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The Prevalence of Metabolically associated Steatotic Liver Disease in Patients with Inflammatory Bowel Disease in Erbil City

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Abstract

Background and Objective: The non-alcoholic fatty liver disease is prevalent in about one-fourth of the world population. The link between inflammatory bowel diseases and non-alcoholic fatty liver disease has been of great concern in last decades. This study aimed to determine the prevalence of non-alcoholic fatty liver disease in patients with inflammatory bowel disease.

Methods: A descriptive cross-sectional study was conducted in Hawler Gastroenterology and Hepatology center at Rzgari teaching hospital in Erbil city-Kurdistan region/Iraq in duration of twelve months (5th of April 2023 to 5th of April 2024) on a sample of one hundred patients with inflammatory bowel disease. The prevalence of non-alcoholic fatty liver disease and factors associated with it (past medical history, platelets, C-reactive protein, fasting blood sugar, Hemoglobin A1c…etc) were studied.

Results: The prevalence of non-alcoholic fatty liver disease was (24%) with fibrosis scores of F0-F2 and predominant grading of grade I (23%); in contrast grade II was reported in one inflammatory bowel disease patient only. Past medical history of hypertension diabetes mellitus and dyslipidemia was a significant risk factor of non-alcoholic fatty liver disease in patients with inflammatory bowel disease. Abnormal results of fasting blood glucose, HemoglobinA1c, triglyceride, High-density-lipoprotein, Aspartate-transaminase and Alanine-transaminase levels of inflammatory bowel disease patients were significantly related to non-alcoholic fatty liver disease.

Conclusion: The prevalence of non-alcoholic fatty liver disease in patients with inflammatory bowel disease is close to prevalence of non-alcoholic fatty liver disease in general population.

Keywords: Inflammatory bowel disease, Non-alcoholic fatty liver disease

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Introduction

The Metabolically associated Steatotic Liver Disease (MASLD), previously known as non-alcoholic fatty liver disease, is defined as a spectrum of conditions resulted from fat accumulation in 5% or more in liver cells with lack of alcohol consumption or medications history, autoimmune and infectious liver diseases.[1] Nowadays, the MASLD is the commonest cause of chronic liver diseases and its incidence rate was elevated three folds in last two decades with global prevalence of about (25%) detected by imaging.[2-4] Approximately, one quarter of worldwide population had MASLD that is related to different metabolic abnormalities such as increased body mass index, resistance to insulin, type 2 diabetes mellitus, dyslipidemia, elevated blood pressure and metabolic syndrome.[5] In addition to liver damaging, the MASLD is accompanied with high rates of cancers and cardiovascular diseases which all increases the mortality rates.[6,7] The inflammatory bowel diseases (IBDs) are chronic debilitating disorders featured by inflammatory remissions and relapses of gastrointestinal tract leads to intestinal and extraintestinal manifestations affecting social status and life quality of patients.[8,9] Inflammatory bowel disease included mainly two common types according to site and depth of involvement which are Crohn's disease(CD) and ulcerative colitis(UC) and recently both of them characterized by higher incidence and prevalence rates globally.[10] The extraintestinal manifestations are common in Crohn's disease and ulcerative colitis especially liver co-morbidities.[11] The etiology of MASLD is multifactorial as many risk factors combine and lead to hepatic steatosis, inflammation and progressive damaging of liver.[12] The MASLD advancing is accomplished by inflammatory changes represented by activating immune cells and high cytokine production in addition to effects of insulin resistance and oxidative stress.[13] The metabolism abnormalities play significant role in MASLD development.[14] Recent reports linked the metabolic dysfunction to liver steatosis and any cardiometabolic risk factors.[15] The MASLD etiology is related to immune-mediated inflammatory disorders as the IBD patients are prevalent by liver diseases and bad liver profile tests of IBDs patients are commonly caused by fatty changes of liver.[16-18] Both Crohn's disease and ulcerative colitis are sharing the same genetic, environmental and infectious etiology of MASLD.[19,20] Additionally, intestinal wall characteristics like permeability are close for IBD and MASLD.[21] Many authors reported higher MASLD prevalence among patients with IBDs in comparison to healthy peoples.[22] The IBDs also are the common risk factor for different cardiovascular disorders and with MASLD these risk were maximized disease.[23] The prevalence of in patients with IBDs varies with range between 1.5-40% depending on variability of criteria of definitions.[24,25] The aim of this study was to assess the prevalence of non-alcoholic fatty liver disease in patients with inflammatory bowel disease and factors associated with it.

