Review of chronic ulcerative colitis cases at King Hussein Medical Centre, Jordan

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استعراض لحالات التهاب القولون التقرُّحي المزمن في مركز الملك حسين الطبي

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الخلاصة: تتزايد الإصابة بالتهاب القولون التقرُّحي المزمن في البلدان النامية. وقد روجعت، في عمَّان، بالأردن، الملفات الطبية لـ 372 مريضاً شخِّصت حالاتهم على أنها التهاب القولون التقرُّحي المزمن، بين عامَيْ 1994 و2001. وتبيَّن أن الإسهال الدموي، وآلام البطن المغصيَّة، هي أكثر الأعراض شيوعاً (84٪ من المرضى). وبلغ متوسط العمر عند بداية ظهور المرض 31.8 عاماً. وتبيَّن أن المرض قد شُخِّص بعد مرور أكثر من عام على بدء ظهور أعراضه لدى ثُلُثَيْ المرضى. واختلف طراز المرض عمَّا هو عليه في البلدان الصناعية من حيث مساره الخفيف، وغياب التظاهرات الجلدية، وندرة إصابة مرضاه بالسرطان القولوني المستقيمي. وقد بلغ معدل الوفيات 6٪.

ABSTRACT Chronic ulcerative colitis is being encountered with increasing frequency in developing countries. In Amman, Jordan, the records of 372 patients with chronic ulcerative colitis diagnosed between 1994 and 2001 were reviewed. Bloody diarrhoea and crampy abdominal pain were the most common presenting symptoms (84% of patients). The mean age at onset was 31.8 years. In two thirds of patients the diagnosis was made more than 1 year after the onset of symptoms. The pattern of the disease differed from that in industrialized countries in the mild course of the disease, the absence of skin manifestations, and the rarity of colorectal cancer in our patients. The mortality rate was 6%.

Étude de cas de rectocolite hémorragique au Centre médical Roi Hussein en Jordanie

RÉSUMÉ Dans les pays en développement, la fréquence de la rectocolite hémorragique est en augmentation. À Amman, en Jordanie, les dossiers de 372 patients présentant une rectocolite hémorragique diagnostiquée entre 1994 et 2001 ont été analysés. Les diarrhées sanglantes et les douleurs abdominales à type de crampes étaient les signes d'appel les plus fréquents (84 % des patients). L'âge moyen de début de la maladie était de 31,8 ans. Chez les deux tiers des patients, le diagnostic a été posé plus d'un an après l'apparition des symptômes. Le tableau clinique se distinguait de celui observé dans les pays industrialisés par l'évolution bénigne de la maladie, l'absence de manifestations cutanées et la rareté du cancer colorectal chez nos patients. La mortalité était de 6 %.

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Introduction

Ulcerative colitis (UC) is a relatively uncommon, chronic, recurrent inflammatory disease of the colon or rectal mucosa [*1*]. Often a lifelong illness, the condition can have a profound emotional and social impact on the affected individual. Chronic UC is defined as continuous idiopathic inflammation of the colonic or rectal mucosa [*1*]. Differences in the pattern of incidence and natural history of chronic UC in various parts of the world may offer some clues as to the cause of the disease. The understanding of the pathogenesis has expanded greatly over the last decade. The combination of genetic risk factors, abnormalities in the immune system, vascular and neural factors, and random environmental factors may all play an important role.

There are various manifestations in the natural course of ulcerative colitis. Chronic UC is traditionally considered a disease of industrially developed countries, and its epidemiological features and natural history have been well-defined by numerous studies in North America and Europe [*2–7*]. Israel, Japan, and South Africa (white populations) also have a relatively high incidence of chronic UC though, with the exception of Ashkenazi Jews, lower than in North America/Europe [*8–10*]. Chronic UC is considered to be rare in developing countries and even more so in black Africans [*10*].

