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A decade of inflammatory bowel disease: a single center experience in Egypt

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Abstract

Background: Inflammatory bowel disease is a chronic inflammatory disorder of the gastrointestinal tract and includes ulcerative colitis and Crohn's disease. Inflammatory bowel disease has always seemed to be rare in the Middle East and Northern Africa. In this study, we explored the clinical characteristics of inflammatory bowel disease patients in our center.

Methods: This retrospective study was conducted on patients with an established diagnosis of inflammatory bowel disease over 10 years from September 2009 to September 2019 who were referred to our inflammatory bowel disease center. Clinical information was obtained from medical records and patient interviews. We included all patients in whom the diagnosis of ulcerative colitis or Crohn's disease was confirmed by clinical, laboratory, endoscopic, and histological examination over a 10-year period from 2009 to 2019.

Results: Our study had one hundred and sixty-nine inflammatory bowel disease patients; one hundred and thirty-six ulcerative colitis patients and the remaining thirty-three patients had Crohn's disease. The main presenting symptom was bloody diarrhea (78 patients) representing 46.2% of the patients in our study. The majority of ulcerative colitis patients (55.9%) had moderate disease (Truelove & Witts score), while the majority of Crohn's disease patients (66.7%) had moderate to severe disease (Crohn's Disease Activity Index).

Conclusions: The prevalence of inflammatory bowel disease is still low in Egypt despite the rising curve of newly diagnosed cases.

Keywords: Inflammatory bowel disease, Ulcerative colitis, Crohn's disease, Egypt, Epidemiology

Background

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder of the gastrointestinal tract and includes ulcerative colitis (UC) and Crohn's disease (CD) [1]. They mainly affect young populations, altering their quality of life and increasing morbidity, compared to the general population [2]. The etiology and pathogenesis of IBD are still poorly understood. The pathogenesis of IBD involves genetic factors and environmental factors [1].

IBD was first recognized in European countries during the industrial revolution. The incidence and prevalence of IBD significantly increased in the twentieth century [3]. IBD occurs with different frequencies around the world. The countries reporting the highest incidence of UC are the USA, the UK, and Sweden [4].

IBD has always seemed to be rare in the Middle East and Northern Africa. In Mediterranean countries, the prevalence of UC was estimated at 5/100000 in urban areas [5].

In a recent review of the natural history of IBD, it was noted that as countries become westernized, the incidence of UC increases first followed by CD [6]. Both diseases have emerged in countries in which they had

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Table 1 Harvey Bradshaw score [8]

Parameter	Input and score
1. Patient well-being (previous day)	0 = Very well 1 = Slightly below par 2= Poor 3 = Very poor 4 = Terrible
2. Abdominal pain (previous day)	0 = None 1 = Mild 2 = Moderate 3 = Severe
3. Number of liquid or soft stools (previous day)	An integer, from 1 to 25
4. Abdominal mass	0 = None 1 = Dubious 2 = Definite 3 = Definite and tender
5. Complications	No (0 points) Yes (each selected complication below is counted with 1 point) Arthralgia Uveitis Erythema nodosum Aphthous ulcer pyoderma Gangrenosum anal fissures

rarely been previously reported, including Japan, South Korea, India, Iran, Lebanon, Thailand, the French West Indies, and North Africa [7]. In these countries, the occurrence of UC preceded that of CD by approximately 10 years. The overall incidence of IBD can be broken down into several geographic zones: those with a high incidence, those with a moderate incidence, those with a low incidence 15 years ago but with a consistently increasing incidence, and those with an unknown incidence [6].

In this study, we studied the sociodemographic and clinical characteristics of patients diagnosed with CD and

Table 2 Crohn's Disease Activity Index (CDAI) [9]

Parameter	Clinical evaluation (single choice)	Score
1. Stool frequency (per day)	• Normal number of stools	0
	• 2 more than normal	1
	• 3–4 more than normal	2
	• ≥ 5 more than normal	3
2. Rectal bleeding (indicate the most severe bleeding of the day)	• None	0
	• Streaks of blood with stool in less than half of the cases	1
	• Obvious blood with stools in most cases	2
	• Blood alone passes	3
3. Endoscopic findings	• Normal mucosa or inactive disease	0
	• Mild activity (erythema, decreased vascular pattern, mild friability)	1
	• Moderate activity (marked erythema, lack of vascular pattern, friability, erosions)	2
	• Severe activity (spontaneous bleeding, large ulcerations)	3
4. Physician's global assessment	• Normal	0
	• Mild disease	1
	• Moderate disease	2
	• Severe disease	3

Calculated by summing the scores of the four parameters. Clinical response is defined as a decrease of at least 3 points and at least 30% versus baseline, which must include a decrease in the score for rectal bleeding of at least 1 point, or an absolute score for rectal bleeding not exceeding 1