Patients and methods

A descriptive cross-sectional study was conducted in Hawler Gastroenterology and Hepatology center at Rizgari Teaching Hospital in Erbil City-Kurdistan Region/Iraq for a duration of twelve months (5th of April 2023 to 5th of April 2024). All patients with previous diagnoses of CD or UC based on a combination of symptoms, endoscopy, histology and abdominal imaging were included in the study. Exclusion criteria include younger age patients less than 12 years, previous diagnosis of chronic liver disease with an etiology different from MASLD (autoimmune, cholestatic, viral and genetic, etc.) and secondary causes for hepatic fat overload, such as daily alcohol

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consumption higher than 20 g in women and 30 gm in men and parenteral nutrition. Ethical approval of this study was obtained from Research Protocol Ethics Committee of Kurdistan Higher Council for Medical Specializations with the consent of selected patients and continuing their monitoring and management. The selected sample size was one hundred patients with inflammatory bowel disease. Information of patients was acquired directly by interviewing them and saved in a well-designed questionnaire by a researcher that included general characteristics of IBD patients, clinical history, inflammatory bowel disease characteristics, investigations findings of patients and non-alcoholic fatty liver abnormalities of studied patients. All patients including both CD and UC had been diagnosed previously by local gastroenterologists based on a combination of symptoms, endoscopy, histology and abdominal imaging. The diagnosis of MASLD was based on presence of ultrasonographic steatosis and the exclusion of secondary causes of fat accumulation in the liver. The statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS), version 24. Categorical variables were presented as percentages, and the chi-square test or Fisher's exact test was applied to determine statistical significance. A significance level of 0.05 or lower was considered.

Results

This study included one hundred patients with inflammatory bowel disease (IBD). The prevalence of MASLD was (24%) with fibrosis scores of F0-F2 and predominant grading of grade I (23%), while grade II was reported in one IBD patient only Table (1). There were no significant relationships between MASLD prevalence and IBD patients' general characteristics (p>0.05), Table (2).

Table (1): Non-alcoholic fatty liver abnormalities of IBD patients.

Variable	No.	%
Non-alcoholic fatty liver disease		
Yes	24	24.0
No	76	76.0
MASLD fibrosis score		
Normal	76	76.0
F0-F2	24	24.0
MASLD grading[26]		
Normal	76	76.0
Grade I	23	23.0
Grade II	1	1.0
Total	100	100.0

Table (2): Patients' general characteristics according to MASLD prevalence.

Variable	MASLD				P
	Yes		No		
	No.	%	No.	%	
Age (years)					0.1 NS
<20	4	16.7	9	11.8	
20-29	5	20.8	27	35.5	
30-39	7	29.2	24	31.6	
40-49	3	12.5	12	15.8	
≥50	5	20.8	4	5.3	
Gender					0.8 NS
Male	13	54.2	43	56.6	
Female	11	45.8	33	43.4	
Ethnicity					0.4 NS
Kurd	20	83.3	69	90.8	
Arab	4	16.7	6	7.9	
Others	0	-	1	1.3	
Smoking					0.43 NS
Yes	1	4.2	5	6.6	
Ex	2	8.3	2	2.6	
No	21	87.5	69	90.8	

S=Significant, NS=Not significant.