There appears to be an increased risk for developing colon carcinoma, rectal carcinoma and hepatobiliary carcinoma among patients with UC [*1,11*]. Severe colitis is a life-threatening complication of ulcerative colitis. Early recognition of the severity of the colitis, intensive medical therapy and prompt surgery when necessary have all contributed to improved outcome.

In view of the lack of information about chronic UC in developing countries this study was undertaken to assess the epidemiology, course and outcome of UC patients attending a hospital in Jordan.

Methods

This retrospective review included 372 patients who were diagnosed with UC at King Hussein Medical Centre in Amman between January 1994 and January 2001. King Hussein Medical Centre is a tertiary hospital which receives referrals from 6 other hospitals throughout Jordan. It mainly cares for army personnel and their families but over last 10 years certain civilians who have chronic illnesses and cannot afford to pay are treated free of charge.

The diagnosis of UC was based on accepted clinical, endoscopic, and radiological criteria. UC was distinguished from Crohn's disease by the biopsy findings; if the biopsy was indeterminate, endoscopic features were considered in the diagnosis (colon involvement, mucosa bleeds easily on contact, and no features suggestive of Crohn's disease). In all patients, biopsy and/or surgical specimens were examined pathologically and the findings were consistent with chronic UC. UC was classified as mild, moderate or severe according to Truelove and Witts [*12*].

Infection was excluded by parasitology and stool cultures. Ten (10) patients were included who demonstrated cysts or trophozoites of *Entamoeba histolytica* on stool examination, but did not improve despite repeated treatment with antiamoebic drugs; however, they did respond to treatment for chronic UC. Primary intestinal lymphoma and intestinal tuberculosis were excluded.

Patients were actively followed up for an average of 4.4 years (range 1–7 years) until 2004/05 with periodic sigmoidoscopy (when necessary) radiological examination of the colon, and flexible colonoscopy.

Simple descriptive statistics were used to analyse the results.

Results

Demographic profile

There were 149 men (40%) and 223 women (60%), and the female predominance was observed in all decades, except for age 60–69 years, when there were more males than females (Table 1). The mean age of patients in the study was 31.8 years (range 14–69 years). In about half of the patients, colitis began before the age of 29 years; in 37 patients (9.9%) it began before the age of 16 years. The peak age group was 20–29 years; no bimodal age distribution was observed. The family history was positive for chronic UC in the case of 9 patients (2.4%). A majority of patients were city dwellers; 230 (61.8%) resided in Amman, with the remaining 38.2% coming from other cities in Jordan (King Hussein Medical Centre is a tertiary referral hospital). All but 9 of the patients were Jordanian nationals, and all but 24 patients were Muslims.

Diagnosis and symptoms

The interval between the onset of symptoms and the diagnosis of chronic UC ranged between 10 days and 10 years (mean 2 years). In only one third of patients was the diagnosis made within 1 year after onset (Table 2).

Bloody diarrhoea and crampy abdominal pain were the most common presenting symptoms (84% of patients); 9% of patients complained of constipation and the remaining 7% of patients had tenesmus, urgency, rectal pain or passage of faeces with mucus. Systemic manifestations included fever (30%), weight loss (32%), and anaemia (haemoglobin < 12 g/l00 mL) (49%).

In 3 patients (< 1%), chronic UC had begun during either pregnancy or puerperium.

A total of 156 patients (42%) had distal colitis (distal to the splenic flexure), 82 (22%) had substantial colitis (distal to the hepatic flexure) and 104 (28%) had total colitis. In 30 patients (8%) the extent of colonic involvement could not be determined (Table 3). Chronic UC was mild in 203 patients (55%), moderate in 136 (37%), and severe in 33 (9%) (Table 3).

