ORIGINAL ARTICLE

Epidemiological Study of Ulcerative Colitis: A Single-center Experience in the Western **Region of Saudi Arabia**

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Abstract

This retrospective chart review was conducted at the King Abdulaziz University Hospital, and covered the data for the period 2010–2019. The clinical data, include the presenting symptoms, extraintestinal symptoms, time elapsed from the onset of the symptoms to the confirmed diagnosis of ulcerative colitis, and endoscopic severity. A total of 413 patients with a confirmed diagnosis of ulcerative colitis were included. Approximately 94.3% (n = 299) of the patients were presented with diarrhea, with 86.9% of the cases had bloody stools, and 64.5% reported lower abdominal pain. About 4.8% of the patients (n = 18) lost >10% of their body weight within six months. Extraintestinal manifestations were documented in 127 (30.8%) patients, including the most common manifestations, such as aphthous ulcers (n = 41, 9.9%), large joint arthralgia/arthritis (n = 34, 8.2%), and erythema nodosum (n = 25, 6.0%). Based on the Montreal classification, 76 (18.5%) patients had ulcerative proctitis, 211 (51.0%) had left-sided ulcerative colitis, and 126 (30.5%) had extensive or pancolitis. The clinical presentation of ulcerative colitis is variable, resulting in the delay of their diagnoses. Research and clinical efforts should be directed to facilitate the conduct of early diagnosis.

Keywords

Colitis; Diagnosis; Diarrhea; Ulcerative colitis; Colonoscopy

Introduction

Icerative colitis (UC) is a chronic inflammatory condition of the large intestine characterized by a chronic remitting and relapsing course. The precise etiology of UC is still unknown. The hallmark symptoms include intermittent bloody diarrhea, abdominal pain, and rectal urgency, and in most cases, the severity and extent of colonic involvement can be predicted by the intensity of the patient's symptoms. Patients with a more fulminant disease course are more likely to have severe inflammation, pancolitis, or both. In addition, extraintestinal manifestations are reported in approximately 11.9% of patients with UC^[1].

In cases, where UC is suspected, alternative etiologies must be excluded by performing stool microscopy for the presence of pus cells, ova, and parasites. Additionally, Clostridium difficile cytotoxin testing should be performed to exclude pseudomembranous colitis. Other laboratory tests, such as C-reactive protein (CRP) and fecal calprotectin,

are important non-invasive surrogate biochemical markers that can also help differentiate UC from other chronic gastrointestinal diseases and can predict active and inactive UC with high accuracy, sensitivity, and specificity^[2,3]. Recent studies have also shown that fecal calprotectin can predict both endoscopic and histological activity of the disease^[4–6]. Other laboratory investigations, including a complete blood count, may demonstrate iron deficiency anemia due to chronic colonic blood loss and electrolyte abnormalities, such as hypokalemia, resulting from persistent diarrhea.

The American College of Gastroenterology and the British Society of Gastroenterology do not recommend radiographic testing in suspected cases of UC^[7,8]. Colonoscopy or proctosigmoidoscopy and biopsy are the standard diagnostic tests for UC. Early diagnosis and proper treatment of UC represent a challenge for many primary care physicians, who still consider inflammatory bowel disease (IBD) a "diagnosis of exclusion"[8], leading to delays in diagnosis and treatment. Although it can be sometimes challenging to differentiate Crohn's disease (CD) from UC, especially during the early stages of the disease, it is crucial that clinicians diagnose these conditions correctly, because their treatments and complications differ. Moreover, primary care physicians might miss many cases of UC, because accurate diagnosis is based on endoscopic and histological examinations, which are primarily performed by gastroenterologists. Further, experienced pathologists should review biopsies from suspected UC cases to establish a definitive diagnosis. Despite this recommendation, up to 5–15% of patients may still have a diagnosis of indeterminate colitis after an initial evaluation^[9].

Until 2012, the clinical and natural course of IBD in Saudi Arabia was mostly unknown. Previous hospital-based studies conducted in Saudi Arabia^[10,11] focused mainly on the epidemiologic features of UC, and only a limited number of studies described the clinical characteristics of these patients^[12,13]. Although a national, multicenter, observational study was recently conducted, it mainly described the clinical pattern of early-onset IBD in children aged 0–14 years, leaving a gap in knowledge of UC diagnosis in the general population^[10]. The goal of this study was to assess the clinical features, biochemical characteristics, pathogenesis, and diagnosis of UC at a tertiary care center in the Western Region of Saudi Arabia.

