Prevalence of microscopic colitis in Upper Egypt among patients with chronic diarrhea and patients with irritable bowel syndrome

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Aim
The aim of this study was to evaluate the prevalence of microscopic colitis (MC) in patients with chronic watery diarrhea and irritable bowel syndrome–diarrhea (IBS-D) predominant.

Patients and methods
We studied 61 patients with chronic nonbloody diarrhea and normal endoscopic findings prospectively for 2 years' duration; 37 patients had chronic watery diarrhea for investigation and 24 had IBS-D predominant.

Results
Our results showed that 18 (29.5%) patients had MC, 10 (16.4%) patients had collagenous colitis, and eight (13.1%) had lymphocytic colitis. Four (16.7%) patients out of the 24 patients with IBS-D predominant had MC. Abdominal pain, nocturnal diarrhea, and weight loss are the most common clinical presentation in MC.

Conclusion
MC is not uncommon in Upper Egypt patients with chronic watery diarrhea and normal colonoscopic findings. Biopsy of normal colonic mucosa in patients with chronic watery diarrhea is emphasized to reach to definite diagnosis of MC.

Keywords:
Microscopic colitis, collagenous colitis, lymphocytic colitis, Irritable bowel syndrome-diarrhea predominant, chronic watery nonbloody diarrhea, chronic diarrhea with normal colonoscopic findings

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Introduction

Chronic diarrhea with no obvious reason is one of the challenges of gastroenterology. In 1980, Read and colleagues introduced microscopic colitis (MC) characterized by chronic diarrhea with normal endoscopic and radiologic findings, but with increased colonic mucosal inflammatory cells and epithelial lymphocytic infiltration on histological examination [1].

MC is a clinical syndrome of unknown etiology, characterized by chronic watery diarrhea in the absence of macroscopic changes in the large bowel. Once a rare diagnosis, its prevalence is now increasing because of the reduction in misdiagnoses and it is included more in the differential diagnosis of watery diarrhea [2].

In the past, MC was thought to be a rare disorder and very little was known about its etiology or epidemiology. MC is now regarded as a common cause of diarrhea in middle-aged and elderly patients [3].

Epidemiological data on MC mainly originate from the Western world. MC accounts for 4–13% of cases of chronic diarrhea [2].

Established risk factors for MC are female sex, higher age, concomitant autoimmune diseases such as thyroid disease or celiac disease, a past or current diagnosis of malignancy, and a history of solid organ transplant [4].

Not surprisingly, a significant number of patients who have MC also fulfill the Rome criteria for irritable bowel syndrome (IBS). Therefore, a subset of IBS patients, in particular those with diarrhea (IBS-D) who do not undergo colonoscopy and biopsies would have missed a diagnosis of MC [5].

Histology is essential in the evaluation of chronic diarrhea because of the fact that many etiologies are not macroscopically evident [e.g. quiescent inflammatory bowel disease (IBD), MC, eosinophilic colitis, and amyloidosis]. The diagnostic yield of colonoscopy in patients with chronic diarrhea ranges from 7 to 32%, with IBD and MC being the most common [6].

Histological characteristics of MC are well defined. The condition can be divided into two subgroups: collagenous colitis (CC) and lymphocytic colitis (LC). CC was first described as a case report by Lindström in 1976 and LC by Lazenby *et al.* in 1989. In MC, a macroscopically normal or near normal mucosa is observed [7] (Table 1).

The long-term prognosis of MC is generally good. In a follow-up study, 63% of the patients with CC had lasting remission after 3.5 years, and in another cohort study, all 25 patients' condition improved 47 months after diagnosis and only 29% of them required ongoing medication [8].

Patients and methods

This prospective, cross-sectional study was conducted in Assiut University Teaching Hospital over 2 years' duration on 61 patients: 37 patients had chronic watery nonbloody diarrhea (CWND) for investigation and 24 patients had IBS-D predominant. The study protocol for patients has been approved by the Ethics Committee of Faculty of Medicine at Assiut University. The participants have been informed about the study and its aim as well. The diagnosis was based on Rome II criteria: a patient must have abdominal pain or discomfort for at least 12 weeks, which need not to be consecutive, during the past 12 months. This pain or discomfort must have at least two of the following three features.

