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Prevalence of Microscopic Colitis among Egyptian Patients with Diarrhea Predominant Irritable Bowel Syndrome

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Abstract

Background: Microscopic colitis (MC) is more prevalent in women than in men. In middle-aged patients, it is the most prevalent chronic inflammatory disease of the colon. Although there is no defined and organic pathology, irritable bowel syndrome (IBS) is the most prevalent functional gastrointestinal disorder. Abdominal distress and altered defecation habits are its distinguishing characteristics. **Aimed to** an examination of the prevalence of MC among Egyptian patients with IBS-D. **Methods:** This observational cross-sectional study included 100 patients with IBS-D who were 18 years of age or older and were seen in the outpatient clinic at Benha University Hospitals' Department of Internal Medicine. **Results:** The history of use of PPI was significantly lower in patients with MC compared to patients without MC (P<0.05). Among the different clinical manifestations, abdominal distention, weight loss and fever, the duration of diarrhea and the bowel motion frequency, C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR) and fecal calprotectin level were significantly higher in patients with MC compared to patients without MC (P<0.05). **Conclusion:** The diagnosis of MC is not uncommon. It is easy to confound colonoscopy specimens derived from the typically appearing mucosa with IBS-D, which is why the primary method of differentiation is the histopathological examination. It is imperative to perform a Colonoscopic biopsy evaluation in patients with IBS-D, as it increases the likelihood of MC, nocturnal diarrhea, and weight loss. However, these markers are non-specific and do not serve as diagnostic indicators for MC. Inflammatory markers (ESR, FC, and CRP) may exhibit modest increases in patients with IBS-D.

Keywords: Microscopic Colitis; Egyptian Patients; Diarrhea Predominant Irritable Bowel Syndrome.

Introduction

Chronic inflammatory colon disease known as microscopic colitis (MC) is more common in middle-aged people and affects women more than men [(1)]. This clinical syndrome is distinguished by chronic diarrhea that is bloodless and watery, in contrast to "classical" inflammatory bowel disease (IBD). In addition, it does not necessitate any particular macroscopic modifications to the large intestine. The cause of the syndrome is still uncertain. The diagnosis is confirmed by the colonic mucosa biopsy, which indicates specific histologic changes, including increased lymphocytic infiltrates and collagen fiber expansion, among other things.[(2)]. Lymphocytic colitis (LC), which was more specifically defined in 1989, and collagenous colitis (CC) are the two primary histologic subtypes of MC, which was initially described in 1980 [(3)].

In the past, MC was considered a rare disorder, and there was a lack of knowledge regarding its epidemiology and etiology. Incidence of MC has been consistently increasing since its description. Especially in the geriatric population, MC should be regarded as a differential diagnosis in the workup of chronic diarrhea. In LC, the incidence of MC is 4.9/100 per person year, while in CC, it is 4.1. The median age at diagnosis is approximately 65 years [(4)].

Normal is the typical endoscopic morphology of the colon. Macroscopic features may encompass scars, exudative lesions, friability, erythema, and minor edema; however, none are distinctive to the disease [(5)]. Numerous potential biomarkers for MC have been investigated in a manner similar to this; however, none are currently available for diagnostic purposes [(6)]. For this reason, the sole method of diagnosing MC is the histological examination of colonic biopsies. A significant obstacle to the evaluation of colonic biopsy in patients with MC is the clinical comorbidity with IBS [(7)].

The most prevalent functional gastrointestinal disorder is IBS, which is defined by altered bowel habits and abdominal discomfort in the absence of a specific and distinctive organic pathology[(8)].

The chronic gastrointestinal disorder irritable bowel syndrome (IBS) is characterized by four underlying subtypes: diarrhea-predominant (IBS-D), constipation-predominant (IBS-C), mixed (IBS-M), and undefined (IBS-U). IBS is diagnosed by gastroenterologists using the Rome criteria, as there are no biomarkers or organic lesions. The primary foundation for this diagnosis is clinical manifestations [(9)].

To diagnose IBS, the Rome IV criteria require that patients have experienced recurrent abdominal discomfort on an average of at least one day per week for the three months prior. This diagnostic condition is associated with two or more of the following attributes: alterations in

the frequency of excrement production and the appearance or form of feces in relation to defecation [10].