Table 3 Vienna and Montreal classification for Crohn's disease [10]

	Vienna	Montreal
Age at diagnosis	A1 below 40 years	A1 below 16 years
	A2 above 40 years	A2 between 17 and 40 years
		A3 above 40 years
Location	L1 ileal	L1 ileal
	L2 colonic	L2 colonic
	L3 ileocolonic	L3 ileocolonic
	L4 upper	L4 isolated upper disease[a]
Behavior	B1 non-stricturing, non-penetrating	B1 non-stricturing, non-penetrating
	B2 stricturing	B2 stricturing
	B3 penetrating	B3 penetrating
		p perianal disease modifier△

△"p" is added to B1–B3 when concomitant perianal disease is present

[a] L4 is a modifier that can be added to L1–L3 when concomitant upper gastrointestinal disease is present

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Methods

As we are lacking the data regarding IBD patients in addition to the absence of solid databases to follow up the patients in Egypt as well as most African countries. This study aimed to identify the sociodemographic and clinical characteristics of IBD patients in our country.

Our department's gastroenterology center serves patients from all parts of Egypt. We considered patients with chronic diarrhea, bleeding per rectum, recurrent abdominal pain or discomfort, melena, weight loss, and/or perianal fistula or abscess. The diagnosis was established by clinical, laboratory, and radiological findings and endoscopic and histopathological criteria.

This retrospective study was conducted on patients with an established diagnosis of IBD over the 10 years from September 2009 to September 2019 who were referred to our IBD center. The following data were collected at index presentation for assessment: demographical data, occupation and the impact of the disease, criteria of activity, area of residency, symptoms (diarrhea, weight loss, abdominal pain, and blood in the stool), family history of IBD, smoking history, extraintestinal manifestations (EIMs), the use of corticosteroids at the time of presentation, and the subsequent decision of treatment by azathioprine, or monoclonal antibodies against tumor necrosis factor (anti-TNF), or colectomy. Clinical information was obtained from medical records including the patients' interviews at their index presentation. We included all patients in whom the diagnosis of UC or CD was confirmed by clinical, laboratory, endoscopic, and histological examination over a 10-year period from 2009 to 2019.

As infection is an important cause of deterioration in our patients even being confused with the activity of the disease and also Egypt is in a region endemic for many parasitic infections, so stool analysis was performed for all our patients at index presentation.

CD was diagnosed if there were histopathologic findings suggestive of Crohn's disease (non-caseating granuloma) in patients with skip lesions; a cobblestone

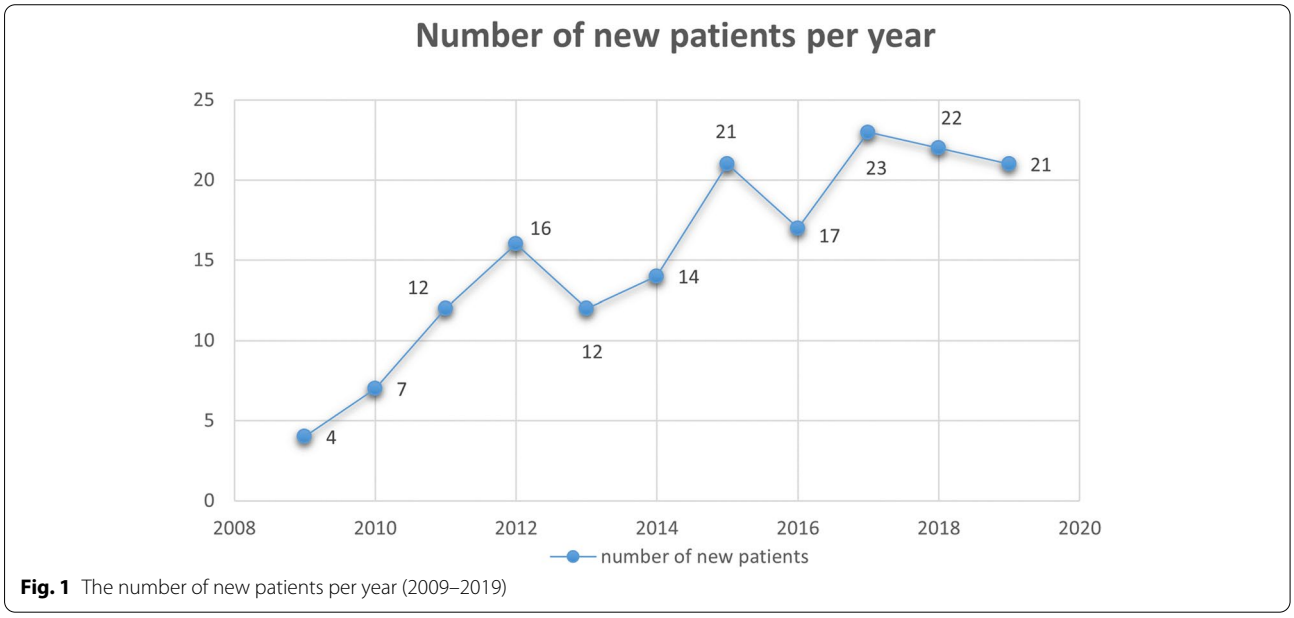

Fig. 1 The number of new patients per year (2009–2019)

