Inflammatory Bowel Disease and Metabolic DysfunctionAssociated Steatotic Liver Disease: Prevalence and Predictive Factors from a Moroccan CaseControl Study

Abstract

Background:
Metabolic dysfunction–associated steatotic liver disease (MASLD) is increasingly recognized as a common comorbidity in patients with inflammatory bowel disease (IBD), potentially impacting disease progression and management. While metabolic factors are central to MASLD, non-metabolic contributors such as chronic inflammation, microbiota alterations, and IBD-related therapies may also play a role.

Objective:
To evaluate the prevalence and predictive factors of hepatic steatosis in patients with IBD through a case-control study.

Methods:
We conducted a retrospective-prospective study at the Hassan II University Hospital in Fez, including patients with Crohn's disease (CD) or ulcerative colitis (UC) who underwent abdominal ultrasound between 2019 and 2025. Patients with ultrasound-diagnosed steatosis comprised the CASE group, while those without steatosis formed the CONTROL group. Demographic, clinical, metabolic, therapeutic, and paraclinical data were collected and analyzed using univariate and multivariate statistical methods.

Results:
Among 403 screened patients, 156 met inclusion criteria (52 CASE, 104 CONTROL). The prevalence of hepatic steatosis was 13.4%. MASLD was significantly associated with age <45 years (p=0.018), presence of metabolic syndrome (p=0.012), hypertension (p=0.018), undernutrition (p=0.024), active IBD (p=0.018), and extensive Crohn's disease (p=0.039). Notably, corticosteroid exposure was more frequent in the steatosis group (55.76% vs. 21.15%). Abnormal liver function tests, especially combined cholestasis and cytolysis, were common findings. Histological analysis confirmed steatosis in two biopsy-proven cases.

Independent predictors included metabolic syndrome (OR 3.6, 95% CI 1.6–10.3), prolonged corticosteroid therapy (OR 14.12, 95% CI 5.7–34.53), malnutrition (OR 2.6, 95% CI 1.11–6.23), active disease (OR 2.6, 95% CI 1.15–5.23), azathioprine (OR 2.7, 95% CI 1.16–4.66) and methotrexate (OR 2.58, 95% CI 1.73–6.24).

Conclusion:
Hepatic steatosis in IBD patients is driven by both metabolic and disease-specific factors. Early identification of at-risk patients may allow for targeted interventions, potentially reducing liver-related morbidity. Routine hepatic screening and metabolic–nutritional assessment should be integrated into IBD management protocols.

Keywords:
MASLD, inflammatory bowel disease, Crohn's disease, ulcerative colitis, hepatic steatosis, metabolic syndrome, corticosteroids, liver ultrasound.

Introduction:

Metabolic dysfunction–associated steatotic liver disease (MASLD) has become one of the leading causes of liver cirrhosis and hepatocellular carcinoma [1]. IMetabolic steatotic liver diseases encompass a histological spectrum ranging from simple steatosischaracterized by the accumulation of lipid vacuoles within hepatocytesto cirrhosis, defined by the presence of parenchymal nodules surrounded by bridging fibrous septa. This spectrum typically develops in the context of insulin resistance. Metabolic dysfunction–associated steatotic liver disease (MASLD) is defined by the presence of hepatic steatosis in association with at least one cardiometabolic risk factor, in the absence of other identifiable causes [2].
The global prevalence of MASLD is approximately 30%. Between 1991 and 2019, its prevalence increased from 22% to 37%. This rising trend closely parallels the global increase in type 2 diabetes and obesity-related diseases, underscoring the strong association between MASLD and cardiometabolic risk factors.[3]. Metabolic syndrome is the most important predisposing factor, consisting of insulin resistance with or without diabetes, dyslipidemia, and obesity [4]. The controlled attenuation parameter (CAP) measured by transient elastography offers high diagnostic accuracy in identifying hepatic steatosis [5].

The prevalence of inflammatory bowel disease (IBD) is increasing in Asia. It would be relevant to study the association between MASLD and IBD, whose prevalence is similar in Asia and Western countries, and is rising in Asia. There are shared pathogenic mechanisms between NAFLD and IBD [6].