(1) Relief with defecation
(2) Association with a change in stool frequency
(3) Association with a change in stool consistency [9].

The patients were included according to the following inclusion criteria.

All patients with CWND (defined by persistent symptoms lasting for more than 1 month) or IBS-D who fulfilled the diagnostic criteria of Rome II and had normal colonoscopic findings.

The exclusion criteria including any one of the following.

- Patients having bloody diarrhea
- All patients with a history of acute diarrhea
- Patients with a history of IBDs
- Patients with abnormal colonoscopic findings
- Patients with a history of steatorrhea
- Patients who had previous gastrointestinal (GI) or colonic surgery except appendectomy.

Detailed history taking and thorough complete physical examination were performed; lab investigations included complete blood count, liver function test, renal function test, erythrocyte sedimentation test, C-reactive protein, antinuclear antibody, thyroid function test, and stool examination.

Colonoscopy and biopsy sampling procedure

Endoscopy was performed for all patients at the GI endoscopy center in Assiut University Teaching Hospital using the Pentax EC-3840M endoscope; the patients underwent the procedure after written informed consent; the procedure was carried out under conscious sedation in the majority of them, but some patients required general anesthesia.

Complete colonoscopy was performed for the majority of our patients without any complications to sedation, anesthesia, or the procedure itself in all examined cases; random multiple biopsies were obtained with the aid of standard, open-type endoscopic biopsy forceps from endoscopically normal appearing mucosa at different segments of the possible reaching examined part with at least two biopsies from each location: the proximal colon (cecum, ascending colon, and transverse colon), distal colon (descending colon and sigmoid colon) and rectum, They were immediately placed in bottles with 10% formalin and sent for processing in the pathology lab at the same hospital.

The tissues were routinely processed for light microscopic examination; the specimens were processed conventionally in paraffin blocks and cut into 5-μm-thick unstained sections and evaluated by a pathologist.

The biopsies were regarded as normal when there were less than five intraepithelial lymphocytes/100 surface epithelial cells, the collagen layer was less than 5 μm and no other pathological changes in the epithelium and lamina propria were found.

Table 1 Histopathological features of collagenous colitis and lymphocytic colitis

Collagenous colitis	Lymphocytic colitis
Thickening of a subepithelial collagen layer of more than 10 μm	Intraepithelial lymphocytosis (≥20 IEL per 100 surface epithelial cells)
Inflammation in the lamina propria consisting mainly of lymphocytes and plasma cells	Inflammation in the lamina propria consisting mainly of lymphocytes and plasma cells
Epithelial damage, such as flattening and detachment	Epithelial damage, such as flattening and detachment
Intraepithelial lymphocytosis (IEL) could be present, but is not necessary for the diagnosis of CC	Subepithelial collagen layer not present or less than <10 μm

Quoted from Storr [4].

Statistical analysis

Data entry, tabulation, and analysis were performed using statistical package for the social sciences (version 16) program for Windows, version 7. Descriptive data are presented as percentage; a *P* value of less than 0.05 was considered statistically significant, continuous data were described using mean, median, SD, and range wherever appropriate. Categorical variables were described using proportions.

Results

A total of 61 consecutive patients with chronic nonbloody diarrhea and IBS-D predominant and normal colonoscopic finding who fulfilled our inclusion criteria were recruited.

The study was conducted in Assiut University Teaching Hospital, which is considered as a tertiary-level hospital providing medical services to all patients in Upper Egypt; there is a well-equipped specialized unit for GI endoscopy where both diagnostic and therapeutic upper and lower GI endoscopy were performed as daily practice; cases with chronic diarrhea for investigation were referred to this unit from most of the governorates in Upper Egypt; in our study, patients came from Assiut, Al-Minia, Qena, Sohaj, and Aswan (Table 2).

