Clinical Patterns and Risk Factors for Non-Alcoholic Fatty Liver Disease in Patients with Inflammatory Bowel Disease in Upper Egypt

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Abstract

Background: Most studies agreed that patients with inflammatory bowel disease are more likely to develop non-alcoholic fatty liver disease because of the presence of chronic infections, toxic drugs and altered gut microbiota.

Objectives: To evaluate and estimate the relationship between NAFLD and IBD and to discover the most important causes and risk factors among IBD patients.

Patients and methods: The study was done on a sample of (200) Egyptian cases diagnosed with inflammatory bowel disease. The criteria for including patients in this study included proving the disease through clinical examination, laboratory tests, imaging, and performing all necessary examinations for patients within this study. Patients with chronic viral hepatitis (B and C) as well as patients with hepatocellular carcinoma and all other liver diseases were excluded from this study because they affect the measure of liver stiffness.

Results: The mean age of all studied patients was 36.2 ± 6.2 years, 108 were females (54%)**,** 37 patients were diabetic (18.5%), the mean BMI of all studied patients was 27.4 ± 3.3 kg/m²**.** The prevalence of NAFLD between IBD patients was 36%. The mean liver stiffness measurement (LSM) of patients was 6.8 ± 3.6**,** the mean controlled attenuation parameter (CAP) was 223.5 ± 67.9.Risk factors responsible for the occurrence of NAFLD between IBD patients included DM, Insulin resistance, high anthropometric findings and dyslipidemia.

Conclusion: NAFLD is a common and recurrent disease in IBD patients. DM, Insulin resistance, high anthropometric findings and dyslipidemia are most important risk factors for occurrence of NAFLD between IBD patients.

Key Words: IBD; Insulin resistance; NAFLD.

DOI: 10.21608/svuijm.2022.129784.1298

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Received: 7 April,2022.

Revised: 7 April,2022.

Accepted: 20 April, 2022.

Cite this article as: Hasan Sedeek Mahmoud, Mohammed Tag-Adeen Said Hussien, Hager Seleem Abdelghaffar, Heba Ahmed Osman. (2022). Clinical Patterns and Risk Factors for Non-Alcoholic Fatty Liver Disease in Patients with Inflammatory Bowel Disease in Upper Egypt. *SVU-International Journal of Medical Sciences*. Vol.5, Issue 2, pp: 209-215 .

Introduction

Most patients with obesity are the most among them non-alcoholic fatty liver disease, which indicates a high indicator of the presence of the relationship, which leads to severe inflammation in the liver and in some cases to fibrosis and cancer, and it has reached a high epidemic rate **(Loomba et al., 2013).** This is what was recently discovered, and fatty liver is the most prevalent among chronic liver diseases in many places of the world, with a percentage of approximately 25%, as stated in a study **(Younusi et al., 2016).**

The severity of the disease and mortality is due to the liver disease itself, as well as to extrahepatic complications, which are associated with NAFLD, as well as its close relationship to metabolic syndrome, as indicated by a study **(Targher et al., 2016),** for some reasons, including cardiovascular disease.

Regional enteritis, which is known as (CD) as well as ulcerative colitis (UC), are two of the most major causes among the inflammatory bowel diseases. Diarrhea, bleeding , abdominal pain and weight loss are the most clinical presentations and thus affect the quality of life as confirmed by a study **(Saroli Palumbo et al., 2019).**

There are other symptoms that may appear in those patients including arthropathy, metabolic bone disease, cardiovascular, and hepatobiliary, ocular and skin manifestations in addition to urological complications which accounts for approximately 50% **(Jaspar et al., 2021).**

There are also some differences in the data about the existence of an association between the presences of fatty liver disease in patients with IBD. The cause of this association is not clear. But researchers draw this to the complex relationship between the environment and multiple genes, and it clearly shows the factor of immune dysregulation and its main role in the occurrence of this disease (**Liu and Stappenbeck, 2016**). We aimed to evaluate and estimate the relationship between NAFLD and IBD and to discover the most important causes and risk factors among IBD patients.

Patients and methods

A sample of (200) Egyptian cases diagnosed with inflammatory bowel disease were selected for the study.

The inclusion criteria included: patients once diagnosed and proved as having inflammatory bowel disease by combination of clinical, laboratory, imaging and histological examination.

Exclusion criteria included Patients having chronic viral hepatitis (B and C), hepatocellular carcinoma, and all other liver disease because they affect liver stiffness measurement. Also, Patients consuming alcohol more than 20g/day were excluded from this study.