Materials and Methods

This retrospective study included patients diagnosed with UC, who were followed up at the Department of Medicine, King Abdulaziz University Hospital, Jeddah, between January 2010 and December 2019. We included all patients aged \geq 14 years with a diagnosis of UC and excluded those with indeterminate colitis. The diagnosis was based on the World Health Organization's definition of UC, and only patients, who fulfilled the criteria of symptoms, biochemical markers, endoscopy, and histology, when the patients were initially examined in our institution, were included in the study. Patients were excluded, if they had a diagnosis of familial adenomatous polyposis or indeterminate colitis. The Research Ethics Committee at King Abdulaziz University approved the study (Reference Number 58-15).

The data collected included demographic characteristics, clinical features, including the time from the onset of symptom to diagnosis, and endoscopic and biochemical features of the UC. The results of laboratory investigations, such as hemoglobin, CRP, ferritin, albumin, and fecal calprotectin levels, were collected. The data collected were based on the initial assessment of the patients during their visits to the outpatient department of the gastroenterology unit.

For the purpose of this research, significant weight loss was defined as a 5% loss of body weight within one month, 7.5% loss of body weight within three months, or 10% loss of body weight within six months. Severe weight loss was defined as > 5% loss of body weight within one month, > 7.5% loss of body weight within three months, or loss of >10% body weight within six months. A normal hemoglobin level was considered > 12 g/dL. Mild anemia was defined as a hemoglobin level \geq 10 g/dL and severe anemia as a hemoglobin concentration < 12 g/dL.

Demographic Characteristics	Frequency	Percent
Gender		
Male	203	49.1
Female	210	50.9
Age group (years)		
14–20	67	16.2
21–40	273	66.1
>40	73	17.7
Nationality		
Saudi	284	68.7
Non-Saudi	129	31.3

Table 1. Demographic characteristics of the patients

The IBM SPSS Statistics for Windows, Version 222 (IBM Corp., Armonk, NY USA) was used to process the data. The results were expressed as percent frequency, median, and mean ± standard deviation (SD).

Results

We reviewed the electronic medical records of 413 patients, including 210 females (female to male ratio = 1.03:1). The mean age at diagnosis was 36.6 ± 16.4 years (range, 12-84 years). Saudis comprised 68.7% of the sample (Table 1). Only two (0.5%) patients had a documented family history of UC.

The estimated duration from the onset of symptom to diagnosis varied considerably (mean at 7.1 months). It ranged between 0-3 months in 63 patients, 4-6 months in six patients, 7-12 months in three patients, 1-24 months in five patients, and > 24 months in three patients. In most cases, the diagnosis was established by gastroenterologists (82.5%) and internists (8.5%). Diarrhea was one of the most common presenting symptoms, found in approximately three-quarters of the patients (n = 299), with 86.9% reporting bloody stools at presentation (Table 2). Of these, 4.8% had continuous bloody stools. Approximately 64.5% of the patients reported abdominal pain, and 4.8% reported

Clinical Characteristics	Frequency*	Percent		
Specialty of diagnosing physician				
General practitioner	34	9.0		
Internist	32	8.5		
Gastroenterologist	311	82.5		
Diarrhea (Frequency)				
Normal formed stool	18	5.7		
<4 times/day (mild cases)	138	43.5		
>6 times/day (moderate to severe cases)	146	46.0		
>10 times/day (fulminant colitis)	15	4.8		
Bloody stool				
None	51	13.1		
Intermittent	156	40.1		
Frequent	159	40.8		
Continuous	23	5.9		
Bowel urgency				
None	79	21.3		
Mild or occasional	234	63.2		
Often	50	13.5		
Continuous	7	1.9		
Abdominal pain				
Yes	260	64.5		
No	143	35.5		
Weight loss				
No weight loss	206	54.9		
Significant weight loss	151	40.0		
Severe weight loss	18	4.8		
Extraintestinal symptoms				
Erythema nodosum	25	6.0		
Pyoderma gangrenosum	0	0		
Hidradenitis suppurativa	3	0.7		
Arthritis of the small joints	1	2.6		
Oligoarthritis (large joints), disease activity related	34	8.2		
Sacroiliitis (CT proven)	15	3.6		
Scleritis	2	0.5		
Episcleritis	4	1.0		
Aphthous ulcers	41	9.9		
Primary sclerosing cholangitis	2	0.5		

CT: computed tomography

*The total is <413 in some cells due to missing data.

Table 3. Summary	y of laboratory results
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Variables	Frequent*	Percent		
Hemoglobin at diagnosis				
<10 g/dL	105	25.4		
10–12 g/dL	175	42.4		
>12 g/dL	133	32.2		
Serum ferritin				
Normal	75	50.7		
Low	73	49.3		
C-reactive protein				
Normal	88	28.5		
Elevated	221	71.5		
Serum albumin				
Normal (≥35 g/dL)	115	40.4		
Low (<35 gm/L)	170	59.6		
Fecal calprotectin				
<100 µg/g	15	18.7		
100—250 µg/g	17	21.3		
>250 µg/g	48	60.0		

*The total is <413 due to missing values in some cells.

losing more than 10% of their body weight over a sixmonth period. Extraintestinal manifestations were documented in 127 (30.8%) patients, with the most common being aphthous ulcers (9.9%), large joint arthralgia/arthritis (8.2%), and erythema nodosum (6.0%).