Our patients who were diagnosed with MC were 50% female patients and 50% male patients; their age ranged from 22 to 58 years and their mean age was 37.39 ± 11.25 years; past drug history of NSAIDs and proton pump inhibitors was positive in 61.1% of them (Table 3).

Abdominal pain, nocturnal diarrhea and weight loss were the most common symptoms with no reported case associated with stool incontinence. About 18 (29.5%) patients in our study were diagnosed with MC based on the histopathological criteria, whereas the rest had nonspecific colitis.

There were 24 patients with IBS-D predominant; their diagnosis was based on Rome II criteria; four patients from this group proved to have MC after undergoing endoscopy and biopsy, two had CC, and two had LC (Figs. 1–4).

Table 2 Demographic data of patients with microscopic colitis

	n=18 (*n* (%))
Age	
Mean±SD	37.39±11.25
Range	22.0-58.0
Sex	
Male	9 (50.0)
Female	9 (50.0)
Smoking	
Smoker	5 (27.8)
Nonsmoker	13 (72.2)
Drugs	
Yes	11 (61.1)
No	7 (38.9)

Table 3 Clinical symptoms of patients with microscopic colitis

	n=18 (*n* (%))
Abdominal pain	15 (83.3)
Nocturnal diarrhea	14 (77.8)
Weight loss	11 (61.1)
Vomiting	6 (33.3)
Anorexia	4 (22.2)
Tenesmus	4 (22.2)
Fever	1 (5.6)
Stool incontinence	0 (0.0)

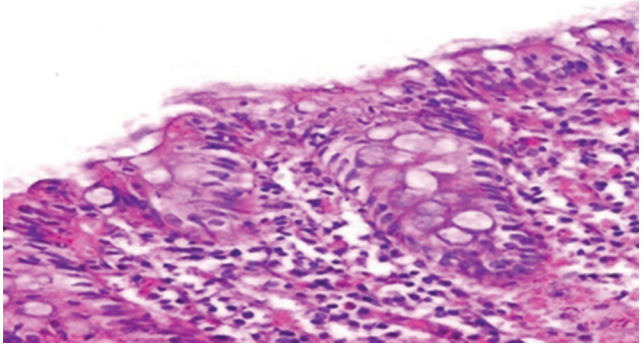
Discussion

This was a cross-sectional study conducted on a total of 61 patients with chronic watery diarrhea: 37 patients had chronic watery diarrhea on investigation and 24 patients had IBS-D predominant; their diagnosis was based on Rome II criteria.

Demographic data of our patients were as follows: age range: 15–72 years, with mean age 37.49 ± 12.28 years, 33 (54.1%) patients were male and 28 (45.9%) patients female; about 18 (29.5%) patients from the total group were diagnosed with MC, and their age ranged from 22 to 58 years, with mean age of 37.39 years: nine (50%) of them were female and nine (50%) were male.

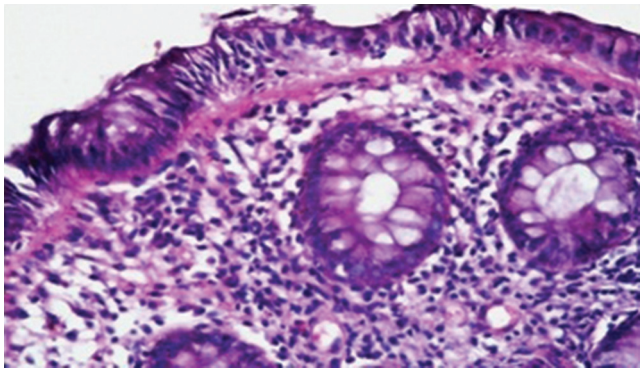
This study demonstrates that MC is a relatively common cause of chronic watery diarrhea of unknown cause in Upper Egypt; we found that 18 (29.5%) patients in our study had MC; a previous retrospective study conducted in Egypt by Gado *et al.* [10] on 44 patients with chronic watery diarrhea and normal endoscopic finding found that 22 (50%) had MC.

