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## Original Article

# Prevalence of Microscopic Colitis in Chronic Diarrhea Patients Attending Al-Azhar University Hospital in New Damietta

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## Abstract

**Background:** Microscopic colitis [MC] is an underdiagnosed cause of chronic diarrhea that characterized histologically as lymphocytic colitis [LC] or collagenous colitis [CC]. The condition can manifest with watery, non-bloody diarrhea, and is frequently misdiagnosed, owing to the lack of endoscopic findings. The purpose of this study is to evaluate the frequency of MC in patients presented with chronic diarrhea attending Al-Azhar University Hospital in New Damietta.

**Patients and Methods:** A cross-sectional study was carried out in the Department of Hepato-gastroenterology and Infectious Diseases, Al-Azhar University Hospital, New Damietta, from December 2023 to December 2024. A total of 262 adult patients [≥18 years old] diagnosed with chronic diarrhea [≥4 weeks] were enrolled. We excluded patients with infectious colitis or inflammatory bowel disease or systemic diseases affecting diarrhea, drug-induced diarrhea and major comorbidities. All subjects were assessed through detailed clinical examination, laboratory tests and colonoscopy with thorough biopsy sampling of the various colonic segments. Microscopic subtypes of colitis were identified by histopathological examination.

**Results:** Among the 262 patients, 22 [8.4%] were diagnosed with microscopic colitis. Lymphocytic colitis was found in 12 patients [4.6%], while collagenous colitis was identified in 10 patients [3.8%]. Endoscopic findings were unremarkable in 59.5% of cases, highlighting the importance of biopsy in diagnosing MC. MC patients had a significantly longer duration of diarrhea [4.5 ± 1.5 months vs. 1.8 ± 0.9 months; p<0.001], higher prevalence of nocturnal diarrhea [p=0.005], weight loss [p=0.012], and bloating [p=0.020]. Proton pump inhibitor [PPI] use was significantly higher in MC patients compared to non-MC patients [63.6% vs. 39.6%, p=0.02].

**Conclusion:** Microscopic colitis was proven in 8.4% of all patients with chronic diarrhea, where lymphocytic colitis appeared a little bit more often than collagenous colitis. The case highlights the importance of performing colonic biopsies in patients with chronic diarrhea and normal endoscopy.

**Keywords:** Microscopic colitis; Chronic diarrhea; Lymphocytic colitis; Collagenous colitis; Colonoscopy; Histopathology.

## INTRODUCTION

Chronic diarrhea is a frequent gastrointestinal complaint that profoundly affects patients' quality of life and proves a diagnostic challenge to clinicians. Chronic diarrhea is defined as diarrhea lasting more than 4 weeks, and may be seen in a variety of etiologies including infectious, inflammatory, functional, and malabsorptive disorders [1] .

Microscopic colitis [MC] is an increasingly recognized cause of chronic watery diarrhea, especially in the elderly, among these. Microscopic colitis includes two primary subtypes: lymphocytic colitis [LC] and collagenous colitis [CC], both of which are defined by specific histopathological findings and the lack of significant endoscopic findings [2].

Despite its clinical significance, MC remains underdiagnosed, often due to the reliance on endoscopic findings alone, which are typically normal or nonspecific [3].

Microscopic colitis is a non-idiopathic inflammatory bowel disease that affects the colon; its prevalence is geographically heterogeneous and has been claimed to be rising over the last few decades, likely due to increased awareness and better diagnostics. Prevalence rates have been reported in studies from Western countries to vary between 4 and 19 per 100 000 people/year and to be more common in older populations and women [4].

Nonetheless, there is scant data regarding the prevalence of MC in Middle Eastern and North African populations including Egypt. A gap in the literature exists, emphasizing the importance of exploring region-specific studies describing the epidemiology and clinical characteristics of MC in these regions. Endoscopic findings are often bland so the diagnosis of microscopic colitis depends on the histopathological examination of colonic biopsies. Lymphocytic colitis is defined by an increased number of intraepithelial lymphocytes [>20 lymphocytes per 100 epithelial cells], while collagenous colitis is diagnosed by the presence of a thickened subepithelial collagen band [>10 µm] and inflammatory change [5].

