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Prevalence of Microscopic Colitis among Egyptian Patients Presented with Chronic None Bloody Diarrhea

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ORIGINAL ARTICLE

Prevalence of Microscopic Colitis among Egyptian Patients Presented with Chronic None Bloody Diarrhea

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Abstract

Background: ***Chronic watery diarrhea(CWD) is a hallmark of the inflammatory colon condition known as microscopic colitis (MC). It usually affects middle-aged and older people, with a higher proportion of females. When people with microscopic colitis have colonoscopies, their colons seem normal.***

Aim of the work: ***To assess the prevalence of microscopic colitis among chronic watery non-bleeding diarrhea among Egyptian patients over 24 months using cross-sectional data and fecal calprotectin test.***

Patient and method: ***The Departments of Endemic Medicine and Pathology at Al-Hussein University Hospital, Faculty of Medicine, Al-Azhar University collaborated to perform and assess the incidence of microscopic intestinal colitis during this cross-sectional study. Eighty-eight individuals were enrolled in this trial from July 2017 to December 2019.***

Results: ***Histological appearance of microscopic colitis was identified in (9.1%), two in males (25%) and six females (75%), with mean age 48,75 -+ 8,88 (range 34-59). All of these cases were identified as lymphocytic colitis.Fecal calprotectin is positive in 25% from this microscopic colitis patient, ranging between 20 to 100, with a cutoff value above 47 microgram/stool with a high specificity of 100% and sensitivity of 25%.***

Conclusion: ***The prevalence of microscopic colitis in Egyptian patients with chronic watery, non-bloody diarrhea is high when compared to other developed countries. That mainly affects young and middle-aged patients and is more commonly lymphocytic.***

Keywords: Microscopic Colitis; Chronic; None Bloody Diarrhea

1. Introduction

Individuals who have microscopic colitis frequently experience arthritis and other autoimmune diseases, such as psoriasis, rheumatoid arthritis, and thyroid problems.[1]

According to a population-based study conducted in Scandinavia, the yearly incidence rate of Crohn's disease and ulcerative colitis was comparable to that of collagenous colitis (CC) and lymphocytic colitis (LC).[2]

The most common symptom is non-bloody diarrhea, including weight loss and stomach discomfort.[3]

Microscopic colitis consists of two main subtypes, (CC) and (LC), distinguished mainly by the presence or absence of a thickened subepithelial collagen band.[4]

Brainerd diarrhea, named after the US town where the outbreak occurred, is a chronic watery diarrhea outbreak with abrupt onset and prolonged duration that shares histological similarities with LC. An infectious cause has been proposed for this illness.[5]

According to a study conducted in Egypt, 21.7% of patients with persistent non-bloody diarrhea had microscopic colitis.[6]

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.[7]

This study aims to evaluate the prevalence of microscopic occurrences of colitis among different etiologies of chronic, non-bloody diarrhea in Egyptian patients throughout the following 24 months using a cross-sectional and fecal calprotectin test.

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2. Patients and methods

The GIT and Endemic Medicine of Al-Hussein University Hospital, Faculty of Medicine, Al-Azhar University collaborated to perform this cross-sectional study. The Ethics Committee of Al-Azhar University's Faculty of Medicine has approved the study methodology, and the participants have been made aware of the purpose of the investigation.

2.1.Patient recruitment and study design

Patients who presented with Chronic Watery Non-bloody Diarrhea (CWND), defined as more than three loose or liquid bowel motions every day for at least four weeks, were seen in the GI Endoscopy Unit at Al-Hussein University Hospital Lamont et al.,[8] and had normal macroscopic appearances at colonoscopy (apart from mild hyperemia and piles).

In this study, 88 patients were recruited from July 2017 to December 2019. Patient selection depended upon the following:

2.2.Inclusion criteria:

The study enrolled all CWND patients who were at least 15 years old, had normal colonoscopic findings, were willing to participate, and could provide informed consent.

2.3.Exclusion criteria:

Patients with a history of bloody diarrhea, patients with a history of steatorrhea, and abnormal colonoscopic findings (apart from mild hyperemia and piles). All cases with a history of acute diarrhea, patients known to have inflammatory bowel diseases, patients with known colonic diseases, e.g., Diverticulosis, CA colon, colonic polyps, and those with acute coronary syndrome. Megacolon, known or suspected intestinal obstruction, unstable angina, congestive heart failure, and other conditions that would make a colonoscopy difficult.