Figure 1



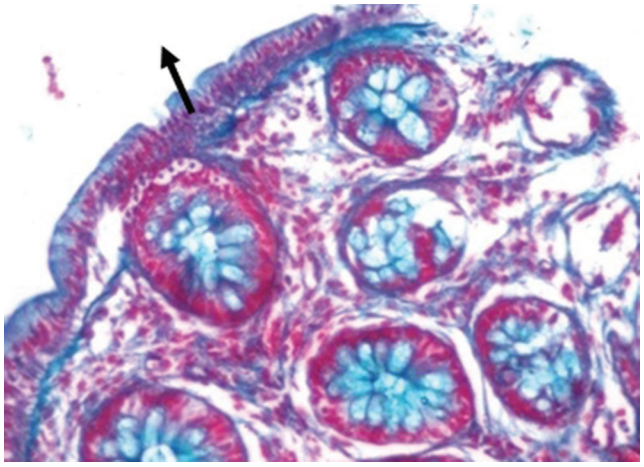
High-power view of lymphocytic colitis showed increased intraepithelial lymphocytes (hematoxylin and eosin, ×400).

Figure 2



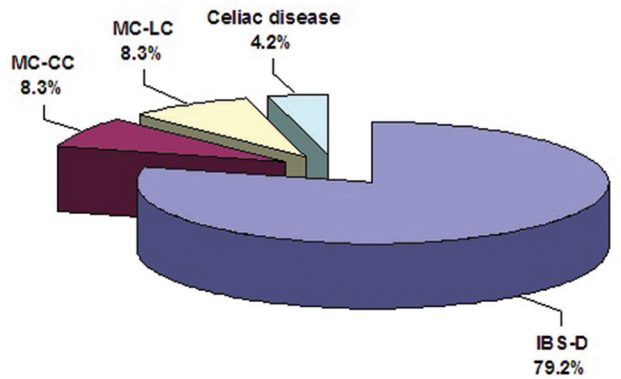
Collagenous colitis showing thickening of the subepithelial collagen band and inflammatory cells in the lamina propria (hematoxylin and eosin, ×400).

Figure 3



Collagenous colitis with a thickened subepithelial collagen band (arrow) Masson trichrome (×400).

Figure 4



Frequency of microscopic colitis (MC) in patients with predominant irritable bowel syndrome–diarrhea (IBS-D). CC, collagenous colitis; LC, lymphocytic colitis.

Larrson *et al.* [7] conducted a similar study on 78 patients with chronic nonbloody diarrhea and normal colonoscopic findings and found that 15 (19%) patients had MC; another study conducted on 129 Turkish patients with chronic watery diarrhea of unexplained etiology with normal colonoscopic finding found that 15 (11.6%) of them had MC [11]; our results were most similar to those found in a study conducted in Iran on 90 patients with chronic watery diarrhea and normal colonoscopic finding, which found that 25 (27.8%) patients showed MC [12].

The etiology of MC is still unknown, but leading models of pathogenesis point toward autoimmunity, an immune or inflammatory response to luminal factors and medications; in the case of CC, myofibroblast dysfunction is a probable factor [13].

Several potential mechanisms have been proposed to explain the pathophysiology of MC, although no dominant mechanism has emerged. The distribution differences for various geographic areas could be justified by exposure to different risk factors [14].

In our study, MC patients showed an equal ratio between women and men; previously published data regarding the sex distribution of MC in some studies found a high female-to-male ratio ranging from 3:1 to 9:1 [1,7,13,15–17].

Although MC can be diagnosed in patients of any age, previously published studies showed that it is more common at an older age [1,7,13,17–22]. In our study, the mean age at diagnosis was lower in comparison with other studies, although this result needs to be confirmed in a larger sample size in future studies.

MC and predominant IBS-D share similar symptoms and endoscopic appearances; in fact, there are no markers that the predict differential diagnosis between the two; currently, the general view is that a patient with CWND who fulfills the criteria for predominant IBS-D should be administered only a limited number of tests if he/she has neither alarming symptoms nor any abnormalities in standard blood analyses [19]

The fact that there is considerable overlap between symptoms of IBS-D and those of MC was demonstrated in a recent retrospective study performed on a population-based cohort of MC patients using the 'Rochester Epidemiological Project' database, which showed that 56% of MC patients fulfilled the Rome II criteria for predominant IBS-D [23].