Anemia was documented in 280 (67.8%) patients. Approximately 49.3% of the patients had low serum ferritin levels, and 71.5% had elevated CRP levels. A summary of the results of other laboratory investigations are presented in Table 3.

Based on the Montreal classification, 76 (18.5%) patients had ulcerative proctitis, 211 (51.0%) had left-sided UC, and 126 (30.5%) had extensive or pancolitis.

Discussion

Generally, patients with UC, especially those with poorly controlled disease, have a poor quality of life^[11]. One of the contributing factors to poor disease control is a delay in the diagnosis, which prevents early therapeutic intervention and, consequently, leads to the worsening of the disease^[12]. Despite the presence of classic symptoms, such as abdominal pain, bloody diarrhea, hematochezia, and sometimes, weight loss, general practitioners are often unfamiliar with the extent and variations of UC presentations, which can be inconsistent or consist of nonspecific symptoms, and therefore, can be misdiagnosed as amoebic colitis, infectious colitis, or irritable bowel syndrome^[13,14].

Consequently, UC is often under-diagnosed or is diagnosed after a considerable delay.

The average time of 7.1 months from the onset of symptom to diagnosis in patients, who were followed up in our center, is longer than that reported in other studies, which was four months^[15]. This diagnostic delay can be shortened by increasing the awareness about the disease among the general practitioners and educating the population about its increasing incidence in our setting^[16]. Furthermore, the routine use of highly accurate diagnostic tools, such as fecal calprotectin, in suspected cases of UC may help shorten diagnostic delays. Evidence shows that fecal calprotectin is a reliable marker of intestinal inflammation, and it has a sensitivity of 90% and a specificity of 85% in diagnosing UC^[4]. Unfortunately, many general practitioners and internists are unaware of the importance of fecal calprotectin in both the diagnosis and the follow up of patients with IBD, despite the growing evidence that supports its use as a standard test and surrogate marker for the diagnosis of UC and its activity^[17-19]. However, there are some issues that are related to its lack of consistent evidence, which validates the cut-off values in clinical practice^[20].

Although gastroenterologists had diagnosed most cases of UC (82.5%) in our center, it is noteworthy that the general practitioners managed 9.0% of the cases without considering referring patients to a gastroenterologist during the early disease course,

thereby, delaying the diagnosis and, consequently, early therapy. This finding, in addition to the patients' lack of awareness regarding UC and its increasing incidence in the Saudi society^[21], may partly explain the observed delay in definitive diagnosis. Furthermore, patients may self-medicate to treat UC symptoms, a globally reported problem, which may further delay the diagnosis^[22]. Another contributor to the delay in diagnosis and a common barrier to care in tertiary centers is the long delay between referral by the general practitioners to the specialty services, such as gastroenterology. A potential solution to this problem is to use a dedicated triage system to streamline referrals from primary health care physicians to the tertiary health care specialists. Specialized nurse practitioners may also serve as a useful resource in this process. National campaigns aimed at educating both general practitioners and the general population regarding the increasing incidence of UC has the potential to help decrease diagnostic delays, increase delivery of timely and effective therapy, prevent UC related complications, and ultimately, preserve and improve the quality of life of patients.

Generally, we observed similar phenotypic characteristics in our sample compared to those reported in UC patients in studies conducted both within Saudi Arabia and abroad^[23-27]. Our results support those of other investigators, who reported that the most common presenting symptoms in UC included diarrhea, bloody stools, abdominal pain, and weight loss^[28,29]. Extraintestinal manifestations, such as episcleritis, scleritis, and uveitis, peripheral arthropathies, erythema nodosum, and pyoderma gangrenosum, have been reported in 10-30% of UC patients^[29], which is consistent with the 30.8% in our sample. In a large study conducted on 394 UC patients at the King Khalid University Hospital in Riyadh, the authors documented arthritis in 16.4% of the cases^[23], which is comparable to the result in our study (14.4%). In their report, other common extraintestinal manifestations included osteopenia (31.4%), osteoporosis (17.1%), and cutaneous manifestations (7.0%).

More than half (67.8%) of our patients had anemia, which represents the most common systemic complication or extraintestinal manifestation in IBD^[30]. A systemic review of six studies, including 2,092 patients, showed that anemia was prevalent in UC patients, with 57% of the cases reported to be iron deficient^[30]. In another study, including 17,059 IBD patients, 85.1% of those with UC were reported to have iron-deficiency anemia^[31]. Iron-deficiency is suggested to occur in UC as a result of chronic blood loss secondary to bleeding from the inflamed colonic mucosa. According to prior reports^[32,33], anemia is often insufficiently treated in patients with IBD, despite a prevalence of up to 60–80% of patients, with a low mean corpuscular volume and low mean corpuscular hemoglobin^[26,33].