Detailed history taking: Demographic information and symptom data were obtained prospectively before the colonoscopy procedure. The demographic variables of interest encompass the patient's age at the point of recruitment, gender, and the present utilization of any medications that may have potential relevance in the etiology of MC, such as nonsteroidal anti-inflammatory drugs (NSAIDs), proton pump inhibitors (PPIs), H2 receptor blockers, statins, lisinopril, or selective serotonin reuptake inhibitors(SSRIs), Beaugerie et al.,[9]

Stool consistency, frequency of daily defecations, length of diarrhea, duration of nocturnal symptoms, and other gastrointestinal symptoms, including vomiting, anorexia, and weight loss. Symptom data include fever, a medical history of autoimmune illnesses, and a medical history of other systemic affections.

2.4.Laboratory tests

Complete blood counts, liver profiles, renal function tests, fasting blood sugar, erythrocyte sedimentation rate (ESR), and serum electrolytes were measured when blood samples were taken. Thyroid function tests (FT3, FT4, and TSH) and sodium and potassium levels. By established protocols, tissue transglutaminase (TTG), antibodies, and antinuclear antibodies (ANA) were examined at the Al-Hussein University Hospital's Department of Clinical Pathology.

At the Parasitology Department, Faculty of Medicine, Al-Azhar University, fresh stool specimens were analyzed for ova and parasites in cases suspected of having a parasitic infestation. Fecal calprotectin testing was performed in different specialized labs. For each patient, an abdominal ultrasound was performed.

Complete colonoscopy examination with multiple biopsies

Using the Pentax EC-3840M endoscope, colonoscopies have been performed on all patients at the Gastrointestinal Endoscopy Unit of Al-Hussein University Hospital. They were prepared using the approved protocol of the gastrointestinal endoscopy center. The facility stopped providing substantial meals on the day preceding the examination. Instead, individuals are advised to consume only clear liquids on the day of preparation, which corresponds to the day immediately preceding the colonoscopy. The administration of divided dosages of laxative formulations was conducted. Patients were instructed to utilize magnesium citrate ingestion or polyethylene glycol-electrolyte lavage solution (PEG-ELS). The patients were informed that it was permissible to take more clear beverages till the morning of the surgical procedure.

Most patients underwent colonoscopy under severe sedation (Propofol), while a few underwent it under conscious sedation (Midazolam). Using typical, open-type endoscopic biopsy forceps, multiple samples were obtained from visually normal mucosa at different regions of the colon during the procedure.

Mucosal biopsy sampling was taken as follows, Yantiss et al.,[10]: A minimum of two colon biopsies should be taken from the right colon, two transverse colon biopsies, two descending colon biopsies, and two sigmoid colon biopsies. They were promptly put in vials containing 10% formalin solution and submitted to the hospital's pathology department for processing.

2.5.Histopathological examination for the obtained specimens

The biopsy specimens underwent standard processing techniques, where they were embedded in paraffin blocks and subsequently sliced into unstained sections with a thickness of 5 micrometers. The slides were subjected to staining using Eosin and (H and E) and Masson's Trichrome dyes.

2.6.Diagnostic criteria for the diagnosis of MC

Multiple cancers (MC) diagnosis is based on

certain diagnostic criteria, such as increased colonic intraepithelial lymphocytes(IELs), increased chronic inflammatory infiltration in the lamina propria, surface epithelium degradation, and increased mitotic in crypts. For the diagnosis of (LC), more than 20 (IELs) per 100 intercryptal epithelial cells (normal <1-5/100). In specimens stained with Masson's Trichrome, the subepithelial collagen band thickness for (CC) is assessed using an ocular micrometer. For the diagnosis of (CC), a collagen band thickness greater than 10µm is necessary, Erdem et al.,[11]

Patients who exhibit clinical signs of MC but whose biopsies do not meet the precise histological requirements of CC and LC are classified as incomplete MC (MCi). When there is lamina propria inflammation, the collagenous band's thickness is somewhat enhanced (>5 but <10 µm In the scenario of incomplete collagenous colitis (CCi), the count of intraepithelial lymphocytes (IELs) exceeds ten but falls below 20 in the situation of incomplete lymphocytic colitis (LCi), Chang et al.,[12]