Table 4 Sociodemographic characteristics of our patients

Sociodemographic data		Total no. = 169
Diagnosis	Ulcerative colitis	136 (80.5%)
	Crohn's disease	33 (19.5%)
Age	Mean ± SD	33.49 ± 11.31
	Range	9–76
Gender	Male	78 (46.2%)
	Female	91 (53.8%)
Smoking	Smoker	14 (8.3%)
	Ex-smoker	13 (7.7%)
	Non smoker	142 (84.0%)
Residency	Rural	45 (26.6%)
	Urban	124 (73.4%)
Marital status	Single	78 (46.2%)
	Married	86 (50.9%)
	Divorced	5 (3.0%)

SD standard deviation

appearance; mucosal ulceration; or aphthous lesions at endoscopy, deep inflammation or chronic terminal ileal inflammation, with or without radiologic evidence of stricturing disease, fistulizing disease, or existence of recurrent perianal disease (abscess, fistula), were also included in the diagnosis. Endoscopic and histopathological examinations were performed by 2 senior experts.

UC was diagnosed when there was evidence of superficial inflammation, crypt abscesses, and cryptitis in diffuse mucosal disease of the colon extending from the rectum to different proximal extensions. For cases of UC, the Truelove classification was used to assess severity, and the Montreal classification was used to assess the extent of the disease.

A diagnosis of IBD was established according to the corresponding criteria. Endoscopic grades were assigned according to the Mayo score as (1) mild activity (erythema, decreased vascular pattern, and mild friability), (2) moderate activity (marked erythema, lack of vascular pattern, friability, and erosions), and (3) severe activity, spontaneous bleeding, and large ulcerations). The histopathological findings included the following: vascular congestion, crypt abscesses, mucin depletion, cellular infiltrate, cryptitis, and crypt branching.

The activity of the disease (whether UC or CD) was determined according to the patient's condition when first presented to our center (index presentation). The relatively simple Harvey-Bradshaw score [8] (Table 1) and the more complicated Crohn's Disease Activity Index [9] (CDAI) (Table 2) were used to assess the disease activity of CD patients at their index presentation. The CDAI is the sum of 8 components calculated online depending on the evaluation within one previous week of the number of liquid or soft stools, daily abdominal pain, patient well-being, complications, use of antidiarrheal, hematocrit, body weight. The Montreal classification [10] (Table 3) and endoscopic grades assessed the activity as follows: (1) inactive (the vascular pattern is only slightly distorted and there is, fine granularity without friability or epithelial defects); (2) mildly active (there is unequivocal erythema, either focal or confluent, and some friability without epithelial necrosis); (3) moderately active (a few aphthoid erosions or small ulcers are noted); or (4) severe (ulcers are larger and more numerous). The histopathological findings included the following: cellular infiltrate, focal