Our results showed that the frequency of MC in patients fulfilling the Rome II criteria of IBS-D is 16.7%.

Ozdil *et al.* [24] conducted a study and found that seven (4.325) out of 162 patients with IBS-D had MC; Hilmi *et al.* [5] conducted a study on 58 Malaysian patients with IBS-D and normal colonoscopic findings and found that 14.9% showed microscopic inflammation; Stoicescu *et al.* [25] conducted a study to evaluate the

prevalence of MC in IBS-D and found that 6% of their patients had histologically confirmed MC; Tavakkoli *et al.* [26] conducted another study in Iran and found that 9.4% of their IBS-D patients had MC.

Conclusion

Our study showed that MC is not uncommon in Upper Egypt patients with chronic watery diarrhea and normal colonoscopic findings. Biopsy of the normal colonic mucosa in patient with chronic watery diarrhea is emphasized to reach to a definite diagnosis of MC.

Abdominal pain, nocturnal diarrhea and weight loss were the most common clinical manifestations of MC.

MC types, LC, and CC have almost similar clinical presentations and there is no diagnostic laboratory marker; thus, histopathologic diagnosis is the only reliable method for differentiation between these subtypes.

Collaboration between treating physicians, endoscopists and pathologists is crucial for diagnosing MC. Our results reinforce the idea that MC should be suspected not only in older patients but also in the younger population. IBS-D patients have presentations almost similar to MC patients and a few of them can be misdiagnosed as having functional GI disease.

Recommendations

Large-scale prospective studies are encouraged to evaluate the real magnitude of this disease and study the response to treatment and the outcome of this missed subject in our locality.

To gain further insight into this subject and differentiate it well from functional bowel syndromes, prospective studies are needed to identify the risk factors and main distinguishing features between predominant IBS-D and MC.

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Conflicts of interest

There are no conflicts of interest.

References

1 Williams J, Kaplan GG, Makhija S, Urbanski SJ, Dupre M, Panaccione R, Beck PL. Microscopic colitis – defining incidence rates and risk factors: a population-based study. Clin Gastroenterol Hepatol 2008; 6:35–40.

2 Ianiro G, Cammarota G, Valerio L, Annicchiarico BE, Milani A, Siciliano M. Microscopic colitis. World J Gastroenterol 2012; 18:6206–6215.

3 Mohamed N, Marais M, Bezuidenhout J. Microscopic colitis as a missed cause of chronic diarrhea. World J Gastroenterol. 2011; 17:1996–2002.

4 Storr MA. Microscopic colitis: epidemiology, pathophysiology, diagnosis and current management – An update 2013. ISRN Gastroenterol 2013; 15:2–12.

5 Hilmi I, Hartono JL, Pailoor J, Mahadeva S, Goh KL. Low prevalence of 'classical' microscopic colitis but evidence of microscopic inflammation in Asian irritable bowel syndrome patients with diarrhoea. BMC Gastroenterol 2013; 13:80.

6 Shen B, Khan K, Ikenberry SO, Anderson MA, Banerjee S, Baron T. The role of endoscopy in the management of patients with diarrhea. Gastrointest Endosc 2010; 71:887–892.

7 Lazenby AJ, Yardley JH, Giardiello FM, Jessurun J, Bayless TM: Lymphocytic ("microscopic") colitis: a comparative histopathologic study with particular reference to collagenous colitis. Hum Pathol 1989;20:18–28.

8 Calabrese C, Gionchetti P, Liguori G, Areni A, Fornarini GS, Campieri M, *et al.* Clinical course of microscopic colitis in a single-center cohort study. J Crohns and Colitis 2011; 5:218–221.