Both subtypes share similar clinical presentations, including chronic watery diarrhea, abdominal pain, and weight loss, which can mimic other gastrointestinal disorders such as irritable bowel syndrome [IBS] or inflammatory bowel disease [IBD]. This overlap in symptoms often leads to delayed or missed diagnoses, highlighting the importance of routine colonic biopsies in patients with chronic diarrhea and normal endoscopic findings [6].

Microscopic colitis has been linked to a number of risk factors, with autoimmune diseases, smoking, and certain medications like nonsteroidal anti-inflammatory drugs [NSAIDs], proton pump inhibitors [PPIs] and selective serotonin reuptake inhibitors [SSRIs] being among them [7].

The role of PPIs involved in the pathogenesis of MC is of particular concern as these drugs are universally prescribed and have been associated with alterations in intestinal microbiota and intestinal permeability[8].

Understanding these associations is crucial for identifying at-risk populations and optimizing diagnostic and therapeutic strategies.

## THE AIM OF THE WORK

This study aims to assess the prevalence of microscopic colitis in patient admitted with chronic diarrhea to al-Azhar hospital in new Damietta.

## PATIENTS AND METHODS

**Study Design:** A cross-sectional study was conducted in the Department of Hepato-gastroenterology and Infectious Diseases at Al-Azhar University, New Damietta Hospitals. Between December 2023 to December 2024.

**Sample Size:** Based on a previous study where the prevalence of microscopic colitis in chronic diarrhea patients was 21.7%, the sample size was estimated using Epi Info version 3, an open-source calculator, with a 95% confidence level. The required sample size was 262 patients with chronic diarrhea. All participants were informed about the study's aim, and informed consent was obtained from each participant [9].

**Inclusion Criteria:** All adult patients [aged 18 or older] who met the criteria for chronic diarrhea defined as more than three loose or liquid bowel motions every day for at least four weeks were referred to the colonoscopy unit for diagnostic colonoscopy.

**Exclusion Criteria:** Patients with Infectious colitis; patients with pervious colonoscopy or histopathologic documentation of IBD [ulcerative colitis, Crohn's disease]; Systemic diseases associated with chronic diarrhea (e.g., diabetes mellitus and Thyroid disease); drugs causing chronic diarrhea (e.g., antibiotics, antidepressants, and ACE inhibitors); chronic diarrhea due to decreased digestion, e.g., pancreatic insufficiency and bile acid deficiency; inadequate bowel preparation; recent myocardial infarction and major comorbidities; uncooperative patients.

All patients underwent full history, clinical examination, laboratory investigations and colonoscopy with biopsy. The laboratory workup included complete blood count [CBC], Electrolytes, including serum sodium [Na] and potassium [K], Liver function tests, including serum transaminases [AST, ALT], serum albumin, serum bilirubin [total, direct], prothrombin time, and concentration, Inflammatory markers [CRP, ESR], Thyroid-stimulating hormone [TSH], fasting blood sugar [FBS], and 2-hour postprandial blood sugar [PPBS], and Stool analysis and culture

**Colonoscopy and Biopsy Procedure:** All included patients underwent a full colonoscopy under conscious sedation following bowel preparation for two days prior to the procedure. Written informed consent was obtained from each patient before the procedure.

**Equipment and Procedure:** The colonoscopy was performed using a high-definition video endoscope [Fujifilm] by an experienced endoscopist. The entire colon was thoroughly examined, starting from the rectum and advancing through the left-sided colon [descending colon, sigmoid colon], right-sided colon [cecum, ascending colon, transverse colon], and rectum. Any obscured mucosal areas were carefully washed to ensure a clear view of the mucosa.

**Biopsy Sampling:** Multiple biopsies were taken from normal-appearing mucosa in various parts of the colon. At least two biopsies were obtained from each site:

- **Right-sided colon:** Cecum, ascending colon, and transverse colon.
- **Left-sided colon:** Descending colon and sigmoid colon.
- **Rectum**: Each biopsy sample was immediately placed in bottles containing 10% formalin and transported to the pathology lab for processing. The biopsies were handled under the supervision of a gastrointestinal pathologist to ensure quality and consistency in preparation for histological examination.