2.7.Definition of the diagnosis of non-specific colitis (NSC)

The microscopic examination reveals an elevated presence of inflammatory cells that exceeds the normal physiological levels in the corresponding anatomical locations. The major cellular infiltrate observed in this study is chronic, characterized by the absence of architectural deformation. Many basal lymphoid aggregates or plasma cells are also observed near the muscularis mucosae. Crypts may exhibit an elevation in mitotic activity and a subtle deviation in morphology, Tsang,.[13]

2.8.Statistical analysis:

The data was subjected to coding and input methods using SPSS (Statistical Package for the Social Sciences) version 25, statistical software developed by SPSS Inc. in Chicago, IL. The data were summarized by the computation of various statistical measures for quantitative variables, including the mean, standard deviation, median, minimum, and maximum. For categorical variables, the summary involved the determination of frequency (count) and relative frequency (%). The non-parametric Mann-Whitney test was employed to conduct comparisons between variables of a quantitative kind Chan,(a).[14]

The Chi-square (X2) test was employed to compare categorical data. In cases when the expected frequency is below five, an exact test was employed instead, Chan,(b).[15]

Using univariate logistic regression, the study examined the associations between the data and the presence of MC. These were analyzed and reported as odds ratios (ORs) and a 95% confidence interval (CI). A diagnostic grading system was developed to predict the existence of MC using the variables that showed statistically significant univariate ORs, as detailed . [16]

3. Results

Table 1. Demographic data and characteristics of the studied patients.

		Total no.=88
Age (years)	Mean±SD	38.03±12.67
	Range	15-72
Gender	Male	46 (52.3%)
	Female	42 (47.7%)
Smoking	Yes	25 (28.4%)
	No	63 (71.6%)
Duration (months)	Median(IQR)	9 (7-15)
	Range	3-96
Duration (years)	Median(IQR)	0.75 (0.58-1.25)
	Range	0.08-8
Duration of diarrhea	≤6 months	18 (20.5%)
	>6 months	70 (79.5%)
Bowel motion frequency	Mean±SD	5.84±1.92
	Range	3-12

The age of the studied patients ranged from 15-72 y with mean of 38.03±12.67. Regarding the gender, the study including 46 males representing (52.3%) and 42 females representing (47.7%).

Table 2. Prevalence of MC among patient with CWND.

PATHOLOGICAL DIAGNOSIS	NO	PERCENT (%)	TOTAL (N=88)
MICROSCOPIC COLITIS (MC)	8	9.1	8
NON-SPECIFIC COLITIS (NSC)	54	61.4	80
NORMAL	21	23.9	
EOSINOPHILIC COLITIS	1	1.1	
INFLAMMATORY BOWEL DISEASE (IBD)	1	1.1	
INCOMPLETE MICROSCOPIC COLITIS (MCI)	3	3.4	

A histopathological examination was performed on biopsied samples collected during colonoscopy in order to determine the occurrence rate of (MC) among persons experiencing (CWND). The presence of microscopic colitis (MC) was pathologically established in eight patients, accounting for 9.1% of the total sample. All of these cases were identified as lymphocytic colitis. (NSC) was observed in 54 patients, representing 61.4% of the sample. Normal histology was found in 21 patients (23.9%), while incomplete microscopic colitis (Mci) was present in 3 patients (3.4%). Eosinophilic colitis was identified in one patient (1.1%), and inflammatory bowel disease (IBD) was diagnosed in another patient (1.1%).

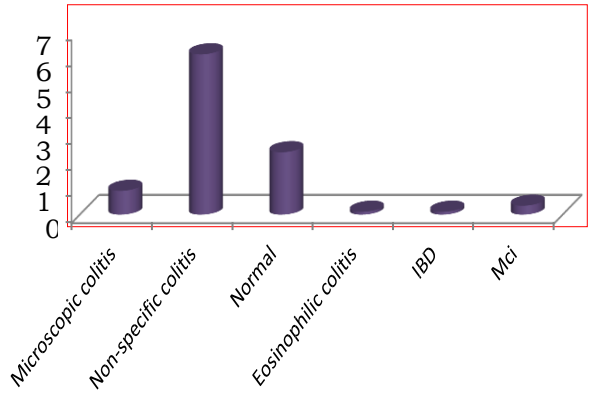

Figure 1. Prevalence of MC among patient with CWND.