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A significant association was observed between positive past medical history of hypertension (HTN), diabetes mellitus (DM) and dyslipidemia of IBD patients and MASLD (p=0.03). There were no significant relationships between MASLD prevalence and other IBD patients' clinical characteristics such as BMI and past surgical history (p>0.05), Table (3).

Table (3): Distribution of clinical characteristics and outcomes according to MASLD prevalence.

Variable	MASLD				P
	Yes		No		
	No.	%	No.	%	
Body mass index					0.2 NS
Underweight	2	8.3	11	14.5	
Normal	10	41.7	37	48.7	
Overweight	7	29.2	23	30.3	
Class I obesity	4	16.7	4	5.3	
Class II	1	4.2	0	-	
Class III	0	-	1	1.3	
Blood pressure					0.07 NS
Normal	23	95.8	76	100.	
High	1	4.2	0	-	
Past medical history					0.03 S
Clear	21	87.5	74	97.4	
Hypertension	2	8.3	0	-	
DM &	1	4.2	0	-	
DM & HTN	0	-	1	1.3	
Others	0	-	1	1.3	
Past surgical history					0.2 NS
No	15	62.5	57	75.0	
Yes	9	37.5	19	25.0	

S=Significant, NS=Not significant.

There were no significant relationships between MASLD prevalence and IBD characteristics (p>0.05), Table (4).

Table (4): Distribution of IBD characteristics according to MASLD prevalence.

Variable	MASLD				P
	Yes		No		
	No	%	No	%	
Inflammatory bowel disease type					1.0 NS
UC	12	50.0	38	50.0	
CD	12	50.0	38	50.0	
Inflammatory bowel disease duration					0.8 NS
<5 years	13	54.2	41	53.9	
5-10 years	10	41.7	29	38.2	
>10 years	1	4.2	6	7.9	
Current medications					0.14 NS
Immunomodulato	0	-	3	3.9	
Biologic agent	2	8.3	1	1.3	
5ASA	2	8.3	9	11.	
Immunomodulator & biologic agent	14	58.3	32	42.1	
Immunomodulator & 5ASA	3	12.5	11	14.5	
Biologic agent & 5ASA	0	-	3	3.9	
Immunomodulator, biologic agent & 5ASA	0	-	13	17.1	
Steroid, immunomodulator & 5ASA	2	8.3	1	1.3	
Steroid, immunomodulator, biologic agent & 5ASA	1	4.2	1	1.3	
Steroid & 5ASA	0	-	1	1.3	
Steroid & biologic agent	0	-	1	1.3	

S=Significant, NS=Not significant.

Abnormal results of fasting blood sugar, HbA1c, triglyceride, HDL, AST and ALT levels of IBD patients were significantly related to MASLD (p≤0.05), however, levels of platelets, C-reactive protein, LDL, ALP

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and GGT levels were not significantly related to MASLD (p>0.05), Table (5).

Table (5): Distribution of investigations findings according to MASLD prevalence.

Variable	MASLD				P
	Yes		No		
	No.	%	No.	%	
Platelets					0.5 NS
Normal	24	100.0	75	98.7	
Low	0	-	1	1.3	
C-reactive protein					0.3 NS
Normal	21	87.5	71	93.4	
Elevated	3	12.5	5	6.6	
Fasting blood sugar level					0.005 S
≤110 mg/dl	19	79.2	74	97.4	
111-126 mg/dl	3	12.5	2	2.6	
>126 mg/dl	2	8.3	0	-	
HbA1c level					0.001 S
<5.8%	19	79.2	75	98.7	
5.8-6.4%	2	8.3	1	1.3	
≥6.5%	3	12.5	0	-	
Triglyceride level					0.01 S
<150 mg/dl	15	62.5	65	85.5	
≥150 mg/dl	9	37.5	11	14.5	
HDL level					0.01 S
Normal	10	41.7	52	68.4	
Low	14	58.3	24	31.6	
LDL level					0.1 NS
Normal	20	83.3	71	93.4	
Elevated	4	16.7	5	6.6	
AST level					0.002 S
Normal	21	87.5	76	100.0	
Elevated	3	12.5	0	-	
ALT level					<0.001 S
Normal	20	83.3	76	100.0	
Elevated	4	16.7	0	-	
ALP level					0.4 NS
Normal	24	100.0	74	97.4	
Elevated	0	.0	2	2.6	
GGT level					0.5 NS
Normal	24	100.0	75	98.7	
Elevated	0	-	1	1.3	