The approval was obtained from all patients before they were admitted to the study and the necessary examinations were conducted for them, as is the case in the Scientific Research Ethics Committee at the Faculty of Medicine in Qena

All patients underwent the following:

I. History and Clinical Examination: -

1- Complete history taking, which include history of comorbid conditions such as DM, HTN and cardiac disease. History of drug intake was taken.

2- Full Clinical Examination: which include manifestations of chronic liver diseases and inflammatory bowel disease.

3- Measurements known as anthropometric measurements such as height, weight and body mass index (BMI). Hence the waist circumference (WC) of each

subject. WHR was calculated as WC (cm)/HC (cm).

II. Laboratory Investigations include:

1. Fasting blood glucose, lipid profile (low-density lipoprotein, high-density lipoprotein, T.cholesterol, triglyceride).
2. Complete blood picture (CBC): white blood cells, hemoglobin concentration, and platelet count.
3. Liver profile: albumin, total bilirubin, direct bilirubin, alanine aminotransferase & aspartate aminotransferase, prothrombin time and INR.
4. TSH
5. Renal function tests: serum creatinine.
6. Viral markers (HCV-Ab, Hbs-Ag).

III. Imaging:- Studied patients were submitted to screening with the following procedures:

1- Abdominal ultrasonography was done and Scanning process will include the following:- NAFLD was detected by ultrasonography utilising a high resolution B-mode ultrasound system by experienced ultrasound specialists, who measured the liver's size in the midline and mid-clavicular lines, as well as its surface and echogenicity. Participants with two of the following three criteria could be diagnosed with fatty liver, according to the recommendations for the diagnosis and therapy of nonalcoholic fatty liver disease; update 2010: I The liver's near-field echo is diffusely enhanced, more so than the kidney's; (ii) the intrahepatic duct structure is unclear; (iii) the liver's far-field echo is gradually decreasing. **(Fan et al., 2011).**

2- Transient elastography Fibroscan S502 echosens (France):- By experienced technicians, the stiffness of the liver was measured using FibroScan as well as (M-probe). By performing the technique on the right liver lobe (intercostal space), where the patient is in a state of supine position and in a state of fasting, with the right arm abducted to the maximum extent and assisted by the help of ultrasonography time-motion and A-mode imaging. Success rate was 100%, 10 shots obtained successful. The range of potential liver stiffness values obtained using TE imaging ranges from 2.5 to 75.0 kPa, with the liver stiffness value of healthy subjects about 5.5 kPa **(Pang et al., 2014)**.

IV. Assessment of Metabolic Syndrome:
The IR index was measured by the Homoeostasis Model Assessment (HOMA)-IR which is calculated by the following equation (**Matthews et al 1985**).

HOMA-IR = fasting glucose (mg/dl) X fasting isulin (mU/l)/22.5.

Statistical analysis

Version 26 of the statistical program was used, quantitative data and qualitative data were used. Quantitative data were shown as mean ± standard deviation (M ± SD) while qualitative data were shown as frequency and percentage number (%) and were compared by Student's t-test. Comparison non-parametric data was calculated by Chi-square test. $P < 0.05$ was considered significant.

Results

Baseline characteristics

Our results showed that more than one third of IBD patients have NAFLD. We observed fatty liver in 73 patients (36.5%) of all studied patients. The mean liver stiffness measurement (LSM) of patients was 6.8 ± 3.6**,** the mean controlled attenuation parameter (CAP) was 223.5 ± 67.9.
Fig.1.

The mean value of laboratory data in all studied patients are illustrated in (**Table .1).** Multivariate logistic regression analysis for predictors of NAFLD among IBD patients, with confidence interval 95%; showed that DM, BMI, WC, WHR, ALT, AST, ALP, FBS, LDL, HDL,TG, HOMA-IR, LSM, CAP ($p < 0.001$) each, and Cholesterol ($p = 0.002$) were the predictive risk factors. **Table (2)** .

Table 1. Description of laboratory data in all studied patients.