Table 3. Comparison of the patient features and demographic information between instances with and without microscopic colitis.

		No microscopic colitis	Microscopic colitis	Test-value	P-value	Sig.
		No.=80	No.=8			
Age (years)	Mean±SD	36.96±12.53	48.75±8.88	-2.590•	0.011	S
	Range	15-72	34-59			
Gender	Male	44 (55.0%)	2 (25.0%)	2.624*	0.105	NS
	Female	36 (45.0%)	6 (75.0%)			
Smoking	Yes	24 (30.0%)	1 (12.5%)	1.095*	0.295	NS
	No	56 (70.0%)	7 (87.5%)			
Duration. (months)	Median(IQR)	9 (8-15.5)	5 (4.5-7)	-3.414≠	0.001	HS
	Range	3-9	3-9			
	≤6 months	12 (15.0%)	6 (75.0%)	16.091*	0.000	HS
	>6 months	68 (85.0%)	2 (25.0%)			
Bowel motion frequency	Mean±SD	5.58 ± 1.7	8.5 ± 2.07	-4.541•	0.000	HS
	Range	3-10	6-12			

P-value>0.05: Non-significant (NS); P-value<0.05: Significant (S);P-value<0.01: Highly significant (HS)

*: Chi-square test; •: Independent t-test; ≠: Mann-Whitney test

The age of the studied patients ranged from 15-72 y with mean of 38.03±12.67. Regarding the gender, the study including 46 males representing (52.3%) and 42 females representing (47.7%), regarding the duration of diarrhea in months as median 9 (7-15) in range (3-9) months, 18 patients represent chronic diarrhea less than 6months and 70 patients represent it more than 6 months. Also by range 3-12 bowel motions frequency in included patients study.

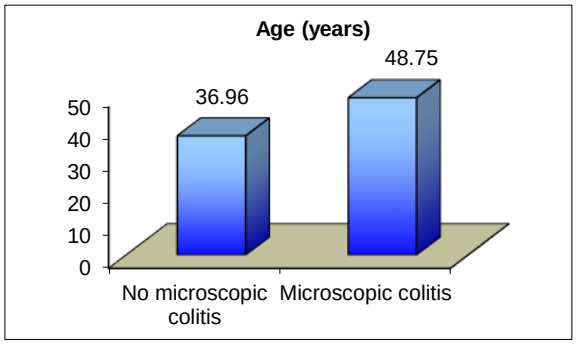

Figure 2. Comparison between cases with and without microscopic colitis regarding mean age of the studied patients.

Table 4. Comparing the symptoms of cases with and without microscopic colitis.

Symptoms	No microscopic colitis	Microscopic colitis	Test-value	P-value	Sig.
	No.=80	No.=8			
Abdominal pain	69 (86.2%)	4 (50.0%)	6.759*	0.009	HS
Nocturnal diarrhea	11 (13.8%)	5 (62.5%)	11.619*	0.001	HS
Weight loss	16 (20.0%)	6 (75.0%)	11.733*	0.001	HS
Vomiting	17 (21.2%)	1 (12.5%)	0.342*	0.559	NS
Tenesmus	7 (8.8%)	2 (25.0%)	2.092*	0.148	NS
Anorexia	2 (2.5%)	0 (0.0%)	0.205*	0.651	NS
Fever	9 (11.2%)	3 (37.5%)	4.255*	0.039	S
Stool incontinence	2 (2.5%)	1 (12.5%)	2.209*	0.137	NS

P-value>0.05: Non-significant (NS);P-value<0.05: Significant (S); P-value<0.01: Highly significant (HS)

*: Chi-square test

Regarding weight loss, nocturnal diarrhea, and abdominal pain, there is a substantial statistical difference between the two groups (p values of 0.009, 0.001, and 0.001, respectively). Additionally, fever has a statistically significant p value of 0.039.