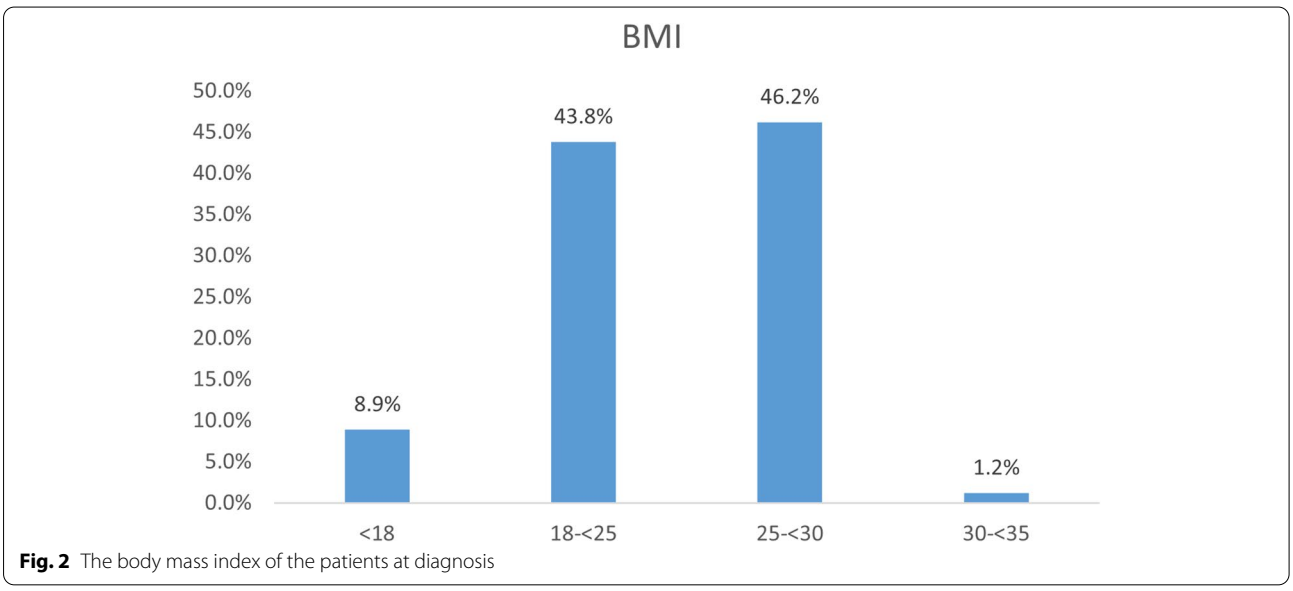

Fig. 2 The body mass index of the patients at diagnosis

Table 5 Symptoms of the patients at index presentation

Clinical presentation		Total no. = 169
Main presenting symptom	Diarrhea	30 (17.8%)
	Bleeding	42 (24.9%)
	Diarrhea & bleeding	78 (46.2%)
	Abdominal pain	19 (11.2%)
Extraintestinal manifestations	Negative	137 (82.0%)
	Hepatobiliary	7 (4.2%)
	Cardiovascular symptoms	1 (0.6%)
	Respiratory symptoms	1 (0.6%)
	Urinary symptoms	1(0.6%)
	Eye symptoms	1 (0.6%)
	Joint symptoms	15 (9.0%)
	Skin symptoms	6 (3.6%)

inflammation, microfistulization, non-caseating granulomas, cobblestoning, and lymphoid hyperplasia.

Results

This retrospective study was conducted on patients with an established diagnosis of IBD over 10 years from September 2009 to September 2019 who were referred to our IBD unit at Tropical Medicine Department, Ain Shams University Hospitals. The total number of IBD patients was 169 patients, 136 of them were UC patients (80.5%) and the other 33 patients (19.5%) were diagnosed to have Crohn's disease. The number of new patients received by our unit each year during the time period of the study is shown in Fig. 1.

Females were slightly more than males (53.8% vs 46.2%). The age of patients ranged between 9 and 76 years. The basic demographic characteristics of our patients are shown in Table 4 and Fig. 2. The clinical picture of the patients ranged between diarrhea, bleeding, and abdominal pain, with the majority of the patients having no extraintestinal manifestations at index presentation as in Table 5.

Exploration of the patients' blood investigations at index presentation showed mostly normal laboratory markers except for anemia and elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) (Table 6). Most of our patients (95.3%) had stool examination free from parasites, with only 4.7% of the patients having *Entamoeba histolytica* cysts (Fig. 3).

Macroscopic and microscopic appearance of the disease (Tables 7 and 8)

All of our patients naturally had undergone colonoscopy at or around the time of presentation with biopsies taken for histopathological examination. As for UC patients, the most frequent endoscopic finding was a loss of vascular pattern (89.7%), while aphthous ulcers were the commonest finding in CD patients (60.6%). Histopathological examination showed that aggregation of polymorph nuclear leucocytes (PMN), cryptitis, infiltration of the lamina propria, and depletion of goblet cells were the most common microscopic findings. Only a minority of patients (4.1%) had dysplasia with no patients showing any evidence of malignancy fortunately.