Although metabolic factors are the most significant predisposing factors for MASLD, non-metabolic factors such as alterations in the gut microbiota, genetic predisposition, and increased visceral fat also contribute to the risk and outcomes in patients with IBD [6]. On the other hand, commonly used medications in IBD, such as corticosteroids and methotrexate, may promote the development of MASLD [7].

The overall prevalence of MASLD in IBD ranges from 24% to 50%. This variation in prevalence across studies can be attributed to heterogeneity in patient populations and methods of steatosis assessment. However, most observational studies on MASLD in IBD are retrospective or cross-sectional and include both ulcerative colitis (UC) and Crohn's disease (CD). Prospective studies focusing on the prevalence of MASLD in UC are limited, and very few have investigated the impact of MASLD on long-term IBD outcomes [8].

Despite increasing awareness of MASLD in IBD, data from Africa and the Middle East remain scarce. Our study, conducted in a Moroccan tertiary center, addresses this gap by providing prospective and retrospective data on predictive factors in a North African population, potentially reflecting different genetic, nutritional, and therapeutic profiles compared to Western cohorts.

The aim of our study is to investigate the predictive factors of hepatic steatosis in patients with IBD through a case-control study.

MATERIALS AND METHODS

1. Materials:

Study period and type:

This is a retrospective, prospective, descriptive, and analytical study including all patients followed for inflammatory bowel disease (IBD) in the Department of Hepato-Gastroenterology at Hassan II University Hospital in Fez. The study was conducted over a five-year period, from 2019 to 2025.

Data collection:

For the purposes of this study, we used the following data sources:

- Hospitalization records from the Department of Hepato-Gastroenterology at Hassan II University Hospital in Fez
- Patients' electronic medical records in the "Hosix" system
- A data collection sheet was used to gather all necessary information to meet the study objectives, including: epidemiological, clinical, paraclinical, therapeutic and evolutionary data.

Inclusion criteria:

We included all patients followed for IBD, either Crohn's disease (CD) or ulcerative colitis (UC), who underwent abdominal ultrasound during disease follow-up:

- Patients in whom the ultrasound revealed hepatic steatosis were classified as the CASE group.
- Patients with no evidence of steatosis on ultrasound constituted the CONTROL group.

Exclusion criteria: We excluded all patients with a known diagnosis of hepatic steatosis prior to the diagnosis of IBD and patients with a history of alcohol abuse.

2. Methods:

Variables studied:

Epidemiological data:We collected information on age, sex, admission date, family and personal medical history, risk factors, and elements of metabolic syndrome including hypertension, diabetes, and dyslipidemia.

Clinical data: We recorded the type of IBD (CD or UC), disease extent, activity using the Harvey-Bradshaw index for CD and the Mayo score for UC.

We also noted general condition using the WHO performance score, body mass index (BMI), and the mode of steatosis discovery (incidental or symptomatic).

Paraclinical data: Diagnostic tests mainly included abdominal ultrasound, which assesses liver echogenicity in comparison to that of the adjacent renal cortex. In the absence of steatosis, the liver parenchyma appears isoechoic to the renal cortex. As steatosis severity increases, the liver becomes more hyperechoic. Additional investigations in cases of jaundice or pruritus included liver function tests.

All ultrasound examinations were performed by senior hepathologist with more than five years' experience in hepatobiliary imaging, following standardized protocols to ensure reproducibility and minimize interobserver variability.

In cases of steatosis, etiological workup included:Viral serologies: Hepatitis B (HBsAg, anti-HBs, anti-HBc), Hepatitis C , lipid profile, fasting blood glucose, HbA1C, serum protein electrophoresis (SPE), autoimmune panel, wilson's disease workup, ferritin and transferrin saturation,alpha-1 antitrypsin level , BILI MRI, fibrosis evaluation using NAFLD fibrosis score, liver stiffness by FibroScan, or liver biopsy.

Therapeutic data: treatment for IBD: corticosteroids and duration of use, azathioprine, methotrexate and cumulative dose, biologics such as anti-TNF alpha agents (infliximab, adalimumab). For surgical cases: indications, type of surgery, and extent of resection.