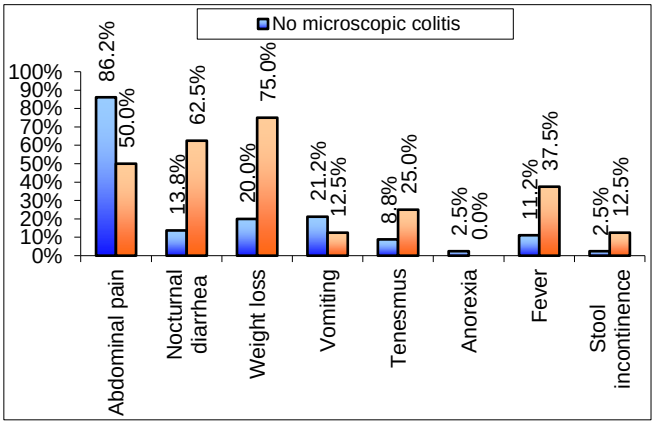

Figure 3: Comparison between cases with and without microscopic colitis regarding symptoms.

Table 5. Comparison of family history and drug history among the patients under study between instances with and without microscopic colitis.

		No microscopic colitis	Microscopic colitis	Test-value	P-value	Sig.
		No.=80	No.=8			
Family history of chronic diarrheal disease	Yes	5 (6.2%)	0 (0.0%)	0.530*	0.467	NS
	No	75 (93.8%)	8 (100.0%)			
Drugs	Yes	43 (53.8%)	7 (87.5%)	3.376*	0.066	NS
	No	37 (46.2%)	1 (12.5%)			
	NSAID	9 (11.2%)	2 (25.0%)	1.257*	0.262	NS
	Aspirin	4 (5.0%)	1 (12.5%)	0.763*	0.382	NS
	PPI	17 (21.2%)	6 (75.0%)	10.884*	0.001	HS
	PPI and/or H_2 receptor antagonist	20 (25.0%)	7 (87.5%)	13.358*	0.000	HS
	H_2 receptor antagonists	12 (15.0%)	7 (87.5%)	22.581*	0.000	HS
	Lisinopril	1 (1.2%)	0 (0.0%)	0.101*	0.750	NS
	Statins	2 (2.5%)	0 (0.0%)	0.205*	0.651	NS

P-value>0.05: Non-significant (NS); P-value<0.05: Significant (S); P-value<0.01: Highly significant (HS)

*: Chi-square test

Regarding PPI, PPI with H2 receptor antagonist, and H2 receptor antagonist, there was a substantial statistical difference between the two groups, with p values of 0.001, 0.000, and 0.000, respectively.

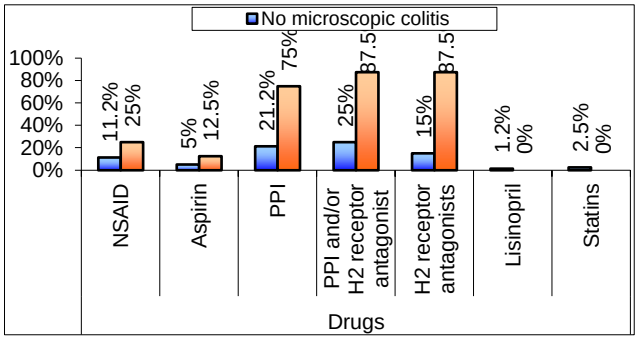

Figure 4. Comparison between cases with and without microscopic colitis regarding history of drugs among the studied patients.

Table 6. Comparison of the laboratory results of the individuals under study in cases with and without microscopic colitis (cont.).

		No microscopic colitis	Microscopic colitis	Test-value	P-value	Sig.
		No.=80	No.=8			
Serum sodium	Mean±SD	139.28±4.78	137.88±7.1	0.758•	0.451	NS
	Range	120-148	129-147			
S.sodium level	Normal	74 (92.5%)	5 (62.5%)	7.129*	0.008	HS
	Low	6 (7.5%)	3 (37.5%)			
Serum potassium	Mean±SD	3.83±0.5	3.43±0.75	2.064•	0.042	S
	Range	1.7-4.7	2.4-4.4			
S.potassium level	Normal	72 (90.0%)	4 (50.0%)	9.881*	0.002	HS
	Low	8 (10.0%)	4 (50.0%)			
S.potassium and/or sodium level	Normal	71 (88.8%)	4 (50.0%)	8.674*	0.003	HS
	Low	9 (11.2%)	4 (50.0%)			
ESR	Median(IQR)	15 (10-20)	23 (19-25)	-2.869≠	0.004	HS
	Range	5-33	15-30			
ESR level	Normal	50 (62.5%)	4 (50.0%)	0.479*	0.489	NS
	Elevated	30 (37.5%)	4 (50.0%)			
ANA (IU)	Median(IQR)	0.51 (0.34-0.76)	0.45 (0.2-0.63)	-0.820≠	0.412	NS
	Range	0.08-1.3	0.09-1.02			
ANA	Normal	79 (98.8%)	7 (87.5%)	4.144*	0.042	S
	High	1 (1.2%)	1 (12.5%)			