Table 6 Laboratory parameters of the patients at index presentation

Laboratory investigations		Total no. = 169
White blood cells (/uL)	Mean ± SD	7.84 ± 2.9
	Range	2.28–20.4
Hemoglobin (gm/dL)	Mean ± SD	10.89 ± 1.77
	Range	6–14.9
Platelets (/uL)	Mean ± SD	311.73 ± 121.93
	Range	62.3–807
INR	Mean ± SD	1.05 ± 0.15
	Range	0–1.91
AST (U/L)	Median (IQR)	20 (15–29)
	Range	5–126
ALT (U/L)	Median (IQR)	20 (14–27)
	Range	5–159
Total proteins (gm/dL)	Mean ± SD	6.85 ± 0.78
	Range	4–9.2
Albumin (gm/dL)	Mean ± SD	3.62 ± 0.6
	Range	1.5–6
Total bilirubin (mg/dL)	Median (IQR)	0.8 (0.6–1)
	Range	0.2–8.9
Direct bililrubin (mg/dL)	Median (IQR)	0.3 (0.2–0.5)
	Range	0.03–5
Sodium (mmol/L)	Mean ± SD	136.28 ± 8.47
	Range	35–148
Potassium (mmol/L)	Mean ± SD	3.85 ± 0.4
	Range	2.5–5.1
Blood urea nitrogen (mg/dL)	Mean ± SD	12.23 ± 6.14
	Range	4–45
Creatinine (mg/dL)	Mean ± SD	0.81 ± 0.21
	Range	0.2–1.5
C-reactive protein (mg/dL)	Median (IQR)	10 (6–20)
	Range	1.2–280
ESR (mm/h)	Median (IQR)	30 (16–50)
	Range	0–140

SD standard deviation, *INR* international normalized ratio, *AST* aspartate aminotransferase, *IQR* interquartile range, *ALT* alanine aminotransferase, *ESR* erythrocyte sedimentation rate

Ulcerative colitis patients

Our records showed 136 patients with UC; the site of the colon most affected was recto-sigmoid (36.8%), with the

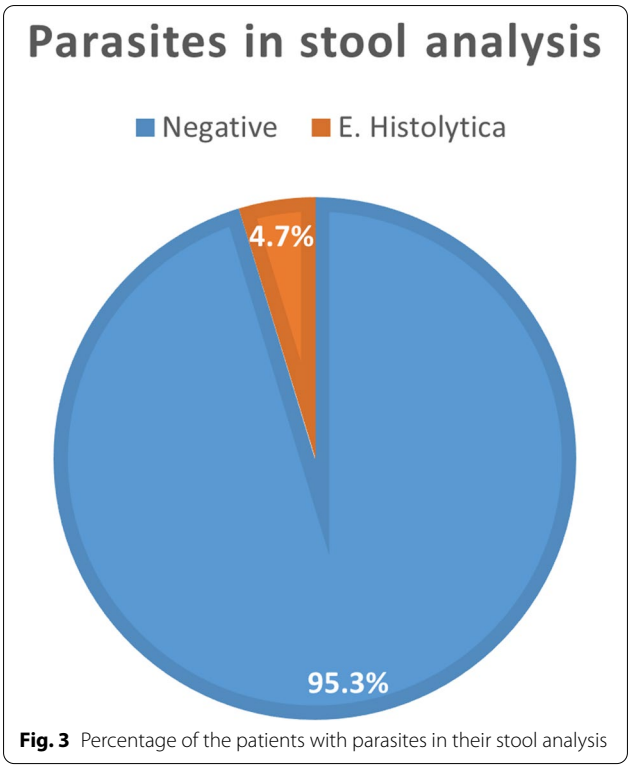

Fig. 3 Percentage of the patients with parasites in their stool analysis

main presenting symptom being bloody diarrhea (52.9%) (Table 9). The activity of the disease at index presentation was evaluated by Truelove & Witts criteria and by Mayo score (Figs. 4 and 5).

Crohn's disease patients

For patients affected by CD, the main site of affection was the ileum (48.5%), and abdominal pain was the most common presentation (42.4%) (Table 10). Crohn's Disease Activity Index was used to assess the disease activity at index presentation (Fig. 6).

Table 7 Colonoscopy findings (at index presentation) in our study

Ulcerative colitis	**Total no. = 136**
Loss of vascular pattern	122 (89.7%)
Opacity of mucosa	69 (50.7%)
Bleeding on touch	76 (55.9%)
Excess exudates	64 (47%)
Diffuse ulcerations	91 (66.9%)
Pseudopolyps	39 (28.7%)
Crohn's disease	**Total no. = 33**
Linear ulcers	14 (42.4%)
Aphthous ulcers	20 (60.6%)
Cobblestone appearance	16 (48.5%)

Table 8 Histopathological findings

Biopsy findings		
Aggregation of polymorph nuclear leukocytes	Positive	133 (78.7%)
	Negative	36 (21.3%)
Cryptitis	Positive	133 (78.7%)
	Negative	36 (21.3%)
Infiltration of lamina propria	Positive	116 (68.6%)
	Negative	53 (31.4%)
Depletion of goblet cells	Positive	114 (67.5%)
	Negative	55 (32.5%)
Thickened muscularis mucosa	Positive	30 (17.8%)
	Negative	139 (82.2%)
Dysplasia	Positive	7 (4.1%)
	Negative	162 (95.9%)
Degree of dysplasia	Mild	6 (85.7%)
	Moderate	1 (14.3%)
Malignancy	Positive	0 (0.0%)
	Negative	169 (100.0%)
Granuloma (CD patients)	Positive	23 (69.7%)
	Negative	10 (30.3%)