**Histopathological Examination:** The biopsy tissues were prepared for light microscopic examination using Hematoxylin-Eosin [H&E] staining. In cases where the initial results were inconclusive or ambiguous, Masson trichrome staining was performed to assess the presence and thickness of the subepithelial collagen layer, which is essential for diagnosing microscopic colitis.

**Intraepithelial Lymphocyte [IEL] Count:** The number of intraepithelial lymphocytes [IELs] was calculated by counting lymphocytes per 100 inter-cryptal epithelial cells. A minimum of five non-contiguous inter-cryptal spaces were examined, excluding lymphoid follicle zones. The mean IEL count was expressed as the number of IELs per 100 epithelial cells.

**Subepithelial Collagen Layer Thickness:** The thickness of the subepithelial collagen band was measured using an optical micrometer. Biopsies were considered normal when the collagen layer was less than 5 µm, and abnormal if the collagen layer exceeded 10 µm in thickness.

**Diagnostic Criteria for Biopsies findings:**

**Normal Findings:** Less than five IELs per 100 surface epithelial cells, a collagen layer thinner than 5 µm, and no pathological changes in the epithelium or lamina propria [5].

**Lymphocytic Colitis [LC]:** The diagnosis of lymphocytic colitis diagnosed by increase in intraepithelial lymphocytes [IELs] to more than 20 IELs per 100 surface epithelial cells, along with an increased inflammatory infiltrate in the lamina propria. The collagenous band is not significantly thickened [<10 µm]. Additional immune-histochemical staining, such as CD3 staining, was applied in borderline cases [25].

**Collagenous Colitis [CC]:** Collagenous colitis is diagnosed by the presence of a thickened subepithelial collagen band [>10 µm] combined with increased inflammatory infiltrate in the lamina propria. In cases where further clarification is needed, Masson's Trichrome stain may be applied to assess collagen thickness [25].

**Incomplete Microscopic Colitis [MCi]:** Patients who exhibit clinical signs of microscopic colitis [MC] but whose biopsies do not fully meet the histological criteria for LC or CC are classified as having incomplete MC.

**Incomplete Collagenous Colitis [CCi]:** Subepithelial collagen band thickness is moderately increased [5–10 µm], and IEL count remains below 20.

**Incomplete Lymphocytic Colitis [LCi]:** The number of IELs ranges between 10 and 20 per 100 epithelial cells [25].

**Nonspecific Colitis [NSC]:** Nonspecific colitis is characterized by fewer than 5 IELs per 100 surface epithelial cells and a collagen layer less than 5 µm. Inflammatory changes exceed the normal limits but are not specific to any disease [25].

**Statistical analysis:** Data were analyzed using SPSS version 26 [IBM, Chicago, IL, USA]. Descriptive statistics were presented as means ± standard deviation [SD] for continuous variables and as numbers and percentages for categorical variables. The Kolmogorov-Smirnov test was used to assess data normality. Comparisons between groups were performed using: Chi-square test or Fisher's exact test for categorical variables. Independent t-test or Mann-Whitney U test for continuous variables, depending on data distribution. A p-value <0.05 was considered statistically significant.

**Prevalence Calculation:** Microscopic colitis prevalence was determined in chronic diarrhea patients after exclusion of all identifiable causes according to predefined exclusion criteria. Inclusion criteria were rigorously applied, and only patients who underwent the complete diagnostic work-up including colonoscopy with sufficient biopsy sampling and histo-pathological examination were included in the final analysis. Prevalence was defined as the number of patients diagnosed with microscopic colitis [lymphocytic or collagenous] divided by the total number of eligible patients included in the study.

**Ethical Considerations:** The study was approved by the Faculty of Medicine Ethics Committee, Al-Azhar University, New Damietta. Permissions were obtained from the hospital administration. Written informed consent was obtained from all participants prior to study enrollment. The study adhered to the principles of the Declaration of Helsinki [1975].