Parameter	Mean	±SD
ALT	35.8	18.9
AST	36.5	16.4
T. Bilirubin	0.7	0.2
D. Bilirubin	0.3	0.8
ALB	4.1	0.4
ALP	122.0	41.3
GGT	25.2	13.7
PT	12.6	1.2
PC	92.5	9.4
INR	1.1	0.1
PLTs	221.3	50.2
TSH	2.0	1.4
FBS	104.7	42.2
Creatinine	0.9	0.2
CHOL	194.1	50.8
LDL	104.2	24.9
TG	177.3	87.3
HDL	42.3	10.6
HOMA IR	3.9	3.5

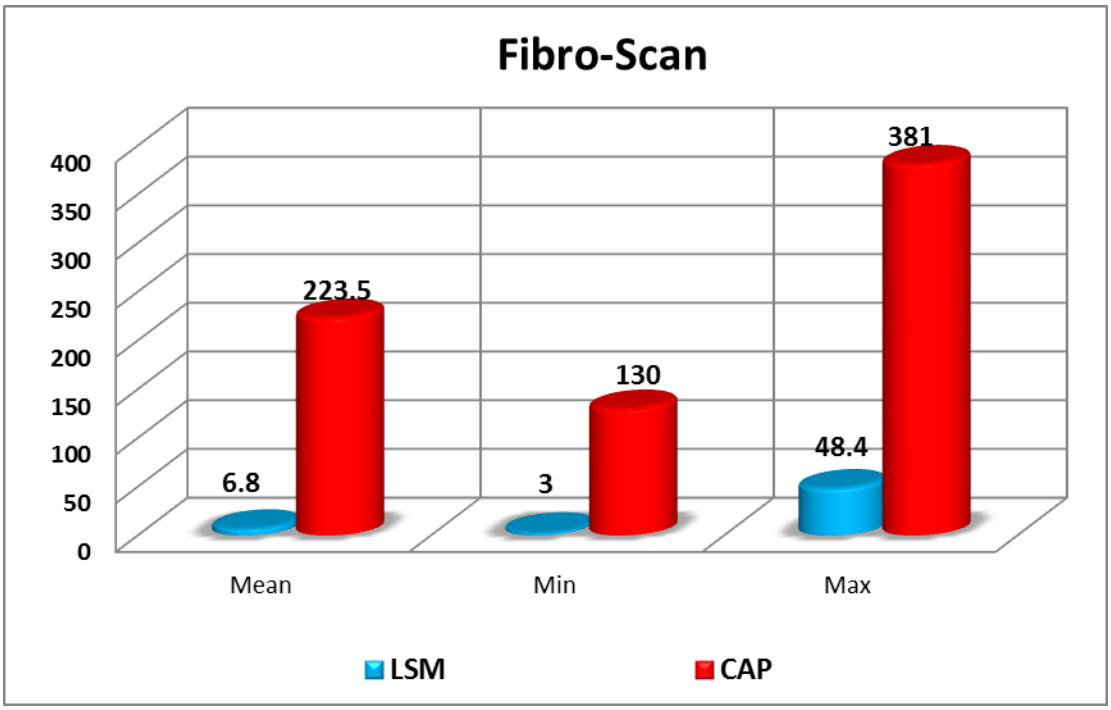

Fig.1. Description of Fibro-Scan measurements in all studied patients.

Table 2. Multivariate logistic regression analysis of predictive factors for fatty liver.

Variables	B	p-value	Odds
DM	2.28	< 0.001	9.8
BMI	0.77	< 0.001	2.17
WC	0.51	< 0.001	1.66
WHR	33.6	< 0.001	
ALT	0.5	< 0.001	1.66
AST	0.49	< 0.001	1.63
ALP	0.054	< 0.001	1.05
FBS	0.018	< 0.001	1.01
Cholesterol	0.01	0.002	1.01
LDL	- 0.03	< 0.001	0.97
TG	0.008	< 0.001	1.0
HDL	- 0.07	< 0.001	0.93
HOMA-IR	0.77	< 0.001	2.1
LSM	0.46	< 0.001	1.59
CAP	0.089	< 0.001	1.09

B: Regression coefficient.

Discussion

This is what was recently discovered, and fatty liver is the most prevalent among chronic liver diseases in most parts of the world, with a percentage of approximately 25%, as stated in a study **(Younusi et al., 2016).**

Prevalence of NAFLD was more than one third of IBD patients.

In accordance with the current study, **Saroli Palumbo et al.** found that, Prevalence of NAFLD among his included patients was 32.8% **(Saroli Palumbo et al. 2019)**.