The most common complications were pseudopolyps in 56 patients (15%), haemorrhoids in 33 (9%) and toxic megacolon in 23 (6%) (Table 4). Only 3 patients (0.8%) had colon cancer, which was associated

Table 1 **Age and sex of 372 patients with chronic ulcerative colitis**

Age (years)	Males No.	%	Females No.	%	Total No.
14–19	16	31	36	69	52
20–29	54	42	75	58	129
30–39	38	46	45	54	83
40–49	21	32	43	68	64
50–59	17	44	22	56	39
60–69	3	60	2	40	5
Total	149	40	223	60	372

Table 2 **Duration of symptoms before diagnosis of chronic ulcerative colitis**

Duration (years)	No.	%
< l	116	31
1–2	77	21
2–3	36	10
3–4	39	11
4–5	14	4
> 5	53	14
Unknown	37	10
Total	372	100

Table 3 **Relationship between extent and severity of illness in 372 patients with chronic ulcerative colitis**

Extent	Severity						
	Mild		Moderate		Severe		Total
	No.	%	No.	%	No.	%	No.
Distal colitis	130	83	26	17	0	0	156
Substantial colitis	39	48	36	44	7	9	82
Total colitis	20	19	60	58	24	23	104
Undetermined	14	47	14	47	2	7	30
Total	203	55	136	37	33	9	372

with high-grade epithelial dysplasia. Common extracolonic complications included polyarthritis and ankylosing spondylitis in 16 patients (4%) and liver cirrhosis in 13 patients (3.5%) (Table 4). Skin lesions were erythema nodosum 10 (3%) patients and pyoderma gangrenosum in 5 patients (1%).

Table 4 **Intestinal complications and extracolonic manifestations in 372 patients with chronic ulcerative colitis**

Item	No.	%
Intestinal complications		
Pseudopolyp	56	15.1
Haemorrhoids	33	8.9
Toxic megacolon	23	6.2
Stricture	13	3.5
Perforation	10	2.7
Anal fissure	10	2.7
Colon cancer	3	0.8
Perianal abscess	3	0.8
Total	151	40.6
Extracolonic manifestations		
Polyarthritis	13	3.5
Liver cirrhosis	13	3.5
Thromboembolism	10	2.7
Erythema nodosum	10	2.7
Finger clubbing	7	1.9
Sclerosing cholangitis	7	1.9
Pyoderma gangrenosum	5	1.3
Ankylosing spondylitis	3	0.8
Uveitis	3	0.8
Total	71	19.1

Treatment and outcome

Because of the endemic nature of *E. histolytica* in our region, 116 (31%) patients were repeatedly treated with antiamoebic drugs, although with no improvement. In 33 (9%) other patients whose stools contained cysts or trophozoites of *E. histolytica*, antiamoebic treatment was ineffective and only chronic UC-specific treatment resulted in remission. Salicylazosulfapyridine was given to 349 (94%) patients, either alone (123 patients, 33%) or in combination with adrenal steroids (226 patients, 61%); 13 patients (3.5%) received only steroids and 10 (2.6%) received neither.

A total of 33 patients (8.9%) underwent either total or subtotal colectomy with ileorectal anastomosis; 13 patients (3.5%) died postoperatively. Indications for surgery in 30 patients included toxic megacolon, perforation and lack of response to medical treatment (all were operated on within 3 years from the onset of bowel disease). The remaining 3 patients (< 1%) were operated on because of colon cancer. In addition to these 33, 5 others had surgery: 2 underwent exploratory laparotomy and in the other 3 biliary drainage was attempted for sclerosing cholangitis. Of the 334 unoperated

patients, 10 died; 3 of chronic UC 2 years after the onset of bowel disease and 7 others of unrelated causes.

The overall mortality rate was 6% (23 patients).

Discussion

Chronic UC is considered rare in developing countries [*1,13*]. However, it is being reported with increasing frequency from various developing countries [*13–15*]. The incidence and prevalence of chronic UC are well defined in the industrialized countries, amounting to 4 to 6 cases per 100 000 white adults per year and 40 to 100 cases per 100 000 members of the total population [*2,3*]. Figures for developing countries are around 7.57 per 100 000 population [*13*].