## RESULTS

The present study was a cross sectional study included 262 patients with chronic diarrhea conducted in the Department of Hepato-gastroenterology and Infectious Diseases at Al-Azhar University, New Damietta Hospitals. Demographic and lifestyle characteristics of the study population, including age [mean: 45.3 ± 12.4 years; range: 18–75], age groups [18–30: 28.6%, 31–50: 42%, >50: 29.4%], gender [male: 54.2%, female: 45.8%], smoking status [smokers: 29.8%, non-smokers: 70.2%], and residency [urban: 61.1%, rural: 38.9%] [**Table 1].**

**Table [2]** showed that The prevalence of microscopic colitis was 8.4%, with lymphocytic colitis accounting for 4.6% and collagenous colitis for 3.8%.

Comparing endoscopic findings with histological diagnoses in 262 individuals. Normal histology [74 cases] was most common, often with normal endoscopy [61 cases] or mild erythema [10 cases]. Microscopic colitis [22 cases] showed normal endoscopy, while chronic nonspecific colitis [113 cases] was linked to varied findings. Colorectal cancer [16 cases] and polyps [12 cases] were also noted, alongside less frequent conditions like ulcerative colitis [14 cases] and Crohn's disease [3 cases] (Table 3). Comparing patients with microscopic colitis [MC, N=22] and without MC [N=240] across variables like age, gender, smoking status, and diarrhea characteristics. Patients with MC had a longer duration of diarrhea [4.5 ± 1.5 months vs. 1.8 ± 0.9 months, p<0.001], but no significant differences were found in age, gender, smoking status, or daily stool frequency [p>0.05] (Table 4).

Comparing symptoms, comorbidities and drug intake between patients with microscopic colitis [mc, n=22] and without mc [n=240].

mc patients had significantly higher rates of nocturnal diarrhea [36% vs. 14.6%, p=0.005], weight loss [41% vs. 18.8%, p=0.012], bloating [45% vs. 25%, p=0.020], and flatulence [50% vs. 20.8%, p=0.003], but lower abdominal pain [55% vs. 75%, p=0.011]. bronchial asthma [9.1% vs. 2.1%, p=0.01] and PPI use [63.6% vs. 39.6%, p=0.02] were more common in mc patients, while other variables showed no significant differences (Table 5).

**Table [1]:** Demographic Data of the studied Patients

| Characteristic | | Mean ± SD or Number | Percentage | Range |
|---|---|---|---|---|
| Age [years] | | 45.3 ± 12.4 | - | 18 - 75 |
| Age groups | **18-30** | 75 | 28.6% | |
| | **31-50** | 110 | 42.0% | |
| | **>50** | 77 | 29.4% | |
| Gender | **Male** | 142 | 54.2% | - |
| | **Female** | 120 | 45.8% | - |
| Smoking Status | **Smoker** | 78 | 29.8% | - |
| | **Non Smoker** | 184 | 70.2% | - |
| Residency | **Urban** | 160 | 61.1% | - |
| | **Rural** | 102 | 38.9% | - |

**Table [2]:** Histopathological Finding and Prevalence of Microscopic Colitis among Studied Patients

| Variables | | Number | Percentage [%] |
|---|---|---|---|
| Microscopic colitis | **Lymphocytic colitis** | 12 | 4.6% |
| | **Collagenous colitis** | 10 | 3.8% |
| Prevalence | | 22 | 8.4% |

**Table [3]: Correlation between endoscopic findings and histological diagnoses for the studied patients:**

| Endoscopic Findings | Normal | Mild Erythema | Ulcerative Colitis | Crohn's Disease | Colorectal Mass | Diverticulosis | Colonic Polyps | Total |
|---|---|---|---|---|---|---|---|---|
| Normal Histology | 61 | 10 | _ | _ | _ | 3 | _ | **74** |
| Microscopic Colitis [Total] | 22 | - | - | - | - | - | - | **22** |
| Ulcerative Colitis | _ | _ | 14 | | | | | **14** |
| Crohn's Disease | _ | _ | 2 | 1 | _ | _ | _ | **3** |
| Eosinophilic Colitis | 1 | 1 | - | - | - | - | - | **2** |
| Chronic Nonspecific Colitis | 69 | 26 | 5 | 3 | | 10 | | **113** |
| Bilharzial Colitis | _ | 3 | _ | _ | _ | _ | _ | **3** |
| Incomplete Microscopic Colitis [MCI] | 3 | - | - | - | - | - | - | **3** |
| Colorectal Cancer [CRC] | - | - | - | - | 16 | | - | **16** |
| Hyperplastic Polyps | - | - | - | - | - | - | 9 | **9** |
| Adenomatous Polyps | - | - | - | - | - | - | 3 | **3** |
| Total | **156** | **40** | **21** | **4** | **16** | **13** | **12** | **262** |