CD Crohn's disease

Discussion

The current study included (169) Egyptian patients similar to another study from Egypt reflecting a relatively small prevalence of the disease, probably due to a lack of awareness of the disease [11]. The number of newly confirmed cases of IBD in our unit during the 10-year period of the study generally shows a rising trend with a sharper rise at the beginning with the cases rising in a less acute

Table 9 Clinical characteristics of ulcerative colitis patients

In ulcerative colitis patients		**Ulcerative group Total no.= 136 No. (%)**
Main presenting symptom	Diarrhea	21 (15.4%)
	Bleeding	38 (27.9%)
	Diarrhea & bleeding	72 (52.9%)
	Abdominal pain	5 (3.7%)
Site of involvement	Rectum	13 (9.6%)
	Rectum & sigmoid	50 (36.8%)
	Left side of colon	21 (15.4%)
	Extensive	24 (17.6%)
	Pancolitis	24 (17.6%)
	Ileum (backwash ileitis)	4 (2.9%)
Biological therapy	Positive	22 (16.2%)
	Negative	114 (83.8%)
Surgery	Positive	8 (5.9%)
	Negative	128 (94.1%)

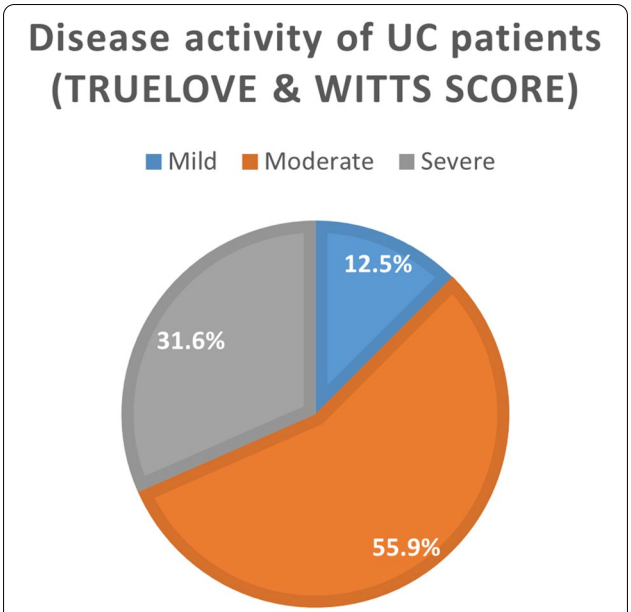

Fig. 4 Degree of severity of ulcerative colitis (Truelove & Witts score) at index presentation

manner in later years. The mean age at diagnosis for the patients in this study was 33.5 years with similar results reported in other studies from India, Brazil, and Iran [12–15].

As for the gender differences in IBD prevalence, our study showed a male to female ratio of 1:1.16, indicating a lack of difference in IBD prevalence between both genders which was similarly reported by Esmat and colleagues [11], regarding UC patients with a higher male predominance in CD patients (2.6:1). Other studies have reported a higher female predominance in both UC & CD [13, 16], while others showed a similar prevalence in both genders [15, 17]. The prevalence of UC was much higher in our study than CD; (4:1.12). This was also reported by Darakhshan and colleagues [18] who found a higher prevalence of UC (6.2:1) and studies in Brazil with a lower incidence of UC (2~1.7:1) [19].

The body mass index (BMI) of the patients in our study was mainly among overweight (46.2%) and average weight (43.8%) groups. Slightly different results were reported by Mentella and colleagues [20] where 49% of the patients had average weight and 25.7% were overweight, which was also stated in other studies [21] that reported a percentage of 20–40% of overweight patients among IBD adult patients. There was no apparent

Table 10 Clinical characteristics of Crohn's disease patients

In Crohn's diseases patients		Crohn's group Total no.= 33
		No. (%)
Main presenting symptom	Diarrhea	9 (27.3%)
	Bleeding	4 (12.1%)
	Diarrhea & bleeding	6 (18.2%)
	Abdominal pain	14 (42.4%)
Site of involvement	Colonic	12 (36.4%)
	Ileum	16 (48.5%)
	Patchy	5 (15.1%)
Biological therapy	Positive	10 (30.3%)
	Negative	23 (69.7%)
Surgery	Positive	12 (36.4%)
	Negative	21 (63.6%)