The Rome criteria for IBS are met by a significant proportion of patients who have MC. Consequently, a subset of IBS patients, specifically those with diarrhea (IBS-D), who failed to undertake colonoscopies and biopsies would have missed a diagnosis of MC. [11].

Quiescent IBD, MC, eosinophilic colitis, and amyloidosis are among the numerous etiologies that are not macroscopically apparent. As a result, histology is indispensable for the assessment of chronic diarrhea. The diagnostic yield for colonoscopy ranges from 7 to 32%, with IBD and MC being the most prevalent diagnoses for patients with chronic diarrhea [12].

Investigation of the prevalence of MC among Egyptian patients diagnosed with IBS-D was the primary objective of this study

Patients and methods

This observational cross-sectional study included 100 patients aged ≥ 18 years attending the outpatient clinic fulfilling Rome IV criteria for diagnosis of IBS-D in the department of internal medicine, Benha University hospitals.

The patients provided written consent that was informed. The study's objective was to provide each patient with a comprehensive explanation, and they were each assigned a secret code number. The research was implemented after the Research Ethics Committee at the Faculty of Medicine at Benha University granted its sanctions. The study begins December 2023 and ends in December 2024.

Exclusion criteria were A patient who is under the age of 18 and has IBD or infectious colitis, bloody diarrhea or steatorrhea, aberrant Colonoscopic findings, systemic diseases associated with chronic diarrhea (e.g., diabetes mellitus (DM) or thyroid disease), and a history of gastrointestinal surgery.

Grouping: Patients were divided into two groups according to the prevalence of MC: **Group I (n=13):** Patients with MC. **Group B (n=87):** Patients without MC.

All studied cases were subjected to the following: Full history taking, including [Personal history including age, gender, occupation, and demographic details, symptom characterization: including stool characteristics, abdominal pain, other symptoms, past medical history, medication history, dietary habits, social history including smoking and alcohol use and stress levels]. **Full clinical examination: General examination including** [Analysis of weight, height, body mass index, temperature, systolic and diastolic blood pressure, vital signs (including blood pressure, heart rate, respiratory rate, and temperature), general appearance, abdominal and

rectal examinations, other pertinent systems, and skin and neurological symptoms]**.Routine laboratory investigations [**Complete blood count (CBC): (Hemoglobin concentration, platelet count, serum creatinine, serum sodium (Na) , red blood cells count, white blood cells count), renal function tests and electrolytes including blood urea, and potassium (K), liver function tests including serum transaminases (aspartate aminotransferase (AST), alanine transaminase (ALT)), serum albumin, serum bilirubin (total, direct) and prothrombin time and concentration, inflammatory markers (C-reactive protein, erythrocyte sedimentation test), HIV testing, TTG- Abs to rule out celiac disease, thyroid stimulating hormone (TSH), HbA1c, Fasting Plasma Glucose (FPG), post prandial blood glucose, to rule out systemic diseases associated with chronic diarrhea like thyroid disease and diabetes mellitus, stool tests: including stool culture and sensitivity, stool for occult blood and fecal calprotectin or lactoferrin]. **Imaging** including **a**bdominal ultrasound (US)

Samples

Six specimens were obtained from each patient: two normal, two EDTA, one citrate, and one ESR. Samples of blood and debris were taken in BD Vacutainer containers (Becton, Dickinson and Company, Franklin Lakes, NJ, USA). For the purpose of conducting a thorough blood count, a single EDTA vial was implemented. The serum was centrifuged at 1200× g for 10 minutes using the standard Vacutainer vial to separate it after it had coagulated for 30 minutes. Centrifuged at 2000× g for 15 minutes, the citrate vial was promptly centrifuged to conduct coagulation testing. By employing the rectum, the left colon (descending colon and sigmoid colon), the right colon (cecum, ascending colon, and transverse colon), and any abnormal-looking regions, the colonic mucosal specimens were obtained.