**Table [4]: Comparison Between MC and Non-MC Patients by Age, Gender, Smoking Status, and Diarrhea Characteristics**

| Variables | Patients with MC [N=22] N [%] / Mean ± SD / Median [Range] | Patients without MC [N=240] N [%] / Mean ± SD / Median [Range] | P Value |
|---|---|---|---|
| **Demographic characteristics** | | | |
| Age [years] | 45.7 ± 7.78 | 40.98 ± 15.2 | 0.15 [NS] |
| Gender | | | |
| - Male | 8 [36.4%] | 134 [55.84%] | 0.12 [NS] |
| - Female | 14 [63.6%] | 106 [44.16%] | |
| Smoking Status | | | |
| - Smoker | 7 [31.8%] | 71 [29.6%] | 1.000 [NS] |
| - Non-Smoker | 15 [68.2%] | 169 [70.4%] | |
| **Diarrhea Characteristics** | | | |
| - Number of motions / day | 7 ± 2 | 5 ± 2 | 0.450* [NS] |
| - Median | 5 | 3 | - |
| - Range | 4 – 9 | 3 – 8 | - |
| - Duration of diarrhea [months] | 4.5 ± 1.5 | 1.8 ± 0.9 | **<0.001* [HS]** |
| - Continuity of loose motions | | | |
| - Continuous | 18 | 157 | 0.100† [NS] |
| - Intermittent | 4 | 83 | |

NS: Non significance, HS: Highly significance, *Mann -Whitney U test., †Chi-square test. And MC, microscopic colitis

**Table [5]:** Comparing Symptoms, Comorbidities, and Drug Intake Between Patients with and Without Microscopic Colitis

| Variables | Patients with MC [N=22] N [%] | Patients without MC [N=240] N [%] | P Value |
|---|---|---|---|
| **Symptoms** | | | |
| - Abdominal pain | 12 [55%] | 180 [75%] | 0.011 [S] |
| - Nocturnal diarrhea | 8 [36%] | 35 [14.6%] | 0.005 [HS] |
| - Weight loss | 9 [41%] | 45 [18.8%] | 0.012 [S] |
| - Vomiting | 4 [18%] | 30 [12.5%] | 0.300 [NS] |
| - Anorexia | 1 [4.5%] | 10 [4.2%] | 0.800 [NS] |
| - Stool incontinence | 1 [4.5%] | 5 [2.1%] | 0.170 [NS] |
| - Bloating | 10 [45%] | 60 [25%] | 0.020 [S] |
| - Flatulence | 11 [50%] | 50 [20.8%] | 0.003 [HS] |
| **Comorbidities** | | | |
| - No Comorbidity | 17 [77.3%] | 211 [87.9%] | 0.20 [NS] |
| - Rheumatoid Arthritis | 1 [4.5%] | 4 [1.7%] | 0.33 [NS] |
| - Ischemic Heart Disease | 1 [4.5%] | 9 [3.8%] | 0.53 [NS] |
| - Bronchial Asthma | 2 [9.1%] | 5 [2.1%] | 0.01 [S] |
| - Hypertension | 1 [4.5%] | 13 [5.4%] | 0.71 [NS] |
| - Chronic Kidney Disease | 1 [4.5%] | 7 [2.9%] | 0.47 [NS] |
| **Drug Intake** | | | |
| - NSAIDs | 3 [13.6%] | 11 [4.6%] | 0.08 [NS] |
| - PPIs | 14 [63.6%] | 95 [39.6%] | 0.02 [S] |
| - P-CABs | 2 [9.1%] | 12 [5.0%] | 0.33 [NS] |
| - Beta Blockers | 1 [4.5%] | 11 [4.6%] | 1.00 [NS] |
| - Statins | 1 [4.5%] | 9 [3.8%] | 0.59 [NS] |

NSAIDs: Nonsteroidal Anti-Inflammatory Drugs, PPIs: Proton Pump Inhibitors, , P-CABs: Potassium-Competitive Acid Blockers, NS: Non significance , S: significance

## DISCUSSION

Microscopic colitis [MC] is an inflammatory bowel disease that may go unnoticed during the diagnostic process due to the less obvious presentation [chronic watery, non-bloody diarrhea], which needs a biopsy to reach a definitive diagnosis. It comprises lymphocytic colitis [LC] and collagenous colitis [CC] and has been associated with autoimmune disorders, certain medications such as NSAIDs and PPIs, and smoking [9].

