



PREVALENCE OF NON ALCOHOLIC FATTY LIVER DISEASE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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ABSTRACT

Introduction: Ulcerative colitis and Crohn's disease are immune mediated inflammatory bowel disease (IBD) which affects the gastrointestinal tract with several extraintestinal manifestations. Hepatic manifestations in IBD vary and range from benign disorders, such as fatty liver to end-stage hepatic failure. Non alcoholic fatty liver disease (NAFLD) is deemed to be hepatic manifestation of metabolic syndrome which is cluster of central obesity, hypertension, hypertriglyceridemia and low HDL. NAFLD is the most common chronic liver disease, characterized by the presence of steatosis in > 5% of the hepatocytes and whose prevalence is steeply increasing in parallel with obesity.^[1] NAFLD includes a wide spectrum of disorders, ranging from hepatic steatosis (NAFL) to non-alcoholic steatohepatitis (NASH). NAFLD patients are at high risk for liver fibrosis, cirrhosis, and hepatocellular carcinoma (HCC).^[1,5] The prevalence of NAFLD in IBD patients is highly variable ranging from 1.5% to even 40%, in dependence of different diagnostic criteria.^[6,8] Despite IBD is commonly considered a wasting disease characterized in some cases by malabsorption and severe weight loss, recent data indicate that the prevalence of NAFLD among IBD patients is increased as compared to the general population.^[9] IBD patients develop NAFLD with fewer metabolic risk factors than general population.^[6] **Materials and methods.** This retrospective analysis was conducted in IBD patients on regular follow up at the Gastroenterology division of the Department of Medicine w.e.f March 2018 to December 2019. The patients were evaluated with detailed clinical history, medical examination and blood investigations. Included were patients with age group of 18 -60 years with biopsy proven diagnosis of Idiopathic ulcerative colitis or Crohns disease. Exclusion criteria included patients with alcohol intake in excess of 20 grams per day, history of jejunoileal bypass surgery or extensive small bowel resection, type 2 diabetes mellitus, usage of drugs known to cause secondary steatosis like corticosteroids, methotrexate, and amiodarone. **Results:** A total of 236 patients were included in the study, out of which 45 were excluded as per the exclusion criteria and only 191 patients participated in the study design. Out of 191 patients, 158(83%) were identified as having idiopathic ulcerative colitis (IUC) and and 33(17%) had Crohns disease (CD). There was no significant difference in the IUC and CD patients when assessed separately, so both the groups were considered together. The prevalence of NAFLD was 55.5%(106/191) in our study group, with grade 1 hepatic steatosis in 61 out of 106 (57.5%), grade 2 steatosis in 27 out of 106 (25%), and grade 3 steatosis in 18 out of 106 patients (17.5%). **Conclusion:** Our study concludes that the prevalence of NAFLD in IBD is very high (55.5%) and regular follow up of the IBD patients for the development of NAFLD is the need of the hour, in order to prevent the further complications of NAFLD.

KEYWORDS: Non-alcoholic fatty liver disease, inflammatory bowel disease, Ultrasonography.

INTRODUCTION

Ulcerative colitis and Crohn's disease are immune mediated inflammatory bowel disease (IBD) which affect the gastrointestinal tract with several extraintestinal manifestations. Hepatic manifestations in IBD vary and range from benign disorders, such as fatty liver to end-stage hepatic failure. Non alcoholic fatty liver disease (NAFLD) is deemed to be hepatic manifestation of metabolic syndrome which is cluster of central obesity, hypertension, hypertriglyceridemia and low HDL. NAFLD is the most common chronic liver

disease, characterized by the presence of steatosis in > 5% of the hepatocytes and whose prevalence is steeply increasing in parallel with obesity.^[1] NAFLD includes a wide spectrum of disorders, ranging from hepatic steatosis (NAFL) to non-alcoholic steatohepatitis (NASH). NAFLD patients are at high risk for liver fibrosis, cirrhosis, and hepatocellular carcinoma (HCC).^[1,5]