Laboratory tests

The XS500i Hematology analyzer (Sysmex, Kobe, Japan) was utilized to conduct the CBC. The blood film was employed to enumerate the differential cells. The Westergren method was employed to measure the ESR. The Sysmex CS2100i (Siemens, Munich, Germany) was employed to conduct coagulation assays. The quantitative analysis of all biochemical assays was conducted using the Cobas 8000 Modular Analyzer (Roche Diagnostics, Mannheim, Germany). By adhering to the manufacturer's instructions, the FC concentration was determined using the Calprest ELISA (Eurospital, Trieste, Italy).

Colonoscopic evaluation

Endoscopy was performed for all patients at the gastroenterology and endoscopy unit of the internal medicine department, Benha University Hospital, using the OLYMPUS EVIS EXTRA III CV-190 endoscope. The patients

underwent the procedure after providing written informed consent. After conducting adequate colonic preparation with Prepawest, the procedure was executed. For the six hours prior to the colonoscopy, patients were prohibited from consuming any oral medications. Additionally, they were obligated to maintain a fluid and liquid diet the day before the procedure. During the procedure, the patient's vital signs, including pulse and oxygen saturation, were closely monitored while they were under conscious sedation with midazolam. Using standard, open-type endoscopic biopsy instruments, multiple specimens were randomly selected from endoscopically normal-appearing mucosa in various segments of the potentially examined part. At least two specimens were collected using the rectum, descending colon, and sigmoid colon, as well as the cecum, ascending colon, and transverse colon as proximal colon techniques.

Histopathologic evaluation

The pathology laboratory at our hospital wasted little time transferring the samples to vials containing 10% formalin. The tissues were examined using standard light microscopy techniques. A specialized pathologist examined the specimens after they were traditionally processed in paraffin blocks and cut into unstained sections that were 5 μm thick. biopsies were classified as follows: Normal or nonspecific colitis (NSC) is defined as the presence of inflammatory changes that exceed the limits of the normal mucosa but are not specific to any particular disease, or a collagen layer that is less than 5 μm thick and has fewer than five intraepithelial lymphocytes per 100 surface epithelial cells (normal condition) [(13)]. MC: The definitive confirmation of LC was achieved by a subepithelial collagen layer thickness of >10 μm and a subepithelial lymphocyte count of ≥ 20 per 100 surface epithelial cells [(14)]. In ulcerative colitis (UC), cryptitis and crypt abscesses develop as a result of active inflammation, a widespread transmucosal inflammatory infiltrate, and distorted crypt architecture [(15)].

Immunohistochemistry protocol

The tissue blocks were deparaffinized in xylene, sectioned into 3–5 μm sections, and rehydrated through a graduated series of alcohols. The blocks were formalin-fixed and paraffin-embedded. Use of a 10 mM citrate buffer (pH 6.0) in a microwave for 20 minutes was employed to perform antigen retrieval. Sections were exposed to 3% hydrogen peroxide for 10 minutes to inhibit the activity of endogenous peroxidase. Following diluting the treated transparencies with PBS, a polyclonal primary anti-CD3 antibody (clone A0452) was introduced to the mixture. As a counterstain, Meyer's hematoxylin was used, and Dako's EnVisionTM polymer detection instrument (Dako, Copenhagen, Denmark) was used to detect the primary antibodies' binding.

Approval code: MS 2-3-2024

Sample size

A minimum number of 1 patient was necessary to meet the desired statistical constraints of 95% confidence level and real value within + or - 5%. Given that, the incidence of MC in literature ranged between 2 and 16 per 100,000 per year.

Statistical analysis

The statistical study was conducted using SPSS v27, which was developed by IBM with headquarters in Armonk, New York, USA. To determine whether the data was normally distributed, the Shapiro-Wilks test and histograms were implemented. The quantitative parametric data, which was provided as the mean + standard deviation (SD), was analyzed using an unpaired student t-test. When necessary, we calculated percentages and frequencies of different qualitative variables using Fisher's exact test and a chi-square test. For statistical purposes, a p-value of less than 0.05 was deemed significant.