In Egypt, where studies in this area are limited but show that MC is a common cause of chronic diarrhea. Prevalence rates differ between studies in Egypt, but with increasing use of the medication, in addition to environmental and genetic factors, the condition may increasingly be recognized by the medical establishment [10].

The primary aim of this study was to evaluate the prevalence and clinical characteristics of microscopic colitis among patients presenting with chronic watery diarrhea. Additionally, the study sought to identify the associated demographic, clinical, and laboratory factors that may serve as predictors for MC, and to compare our findings with those from previous studies conducted in both local and international settings. This gender distribution matches the previous studies in Egypt such as the work by **El-shafei *et al.*,** where males present more frequently in the younger demographic while females tend to present more so with microscopic colitis, particularly in middle-aged individuals. The gender difference observed in our cohort differs also from those observed elsewhere globally, where the incidence is higher in females, particularly collagenous colitis [11].

Another study by **Münch *et al.*** highlighted the importance of smoking as a significant risk factor for microscopic colitis, particularly collagenous colitis [CC]. This European multi-centered study detected higher incidence rates of CC across the different countries based on smoking status and found that both current and former smokers had an increased risk of CC compared to non-smokers. Smoking was found to be one of the most consistent environmental risk factors, contributing to the increased risk of CC in European populations, which presented an increased risk by up to three-fold among smokers. The relationship between smoking and lymphocytic colitis [LC] was shown as well, but did not have the same strength as CC [12].

The findings from **Münch *et al.*** contrast with our study, where no significant association between smoking and microscopic colitis was identified. This discrepancy could be explained by differences in smoking prevalence and patterns between European and Egyptian populations. In Europe, smoking rates, particularly among women, tend to be higher, which may amplify the role of smoking as a risk factor for CC. In contrast, the lower smoking rates in Egypt, especially among women, may reduce the overall impact of smoking

on the development of MC. Furthermore, differences in genetic susceptibility and environmental exposures may contribute to the varying significance of smoking as a risk factor across regions.

Another point of divergence is the age distribution of MC patients. Studies from the United States, such as the one conducted by **Thijs *et al.*** found the mean age at diagnosis to be significantly higher, with most cases occurring in patients over the age of 60. In contrast, the mean age in our study was 45.3 years. This younger age profile in our Egyptian cohort suggests that MC may manifest earlier in developing countries, potentially due to different environmental or infectious exposures that could accelerate the disease's onset [13].

Compared to the study by **Nassar et al.** [14], which found a higher median age of 45 years among MC patients and a predominantly female population, our findings suggest that the age and gender distribution of MC in Egypt are broadly in line with those reported in other regions. However, our study did not find a statistically significant difference between age and gender among MC and non-MC patients, similar to the findings of **El-Shafei *et al.*** [11], who reported no significant gender differences but a higher incidence in women.

Endoscopic findings in our study revealed that 59.5% of patients had normal results, with a smaller proportion showing mild erythema [15.2%] or other significant findings such as ulcerative colitis [8.0%] and colorectal masses [6.1%]. These results underscore the challenges of diagnosing MC based on endoscopic findings alone, as nearly 60% of patients exhibited no macroscopic abnormalities. This observation is consistent with international studies, such as one conducted in Sweden, where endoscopic normalcy was common in MC patients [15]. Similarly, a study from Egypt conducted by **Gado *et al.*** [16] reported that most patients with chronic diarrhea had normal endoscopic results, reinforcing the importance of histopathological examination for diagnosing MC.

