groups regarding complaint, type, and extent of disease or mayo score. Overall, majority of patients complained of abdominal pain (74.0%), while the least common complaint was tenesmus (6.0%).

According to a recent analysis by <sup>(17)</sup>, diarrhea (73.2%) was the most common symptom among all patients at the time of diagnosis, and this was true for both UC and CD. Bowel movements per day ranged from 0 to 20, moreover, 54.6% of patients reported rectal bleeding, which was substantially more common in UC

participants, while 48.6% of patients experienced abdominal pain. Patients with CD reported more abdominal pain, but the difference was insignificant.

This study identifies that there was a statistically significant increase of AST, , FPG, CRP, HbA1C among IBD cases with MAFLD than those without MAFLD. While Bilirubin level was significantly higher among IBD cases without MAFLD. Faecal Calprotectin was higher in IBD cases with MAFLD however, the difference was non-significant. Other tested lab variables were not significantly different among the 3 groups including WBCs, PLT, Albumin, creatinine, ESR

Against our study, it was reported that ALT, and AST were significantly higher among the studied IBD patients without MAFLD, and that WBCs, platelets, CRP were significantly higher among IBD with MAFLD <sup>(16)</sup>.

Sarikaya and co-workers <sup>(18)</sup> observed that there was no statistically significant difference between the groups for any laboratory results including (CRP, serum hemoglobin, and leukocyte count)

This study demonstrated that Plasma FABP levels were significantly elevated in studied IBD cases ( $751.8 \pm 104.3$  pg/mL in MAFLD and  $471.5 \pm 73.2$  pg/mL among cases without MAFLD) compared to control group  $383.1 \pm 102.7$  pg/mL ( $p < 0.001$ ).

Like our results, according to Sarikaya and co-workers <sup>(18)</sup> both newly diagnosed IBD patients and those with established IBD had plasma I-FABP concentrations that were significantly higher than those of controls (plasma I-FABP newly diagnosed IBD: 2104 pg/mL vs controls: 938 pg/mL vs established IBD: 1070 pg/mL;  $p = 0.001$ ). Patients with established IBD and controls did not have significantly different plasma I-FABP levels ( $p = 0.41$ ), however their study was conducted among pediatric population.

Our data revealed that excellent predictive values of plasma FABP levels were observed at cut off 526.0 and 430.5 in IBD



with MAFLD and all IBD patients respectively ( $p < 0.001$ ).

In agreement with our results, Goswami and co-workers<sup>(19)</sup>, study confirmed our diagnostic data and concluded that intestinal fatty acid binding protein is a promising prognostic marker in IBD<sup>(19)</sup>.

In our study there was a significant difference observed between IBD with MAFLD and IBD without MAFLD groups regarding NAFLD score ( $p = 0.005$ ), similarly, a significant difference between IBD with MAFLD compared with controls ( $p = 0.033$ ). In addition to that, the proportion of patients with intermediate or high probability of advanced liver fibrosis was higher in IBD patients with MAFLD (20.0%) compared to the other 2 groups (4.0%), however the difference was not enough to make it significant.

Similarly, Martinez-Dominguez and co-workers<sup>(20)</sup> suggested that the prevalence of NAFLD and significant liver fibrosis was 45 % and 10 % in IBD group. Longer IBD duration (OR 1.02 95 % CI (1.001–1.04)) and older age at IBD diagnosis (OR 1.02 95 % CI (1.001–1.04)) were independent risk factors for NAFLD in IBD group. Crohn's Disease was an independent risk factor for significant liver fibrosis in participants with IBD and NAFLD (aOR 3.97 95 % CI (1.78–8.96)). Capela and colleagues<sup>(21)</sup> reported that body mass index  $\geq 25$ , type 2 diabetes mellitus, dyslipidemia and arterial hypertension were present in 45.2%, 6.0%, 31.5%, 11.9%, respectively. HS was identified in 45.8% patients, of which 84.4% fulfilled MAFLD criteria. MAFLD screening score (AUROC, 0.929 [95% CI, 0.888–0.971]) had outstanding and Fatty Liver Index (AUROC, 0.882 [95% CI, 0.830–0.934]), and Hepatic Steatosis Index (AUROC, 0.803 [95% CI, 0.736–0.871]), had excellent discrimination in predicting MAFLD.

An interesting finding was declared by a group of researchers<sup>(22)</sup>, where they, proved that IBD patients with NAFLD tend to have stable liver disease over 4–6

years, and the risk of liver disease progression is low. This is the first study to document the progression of NAFLD by noninvasive testing over time.

To sum up, these study findings showed some variations, from many other studies and this could be attributed to many factors. As noted, no previous study has had the exact same aim and grouping as the current study. This inherently limits direct comparisons. For instance, some studies focused on serum I-FABP (intestinal fatty acid-binding protein) levels in specific diseases, while others examined broader metabolic or inflammatory markers in IBD or MAFLD populations.

In the current study, the grouping involved IBD cases with and without MAFLD and a control group. Other studies grouped their populations differently, for example, by disease severity, specific IBD types (UC vs. CD), or pediatric versus adult populations.

## Conclusion

Our study revealed that serum I-FABP is a promising biomarker for the diagnosis of inflammatory bowel disease in patients with IBD with & without MAFLD. Measuring plasma FABP levels should be measured at cut off 526.0 and 430.5 in IBD with MAFLD and all IBD patients respectively. Plasma FABP levels had high sensitivity and specificity in diagnosis of IBD with MAFLD or without MAFLD.

