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Original article

Clinical and Biochemical Profile of Libyan Patients with Biopsy Proven Inflammatory Bowel Diseases

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Abstract

Inflammatory bowel disease (IBD) is a group of inflammatory gastrointestinal diseases (Crohn´s disease and Ulcerative colitis), with remission and relapse periods. IBD arises as a result of inappropriate immune response and consequently causes inflammation and intestinal ulcers and annoying symptoms such as abdominal pain, diarrhea, bleeding per rectum, weight loss and anemia, also there is an extra- intestinal manifestation as arthritis, mouth ulcers, primary sclerosing cholangitis, cholelithiasis, eye and skin manifestation. The aim of the current study is to describe the clinical and biochemical profile of adult Libyan IBD patients. Two-hundred patients with endoscopic biopsy proven IBD were enrolled in this study which was started in January 2021 to December 2023, all patients were negative for HBsAg, anti HCV, HIV., negative Covid-19 PCR test, normal D-Dimer, normal CRP, normal coagulation profile (PT & INR). From these 200 patients 70 patients (35%) were asymptomatic (in remission) and 130 patients (65%) were symptomatic in which 60 patients (30%) were UC presented with frequently rectal bleeding, diarrhea with mucus, and the others 70 patients (35%) were CD presented with frequent abdominal pain, fever, intestinal obstruction, perineal disease, and post-operative recurrence, and both groups associated with high fecal calprotectin. IBD patients' symptoms either UC (bleeding per rectum, diarrhea with mucus) or CD (abdominal pain, fever, perianal disease, intestinal obstruction) with high fecal calprotectin associated with active disease.

Keywords: *IBD, UC, CD, Patient, Symptoms.*

Introduction

Inflammatory bowel disease (IBD) is a long-life disease with remission and relapse periods. IBD arises as a result of inappropriate immune response to intestinal commensal organisms in individual with genetic predisposition and consequently inflammation and intestinal ulcers [1], In addition, IBD has a complex pathogenesis and many factors such as dysbiosis, oxidative stress, and epigenetics that may also be involved [2].

Ulcerative colitis (UC) and Crohn´s disease (CD) are known as two main forms of IBD. Crohn´s disease which can affect any segment of the gastrointestinal tract (from mouth to anus), Ulcerative colitis (which is limited to colonic mucosa) [3]. These diseases cause intestinal ulcers and both commonly presented with some symptoms such as diarrhea, abdominal pain, and rectal bleeding occurs more frequently with UC, but patients with CD often experience weight loss and perianal disease [4]. Occasionally the severity of these symptoms is very high which can lead patients to be hospitalized. In this regard, therapeutic approaches to treat these diseases mainly focus on prolonging remission [5], [6]. Differential diagnosis is a serious challenge because CD and UC have significant similarities in terms of their clinical, endoscopic, and histological features. However, there are some differences between UC and CD which are summarized in Table 1.

Table 1: Clinical features of IBD

Feature	Crohn´s disease	Ulcerative colitis
Rectal bleeding	Occasionally	Frequently
Abdominal pain	Frequently	Occasionally
Fever	Frequently	Not common
Defecation with mucus	Occasionally	Frequently
Intestinal obstruction	YES	NO
Perineal disease	YES	NO
Post-operative recurrence	YES	NO
ASCA positive	Frequently	Not common
ANCA positive	Not common	Frequently

In addition to intestinal complication, UC and CD also have significant extra-intestinal manifestation. For example, UC is significantly associated with primary sclerosing cholangitis and CD is also associated with cholelithiasis especially in cases that the ileum is involved [7], Furthermore, CD can cause fistula to the adjacent structures and leading to recurrent infections [8], Both CD and UC can cause several disorders such as arthritis, erythema nodosum, pyoderma gangrenosum and anemia which are known as the most important extra-intestinal manifestation of IBD [9]. The latest statistics showed that the global prevalence of IBD currently is on the rise [10].

According to a report published in 2018, IBD has the highest prevalence, rate in Europe and its prevalence in the newly industrialized countries of Asia, Africa, and South America also appear to be increased over the past three decades [11].