Statistical analysis:

Data were recorded in an Excel spreadsheet, results were presented as graphs and tables.

Qualitative variables were described using frequencies and percentages, while quantitative variables were expressed using central tendency measures (mean ± standard deviation) or (median, range) and dispersion.

Univariate and multivariate analyses were performed using SPSS software in collaboration with the Epidemiology Department of Hassan II University Hospital in Fez.

The analysis aimed to identify predictive factors of steatosis in IBD by comparing the two groups (CASE vs CONTROL) using the Chi-square test or Fisher's exact test.

A p-value ≤ 0.05 and a confidence interval not including 1were considered statistically significant for all tests.

The study protocol complied with the principles of the Declaration of Helsinki. Given its observational nature and use of anonymized data, it was exempted from formal ethics committee approval according to the policies of the Hassan II University Hospital. Patient consent was obtained for all prospectively collected data.

Results :

Among 403 cases, we included 156 patients, of whom 52 were in the CASE group and 104 in the CONTROL group. The prevalence of steatosis among patients with IBD was 13.4%.

Patients were categorized into age groups: 83 patients were younger than 45 years, 52 patients were between 45 and 60 years old, and 21 patients were older than 60 years. The mean age of the patients was 46 years, ranging from 17 to 70 years.
In Group A (n=52), 57.69% of patients (n=30) were under 45 years of age, 26.92% (n=14) were between 45 and 60 years, and 15.38% (n=8) were older than 60 years.
In Group B (n=104), 50.96% of patients (n=53) were under 45 years, 36.53% (n=38) were between 45 and 60 years, and 12.5% (n=13) were older than 60 years.
A statistically significant difference was observed between the two groups for the <45 years age category (p=0.018).

In Group A (n=52), a female predominance was observed, with 59.61% (n=31) women and 36.53% (n=19) men. In Group B (n=104), there was a slight male predominance, with 50.96% (n=53) men and 49.03% (n=51) women.
Comparative analysis did not reveal a statistically significant difference between the two groups regarding sex distribution (p=0.164 for both females and males).

In Group A (with steatosis), diabetes was present in 26.92% of patients (n=14), hypertension in 25% (n=13), dyslipidemia in 23.07% (n=12), and metabolic syndrome in 28.84% (n=15). In Group B (without steatosis), diabetes was present in 13.46% of patients (n=14), hypertension in 9.61% (n=10), dyslipidemia in 11.53% (n=12), and metabolic syndrome in 11.53% (n=12).
Comparative analysis revealed a statistically significant difference between the two groups for the presence of metabolic syndrome (p=0.012) and hypertension (p=0.018). However, no statistically significant differences were found between the groups regarding diabetes (p=0.084) and dyslipidemia (p=0.134).

Hepatic steatosis was incidentally discovered in 35.7% of cases following an abdominopelvic ultrasound performed during IBD follow-up.
In 64.3% of cases, the ultrasound was performed due to clinical symptoms: biliary colic in 16.7% of cases, and abnormal liver function tests in 47.6% of cases.

In Group A (patients with steatosis), Crohn's disease (CD) was observed in 53.84% of cases (n=28), while ulcerative colitis (UC) was present in 46.15% of cases (n=24). In Group B (patients without steatosis), CD was found in 67.30% of cases (n=70) and UC in 23.07% of cases (n=34). Comparative analysis showed a statistically significant difference between the two groups concerning the prevalence of Crohn's disease (p=0.02), whereas no significant difference was noted for ulcerative colitis (p=0.055).

Regarding the extent of IBD, among patients with Crohn's disease in Group A, 3.57% (n=1) had isolated ileal disease, 89.28% (n=25) had extensive ileocolic or colonic involvement, and 7.14% (n=2) had isolated perianal disease. In patients with ulcerative colitis from the same group, 62.5% (n=15) presented with pancolitis, 20.83% (n=5) with left-sided colitis, and 16.66% (n=4) with distal colitis. In Group B, among patients with Crohn's disease, 11.42% (n=8) had isolated ileal disease, 81.42% (n=57) had extensive ileocolic or colonic disease, and 7.14% (n=5) had isolated perianal disease. For patients with ulcerative colitis in Group B, 47.05% (n=16) had pancolitis,

32.35% (n=11) had left-sided colitis, and 20.58% (n=7) had distal colitis. Statistical analysis revealed a significant difference between the two groups concerning extensive Crohn's disease (p=0.039), whereas no significant differences were observed for isolated ileal disease (p=0.067), isolated perianal disease (p=0.085), or the different forms of ulcerative colitis.