Results

Regarding the prevalence of MC, there was an insignificant difference between patients with MC and those without MC regarding the baseline characteristics including age, sex and residence, family history of colorectal cancer, the associated comorbidities including smoking, hypertension and diabetes mellitus, the manifestations including abdominal pain, nocturnal diarrhea, vomiting and anorexia and the complete blood count including Hb, platelet count, WBCs and HbA1c. The history of use of PPI was significantly lower in patients with MC compared to patients without MC (P<0.05). Among the different clinical manifestations, abdominal distention, weight loss and fever, the duration of diarrhea and the bowel motion frequency were significantly higher in patients with MC compared to patients without MC (P<0.05). **(Table 1)**

There was an insignificant difference between both groups regarding the serum creatinine, urea and serum electrolytes (sodium and potassium) and the liver function tests including (total protein, direct bilirubin, total bilirubin, ALT, AST, albumin, prothrombin time and international normalized ratio (INR)). (**Table 2)**

Patients with MC had significantly higher CRP level and ESR compared to patients without MC (P <0.001, <0.001). There was an insignificant difference between both groups regarding the thyroid function tests including TSH, T3 and T4. (**Table 3)**

All the studied patients in both groups were HIV negative and the HIV testing was insignificantly different between both groups. The Fecal calprotectin level was significantly higher in patients with MC compared to patients without MC (P <0.001). (**Table 4)**

Table 1: Baseline characteristics, history, comorbidities, clinical manifestations, clinical data and complete blood count (CBC) and HbA1c of the studied groups regarding the prevalence of MC

		Total (n=100)	Patients with MC (n=13)	Patients without MC (n=87)	P value
Age (years)	**Mean± SD**	44.15± 10.33	43.23± 11.37	43.35± 11.19	0.783
	Range	28-60	21-60	21-60	
Sex	**Male**	7 (53.85%)	57 (65.52%)	64 (64%)	0.611
	Female	6 (46.15%)	30 (34.48%)	36 (36%)	
Residence	**Urban**	6 (46.15%)	43 (49.43%)	49 (49%)	0.825
	Rural	7 (53.85%)	44 (50.57%)	51 (51%)	
Family history of colorectal cancer		2 (2%)	1 (7.69%)	1 (1.15%)	0.244
History of use of PPI		27 (27%)	8 (61.54%)	19 (21.84%)	**0.001***
Smoking		45 (45%)	7 (53.85%)	38 (43.68%)	0.491
HTN		38 (38%)	4 (30.77%)	34 (39.08%)	0.564
DM		22 (22%)	2 (15.38%)	20 (22.99%)	0.537
Abdominal pain		46 (46%)	7 (53.85%)	39 (44.83%)	0.542
Abdominal distention		32 (32%)	9 (69.23%)	23 (26.44%)	**0.002***
Weight loss		20 (20%)	6 (46.15%)	14 (16.09%)	**0.011***
Nocturnal diarrhea		17 (17%)	5 (38.46%)	12 (13.79%)	0.124
Fever		16 (16%)	5 (38.46%)	11 (12.64%)	**0.017***
Vomiting		12 (12%)	2 (15.38%)	10 (11.49%)	0.687
Anorexia		9 (9%)	1 (7.69%)	8 (9.2%)	0.859
Duration of diarrhea (months)	**Mean± SD**	4.67± 1.27	6.08± 1.26	4.46± 1.14	**<0.001***
	Range	3-8	4-8	3-6	
Bowel motion frequency (motion / day)	**Mean± SD**	5.91± 2.24	9.62± 2.02	5.36± 1.68	**<0.001***
	Range	3-12	6-12	3-8	
Hb (g/dl)	**Mean± SD**	12.2± 1.29	12.02± 1.52	12.23± 1.26	0.595
	Range	10-14.5	10.1-14.5	10-14.4	
Platelets (*109/L)	**Mean± SD**	287.07± 38.84	279.38± 27.65	288.22± 40.24	0.447
	Range	223-350	243-337	223-350	
WBCs (*109/L)	**Mean± SD**	8.5± 1.24	9.1± 1.88	8.41± 1.11	0.063
	Range	5.9-12.9	6.8-12.9	5.9-10.5	
HbA1c (%)	**Mean± SD**	4.65± 0.61	4.48± 0.68	4.67± 0.6	0.306
	Range	3.4-5.5	3.4-5.4	3.5-5.5	

Data presents as mean ± SD, range or frequency (%). MC: Microscopic colitis, PPI: proton pump inhibitor. HTN: Hypertension, DM: Diabetes mullites. Hb: hemoglobin, WBCs: white blood cells count, HbA1c: Glycated hemoglobin. MC: Microscopic colitis, Hb: hemoglobin, WBCs: white blood cells count, HbA1c: Glycated hemoglobin. *: statistically significant as *p* value <0.05.