Unfortunately, the peak of the disease is at the young age of 15-30 years old [12], therefore, in addition to the suffering from inflicts on the patients, it also has many negative effects on the society. Moreover, many financial burdens are annually imposed on counties for controlling and treating this chronic disease. Now, the gold standard method for diagnosing IBD and monitoring patient status is performing colonoscopy and histopathological evaluation, which are invasive and expensive measures [13]. Therefore, in recent years many studies have been conducted to find a suitable marker with sufficient sensitivity and specificity for the purpose of non-invasive diagnosing and management of IBD. A high proportion of these studies have investigated the efficacy of fecal calprotectin in diagnosing and monitoring patients.

Calprotectin is an antimicrobial protein mainly secreted by neutrophils, this protein competes with bacteria over zinc, thus kills the bacteria.

However, this is not the only antimicrobial activity but also this protein has many clinical applications. The aim of the current study is to describe the clinical and biochemical profile of adults IBD patients.

METHODS

Study design and setting

A retrospective study was conducted at gastroenterology department in Tripoli University Hospital from January 2021 to December 2023 where two-hundred patients with histological endoscopic biopsy proven IBD was enrolled in this study (110 UC & 90 CD) with different presentations and from different out-patient clinic (indoor and outdoor the hospital).

Eligible subjects of either gender of all ages, who agree to participate in the study with a consent form of all participants were obtained.

Data collection procedure

Detailed clinical examination of each patient was done and each patient underwent endoscopy (gastroscopy / colonoscopy) in a standard way after getting a written consent and necessary investigations like hemoglobin level, blood group, all patients should have negative viral serology, negative Covid-19 PCR test, normal D-Dimer, normal CRP, normal coagulation profile (PT & INR).

Endoscopic biopsies were taken for histopathological examinations and decision to perform endoscopic biopsy for each patient was done on individual basis, CT Scan abdomen and pelvis with CT ernterophraphy were done.

Fecal calprotectin level was sent for all patients, serology for ASCA and ANCA also was sent.

Statistical analysis

The medical records of these patients reviewed and the relevant data for the purpose of this study obtained in predesigned case sheet.

Data was analyzed using statistical package for the social sciences (SPSS Inc. Released 2007. SPSS for Windows, version 16.0. Descriptive statistics were used as mean, SD, and %, Chi square test was used to find the significance between categorical variables, and p value less than 0.05 were considered significant.

RESULTS

During the study period from January 2021 to December 2023 for 200 patients with histological biopsy proven IBD (110 UC & 90 CD) were enrolled in this study.

From these 200 patients 70 patients (35%) were asymptomatic (in remission) and 130 patients (65%) were symptomatic (table 2) in which 60 patients (30%) were UC presented with frequently rectal bleeding, diarrhea with mucus, and occasionally abdominal pain. The others 70 patients (35%) were CD presented with frequent abdominal pain, fever, intestinal obstruction, perineal disease, and post-operative recurrence.

Table 2. IBD patients' number and percentage (types &symptoms)

Character	No(%)
IBD patients (UC & CD)	200 (100)
UC patients	110 (55%)
CD patients	90 (45%)
Asymptomatic (in remission)	70 (35%)
Symptomatic (at presentation or relapse)	130(65%)
Ulcerative colitis (UC)	60 (30%)
Crohns´disease (CD)	70 (35%)

These symptomatic patients have active disease present at the presentation or at the relapse of the IBD.

Thirty patients (15%) with a diagnosis of UC at the time of presentation have high fecal calprotectin > 200 µg/g, and 30 patients (15%) with a diagnosis of UC at relapse have also high fecal calprotectin > 200 µg/g, these two groups of patients have also high ESR and CRP, the remaining 50 patients (25%) with a diagnosis of UC have normal fecal calprotectin < 50 µg/g (figure 1).