Concerning disease activity, overall, 61.9% of patients had active IBD (n=61). For Crohn's disease, activity was assessed using the Harvey-Bradshaw Index (HBI). In Group A, 26.9% of patients (n=14) had active disease (HBI ≥ 4), while 73.07% (n=38) had inactive disease (HBI < 4). In Group B, 23.07% (n=24) had active disease and 76.9% (n=80) had inactive disease. For ulcerative colitis, activity was assessed using the Mayo score. In Group A, 23.07% of patients (n=12) exhibited active disease (Mayo score ≥ 2), compared to 76.9% (n=40) with inactive disease (Mayo score < 2). In Group B, 10.57% (n=11) had active disease and 89.42% (n=93) had inactive disease. Overall, 26 patients had active disease in Group A versus 35 patients in Group B. Comparative analysis showed a statistically significant difference between the two groups, with a higher rate of active disease observed in Group A (p=0.018).

In Group A (patients with steatosis), 40.38% of patients were undernourished (BMI < 18 kg/m²), 25% had a normal BMI (≥ 18 kg/m² and < 25 kg/m²), 9.61% were overweight (BMI ≥ 25 kg/m² and < 30 kg/m²), and 5.76% were obese (BMI ≥ 30 kg/m²). BMI was undefined in 19.23% of patients. The mean BMI was 20.1 kg/m².
In Group B (patients without steatosis), 26.92% of patients were undernourished (BMI < 18 kg/m²), 39.42% had a normal BMI, 11.53% were overweight, and 4.80% were obese. The mean BMI was 22.88 kg/m².
Statistical analysis showed a significant difference between the two groups for the prevalence of undernutrition (BMI < 18 kg/m²), with a higher prevalence in Group A (p=0.024). No significant difference was found for other BMI categories (normal weight, overweight, or obesity).
Clinical examination in the case group (A) revealed abdominal tenderness in 45.2% of patients, hepatomegaly in 11.9%, while 42.9% had a normal physical examination.

In 47.6% of cases, abdominal ultrasound was performed due to abnormal liver function tests. Isolated cholestasis with elevated gamma-GT levels was observed in 25% of patients, isolated hepatocellular injury (cytolysis) in 35%, and a combination of cholestasis and cytolysis in 40% of cases. Bilirubin levels were normal in all patients.

All patients underwent abdominal ultrasound. Hepatic steatosis was identified in 52 cases. In 35.7% of cases, steatosis was detected prospectively during routine IBD follow-up. In 64.3% of cases, ultrasound was performed retrospectively in response to clinical symptoms or abnormal liver function tests.Figure 1 shows an example of hepatic steatosis on abdominal ultrasound, illustrating the characteristic increased echogenicity of the liver parenchyma compared to the renal cortex.

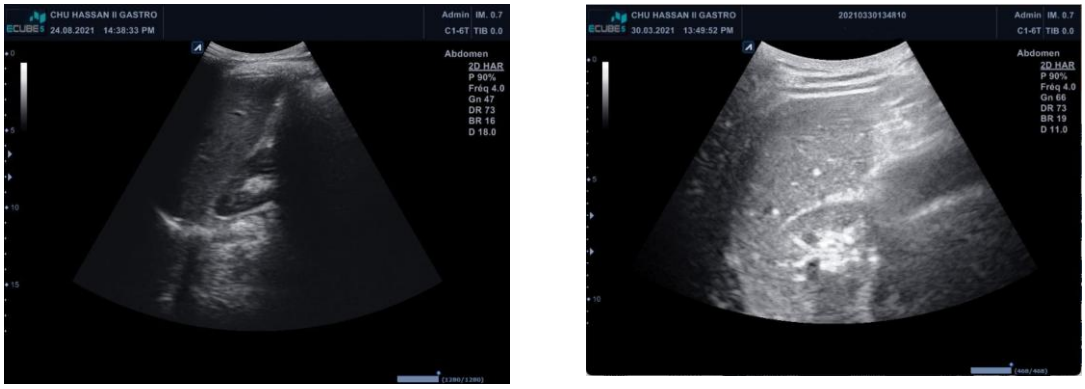

Figure.1 : Ultrasound image showing hepatic steatosis.