The prevalence of NAFLD in IBD patients is highly variable ranging from 1.5% to even 40%, in dependence

of different diagnostic criteria.^[6,8]

Despite IBD is commonly considered a wasting disease characterized in some cases by malabsorption and severe weight loss, recent data indicate that the prevalence of NAFLD among IBD patients is increased as compared to the general population.^[9] IBD patients develop NAFLD with fewer metabolic risk factors than general population.^[6] The increase incidence of NAFLD in IBD can be multifactorial. It can be attributed to intestinal disease specific factors such as chronic inflammatory status, disease duration and activity, intestinal surgery, steroid use, immunosuppressants and gut microbiota.^[10] Ultrasound of the liver is the most common diagnostic tool to detect NAFLD with a sensitivity of 85% and specificity of 94%⁽¹⁵⁾. The main aim of this observational study was to evaluate the prevalence of NAFLD in IBD patients.

MATERIALS AND METHODS

This retrospective analysis was conducted in IBD patients on regular follow up at the Gastroenterology division of the Department of Medicine w.e.f March 2018 to December 2019. The patients were evaluated with detailed clinical history, medical examination and blood investigations. Included were patients with age group of 18 -60 years with biopsy proven diagnosis of Idiopathic ulcerative colitis or Crohns disease. Exclusion criteria included patients with alcohol intake in excess of 20 grams per day, history of jejunoileal bypass surgery or extensive small bowel resection, type 2 diabetes mellitus, usage of drugs known to cause secondary steatosis like corticosteroids, methotrexate, and amiodarone. Pregnant women and subjects with severe co- morbidities such as malignancies, congestive heart failure and chronic kidney disease were excluded. A structured questionnaire was administered to each subject to obtain information such as bio-data, alcohol intake, current medications as well as family history of diabetes and liver disease. All patients were clinically evaluated and weight (kg) and height (m) were measured. The Body Mass Index (BMI=weight (kg) /height (m²) was calculated and classified based on World Health Organisation (WHO) criteria.^[11] BMI cutoff points (Asian) was taken as follows; BMI <18.5 kg/m² (lean or underweight), between 18.5 and 22.9 kg/m² (normal), between 23 and 27.49 kg/m² (overweight) and 27.5 kg/m² or above as (obese).^[11] Waist circumference was measured from the right side in the mid-axillary line, midway between the lower margin of the least palpable rib and the top of the iliac crest (highest point of the hip bone on the right side) as the point of reference. Hip circumference measurement (HC) in centimetres was done at the point of widest circumference of the buttocks with the tape parallel to the floor. Both waist and hip circumference was taken twice and the average was calculated. The cutoffs points for Asians used (0.95 in men and 0.80 in women) denote

abdominal obesity. Average of two readings was used for analysis.^[12,13] The average of three BP readings was calculated. Hypertension was considered at a blood pressure reading of more than or equal to 140/90 mmHg or current intake of anti hypertensive or both.^[14] Blood samples were taken for evaluation of serum alanine transaminase (ALT), aspartate transaminase (AST), mg/dL. Samples were also analysed for detection of antihepatitis C virus antibodies and hepatitis B surface antigen. Abdominal Ultrasound scan (USG) evaluation was performed (Aloka Pro-sound 3500, Japan) using a 3.75 MHz probe. Findings suggestive of hepatic steatosis included "bright liver" with increased echogenicity, hepato-renal contrast and attenuation of the diaphragm. The USG will assess the severity of fatty liver as grade I, II or III.^[20,21] The diagnosis of NAFLD was based on the absence of alcohol consumption (or alcohol intake less than 20 grams per day) and the presence of hepatic steatosis on USG evaluation.