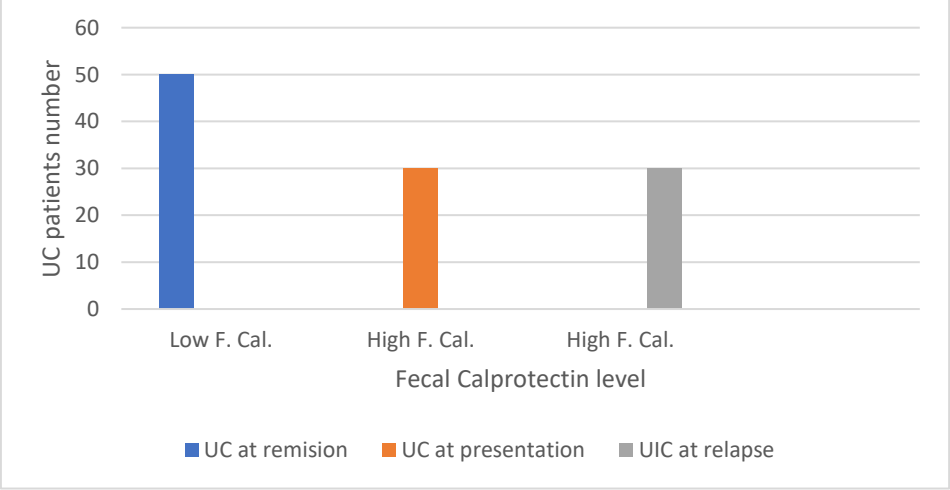

Figure 1. Relation between UC patients and Fecal Calprotectin

Twenty-five patients (12.5%) with a diagnosis of CD at the time of presentation have high fecal calprotectin > 200 µg/g, and 45 patients (22.5%) with a diagnosis of CD at relapse have also high fecal calprotectin > 200 µg/g, these two groups of patients have high ESR

and CRP, the remaining 20 patients (10%) with a diagnosis of CD have normal fecal calprotectin (figure2).

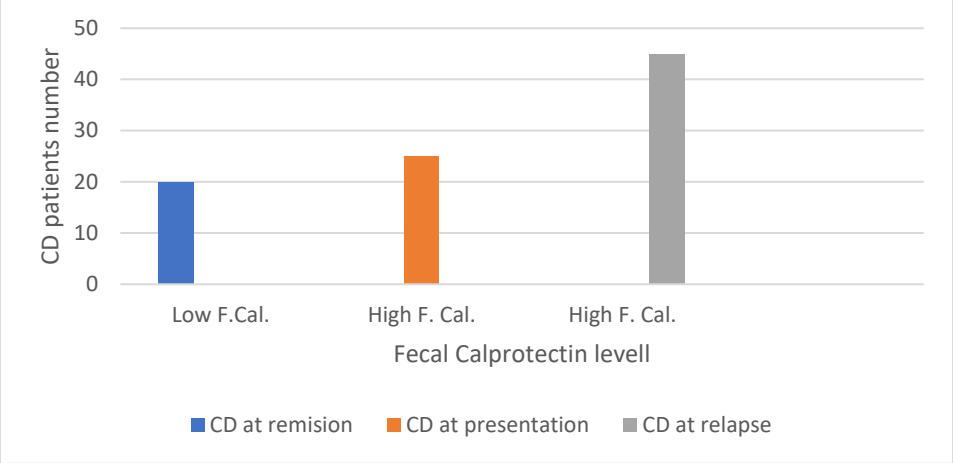

Figure: 2 Relation between CD patients' number and Fecal Calprotectin level

This study demonstrates that 130 patients out of 200 patients (65%) with a histological biopsy proven IBD have a symptomatic disease, UC patients (60 out of 110) have bleeding per rectum, diarrhea with mucus and high fecal calprotectin >200 µg/g either at the disease presentation or its relapse, while in CD patients(70 out of 90) have abdominal pain, fever, perianal disease, and intestinal obstruction and high fecal calprotectin >200µg/g either at the disease presentation or its relapse, this shows that there is a strong relation in UC patients between symptoms as bleeding per rectum and diarrhea with mucus and active disease, on the other hand in CD patients there is a strong relation between symptoms as abdominal pain, fever, perianal disease, intestinal obstruction and active disease, the chi square test was applied to test if there is any relation between these symptoms and IBD activity (p=0.019). moreover, there is significant correlation in IBD patients between active disease and the above mentioned symptoms.

Discussion

During the study period from January 2021 to December 2023 at gastroenterology department of Tripoli University Hospital a total of 200 patients with histological proven biopsy of IBD (110 UC&90 CD) with different presentations and from different departments and outpatient clinics, 120 patients were males (60%), 80 patients were females (40%), and male to female ratio was 3:2, and mean age of patients was 40±25 years.