## References

1. Cosnes J, Gower-Rousseau C, Seksik P, Cortot A. Epidemiology and natural history of inflammatory bowel diseases. *Gastroenterology*. 2011;140:1785-94.
2. Danese S, Fiocchi C. Ulcerative colitis. *N Engl J Med*. 2011;365:1713-25.
3. Peyrin-Biroulet L, Sandborn W, Sands BE, Reinisch W, Bemelman W, Bryant RV, et al. Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE): Determining Therapeutic Goals for Treat-to-Target. *Am J Gastroenterol*. 2015;110:1324-38.
4. Gecse KB, Vermeire S. Differential diagnosis of inflammatory bowel disease: imitations and

- complications. *Lancet Gastroenterol Hepatol*. 2018;3:644-53.
5. Kornbluth A, Sachar DB. Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology, Practice Parameters Committee. *Am J Gastroenterol*. 2010;105:501-23; quiz 24.
  6. DeRoche TC, Xiao SY, Liu X. Histological evaluation in ulcerative colitis. *Gastroenterol Rep (Oxf)*. 2014;2:178-92.
  7. Okada K, Sekino M, Funaoka H, Sato S, Ichinomiya T, Murata H, et al. Intestinal fatty acid-binding protein levels in patients with chronic renal failure. *J Surg Res*. 2018;230:94-100.
  8. Wiercinska-Drapalo A, Jaroszewicz J, Siwak E, Pogorzelska J, Prokopowicz D. Intestinal fatty acid binding protein (I-FABP) as a possible biomarker of ileitis in patients with ulcerative colitis. *Regul Pept*. 2008;147:25-8.
  9. Treeprasertsuk S, Björnsson E, Enders F, Suwanwalaikorn S, & Lindor K D. NAFLD fibrosis score: a prognostic predictor for mortality and liver complications among NAFLD patients. *World journal of gastroenterology: WJG*. (2013) 19: (8), 1219.
  10. Ferraioli, G., & Monteiro, L. B. Ultrasound-based techniques for the diagnosis of liver steatosis. *World Journal of Gastroenterology*. (2019) 25:(40), 6053–6063.
  11. Monstad I, Hovde Ø, Solberg I, Moum B. Clinical course and prognosis in ulcerative colitis: Results from population-based and observational studies. *Annals of gastroenterology : quarterly publication of the Hellenic Society of Gastroenterology*. 2014;27:95-104.
  12. Dave M, Loftus E. Mucosal Healing in Inflammatory Bowel Disease—A True Paradigm of Success? *Gastroenterology & hepatology*. 2012;8:29-38.
  13. Noorian S, Jeon Y, Nguyen MT, Sauk J, Limketkai BN. The Impact of NAFLD on Hospitalization Outcomes in Patients With Inflammatory Bowel Diseases: Nationwide Analysis. *Inflamm Bowel Dis*. 2022;28:878-87.
  14. Rodriguez-Duque JC, Calleja JL, Iruzubieta P, Hernández-Conde M, Rivas-Rivas C, Vera MI, et al. Increased risk of MAFLD and Liver Fibrosis in Inflammatory Bowel Disease Independent of Classic Metabolic Risk Factors. *Clin Gastroenterol Hepatol*. 2023;21:406-14.e7.
  15. Esmat S, El Nady M, Elfekki M, Elsherif Y, Naga M. Epidemiological and clinical characteristics of inflammatory bowel diseases in Cairo, Egypt. *World J Gastroenterol*. 2014;20:814-21.
  16. Sartini A, Gitto S, Bianchini M, Verga MC, Di Girolamo M, Bertani A, et al. Non-alcoholic fatty liver disease phenotypes in patients with inflammatory bowel disease. *Cell Death Dis*. 2018;9:87.
  17. Elbadry M, Nour MO, Hussien M, Ghoneem EA, Medhat MA, Shehab H, et al. Clinico-Epidemiological Characteristics of Patients With Inflammatory Bowel Disease in Egypt: A Nationwide Multicenter Study. *Front Med (Lausanne)*. 2022;9:867293.
  18. Sarikaya M, Ergül B, Doğan Z, Filik L, Can M, Arslan L. Intestinal fatty acid binding protein (I-FABP) as a promising test for Crohn's disease: a preliminary study. *Clin Lab*. 2015;61:87-91.
  19. Goswami P, Sonika U, Moka P, Sreenivas V, Saraya A. Intestinal Fatty Acid Binding Protein and Citrulline as Markers of Gut Injury and Prognosis in Patients With Acute Pancreatitis. *Pancreas*. 2017;46:1275-80.
  20. Martínez-Domínguez SJ, García-Mateo S, Gargallo-Puyuelo CJ, Gallego Llera B, Refaie E, Callau P, et al. Crohn's disease is an independent risk factor for liver fibrosis in patients with inflammatory bowel disease and non-alcoholic fatty liver disease. *Eur J Intern Med*. 2024;120:99-106.
  21. Capela TL, Silva VM, Freitas M, Arieira C, Gonçalves TC, de Castro FD, et al. Identifying inflammatory bowel disease patients at risk of metabolic dysfunction-associated fatty liver disease: usefulness of non-invasive steatosis predictive scores. *BMC Gastroenterol*. 2023;23:437.
  22. Ritaccio G, Stoleru G, Abutaleb A, Cross RK, Shetty K, Sakiani S, et al. Nonalcoholic Fatty Liver Disease Is Common in IBD Patients However Progression to Hepatic Fibrosis by Noninvasive Markers Is Rare. *Dig Dis Sci*. 2021;66:3186-91.

**To cite this article:** Reda M. El-Badawy, Magdy A. Gad, Badawy A. Abd El Aziz, Waled A. Abd Elhalem, Ahmed I. Sakr. Intestinal Fatty Acid Binding Protein (I-FABP) in Patients with Inflammatory Bowel Diseases with and without MAFLD. *BMFJ* 2025;42(4):644-653.