RESULTS

A total of 236 patients were included in the study, out of which 45 were excluded as per the exclusion criteria and only 191 patients participated in the study design. The average age of the patients in the study group was 44.25±12.34 years with a minimum age group of 23 years and maximum age group of 66 years. Out of 191 patients, 79(41%) were males and 112(59%) were females. Out of 191 patients, 158(83%) were identified as having idiopathic ulcerative colitis (IUC) and 33(17%) had Crohns disease (CD). There was no significant difference in the IUC and CD patients when assessed separately, so both the groups were considered together. The prevalence of NAFLD was 55.5%(106/191) in our study group, with grade 1 hepatic steatosis in 61 out of 106 (57.5%), grade 2 steatosis in 27 out of 106 (25%), and grade 3 steatosis in 18 out of 106 patients (17.5%).

Table 1: Demographic characteristics of patients in the study group.

Variables	Number (N)	%age
Age at IBD Diagnosis(years)	44.25±12.34	
IUC	158	83%
CD	33	17%
IUC(Extent)		
Proctitis	32/158	20%
Left sided	107/158	68%
Pancolitis	19/158	12%
CD(Extent)		
Ileal	6/33	18%
Colonic	19/33	57.5%
Ileocolonic	8/33	24%
IBD Duration in years	8±2.34	
More than 1 relapse per year	172	

Table 2: Grades of Hepatic Steatosis in the study group.

Grades of Hepatic Steatosis	Number of patients (N=106)	%age
Grade 1 Steatosis	61	57.5%
Grade 2 Steatosis	27	25%
Grade 3 Steatosis	18	17.5%

DISCUSSION

The prevalence of NAFLD in IBD was 55.5% in our study group. The world wide prevalence of NAFLD has been rising and is now estimated to be 24% (16). The reported prevalence of NAFLD in IBD patients has varied from 8-59%, depending on the diagnostic criteria: 59% based on liver histology, 34% based on hepatic steatosis index score, 8% based on combined multiple imaging modalities and 26-40% based on ultrasonography.^[6,7,10,17,18] The exact pathogenesis of NAFLD in IBD patients is not known but the various postulated are metabolic syndrome, malnutrition, intestinal inflammation, alteration of gut microbiota, steroid exposure and drug induced hepatotoxicity.

Our prevalence of NAFLD in IBD patients is more than that observed in most of the studies. Bargiggia et al reported an over all prevalence of 25.55-39.5% in IBD patients.^[7] A study by Hoffman et al, observed that 48% of CD and 44% of IUC patients suffered from NAFLD.^[19] The higher prevalence in our study can be explained by changes in the dietary habits and nutritional changes which have occurred over the last 2 decades and more prevalence of metabolic syndrome in the over all general population. Another reason could be the emerging therapies of IBD and better management of malnutrition in the IBD patients.

A meta-analysis by Zou ZY et al,^[20] including one study from japan and 18 studies from western countries, found an overall prevalence of NAFLD in 27.5% of IBD patients and they mentioned that the risk factors for NAFLD development were type 2 diabetes mellitus, hypertension, obesity, insulin resistance, metabolic syndrome, chronic kidney disease, methotrexate intake, surgery for IBD and longer duration of IBD.

Further more, as the visceral fat seems to perpetuate inflammation and due to that the IBD patients with NAFLD may develop more aggressive IBD course and may require potent anti-inflammatory treatment modalities for their disease remission.

The limitation of our study is that we could not perform vibration controlled transient elastography or MR spectroscopy in our patients to grade steatosis and fibrosis and nor was liver biopsy done to differentiate between NAFLD and NASH. Also the nutritional status and the exact metabolic status of the study group could have been elaborated. However this is the first study of its kind conducted in this part of the country and more studies are needed to know the prevalence and then to further categorize these patients and manage them to prevent the complications of NAFLD.

CONCLUSION

Our study concludes that the prevalence of NAFLD in IBD is very high (55.5%) and regular follow up of the IBD patients for the development of NAFLD is the need of the hour, in order to prevent the further complications of NAFLD. A routine ultrasound of the IBD patients should be done regularly to diagnose NAFLD. More prospective studies are required to detect the risk factors for the development of NAFLD in IBD patients.

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