P-value>0.05: Non-significant (NS); P-value<0.05: Significant (S); P-value<0.01: Highly significant (HS)

*: Chi-square test; •: Independent t-test; ≠: Mann-Whitney test

Regarding serum potassium, sodium, and ESR, there was a significant statistical difference between the two groups (p values of 0.008, 0.002, 0.003, and 0.004, respectively). Additionally, there was a statistically significant difference (p value of around 0.004) in ANA between the two groups.

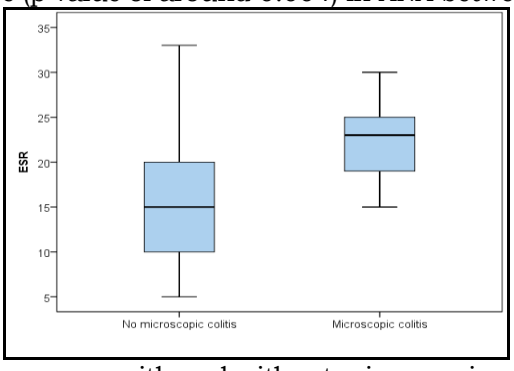

Figure 5. Comparison between cases with and without microscopic colitis regarding ESR level.

Table 7. Comparison of the occurrence of DM, AID, non-specific colitis, eosinophil, IBD, and MCI in the patients under study in cases with and without microscopic colitis.

		No microscopic colitis	Microscopic colitis	Test-value	P-value	Sig.
		No.=80	No.=8			
DM	Yes	8 (10.0%)	1 (12.5%)	0.050*	0.824	NS
	No	72 (90.0%)	7 (87.5%)			
AID	Yes	4 (5.0%)	1 (12.5%)	0.763*	0.382	NS
	No	76 (95.0%)	7 (87.5%)			
Non-specific colitis	Yes	54 (67.5%)	0 (0.0%)	13.976*	0.000	HS
	No	26 (32.5%)	8 (100.0%)			
Normal	Yes	21 (26.2%)	0 (0.0%)	2.758*	0.097	NS
	No	59 (73.8%)	8 (100.0%)			
Eosinophil	Yes	1 (1.2%)	0 (0.0%)	0.101*	0.750	NS
	No	79 (98.8%)	8 (100.0%)			
IBD	Yes	1 (1.2%)	0 (0.0%)	0.101*	0.750	NS
	No	79 (98.8%)	8 (100.0%)			
MCI	Yes	3 (3.8%)	0 (0.0%)	0.311*	0.577	NS
	No	77 (96.2%)	8 (100.0%)			

P-value>0.05: Non-significant (NS); P-value<0.05: Significant (S); P-value<0.01: Highly significant (HS)

*: Chi-square test

Regarding nonspecific colitis, A significant statistical distinction exists between both groups (p=0.000). The remaining variables did not exhibit any statistically significant.

Table 8. Comparison of fecal calprotectin levels in patients under study with and without microscopic colitis

		No microscopic colitis	Microscopic colitis	Test-value	P-value	Sig.
		No.=80	No.=8			
Fecal calprotectin	Negative	80 (100.0%)	6 (75.0%)	20.465*	0.000	HS
	Positive	0 (0.0%)	2 (25.0%)			
	Mean ± SD	28.08 ±8.38	39.50 ± 27.55	-2.742•	0.007	HS
	Range	5-43	20-100			

P-value>0.05: Non-significant (NS); P-value<0.05: Significant (S); P-value<0.01: Highly significant (HS)
*: Chi-square test