Regarding age, one of the most serious challenges to the laboratory of fecal calprotectin is the determination of the upper limit in healthy individual. Among healthy adults, there is a significant agreement on (50µg/g) as an upper limit, one study suggested values up to (118 µg/g) in people over 60 years old and up to (200 µg/g) in children aged 12 to 18 years old [14].

Only a small percentage of patients complaining of abdominal pain and diarrhea have IBD. In many cases IBS (Irritable Bowel Syndrome) as a functional gastrointestinal disorder is a known as the cause of such symptoms, patients with IBS have normal colonoscopy result while IBD have abnormal colonoscopy results with intestinal ulcers. Unfortunately, the significant prevalence of IBS and the overlap between clinical symptoms and IBD can increase the colonoscopy rate. Therefore, a non-invasive diagnostic marker can be very helpful in this regard in spite of fecal calprotectin not specific for IBD.

From these 200 patients 70 patients (35%) were asymptomatic (in remission) and 130 patients (65%) were symptomatic (active disease) either at time of presentation or relapse.

In our study, thirty patients (15%) with a diagnosis of UC at the time of presentation complaining of bleeding per rectum and diarrhea with mucus have high fecal calprotectin > 200 µg/g, and 30 patients (15%) with a diagnosis of UC at relapse have the same symptoms and also high fecal calprotectin > 200 µg/g, the remaining 50 patients (25%) with a diagnosis of UC remission have normal fecal calprotectin < 50 µg/g (figure 1).

And twenty-five patients (12.5%) with a diagnosis of CD at the time of presentation complaining of abdominal pain, fever, perianal disease, and intestinal obstruction have high fecal calprotectin > 200 µg/g, and 45 patients (22.5%) with a diagnosis of CD at relapse have the same symptoms and also high fecal calprotectin > 200 µg/g, the remaining 20 patients (10%) with a diagnosis of CD have normal fecal calprotectin (figure 2).

Our study results showed a significant correlation in IBD patients between these symptoms with high fecal calprotectin > 200µg/g and active disease. The first evidence of the efficacy of fecal calprotectin in the diagnosis of IBD was obtained in 1990s. Roseth et al.in 1992 proposed a method for measuring calprotectin in stool specimen [15]. One of the first and most interesting studies regarding fecal calprotectin utility in IBD diagnosis was the study by Roseth et al published in 1997. This study has also shown that even patients with low disease activity had higher levels of fecal calprotectin compared to healthy individuals [16]. In 2017 study done with a sensitivity of 100% a specificity of 100% at a cut-off of 78.4 µg/g were observed for fecal calprotectin in the diagnosis of IBD, in another study conducted in 2018 on 76 patients with UC, a sensitivity of 98% and a specificity of 96% at cut-off of 188 µg/g have reported in this regard. The results of our study along with other studies showed that fecal calprotectin is preferred over traditional inflammatory biomarkers such as CRP and ESR in the diagnosis of IBD [17].

Therefore, fecal calprotectin helpful in ruling out the possibility of IBD in patients with IBS-like symptoms as well as reducing the rate of colonoscopy, with a sensitivity and specificity above 90% for fecal calprotectin to differentiate between IBD and IBS [18], also helpful in evaluation of endoscopic and histological activity of the disease, and prediction of disease recurrence and response to treatment.

Pregnant patients with IBD have serious limitation for colonoscopy and done only in the second trimester where there is a strong indication [19]. Therefore, non-invasive fecal calprotectin is helpful during pregnancy.

Conclusion

In the management of inflammatory bowel disease (IBD), understanding the relationship between symptoms and disease activity is crucial for effective care. For patients with UC, symptoms like bleeding per rectum and diarrhea with mucus are strongly associated with active disease. Conversely, in patients with CD, symptoms such as abdominal pain, fever, perianal disease, and intestinal obstruction are closely linked to disease activity. By utilizing fecal calprotectin, healthcare providers can reduce the reliance on frequent endoscopies or imaging studies, offering patients a non-invasive alternative that not only enhances their care but also lessens the burden of invasive procedures.

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