In the etiological assessment of steatosis, various biological tests were conducted. The metabolic profile showed normal fasting glucose levels in 10.5% of patients and elevated glucose levels in 3.34%. A total of 13.84% of patients had elevated glycated hemoglobin, indicating diabetes. The lipid profile was normal in 34.61% of patients, while the remaining 65.38% had lipid abnormalities. Liver function tests revealed abnormalities in 47.6% of patients, with isolated cholestasis (elevated gamma-glutamyl transferase) in 25%, isolated hepatic cytolysis in 35%, and a combination of cholestasis and cytolysis in 40%. Bilirubin levels were normal in all patients. Hypoalbuminemia was found in 15.38% of patients, and viral serology revealed a resolved hepatitis B infection in one patient, with negative results for hepatitis B and C in the remaining patients. Protein electrophoresis showed hypogammaglobulinemia in three patients and hypergammaglobulinemia in one patient due to an inflammatory syndrome. Ferritin levels were elevated in 9.61% of patients, with a mean transferrin saturation of 0.32 µmol/l. An autoimmune panel performed in 23 patients (44.23%) revealed positive antinuclear antibodies in four patients, with all other autoimmune markers negative. Wilson's disease testing in 8 patients (15.38%) was normal. Alpha-1 antitrypsin testing was requested in five patients, but results were unavailable.

Imaging with MRI of the liver and biliary tract was conducted in 7 patients, with one showing diffuse steatosis. Non-invasive fibrosis assessment via FibroScan was done in 7 patients, with elasticity ranging from 2.77 kPa to 8.7 kPa. Finally, liver biopsy was performed in two patients. One patient, with a FibroScan elasticity of 8.7 kPa, presented with macrovacuolar steatosis, chronic mildly active hepatitis, and moderate portal fibrosis (Metavir score A2F2), while the other, with unexplained hepatic cytolysis (negative etiology), had macrovacuolar steatosis.

A summary of the biological, imaging, and histological findings obtained during the etiological assessment of hepatic steatosis is presented in Table1

Table 1 : Summary of Biological, Imaging, and Histological Findings in the Etiological Assessment of Hepatic Steatosis

Assessment	Findings
Fasting Glucose	Normal in 10.5%, elevated in 3.34%
Glycated Hemoglobin (HbA1c)	Elevated in 13.84% (indicative of diabetes)

Lipid Profile	Normal in 34.61%; abnormal in 65.38%
Liver Function Tests	Abnormal in 47.6%
– Isolated Cholestasis (γGT elevation)	25%
– Isolated Hepatic Cytolysis	35%
– Combined Cholestasis and Cytolysis	40%
Bilirubin Levels	Normal in all patients
Albumin	Hypoalbuminemia in 15.38%
Viral Serology	Resolved hepatitis B in 1 patient; negative for HBV and HCV in others
Protein Electrophoresis	Hypogammaglobulinemia in 3 patients; hypergammaglobulinemia in 1 patient
Ferritin and Transferrin Saturation	Elevated ferritin in 9.61%; mean transferrin saturation: 0.32 μmol/L
Autoimmune Panel	Positive ANA in 4 patients (among 23 tested); other markers negative
Wilson's Disease Testing	Normal in 8 patients
Alpha-1 Antitrypsin	Test requested in 5 patients; results unavailable
MRI of Liver and Biliary Tract	Performed in 7 patients; diffuse steatosis in 1 patient
FibroScan	Performed in 7 patients; elasticity range 2.77–8.7 kPa
Liver Biopsy	2 patients: macrovacuolar steatosis, mild chronic hepatitis, portal fibrosis (A2F2)