Our observations suggest that chronic UC is not rare in Jordan. However, because of lack of awareness on the part of physicians and inadequate facilities, diagnosis of chronic UC is considerably delayed. In one third of our patients, diagnosis was established more than 3 years after the onset of symptoms, and in only one third, within 1 year. Furthermore, 30% of them were subjected to surgery for "haemorrhoids" or "anal fissures". Socioculturally, patients are reluctant to undergo sigmoidoscopy and not infrequently the physician is tempted to diagnose "haemorrhoids" or "anal fissures" in patients with proctosigmoiditis on the basis of a normal appearance on barium enema examination. The peak age of incidence of chronic UC in our patients was during the 3rd decade. A positive family history of chronic UC was noted in 2.4% of our patients, far less than the 15%–50% reported from Western countries [*15*]. This finding may indicate a lower degree of susceptibility of our population to chronic UC compared to those with a high incidence.

Although the clinical manifestations of chronic UC are similar in various parts of the world, it has been stated that the disease is less often complicated by intestinal and extraintestinal manifestations in developing countries; indeed, some authors have reported none or very few such complications [*16*]. In our patients we found a relatively high rate of occurrence of toxic megacolon, perforation, strictures, and extraintestinal manifestations. However, skin lesions such as erythema nodosum and pyoderma gangrenosum were 2.7% and 1.3% respectively. From other developing countries skin lesions have only occasionally been reported for reasons which are not readily apparent [*16*]. However, joint symptoms, which frequently accompany skin lesions, have been observed in those countries.

Of interest is the fact that colorectal cancer was seen in only 3 (< 1%) of our patients, although its overall incidence in chronic UC is between 3%–5% in the Western countries [*17*]. It is also well known that cancer is more likely to develop in patients with extensive colitis, lasting 8.8–10 years or more [*1,11,17*]. However, a low incidence of colorectal cancer in chronic UC has been reported from other developing nations as well as Israel, Japan, and the former Yugoslavia [*8,18,19*]. In our series, 50% of patients had extensive or total colitis. However, the mean follow-up period was only 4.4 years, and very few of our patients had colitis for more than 10 years. It is possible that because of the short follow-up period, we were not able to detect superimposed bowel cancer in our patients. However, it should be noted that the incidence of colorectal cancer is generally low in several other developing nations [*20*].

Chronic UC is reported to exhibit a milder course and be less extensive in developing countries; mild to moderate forms of chronic UC have been reported in as

many as 74% of patients from Turkey and 93% of patients from Kuwait [*21,22*]. In our patients, a mild course was noted in 55% and involvement of the colon distal to the splenic flexure in 42%. Furthermore, 33 patients (9%) required colectomy, and only 16 (4.3%) died as the result of chronic UC. In industrialized countries, surgery has been reported in 20%–25% of patients with chronic UC, and although mortality rates were high, overall mortality has decreased steadily in recent years and is currently less than 5% [*1*]. Mortality rates reported from developing countries range between 4% and 10% [*21*].

The pathogenesis of chronic UC is unknown, and the influence of lifestyle and socioeconomic factors on its development is a subject of controversy. In developing countries, chronic UC has been observed in subgroups of populations who have attained a higher socioeconomic status and adopted a modern lifestyle and dietary habits [*23*]. Even in the industrialized countries, the disease seems to be more frequent in urban rather than rural populations [*1,3,4*]. The effects of changing socioeconomic status and dietary habits have been particularly impressive in African blacks with chronic UC [*23*]. Almost all of our patients were city dwellers and were likely to belong to middle or high socioeconomic classes. However, the influence of dietary habits on the development of chronic UC in our population is harder to prove because the use of canned and processed foods is neither widespread nor popular in our country. Thus, the importance of food additives such as carrageenan, which can induce haemorrhagic colitis in guinea pigs is doubtful [*24*]. To be considered are factors other than diet such as emotional stress which are also related to changes in lifestyle and socioeconomic status and which may play an important role in this connection.

In conclusion, the epidemiology of UC in Jordan is similar to that in developing countries but the disease seems more severe than in neighbouring countries. Increased awareness among patients and doctors together with modernization of our population is likely to increase the prevalence of UC in Jordan.

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