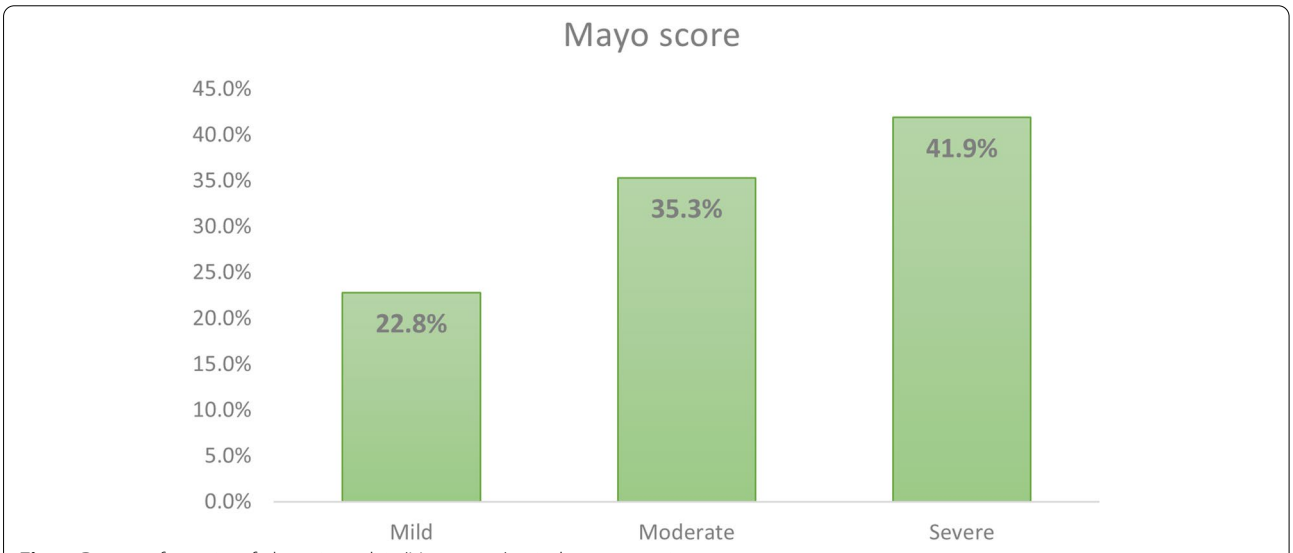

Fig. 5 Degree of severity of ulcerative colitis (Mayo score) at index presentation

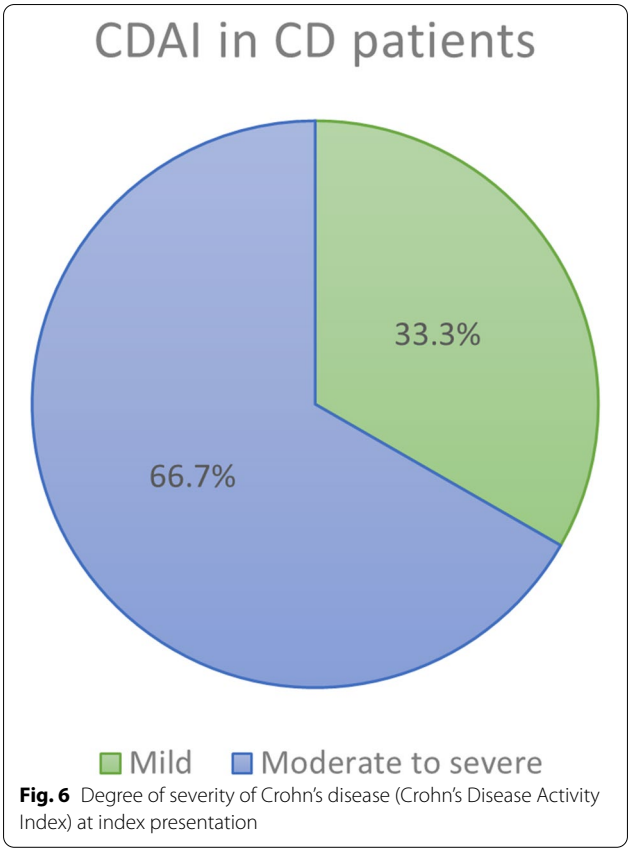

Fig. 6 Degree of severity of Crohn's disease (Crohn's Disease Activity Index) at index presentation

correlation between smoking and IBD in our study as 142 patients (84%) were non-smokers at the time of diagnosis, with the remaining patients being smokers or ex-smokers, which is different from the findings in previous studies showing that smoking was protective against UC [22]. However, it is similar to findings in other studies done in Arabs [11, 23] and Asians [24].