Table 2: Renal and liver function tests and serum electrolytes of the studied groups regarding the prevalence of MC

		Total (n=100)	Patients with MC (n=13)	Patients without MC (n=87)	P value
Serum creatinine (mg/dL)	**Mean± SD**	1.04± 0.17	1.04± 0.16	1.04± 0.17	0.969
	Range	0.7-1.32	0.8-1.32	0.7-1.31	
S. Urea (mg/dL)	**Mean± SD**	27.98± 7.09	25.85± 6.05	28.3± 7.21	0.247
	Range	16-41	18-39	16-41	
Sodium (mEq/L)	**Mean± SD**	137.62± 1.69	138.08± 1.66	137.55± 1.69	0.297
	Range	135-141	136-141	135-140	
Potassium (mEq/L)	**Mean± SD**	4.54± 0.59	4.76± 0.56	4.51± 0.59	0.153
	Range	3.6-5.4	3.7-5.3	3.6-5.4	
ALT (IU/L)	**Mean± SD**	28.95± 6.69	26.62± 6.56	29.3± 6.68	0.179
	Range	19-40	19-38	20-40	
AST (IU/L)	**Mean± SD**	30.13± 6.96	33± 6.71	29.7± 6.93	0.111
	Range	19-41	21-40	19-41	
Albumin (g/dL)	**Mean± SD**	4.4± 0.6	4.61± 0.58	4.37± 0.6	0.190
	Range	3.4-5.5	3.5-5.4	3.4-5.5	
Total protein (g/dL)	**Mean± SD**	70± 5.9	71.15± 3.98	69.83± 6.13	0.452
	Range	60-80	65-77	60-80	
Direct bilirubin (mg/dL)	**Mean± SD**	0.16± 0.05	0.16± 0.05	0.15± 0.05	0.616
	Range	0.09-0.21	0.09-0.2	0.1-0.21	
Total bilirubin (mg/dL)	**Mean± SD**	0.67± 0.31	0.56± 0.29	0.69± 0.31	0.109
	Range	0.2-1.22	0.3-1.2	0.2-1.22	
Prothrombin time (sec)	**Mean± SD**	11.95± 0.6	11.82± 0.62	11.97± 0.6	0.391
	Range	11-13	11-12.6	11-13	
INR	**Mean± SD**	0.95± 0.11	0.98± 0.11	0.94± 0.11	0.298
	Range	0.8-1.1	0.8-1.1	0.8-1.1	

Data presents as mean ± SD, range or frequency (%). MC: microscopic colitis, S. urea: serum urea. ALT: alanine transaminase, AST: aspartate aminotransferase, PT: prothrombin time, INR: international normalized ratio

Table 3: Inflammatory markers and thyroid function tests of the studied groups regarding the prevalence of MC

		Total (n=100)	Patients with MC (n=13)	Patients without MC (n=87)	*P* value
CRP (mg/dL)	**Mean± SD**	4.78± 2.77	9.77± 4.15	4.03± 1.46	**<0.001***
	Range	2-16	4-16	2-6	
ESR (mm/hr.)	**Mean± SD**	6.89± 4.8	17± 5.28	5.38± 2.2	**<0.001***
	Range	2-25	10-25	2-9	
TSH (mIU/L)	**Mean± SD**	1.49± 0.91	1.39± 0.85	1.51± 0.92	0.668
	Range	0.1-3	0.2-2.9	0.1-3	
T3 (pmol/L)	**Mean± SD**	7.23± 1.54	7.38± 1.76	7.21± 1.52	0.701
	Range	5-10	6-10	5-9	
T4 (pmol/L)	**Mean± SD**	80.34± 6.36	77.69± 5.76	80.74± 6.38	0.108
	Range	70-90	70-88	70-90	

Data presents as mean ± SD, range or frequency (%): (CRP): C-reactive protein: (ESR): Erythrocyte Sedimentation Rate, TSH: Thyroid Stimulating Hormone, T3: Triiodothyronine, T4: thyroxine*: statistically significant as *P* value <0.05.