S=Significant, NS=Not significant.

There were no significant relationships between MASLD characteristics and IBD types (p>0.05), Table (6).

Table (6): Distribution of MASLD characteristics according to IBD type.

Variable	IBD type				P
	UC		CD		
	No.	%	No.	%	
Non-alcoholic fatty liver disease					1.0 NS
Yes	12	24.0	12	24.0	
No	38	76.0	38	76.0	
MASLD fibrosis score					1.0 NS
Normal	38	76.0	38	76.0	
F0-F2	12	24.0	12	24.0	
MASLD grading					0.5 NS
Normal	38	76.0	38	76.0	
Grade I	12	24.0	11	22.0	
Grade II	0	-	1	2.0	

S=Significant, NS=Not significant.

Discussion

Studying the relationship between non-alcoholic fatty liver disease and inflammatory bowel diseases is important to clarify the link between two diseases and prevent the extra-intestinal liver complications of inflammatory bowel diseases.[26,27] This study found that the prevalence of MASLD among IBD patients was (24%). This MASLD prevalence among IBD patients is close to that of (23%) reported by Abenavoli et al., cross-sectional study in Italy.[28] This prevalence rate is close to MASLD prevalence among general population in Iraq and globally.[4,29] However, Dias et al., found non-alcoholic fatty liver changes in 32.7% of IBD patients and Hoffmann et al., found that 46.5% of patients with IBDs had MASLD which all indicated higher prevalence than general population.[18,30] Inconsistently, recent

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American study conducted by Ritaccio et al. found that prevalence of MASLD among IBD patients was (12.4%).[31] These differences might related to variances in diagnostic tools for MASLD and the burden of MASLD in general population between different studies in addition to differences in study design and sample size applied in each study. Our study found that liver fibrosis scores were F0-F2 and predominant grading of grade I (23%), while grade II was reported in one IBD patient only. These findings are in agreement with the results of Martínez-Domínguez et al., systematic review study in Spain. This study also showed equal prevalence of MASLD in both types of IBD (UC and CD).[32] This finding is inconsistent with results of Lin et al study in United States of America which revealed a higher prevalence of MASLD in CD and also inconsistent with results of Gizard et al., study in France which revealed higher prevalence of MASLD in UC.[17,24] This inconsistency might be attributed to differences in sample size. The present study showed that positive past medical history of IBD patients was a risk factor for MASLD in IBD patients. Similarly, Sourianarayanane et al., reported that past medical history of IBD patients especially with hypertension represented risk factor for MASLD.[33] Our study showed that abnormal results of fasting blood sugar, HbA1c, triglyceride, HDL, AST and ALT levels of IBD patients were significantly related to MASLD. Consistently, Capela et al., stated that abnormal glycemic and lipid profile measures of IBD patients were useful scores in prediction of MASLD and liver damage which allow the early prevention and management.[34]

Conclusion

The prevalence of non-alcoholic fatty liver disease in patients with inflammatory bowel disease is close to prevalence of non-alcoholic fatty liver disease in general population. Past medical history is the common risk factor of non-alcoholic fatty liver disease in patients with inflammatory bowel disease. This study recommended assessment of glycemic and lipid profiles of inflammatory bowel disease patients routinely.

Conflict of interest

None.

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