In **Group A**, 29 patients (55.76%) received corticosteroid treatment, with 17 patients (32.69%) being treated for more than 3 months. The indication for corticosteroids was severe active disease or acute severe colitis, with an average treatment duration of 3.5 months (ranging from 2 to 6 months) and an average dose of 45 mg per day before tapering. 5-ASA was prescribed to 21 patients (40.38%), azathioprine to 26 patients (50%), methotrexate to 13 patients (25%), purine analogs to 6 patients (11.53%), infliximab to 12 patients (23.07%), and adalimumab to 3 patients (5.76%). Surgical intervention was necessary for 9 patients (17.30%), including emergency surgery for 3 patients with acute severe colitis unresponsive to medical treatment, who underwent subtotal colectomy. One patient had resection for a sigmoid fistula with lateral anastomosis, and 5 patients underwent ileocoecal resections, with 3 of them having resections > 50 cm and 2 having resections < 50 cm.

In **Group B**, 22 patients (21.15%) were treated with corticosteroids, with 11 patients (10.57%) receiving corticosteroids for more than 3 months. The treatment duration ranged from 1 to 7 months, with an average dose of 50 mg per day before tapering. 5-ASA was used by 12 patients (11.53%), azathioprine by 49 patients (47.11%), methotrexate by 23 patients (22.11%), purine analogs by 10 patients (9.61%), infliximab by 48 patients (46.15%), and adalimumab by 17 patients (16.34%). Surgical treatment was required for 15 patients (14.42%), with emergency surgery performed in 5 patients: 2 for acute severe colitis unresponsive to medical treatment, 1 for sigmoid perforation, and 2 for intra-abdominal collections. The remaining patients

underwent ileocoecal resections, with 4 having resections > 50 cm and 6 having resections < 50 cm.

The analytical study revealed statistically significant differences between the two groups for corticosteroid use for more than 3 months, azathioprine, and methotrexate treatment, but no significant difference was found for other medical treatments or surgical interventions.

The following table presents a comprehensive comparison of various epidemiological, clinical, paraclinical, and therapeutic factors between Group A and Group B in patients diagnosed with hepatic steatosis associated with Inflammatory Bowel Disease (IBD). This analysis includes key variables such as age, sex, risk factors, type of IBD (Crohn's disease or ulcerative colitis), disease extent, disease activity, as well as treatment regimens including corticosteroids, immunosuppressants, and surgical interventions. The statistical significance of each factor is also provided, offering insight into the distinct characteristics and treatment patterns between the two groups.

Table 2: Comparison of Epidemiological, Clinical, Paraclinical, and Therapeutic Factors between Group A and Group B in Patients with Hepatic Steatosis Associated with Inflammatory Bowel Disease (IBD)

Factor	Group A (%)	Group B (%)	P-value
Age < 45 years	40.38% (21)	26.92% (28)	0.018
Male Sex	55.76% (29)	50% (52)	0.398
Female Sex	44.23% (23)	50% (52)	0.398
Diabetes	13.46% (7)	15.38% (16)	0.75
Dyslipidemia	30.77% (16)	26.92% (28)	0.65
Hypertension (HTN)	23.07% (12)	28.85% (30)	0.51
Malnutrition (BMI < 18 kg/m²)	40.38% (21)	26.92% (28)	0.024
Overweight (BMI ≥ 25 kg/m²)	9.61% (5)	11.53% (12)	0.447
Obesity (BMI ≥ 30 kg/m²)	5.76% (3)	4.80% (5)	0.177
Metabolic Syndrome	30.77% (16)	10.57% (11)	0.012
UC Type (RCH)	34.61% (18)	50% (52)	0.015
Crohn's Disease (CD)	65.38% (34)	50% (52)	0.015
Active Disease	57.69% (30)	34.61% (36)	0.018
Extent of Disease	53.84% (28)	44.23% (46)	0.22
Corticosteroids > 3 months	55.76% (29)	21.15% (22)	<0.001
5-ASA	40.38% (21)	11.53% (12)	0.06
Azathioprine	50% (26)	47.11% (49)	0.043
Methotrexate	25% (13)	22.11% (23)	0.031
Purinethol	11.53% (6)	9.61% (10)	0.06
Infliximab	23.07% (12)	46.15% (48)	0.304
Adalimumab	5.76% (3)	16.34% (17)	0.871
Surgical Treatment	17.30% (9)	14.42% (15)	0.304
Resection > 50 cm	5.76% (3)	3.84% (4)	0.304
Resection < 50 cm	11.53% (6)	10.57% (11)	0.304