Table 4: HIV testing and fecal calprotectin level of the studied groups regarding the prevalence of MC

		Total (n=100)	Patients with MC (n=13)	Patients without MC (n=87)	P value
HIV testing	**Positive**	0 (0%)	0 (0%)	0 (0%)	-
	Negative	100 (100%)	13 (100%)	87 (100%)	
Fecal calprotectin (µg/mg)	**Mean± SD**	21.84± 19.7	63.92± 24.28	15.55± 7.54	**<0.001 ***
	Range	3-97	27-97	3-30	

Data presents as mean ± SD, range or frequency (%). HIV: Human Immunodeficiency Virus. MC: Microscopic colitis, *: statistically significant as *P* value <0.05

Discussion

In patients who present with chronic diarrhea, in particular those who have a macroscopically normal colonoscopy, the differential diagnosis of both MC and IBS is essential [(16)]. Frequently affecting younger individuals, IBS is a chronic functional bowel disorder that is characterized by abdominal distress that is linked to a disordered bowel habit. Approximately 10–20% of individuals worldwide are affected by the condition [(8)]. Regardless, some research suggests that stomach pain is a negative indicator of MC, and MC often presents as persistent watery diarrhea in middle age. Additionally, there are two primary subtypes of MC identified by histology: CC, which is characterized by intraepithelial lymphocytosis, and LC, which is characterized by a distinct subepithelial collagen band. About 9 cases per 100,000 person-years are reported for CC [(17)].

In spite of the disparities in epidemiology, the significant risk of symptom overlap is posed by the high prevalence of IBS and the similarities in some of the presenting features between IBS and MC. Importantly, this could lead to a misunderstanding between the two, which could cause unnecessary colonoscopies and biopsies for patients suspected of having IBS or a delay in the diagnosis and start of effective treatments for patients with MC [(16)].

Of the patients who were part of the study, two (2%) had a personal or family history of colorectal cancer, and twenty-seven (27%) had used proton pump inhibitors at some point.

The reason for this is that 27% of patients had previously used proton pump inhibitors. Because of the increased risk of GERD and dyspepsia in patients with IBS, PPI therapy is also commonly administered to these patients. Additionally, the overuse of PPI therapy is a prevalent issue, frequently precipitated by an unexplained abdominal discomfort [(18)].

Regarding the results, the histological findings of the biopsy showed normal biopsy in 87 (87%) patients, lymphocytic colitis in 9 (9%) patients and collagenous colitis in 4 (4%) patients. The prevalence of MC was among 13 (13%) of the studied patients.

These results are in agreement with A Abd El-Fattah Badran et al. [(19)] Twenty out of one hundred patients were found to have MC, eighteen (or 90%) to have LC, and two (10%) to have CC, all based

on the Rome IV criteria for IBS-D diagnosis.

Further, Ebeid et al. [20] In a study conducted by the authors, they discovered that out of 86 specimens from patients with normal colonic mucosa and D-IBS diagnosed using Rome III criteria, there were 26 cases of MC, 8 cases of UC, and 26 cases of NSC (71.66%).

Our study finds that the history of use of PPI was significantly lower in patients with MC compared to patients without MC (P=0.001).

On the other hand, Bruno et al. [21] stated that it has been postulated that PPIs may lead to MC via reduction of gastric acidity, which causes changes in the gut microbiome and electrolyte concentration within the colonic lumen. These changes could induce intraepithelial lymphocytosis and subsequently inflammation and resulting diarrhea.

In comparison to patients without MC, patients with MC exhibited significantly higher rates of abdominal distention, weight loss, and fever (P=0.002, 0.011, and 0.017, respectively). Nevertheless, there was no considerable distinction between the two groups in terms of the other manifestations, such as anorexia, vomiting, nocturnal defecation, and abdominal pain.

In alignment with our study, Stoicescu et al. [22] The group of patients with MC exhibited a predominance of nocturnal diarrhea, modest weight loss, and positive fecal calprotectin (p <0.0001, p = 0.0005, p <0.0001). Nevertheless, the investigation produced distinctive findings, as it was determined that patients with IBS-D were more likely to experience abdominal distress and pain (p = 0.0017, p = 0.022).