The main presentation in our study was diarrhea & bleeding per rectum in 46.2% of patients followed by bleeding per rectum alone (24.9%) and diarrhea alone (17.8%). This is similar to the study of Esmat and colleagues [11] where rectal bleeding and diarrhea were the main presenting symptoms in UC patients and diarrhea was the main presentation of CD patients. This was also reported in a study from Iran [15] as bloody diarrhea was the main presenting symptom (97.9%) in their cohort though abdominal pain was the second main presentation (71.4%) where it was the main presenting symptom in only 11% of patients in the current study. Their findings were also different from another study in Iran [18] which stated that the main presenting symptoms of their patients were diarrhea, bleeding, and bloody diarrhea. Abdominal pain was also the main presentation in another study [23] which could be explained by the fact that it was done on patients with CD only with no UC patients included, which is in fact similar to the 33 patients with CD in our study whose main presentation was abdominal pain (42.4%).

The laboratory parameters of our patients showed only mild anemia with a mean hemoglobin of 10.9 gm/dl, with the rest of the parameters being mainly normal. This is quite similar to the average level of hemoglobin in the study of Esmat and colleagues [11] which was 11 gm/dl. The median ESR was 30 mm in the 1st hour and that is slightly similar also to the findings in the study of Esmat and colleagues [11], where the mean ESR in the 1st hour was 36 in UC patients and 49.5 in CD patients.

In our study, most of the patients with UC had a disease affecting the rectosigmoid colon (36.8%), while pancolitis and extensive colitis were presented equally, each in 17.2% of the patients. Similar results were reported by Mostafa and colleagues [25], where most of the patients (50%) had proctosigmoiditis. This is quite different from another study in Egypt [11] which reported that 65.2% of patients had left-sided colitis, 18.5% of patients had proctosigmoiditis, and 16.3% had pancolitis.

The presentations of the disease in the current study showed that the most common activity at index presentation in UC patients is the moderate form (55.9%) followed by the severe form according to the Truelove & Witts score. Using the Mayo score in stratification regarding the disease activity in presentation, the severe form had the highest percentage of the included patients (41.9%) which could be related to built-in differences in criteria for evaluation of both scores and could also be due to the fact that we are a tertiary center receiving complicated patients from other hospitals and centers all over the country.

Crohn's disease group of patients were mainly at moderate to severe form followed by mild form (66.7%) and (33.3%) respectively. This is matched with another Egyptian study that showed 50% of patients presented with the moderate form of the disease [11].

Thirty-two patients were treated by biological therapies. Twenty-two of them were ulcerative colitis (16.17%) patients and the other ten were Crohn's disease (30.3%) patients. These percentages are comparable to those recorded by a Danish study which stated the use of biologics in 28.5% of CD patients and 11.3% of UC patients [26]. That retrospective study included more than 30 thousand patients during 12 years which may reflect the difference in the prevalence of IBD there and in Egypt. It also shows the relatively late use of biologics in Egypt with the standard treatment for severe cases limited to intravenous steroids, and surgery in non-responding cases.

Infliximab was the most commonly used biologic followed by adalimumab. These choices are of course influenced by financial issues, insurance coverage, and availability.

Surgical intervention in the current study was decided in 20 patients; 8 of them were UC and 12 of them were CD which is more than those reported by Esmat and colleagues [11] that were 11 patients only (4 UC and 7 CD), with a comparable percentage of the total number of patients who needed surgical intervention in UC in relation to CD patients' total number who needed surgical intervention.

As a matter of fact, the findings from recent reviews on IBD patients in Africa and the Middle East [27–29] are quite similar to the findings from our study regarding the percentage of smokers, the percentage of female patients, and the proctosigmoid distribution of UC in the majority of their patients, with only slight differences with some of the studies included in these reviews related to the severity of the disease as most of their studies showed a predominance of mild activity of IBD in contrast to our study where the majority of UC and CD patients were moderate to severe which again could be related to the fact that we are a tertiary center dealing with more complicated cases. It is worth noting that in two of these reviews [27, 29] the information related to Egyptian patients was derived from only one study [11], indicating the need for a population-based IBD registry and multicenter studies to pinpoint the real situation of IBD in Egypt which will be surely reflected upon the public awareness of the disease and national health plans.

Conclusion

The prevalence of inflammatory bowel disease is still low in Egypt despite the rising curve of newly diagnosed cases. Further large-scale multicenter studies are needed to obtain accurate figures regarding the IBD pattern and prevalence in Egypt.

Abbreviations

BMI: Body mass index; CRP: C-reactive protein; CD: Crohn's disease; CDAI: Crohn's Disease Activity Index; ESR: Erythrocyte sedimentation rate; EIMs: Extraintestinal manifestations; IBD: Inflammatory bowel disease; PMN: Polymorph nuclear leucocytes; TNF: Tumor necrosis factor; UC: Ulcerative colitis.

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Authors' contributions

All authors read and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Declarations

Ethics approval and consent to participate

This study was conducted according to the Declaration of Helsinki 1975, as revised in 2000 and in accordance with the Faculty of Medicine, Ain shams University ethical committee standards.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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