Analytical Study:

Univariate Analysis: The aim of this analysis was to investigate the relationship between various epidemiological, clinical, paraclinical, and therapeutic factors and the presence of hepatic steatosis in patients with inflammatory bowel disease (IBD). A P value ≤ 0.05 was considered statistically significant. The factors studied included: age (according to age groups), diabetes, dyslipidemia, hypertension, malnutrition, overweight, obesity, metabolic syndrome, type of IBD (Crohn's disease or ulcerative colitis), extent of the disease, disease activity, surgery and extent of intestinal and/or colonic resection, corticosteroid therapy, prolonged corticosteroid therapy > 3 months, treatment with 5-ASA, methotrexate, purine analogs, azathioprine, infliximab, and adalimumab.

The univariate analysis revealed that hepatic steatosis was significantly associated with younger age (<45 years) ($p = 0.018$), malnutrition (BMI < 18) ($p = 0.024$), metabolic syndrome ($p = 0.012$), extensive Crohn's disease ($p = 0.039$), pancolitis in ulcerative colitis ($p = 0.047$), active disease ($p = 0.018$), prolonged corticosteroid therapy ($p < 0.001$), treatment with azathioprine ($p = 0.043$), and methotrexate ($p = 0.031$).

Multivariate Analysis: Of the significant factors, malnutrition (OR: 2.6, 95% CI [1.11-6.23]), metabolic syndrome (OR: 3.6, 95% CI [1.6-10.3]), active disease (OR: 2.6, 95% CI [1.15-5.23]), prolonged corticosteroid therapy (OR: 14.12, 95% CI [5.7-34.53]), azathioprine treatment (OR: 2.7, 95% CI [1.16-4.66]), and methotrexate treatment (OR: 2.58, 95% CI [1.73-6.24]) were identified as independent predictive factors for hepatic steatosis in patients with IBD.

Factor	Odds Ratio (OR)	95% CI	P value
Malnutrition (BMI < 18 kg/m²)	2.6	1.11 – 6.23	0.024
Metabolic syndrome	3.6	1.6 – 10.3	0.012
Active disease	2.6	1.15 – 5.23	0.018
Prolonged corticosteroid therapy (> 3 months)	14.12	5.7 – 34.53	<0.001
Azathioprine treatment	2.7	1.16 – 4.66	0.043
Methotrexate treatment	2.58	1.73 – 6.24	0.031

Univariate and Multivariate Analysis – Independent Predictive Factors for Hepatic Steatosis in Patients with IBD

Discussion:

The study investigates the predictive factors of hepatic steatosis in patients with inflammatory bowel disease (IBD), encompassing both Crohn's disease (CD) and ulcerative colitis (UC). The findings reveal a prevalence of hepatic steatosis at 13.4% among the IBD study, with significant associations identified between steatosis and factors such as undernutrition, metabolic syndrome, active disease, prolonged corticosteroid therapy, and the use of immunosuppressive agents like azathioprine and methotrexate.

Prevalence of Hepatic Steatosis in IBD

The observed prevalence of hepatic steatosis in this study aligns with existing literature, which reports a variable prevalence ranging from 13.3% to 70% among IBD patients [9]. This variability can be attributed to differences in diagnostic modalities, patient populations, and definitions of steatosis across studies. Notably, a study utilizing magnetic resonance imaging reported a prevalence of 54.6%, highlighting the sensitivity of advanced imaging techniques in detecting hepatic steatosis [10].