As well, A Abd El-Fattah Badran et al. [19] Disclosure has been provided to patients who meet the Rome IV criteria for the diagnosis of IBS-D. Patients diagnosed with MC were the only ones to experience nighttime diarrhea and weight loss (15 out of 20 or 75% of the total). A statistically significant difference was found between patients with normal histology and those with metabolic cancer (p-value < 0.001).

The duration of diarrhea and the frequency of gastrointestinal movements were significantly higher in patients with MC than in those without MC, as indicated by the results (P<0.00, <0.001).

These findings are in accordance with Ebeid et al. [20] Diarrhea lasted significantly longer in MC patients compared to NSC and UC patients among those who met the Rome III criteria for D-IBS (P=0.0006).

Additionally, Abdel Monem et al. [23] found in patients with MC compared to patients with IBS-D had higher mean number of motions per day (4>3) but it wasn't statically significant (P=0.451), Also, duration of diarrhea in MC group (4 ± 1.47 months) statically higher than IBS-D (1.64 ± 0.79 months) (P<0.001).

In comparison to patients without MC, patients with MC exhibited significantly higher CRP levels and ESRs (P <0.001, <0.001).

These findings are supported by Elsayed et al. [24] who declared that the ESR levels in MC patients were significantly

elevated, with a range of 5-15 mg/dl, compared to the levels of other patients, which exhibited a range of 3-13 mg/dl, since ESR is an acute phase reactant.

Furtherly, A Abd El-Fattah Badran et al. [19] The results of the study were corroborated by the significant difference in the levels of the inflammatory markers C-reactive protein (CRP) and Erythrocyte sedimentation rate (ESR) between MC patients and normal biopsy patients. Nonetheless, these markers remained within the normal range regarding their levels.

Concerning the results, the fecal calprotectin level was significantly higher in patients with MC compared to patients without MC (P <0.001).

von Arnim et al. [25] Through our investigation, we were able to verify several points. Patients suffering from IBS had a significantly lower median level (2 μg/g [1-111.83]) compared to those with active multiple sclerosis (MC) (48 μg/g [23-106]), as shown by an ELISA test.

Additionally, Batista et al. [26] The median calprotectin level in the control group was 28 (IQR, 16-111) while in the MC group it was 175 (IQR, 59-325) ($p < 0.001$). The fecal calprotectin assay showed a sensitivity of 67% and a specificity of 75%, and the ideal cut-off value was >100 μg/g (AUC, 0.73). When calprotectin levels were high, the likelihood of MC was 5.3 (confidence interval, 2-14.1). When diagnosing chronic watery diarrhea in women older than 60, elevated fecal calprotectin concentrations may be helpful in MC.

As well, Songtanin et al. [27] The results of the meta-analysis supported our own findings, indicating that FCP was slightly higher in MC patients than in controls (SMD = 0.6 [95% CI 0.3, 1.0], P = 0.001). According to the results of the single effect size (SMD = 0.5 [95% CI 0.2, 0.9], P = 0.004), it is evident that patients with MC have a significantly higher FCP than control subjects with chronic diarrhea.

The limitations of the study were that the relatively small sample size inevitably lowered the statistical power of the analysis and single-center study making the results less generalizable.

Conclusion

Elderly individuals are frequently diagnosed with MC, which is not an uncommon condition. Because it is easily confused with IBS-D, the only way to differentiate is by histopathological analysis of colonoscpic specimens taken from the normally appearing mucosa. When patients with irritable bowel syndrome-D have both weight loss and diarrhea at night, the risk of MC rises, which calls for a colonoscopy biopsy. Inflammatory markers (CRP, ESR, and FC) may show modest increases in patients who meet IBS-D criteria; however, these markers are not specific enough to diagnose MC.

As a result, it is recommended that additional research be conducted with a larger and stratified sample, as well as a multi-center study size, to ensure more precise results. According to our research, FC could be incorporated into the clinical workup to ascertain which patients with chronic diarrhea necessitate biopsies for the histological assessment of active MC.

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