Based on the Montreal classification, 30.5% of our patients had extensive colitis (E3), 51.0% had left-sided colitis (E2), and 18.5% had proctitis (E1). In the study by Alharbi et al.^[23], 42.7% of the patients had extensive UC, 35.3% had left-sided colitis, and 29.2% had proctitis. In hospital-based studies conducted abroad, extensive forms of UC have also been reported to be the predominant form^[27]. Approximately two-thirds of patients with UC will have E1 or E2 disease at the initial presentation^[34], which is in line with our finding; however, it is plausible that the lower proportion of patients with E1 disease in our study, compared to those of other investigators^[27], is due to the differences in sample composition and size. Additionally, we believe that the long delay in diagnosis compared to that reported by other investigators^[15] led to more time for disease progression from proctitis to proctosigmoiditis, which has been described in about 30% of the patients with UC^[34].

Although this is a large cohort of UC patients, this study is limited by its retrospective design, and therefore, a cause-effect relationship cannot be inferred from our analysis. Nevertheless, this study was designed as a pilot study, and a subsequent study is planned to enable firm conclusions regarding the diagnosis and clinical characteristics of UC in our institution.

Conclusions

This study has shown that, although UC patients presented with classic symptoms that have been reported in the literature, the clinical presentation is inconsistent, which may result in misdiagnosis and diagnostic delay. Of note is that diagnostic delay is frequent in our institution, suggesting that efforts should be directed at improving the timing of UC diagnosis. Future studies should investigate the factors associated with diagnostic delays in our setting.

Conflict of Interest

The author has no conflict of interest.

Disclosure and Ethical Approval

This study was approved by the Unit of Biomedical Ethics Research Committee at King Abdulaziz University (KAUH), Jeddah, Saudi Arabia (Reference No. 58-15).

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دراسة وبائية لالتهاب القولون التقرحي: تجربة مركزية واحدة في المنطقة الغربية من المملكة العربية السعودية

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جدة - المملكة العربية السعودية

المستخلص. تهدف هذه الدراسة إلى الإبلاغ عن السمات السريرية والخصائص البيو كيميائية والأسباب، وطرق تشخيص التهاب القولون التقرحي، تم إجراء مراجعة بيانات المرضى بأثر رجعي في مستشفى جامعة الملك عبد العزيز، للفترة من ٢٠١٠ - ٢٠٩ و لقد حصلنا على البيانات السريرية ، بما في ذلك السمات المرضية في الأمعاء، والأعراض خارج الأمعاء ، والوقت المنصر م من ظهور الأعراض إلى التشخيص المؤكد، وحدة إصابة الأمعاء في التنظير الداخلي، من واقع السجلات الطبية للمرضى، و تم تضمين ما مجموعه ٢١٢ مريض بتشخيص مؤكد لإلتهاب القولون التقرحي، أي ما يقرب من (٣٤.٣) من المرضى الذين يعانون من الإسهال و (٣٦.٨٪) من الحالات أبلغت عن وجود دم في البراز ، و (٣٤.٦٪) ذكروا آلاما أسفل البطن، و أفاد حوالي (٣٠.٨٪) من المرضى أنهم فقدو ا < ٢٠٪ من وزن الجسم في غضون ستة أشهر ، و تم توثيق العلامات المرضية خارج الأمعاء عند (٣٠.٣٪) وأكثر ها شيوعاً بما في ذلك القرحة القلاعية (٣٩.٩٪)، ألم المفاصل / التهاب المفاصل الكبيرة (٢٠.٨٪)، والعقدة الحمامية (٢٠.٨٪) بناءً على تصنيف مونتريال، و كان (٣٠.٨٪) مصابين بالتهاب المستقيم التقرحي، و (٣٠.٥٪) مصابين بإلتهاب القولون التقرحي بناءً على تصنيف مونتريال، و كان (٣٠.٨٪) مصابين بالتهاب المستقيم التقرحي، و (٣٠.٥٪) مصابين بإلتهاب القولون التقرحي على الجانب الأيسر ، و (٣٠.٥٪) لديهم التهاب في البراز ، و (٣٠.٥٪) منا مراحية خارج الأمعاء عند (٣٠.٦٪)

وخلصت الدراسة إلى أن الأعراض السريرية لإلتهاب القولون التقرحي متباينة، وتظهر على المرضى بأشكال مختلفة، مما يؤدي إلى تأخير تشخيص هذا المرض، ولهذا يجب توجيه الجهود البحثية والسريرية لتسهيل التشخيص المبكر.