9 Thoua NM, Murray CD. Irritable bowel syndrome. Medicine (Baltimore) 2011; 39:214–217.

10 Gado AS, El Hindawi AA, Akl MM, Axon AT. Prevalence of microscopic colitis in patients with chronic diarrhea in Egypt: a single-center study. Saudi J Gastroenterol 2011; 17:383–386.

11 Erdem LL, Yildinm S, Akbayir N, Yilmaz B, Yenice N, Gültekin OS, *et al.* Prevalence of microscopic colitis in patients with diarrhea of unknown etiology in Turkey. World J Gastroenterol 2008; 14:4319–4323.

12 Tabrizchie H, Zahedie M, Hayatbakhsh A, Jafari EA, Haghdoost A, Hosseini S. Frequency and distribution of microscopic findings in patients with chronic non-bloody diarrhea and normal colonoscopy. Iran J Med Sci 2008; 33:101–105.

13 Pardi DS, Loftus EV, Smyrk TC, Kammer PP, Tremaine WJ, Schleck CD, *et al.* The epidemiology of microscopic colitis: a population based study in Olmsted County, Minnesota. Gut 2007; 56:504–508.

14 Münch A, Aust D, Bohr J, Bonderup O, Fernández Bañares F, Hjortswang H, *et al.* Microscopic colitis: current status, present and future challenges. J Crohns Colitis 2012; 6:932–945.

15 Protic M, Jojic N, Bojic D, Milutinovic S, Necic D, Bojic B, *et al.* Mechanism of diarrhea in microscopic colitis. World J Gastroenterol 2005; 11:5535–5539.

16 Kao KT, Pedraza BA, McClune AC, Rios DA, Mao Y, Zuch RH, *et al.* Microscopic colitis: a large retrospective analysis from a health maintenance organization experience. World J Gastroenterol 2009; 15:3122–3127.

17 Vigren L, Olesen M, Benoni C, Sjöberg K. An epidemiological study of collagenous colitis in southern Sweden from 2001–2010. World J Gastroenterol 2012; 18:2821–2826.

18 Bohr J, Wickbom A, Hegedus A, Nyhlin N, Hultgren Hornquist E, Tysk C. Diagnosis and management of microscopic colitis: current perspectives. Clin Exp Gastroenterol 2014; 7:273–284.

19 Fernandez-Banares F, Salas A, Forne M, Esteve M, Espinos J, Viver JM. Incidence of collagenous and lymphocytic colitis: a 5-year population-based study. Am J Gastroenterol 1999; 94:418–423.

20 Olesen O, Eriksson S, Bohr J, Jarnerot G, Tysk C. Microscopic colitis: a common diarrhoeal disease. An epidemiological study in Orebro, Sweden, 1993–1998. Gut 2004; 53:346–350.

21 Tysk C, Wickbom A, Nyhlin N, Eriksson S, Bohr J. Recent advances in diagnosis and treatment of microscopic colitis. Ann Gastroenterol 2011; 24:253–262.

22 Kane JS, Everett SM, Samji S, Michelotti F, Ford AC. Development and validation of a scoring system to identify patients with microscopic colitis. Clin Gastroenterol Hepatol 2015; 13:1125–1131.

23 Limsui D, Pardi DS, Camilleri M, Loftus EV, Kammer PP, Tremaine WJ. Symptomatic overlap between irritable bowel syndrome and microscopic colitis. Inflamm Bowel Dis 2007; 13:175–181.

24 Ozdil K, Calhan T, Kahraman R, Nigdelioglu A, Akyuz U, Sokmen HM. The frequency of microscopic and focal active colitis in patients with irritable bowel syndrome. BMC Gastroenterol 2011; 11:2–6.

25 Stoicescu A, Gheorghe C, Dumbrava M, Diculescu M. Microscopic colitis – A missed diagnosis in diarrhea-predominant irritable bowel syndrome. Maedica (Buchar) 2012; 7:3–9.

26 Tavakkoli H, Esmaeili FS, Emami MH, Mahzouni P, Haghdani S. Is microscopic colitis a missed diagnosis in diarrhea-predominant irritable bowel syndrome? J Res Med Sci 2008; 13:202–206.