The results of this study were repeated with previous studies from the comprehensive systematic review, as there were nearly 7,640 patients who were diagnosed with IBD, and they were in twenty-seven studies, and nearly 1,716 of them had fatty liver disease, which is estimated at an approximate rate of 33%, this constitutes a large spread of up to 33%. The prevalence of fatty liver reached (25.2%) of patients with IBD ($P < 0.001$). They also reported that factors associated with the incidence of nonalcoholic fatty liver disease among IBD patients include age, BMI, diabetes, duration of IBD, and previous history of bowel resection **(Lin et al., 2019).**

The study of Yen et al., which was conducted on a sample of 81 patients suffering from inflammatory bowel disease, NAFLD was observed in nearly one third of patients, with a percentage of 1.2%, have significant fibrosis of the liver **(Yen et al. 2021).**

According to our results, DM, dyslipidemia and high anthropometric findings (high BMI, increased WC and high WHR) were risk factors for the presence of fatty liver in IBD patients. Also, metabolic syndrome as assessed by HOMA-IR test, constitutes a risk for developing NAFLD in our IBD patients.

A retrospective study consists of 694 patients. Nearly half of patients of Crohn's disease (CD) and 44% of ulcerative colitis complaining from NAFLD. And this association was due to body mass index (BMI), older age, hypertension and as well as higher disease activity and dyslipidemia in CD **(Hoffmann et al. 2020).**

Consistently, in 2017, a retrospective study showed that the severity of NAFLD in UC and CD patients was highly correlated with metabolic syndrome (MetS), but not correlated with the degree of the disease severity in IBD. Specifically, UC and CD patients with MetS had a higher NAFLD Fibrosis Score (NFS) than those without MetS **(Carr et al. 2017).**

Conclusion

NAFLD is a common and recurrent disease in IBD patients. DM, Insulin resistance, high anthropometric findings and dyslipidemia are most important risk factors for occurrence of NAFLD between IBD patients.

References

- **Carr RM, Patel A, Bownik H, Oranu A, Kerner C, Praestgaard A, Forde KA, Reddy KR, Lichtenstein GR. (2017)** Intestinal inflammation does not predict Nonalcoholic Fatty Liver Disease severity in Inflammatory Bowel Disease patients. Dig Dis Sci, 62: 1354-1361.

- **Fan JG., Jia JD, Li YM et al. (2011)** Guidelines for the diagnosis and management of nonalcoholic fatty liver disease: update 2010. Journal of Digestive Diseases, 12 (1). 38–44

- **Gaspar R, Branco CC, Macedo G. (2021)** Liver manifestations and complications in inflammatory bowel disease: A review. World J Hepatol, 13(12): 1956 1967

- **Glassner K, Malaty HM, Abraham BP. (2017)** Epidemiology and Risk Factors of Nonalcoholic Fatty Liver

Disease Among Patients with Inflammatory Bowel Disease. Inflamm Bowel Dis, 23: 998-1003

- **Liu TC, Stappenbeck TS. (2016)** Genetics and pathogenesis of inflammatory bowel disease. Annu Rev Pathol, 11:127–148.

- **Loomba R, Sanyal AJ. (2013)** The global NAFLD epidemic. Nat Rev Gastroenterol Hepatol, 10:686–90.

- **Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. (1985)** Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia, 28:412–419.

- **Pang JXQ, Zimmer S, Niu S, et al. (2014)** Liver stiffness by transient elastography predicts liver-related complications and mortality in patients with chronic liver disease. PLoS One, 9:e95776.

- **Principi M, Iannone A, Losurdo G, Mangia M, Shahini E, Albano F, Rizzi SF, La Fortezza RF, Lovero R, Contaldo A, Barone M, Leandro G, Ierardi E, Di Leo A. (2018)** Nonalcoholic Fatty Liver Disease in Inflammatory Bowel Disease: Prevalence and Risk Factors. Inflamm Bowel Dis, 24: 1589-1596

- **Saroli Palumbo C, Restellini S, Chao CY, Aruljothy A, Lemieux C, Wild G, Afif W, Lakatos PL, Bitton A, Cocciolillo S, Ghali P, Bessissow T, Sebastiani G. (2019)** Screening for Nonalcoholic Fatty Liver Disease in Inflammatory Bowel Diseases: A Cohort Study Using Transient Elastography. Inflamm Bow Dis, 25: 124-133.

- **Targher, G, Byrne, CD, Lonardo A, Zoppini G, Barbui C. (2016)** Non-alcoholic fatty liver disease and risk of incident cardiovascular disease: A meta-analysis. J. Hepatol, 65, 589–600.

- **Yen HH, Su PY, Huang SP, Wu L, Hsu TC, Zeng YH, et al. (2021)** Evaluation of nonalcoholic fatty liver disease in patients with inflammatory bowel disease using controlled attenuation parameter technology: A Taiwanese retrospective cohort study. PLoS ONE, 16(5): e0252286.

- **Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. (2016)** Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology, 64:73–84.