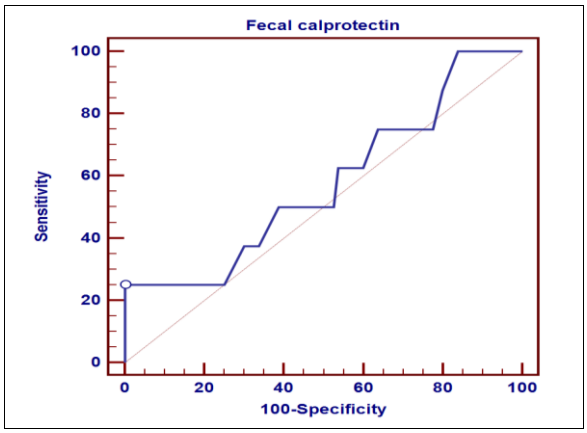

Figure 6. Fecal calprotectin as predictor of microscopic colitis.

4. Discussion

According to this study, MC is a very common cause of CWND with an unknown origin in Egypt; a prior retrospective study conducted in Egypt by[17] and his associates discovered that 22 (50%) of 44 patients with persistent watery diarrhea who had normal endoscopic results in 2011 had MC.

Most patients in our study (87.5% in the MC group and 53.3% in the control group, p=not significant) used medicines. A comparable outcome was clarified .[18] They discovered that most patients (71.7% in the MC group and 67.8% in the control group, p=not significant) had received at least one prescription within the year before the colonoscopy.

Our investigation found a substantial correlation between MC patients' current PPI consumption. This result was in line with the biggest retrospective analysis conducted previously by [19] who performed research on 10 652 people who were diagnosed with MC for the first time (6254 (59%) with cc and 4398 (41%) with LC) and who found a significant correlation between MC and PPI use at the time of diagnosis (OR 6.98; 95% CI: 6.45 7.55).

Additionally, we found a strong correlation in our study between MC patients' current H2 receptor antagonist intakes.

1211 MC patients and 6041 matched controls participated in a case-control study conducted by [20], demonstrating that the higher risk of presenting MC has been linked to H2 receptor antagonist medications (OR 2.40; 1.73-3.31% 95% CI).

In our investigation, there was no statistically significant difference in smoking between the MC patients and the control group. Given that almost all of our patients were female, and that current smoking was found to be more strongly associated with CC than LC, these statistics are even more compelling when one takes into account the disparities in gender and type of MC in these patients.[21]

In our investigation, we observed no noteworthy laboratory abnormalities except hypokalemia in 50% of the patients (n=4) and hyponatremia in 37.5% (n=3). These electrolyte imbalances were predominantly observed in patients experiencing more severe and frequent episodes of diarrhea. This correlation may be attributed to the raised mean blood creatinine levels observed in patients with MC.

Median fecal calprotectin (FC) levels were 30.1 μg/g (15.6, 122.5), 19.5 μg/g (16.5, 64.6), and 33.2 μg/g (15.6, 134.9) in all groups, collagenous colitis, and lymphocytic colitis, respectively. Conclusion: The utility of fecal calprotectin in diagnosing microscopic colitis is limited. Our study suggests the diagnosis should be based on histopathology tissue obtained during colonoscopy. There is a highly significant value of fecal calprotectin (2 (25%) cases positive from 8 positive MC) that showed fecal calprotectin value cutoff above 47microgram /stool with high Specificity (100%) and sensitivity of 25%.

In order to understand the role and importance of (FC), we performed a statistical analysis on the patients suffering from chronic diarrhea. We were admitted to our hospital from 2014 to 2020 and were prescribed Loperamide (Imodium) or Budesonide or a combination of both and had undergone an FC detection test.

The major limitations of our study are the small sample size and the small number of MC cases compared to the control group. Despite the smaller number of cases in this study, the

characteristics of patients with MC, including mean age, gender, and use of PPI and H2 receptor antagonists, were remarkably similar to those in previous studies.

4. Conclusion

Microscopic colitis is a rather prevalent occurrence among Egyptian patients presenting with persistent watery, non-bloody diarrhea and with normal findings during colonoscopy. The need to do a biopsy on the typical colonic mucosa in patients with chronic watery diarrhea is underscored as a means to establish a conclusive diagnosis of (MC).

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

Funding

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Conflicts of interest

There are no conflicts of interest.

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