Metabolic Syndrome and Hepatic Steatosis

The strong association between metabolic syndrome and hepatic steatosis observed in this study corroborates previous findings. Metabolic syndrome, characterized by insulin resistance, hypertension, dyslipidemia, and central obesity, is a well-established risk factor for non-alcoholic fatty liver disease (NAFLD)[11]. In the context of IBD, systemic inflammation may exacerbate insulin resistance, thereby increasing the risk of hepatic steatosis [9].

Undernutrition and Hepatic Steatosis

Interestingly, undernutrition (BMI < 18 kg/m²) emerged as a significant predictor of hepatic steatosis in this cohort. This finding contrasts with the traditional association of hepatic steatosis with obesity. In IBD patients, malnutrition may lead to alterations in gut microbiota and intestinal permeability, contributing to hepatic fat accumulation [9]. Further research is warranted to elucidate the mechanisms linking undernutrition and hepatic steatosis in this population.

Regarding the correlation between malnutrition and the prevalence of NAFLD, Adams et al. [12] reported a prevalence of 87.6% of NAFLD among underweight IBD patients (BMI <18.5), compared to 21.5% in controls ($p < 0.001$). Similarly, Kang et al. [13] identified NAFLD in 11.1% of 443 IBD patients based on CT findings, with 20% of these cases classified as "lean NAFLD" (BMI <23, in the Asian context) ($p < 0.05$).

Disease Activity and Hepatic Steatosis

Active IBD was significantly associated with hepatic steatosis, consistent with studies suggesting that systemic inflammation plays a pivotal role in the pathogenesis of hepatic steatosis [9]. Pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) can promote hepatic fat accumulation by enhancing insulin resistance and lipogenesis [10]. This underscores the importance of effective disease control in mitigating the risk of hepatic steatosis.

Another study identified IBD activity as an independent predictive factor for NAFLD development, with a hazard ratio (HR) of 1.58, suggesting that ongoing intestinal inflammation may contribute to hepatic fat accumulation [14]

Impact of Medications on Hepatic Steatosis

The study identified prolonged corticosteroid therapy and the use of immunosuppressive agents (azathioprine and methotrexate) as independent predictors of hepatic steatosis. Corticosteroids are known to induce insulin resistance and promote fat deposition, thereby increasing the risk of hepatic steatosis [9]. The association between azathioprine and methotrexate with hepatic steatosis may be related to their hepatotoxic potential and effects on lipid metabolism[9]. Clinicians should carefully monitor liver function and metabolic parameters in patients receiving these therapies.

In the series by Adams et al. [12], among malnourished IBD patients (BMI <18.5), severe steatosis (>33%) was twice as frequent when corticosteroid therapy duration exceeded 12 months (OR ≈ 2.2; $p < 0.01$).

In terms of pharmacologic exposure, Hoffmann et al. [15]identified azathioprine use as a factor associated with NAFLD in a large IBD cohort (n = 694; OR = 1.98; p = 0.031). However, a meta-analysis published in 2018 [18] showed that while azathioprine use may increase the risk of NAFLD in IBD patients, the association did not reach statistical significance (OR: 1.19; 95% CI: 0.70–2.01).

similarly, methotrexate use was examined in the same cohort by Hoffmann et al. [15], who reported no statistically significant association with NAFLD (OR = 1.15; 95% CI: 0.99–1.30; p = 0.843). Nevertheless, evidence remains mixed. A systematic review and meta-analysis [17] reported that methotrexate use in IBD patients was associated with an increased risk of NAFLD (OR = 1.76; 95% CI: 1.02–3.06), whereas another study [16] found no significant association, with an OR of 3.62 (95% CI: 0.48–27.39), suggesting a lack of statistical significance.

This study is limited by its single-center design and reliance on ultrasound, which may underestimate steatosis compared to MRI or CAP. Nevertheless, the use of standardized imaging protocols and inclusion of both retrospective and prospective data strengthen the validity of our findings.

Conclusion

This study contributes to the growing body of evidence on the interplay between IBD and hepatic steatosis. The identification of undernutrition, metabolic syndrome, active disease, and specific medications as predictive factors underscores the multifaceted etiology of hepatic steatosis in IBD patients. Comprehensive management approaches that encompass metabolic, nutritional, and inflammatory aspects are essential in mitigating the risk and progression of hepatic steatosis in this population.

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