Histological analysis revealed that 43.1% of patients had chronic nonspecific colitis, while MC was diagnosed in 8.4% of patients, with LC being slightly more common than CC [4.6% vs. 3.8%]. These findings are comparable to reports from the international literature, where LC generally appears to be more prevalent than CC [17]. However, the prevalence of MC in our study is lower than the 21.7% reported by **Abdel Monem *et al.*** [18] and higher than the 5.2% found in a study by **Nassar et al.** [14], highlighting variability in prevalence estimates across different studies.

One of the most striking differences between our study and international studies is the overall prevalence of MC. In our study, the prevalence of MC was 8.4%, which is lower than the rates reported in several Western studies. For example, the study by **Weimers *et al.*** [19] reported a prevalence of 197.9 cases per 100,000 inhabitants in Denmark, while **Thijs *et al.*** [13] found that MC accounted for approximately 10-13% of cases of chronic diarrhea in Western populations. This lower prevalence in our study may reflect differences in diagnostic practices, as well as differences in the underlying risk factors for MC between regions.

In our study, there was no significant difference in age or gender between MC and non-MC patients, which is consistent with findings from other studies that did not observe significant demographic differences between these groups [17].

Patients with MC in our study experienced significantly more nocturnal diarrhea [36% vs. 14.6%, p=0.005] and weight loss [41% vs. 18.8%, p=0.012] compared to non-MC patients. These findings are consistent with **Cotter *et al.*** [20], who reported that nocturnal diarrhea and weight loss are hallmark symptoms of MC. The higher prevalence of abdominal pain [55%] and bloating [45%] in MC patients further supports the notion that MC is associated with significant gastrointestinal symptoms.

As regard drug use, a study by **Cotter *et al.*** [21] evaluated medication use in 200 MC patients and 400 controls, focusing on PPIs and NSAIDs, through patient interviews and medical records. This study found that PPI use was significantly higher in MC patients [65% vs. 40%, p=0.001], which aligns closely with our findings [63.6% vs. 39.6%, p=0.02]. Both studies also found no significant difference in NSAID use, suggesting that NSAIDs may not be a major risk factor for MC.

A retrospective study by **Fernández-Bañares *et al.*** [22] analyzed comorbidities in 150 MC patients compared to 300 controls without MC, using data from electronic health records over a 5-year period. This study found that bronchial asthma was significantly more common in MC patients [12% vs. 3%, p=0.01], aligning with our findings [9.1% vs. 2.1%, p=0.01]. Both studies also reported no significant differences in hypertension and rheumatoid arthritis, supporting the consistency of these results.

In contrast, a study by **Pardi *et al.*** [23] investigated comorbidities in 120 MC patients and 240 controls using a retrospective chart review. Contrary to our findings, this study found no significant association between bronchial asthma and MC [8% vs. 6%, p=0.45]. While our study reported a significant association [9.1% vs. 2.1%, p=0.01].

**Pardi *et al.*** suggested that the link between MC and bronchial asthma might be influenced by regional or environmental factors, which could explain the discrepancy. Additionally, this study found a higher prevalence of hypertension in MC patients [18% vs. 12%, p=0.04], which contrasts with our finding of no significant difference [4.5% vs. 5.4%, p=0.71]. These differences may stem from variations in study populations or diagnostic criteria.

In Egypt, a study highlighted the significance of microscopic colitis. Study by **Abdel Monem et al.** [18] aimed to estimate the prevalence of microscopic colitis [MC] among patients with chronic watery non-bloody diarrhea [CWND] at Zagazig University Hospitals. Sixty patients were included, and the diagnosis of MC was confirmed via colonoscopy and histopathological examination. The study found that 21.7% of the patients had MC, with lymphocytic colitis [LC] being more common [15%] than collagenous colitis [CC] [6.7%]. The study identified a significant association between MC and the use of nonsteroidal anti-inflammatory drugs [NSAIDs] and proton pump inhibitors [PPIs], and the majority of cases were female. These results highlight the need for histopathological evaluation in patients with CWND, particularly those with a history of PPI or NSAID use, to diagnose MC accurately. However, while our study found a significant association between PPI use and MC,

the strength of this association was somewhat lower than that reported in some Western studies. For example, a study by **Bonderup *et al.*** [24] in Denmark found that PPI use was associated with a more than threefold increased risk of developing MC. This discrepancy could be due to differences in the prevalence of PPI use between countries, as well as differences in the types and dosages of PPIs commonly prescribed. It is also possible that other factors, such as genetic predisposition or the use of other medications, may modify the risk of MC in different populations.

