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Risk factors of non-alcoholic fatty liver disease in patients with inflammatory bowel disease☆

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KEYWORDS
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Abstract

Background: Metabolic risk factors are associated with non-alcoholic fatty liver disease (NAFLD), but they are less frequent in inflammatory bowel disease (IBD).
Aim: This study evaluates the frequency of NAFLD and its risk factors among IBD patients including anti-TNF-α therapy.
Methods: IBD patients who underwent abdominal imaging from January, 2009 to December, 2010 were analyzed in this nested, case-controlled study. IBD patients with NAFLD by imaging were compared with those who had no evidence of NAFLD (control).
Results: Among 928 IBD patients, 76 (8.2%) had evidence of NAFLD by imaging, and were compared to 141 patients without NAFLD evaluated (study: control ratio = ~1:2). NAFLD patients were older (46.0 ± 13.3 vs. 42.0 ± 14.1 years; p = 0.018) and had a later onset of IBD compared to the control group (37.2 ± 15.3 vs. 28.7 ± 23.8 years; p = 0.002). Metabolic syndrome was present in 29.0% of NAFLD patients, with a median Adult Treatment Panel risk factor of 2 [Interquartile range 1,3]. Patients not receiving anti-TNF-α therapy had a higher occurrence of NAFLD (p = 0.048). In multivariate analysis, hypertension (OR = 3.5), obesity (OR = 2.1), small bowel surgeries (OR = 3.7), and use of steroids at the time of imaging (OR = 3.7) were independent factors associated with NAFLD.

Abbreviations: ASA, aminosalicylic acids; ATP, Adult Treatment Panel; CD, Crohn's disease; HDL, high density lipoprotein; IBD, inflammatory bowel disease; LDL, low density lipoprotein; MP, mercaptopurine; PEM, protein energy malnutrition; PSC, primary sclerosing cholangitis; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; TG, triglycerides; TNF, tumor necrosis factor; TSH, thyroid stimulating hormone; UC, ulcerative colitis.

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Conclusion: NAFLD occurred in 8.2% of the IBD population. NAFLD patients were older and had a later onset of IBD disease. IBD patients develop NAFLD with fewer metabolic risk factors than non-IBD NAFLD patients. It is also less common among patients who received anti-TNF-α therapy.

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) is a clinico-pathological syndrome with a histologic spectrum ranging from benign steatosis to non-alcoholic steatohepatitis (NASH)[1] along with subsequent development of cirrhosis and its complications in a proportion of these patients. The prevalence of NAFLD is increasing in the Western population, and studies have shown a high prevalence in the US (about 30%),[2,3] where it has become the most common chronic liver disease.[2] The third report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults, Adult Treatment Panel (ATP) III defined metabolic syndrome by the presence of three of five risk factors: waist girth >102 cm (M) or >88 cm (F), or body mass index (BMI) >30; arterial blood pressure ≥130/85 mm Hg; triglycerides (TG) ≥150 mg/dL; high density lipoprotein (HDL) cholesterol <40 mg/dL for males or <50 mg/dL for females; and fasting glucose ≥110 mg/dL.[4] The prevalence of NAFLD is increased in patients who are obese and have metabolic syndrome.[5,6] In patients with NAFLD, metabolic syndrome was present in 60% of women and 30% of men.[7]

Patients with chronic inflammatory diseases, such as inflammatory bowel disease (IBD), which consists of Crohn's disease (CD) and ulcerative colitis (UC), are prone to under-nutrition, and some require nutritional supplementation. Gut inflammation and bowel resection surgery can result in decreased absorptive capacity. Protein energy malnutrition (PEM) is frequently seen in patients with IBD.[8] Depending on the severity of IBD, weight loss has been reported in 65–76% of CD patients and in 18–62% of UC patients.[9] The reported frequency of under-nutrition in active IBD patients ranged from 25.0% to 69.7%, and the frequency of severe malnutrition ranged from 1.3% to 31.6%.[10] On the other hand, metabolic syndrome and obesity are expected to be less common in IBD patients than in NAFLD patients, and normal lipid levels are reported in some patients with short gut syndromes.[11]

Tumor necrosis factor (TNF)-α plays an important role in the pathogenesis of both IBD and NAFLD. Pentoxifylline, an anti-TNF-α agent, was shown to benefit non-alcoholic steatohepatitis (NASH) patients.[12–15] Infliximab, an anti-TNF-α therapy used in IBD, may also benefit NAFLD patients,[16] as it normalized transaminases and improved inflammation, necrosis, and fibrosis in an animal model,[17,18] although it has not yet been proven to be clinically effective. Other treatments for IBD, such as steroids, could also affect the prevalence of NAFLD.

There are a number of other concurrent liver diseases reported in IBD patients, including primary sclerosing cholangitis (PSC).[19,20] Fatty liver is frequently seen (38–49%) in CD or UC patients with abnormal liver test results such as elevated transaminases.[19–22] Recent increasing awareness of NAFLD in IBD is evidenced by the publications of case reports and series.[23] An Italian study[24] found steatosis by ultrasound in nearly 40% of IBD patients, who had a mean BMI of 21; however, to our knowledge, there are no studies from the US evaluating the frequency of NAFLD in IBD patients and the metabolic profiles of these patients. We hypothesized that a subgroup of IBD patients with their "unique" clinical risk factors would develop NAFLD. The hypothesis was tested by the following aims: 1) to assess the frequency of NAFLD in patients with CD or UC, and 2) to evaluate the risk factors for NAFLD in this population, including treatment with anti-TNF-α therapy.

2. Patients and methods

Medical records of consecutive patients undergoing evaluation and treatment for IBD at our tertiary care center between January, 2009 and December, 2010 were reviewed. Detailed demographic and clinical data, including data pertaining to IBD and liver diseases, were obtained. The study was approved by our Institutional Review Board. All patients were seen by IBD/nutrition specialists and, if indicated, by colorectal surgeons, and were managed according to standard of care.

2.1. Inclusion and exclusion criteria

Inclusion criteria were patients with 1) IBD and 2) abdominal imaging performed at our institution. Patients who had other types of liver diseases or who had a prior diagnosis of a liver disease other than NAFLD were excluded.

2.2. Study groups

Various imaging modalities (ultrasound of liver, CT scans with and without contrast, CT enterography, and MRI) were used to evaluate patients for evidence of NAFLD. The study (i.e., NAFLD) group included patients who had evidence of steatosis by any modality of imaging evaluated. This study group was compared with a sample population selected from the remainder of IBD patients who did not have NAFLD on imaging. The control group (i.e., no NAFLD) consisted of patients who did not have fatty liver on imaging. For analysis in this study, the control group of 141 patients (nearly 1:2 compared to study group) was obtained by analyzing patients who had presented in a fixed 2-month period from January, 2009 to February, 2009 and did not have steatosis on imaging.

2.3. Diagnostic criteria

The diagnoses of CD and UC were made based on a combined assessment of symptomatology, endoscopy, histology, and abdominal imaging. The pattern and distribution of CD and UC were obtained from endoscopic, radiological and operative findings. A diagnosis of NAFLD was made by an expert GI radiologist based on imaging of the liver. Typical radiographic findings indicative of NAFLD include a heterogeneous