One of the drawbacks of our study, that we didn't focus on specific tests while there were Another study in egypt was conducted by **El-Shafei and colleagues**, the focus was placed on determining the prevalence of microscopic colitis [MC] among a group of 88 Egyptian patients suffering from chronic watery non-bloody diarrhea [CWND] at Al-Hussein University Hospital. The findings revealed that 9.1% of these patients were diagnosed with MC, all cases falling under the category of lymphocytic colitis. The demographic analysis indicated a predominance of females among the affected individuals, with an average age of 48.75 years. The research utilized the fecal calprotectin test as a diagnostic measure, which demonstrated a strikingly high specificity of 100%, yet it bore a low sensitivity rate of just 25%. This study underscores the critical role those histopathological biopsies play in the accurate diagnosis of MC, particularly given that this condition is frequently overlooked during standard endoscopic evaluations [11].

Furthermore, our findings uncovered a markedly greater occurrence of various autoimmune diseases, including celiac disease, among individuals diagnosed with MC. This noteworthy observation underscores the well-recognized link that exists between MC and various autoimmune conditions, highlighting the importance of understanding this connection for effective patient management and treatment [17].

The above systematic review conducted by **Tong *et al.*** presents a comprehensive meta-analysis encompassing 25 studies focused on the incidence of microscopic colitis [MC]. The analysis revealed that the aggregated incidence rates were 4.14 per 100,000 person-years for collagenous colitis and 4.85 per 100,000 person-years for lymphocytic colitis. Notably, the review identified several significant risk factors associated with MC, including increased age, female gender, and the administration of proton pump inhibitors [PPIs] and selective serotonin reuptake inhibitors [SSRIs]. Furthermore, the findings indicated that the incidence of MC has reached a plateau in developed countries; however, the authors emphasized the necessity for additional data from developing nations to elucidate the global patterns of this condition [17].

Our study confirmed a significant association between drug use and the development of MC, particularly with PPIs. These findings are supported by multiple studies, including a systematic review by **Zylberberg *et al.*** [25] which found that the use of PPIs and SSRIs increased the risk of developing MC by more than twofold. This association has been consistently reported across different populations, including in Egyptian studies, highlighting the global relevance of medication use as a risk factor for MC.

**Study Strengths and Limitations:** This study has several strengths, such as the well-defined sample of 262 patients with chronic diarrhea, serving as an excellent source of epidemiological data on microscopic colitis [MC] in Egypt. The enhanced diagnostic methodology, including detailed clinical assessment, relevant laboratory work-up, colonoscopic biopsy sampling added [systematically] all contributed to enable accurate diagnosis. Histopathological evaluations by H&E and Masson's trichrome staining are included to accurately identify MC subtypes. In addition, the study also assesses potential risk factors, including proton pump inhibitor [PPI] use, to add to the knowledge of medication-associated MC in this population.

But the study also comes with limitations. Its single-center design may restrict generalizability of results to broader populations, particularly those living in rural or primary care settings. The cross-sectional design of the study limits establishing causality between MC and reported risk factors. Moreover, the low number of MC cases [n=22] has an influence on the statistical power for subgroup analyses. Fecal biomarkers including fecal calprotectin were not assessed in the study, and this could have provided additional diagnostic information. In addition, this study did not account for confounders, such as duration and dosage of PPI use. Larger cohorts with longer longitudinal follow-up are required in multicenter studies to confirm these findings and evaluate disease progression, treatment response, and relapses.

**Conclusion:** This study identified microscopic colitis [MC] in 8.4% of patients with chronic diarrhea, emphasizing the importance of colonic biopsies in cases with normal endoscopic findings. Lymphocytic colitis was slightly more common than collagenous colitis. Proton pump inhibitor [PPI] use was significantly associated with MC, highlighting a potential risk factor. Further research is needed to explore long-term outcomes and regional variations in MC prevalence.

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