PREVALENCE OF MICROSCOPIC COLITIS IN PATIENTS WITH NORMAL OR NONSPECIFIC COLONOSCOPIC FINDINGS

ABSTRACT:

***Background*:** Microscopic colitis (MC) is a chronic inflammatory bowel disease in the setting of normal appearing colonic mucosa and distinct histopathologic features. Microscopic colitis has two main subtypes, collagenous colitis (CC) and lymphocytic colitis (LC). Diagnosis of MC is mainly based on pathological examination of colonic biopsy. ***Aim*:** Estimation of MC among patients with normal or nonspecific colonoscopic findings. ***Methods*:** This cross-sectional study was conducted on (172) patients with normal or nonspecific colonoscopic findings. Full history taking, clinical examination, laboratory investigations, pelvi-abdominal ultrasound and complete colonoscopy examination were done. Endoscopic biopsies from the right and left side of the colon were taken for all patients for histopathological examination. ***Results*:** Of all the studied patients, 9 cases (5.2%) had MC with 6 patients (3.5%) having LC and 3 patients (1.8%) having CC. One hundred twenty-one cases were diagnosed as chronic nonspecific colitis (70.3%), 19 cases were diagnosed as chronic active colitis (11.1%) while 23 cases (13.3%) were normal. The median age of patients with MC was about 45 years and most of them were females. Univariate logistic regression analysis of predictors for developing MC showed that chronic diarrhea, chronic diarrhea duration and nonsteroidal anti-inflammatory drugs (NSAIDs) use are significant independent predictors for MC. ***Conclusion*:** MC could be considered in any patient with chronic lower gastrointestinal symptoms and apparently normal mucosa during colonoscopy examination. Multiple colonic biopsies should be taken from any patient with unexplained chronic lower gastrointestinal symptoms even with normal macroscopic picture to reach a definite diagnosis of MC.

KEY WORDS: Microscopic Colitis; Colonoscopy; Biopsy.

ABBREVIATIONS: MC = Microscopic Colitis; CC = Collagenous Colitis; LC = Lymphocytic Colitis; NSAIDs = Nonsteroidal Anti-Inflammatory Drugs.

INTRODUCTION:

Microscopic colitis (MC) is a chronic inflammatory bowel disease characterized by nonbloody diarrhea in the setting of normal appearing colonic mucosa and distinct histopathologic features [(1)]. Microscopic colitis has two main subtypes, collagenous colitis (CC) and lymphocytic colitis (LC) [(2,3)]. In the past, MC was thought to be a rare disorder and very little was known about its etiology or epidemiology. MC is regarded as a common cause of diarrhea in middle-aged and elderly patients [(4)]. MC accounts for 4–13% of cases of chronic diarrhea [(5)].

The etiology of MC is still unknown, various independent risk factors, broadly including medications such as (proton pump inhibitors (PPIs), nonsteroidal anti-inflammatory drugs (NSAIDs), beta-blockers, statins, and selective serotonin reuptake inhibitors), tobacco, and autoimmune conditions, have been identified, which are implicated in both developing and flaring of MC [(6)]. The incidence is higher in women than in men, with a female-to-male

incidence ratio of 3.05 for CC and 1.92 for LC [7]. The hallmark symptom of MC is watery chronic nonbloody diarrhea [8]. The watery diarrhea is often associated with abdominal pain, urgency, incontinence, nocturnal symptoms, and/or weight loss [8]. Fatigue has also been noted to be a prevalent symptom in MC [9].

Colonoscopy usually reveals normal colonic mucosa on endoscopic examination [10]. However, macroscopically visible lesions or alterations were reported in 38.8% of patients in various parts of the colon, including isolated linear ulcerations, pseudomembranes, irregular vascular patterns, mucosal lacerations, erythema, oedema, nodularity and surface textural alterations [11].

Microscopic Colitis shares similar symptoms and endoscopic results with functional bowel disorders, especially in diarrhea-dominant irritable bowel syndrome (IBS) and chronic functional diarrhea [9]. Irritable bowel syndrome (IBS) is a chronic functional bowel disorder, often affecting younger individuals [12] and characterized by abdominal pain in association with a disordered bowel habit [13]. The condition affects approximately 10–20% of individuals globally [12]. Both microscopic colitis (MC) and irritable bowel syndrome (IBS) are important differential diagnoses in individuals presenting with chronic diarrhea, especially among patients with a macroscopically normal colonoscopy [12]. This substantial overlap of symptoms between IBS and MC can lead to confusion between the two, delaying the diagnosis and commencement of effective therapies in patients with MC [14]. The aim of the current study was estimation of microscopic colitis among patients with normal or nonspecific colonoscopic findings.

PATIENTS AND METHODS:

This cross sectional study was conducted on 172 subjects at the Hepatology, Gastroenterology and Infectious Diseases Department and the Pathology Department, Benha University during the period from Mars 2021 to June 2023. The study was done after being approved by the Research Ethics Committee of Benha faculty of medicine, Benha university (study number: M.D.7.12.2020).

An informed consent was obtained from all individual participants included in the study.

Inclusion criteria:

Patients of both sex who had been attended to the endoscopy unit of Hepatology, Gastroenterology and Infectious Diseases Department at Benha Faculty of Medicine University Hospitals with normal or nonspecific colonoscopic findings and had one or more of the following criteria:

1- Symptoms suggesting MC including (chronic watery nonbloody diarrhea defined by persistent symptoms lasting for more than 1 month, fecal urgency, nocturnal stools, fecal incontinence, abdominal pain, weight loss and fatigue) [8,9].
2- Irritable bowel syndrome fulfilling the diagnostic criteria of Rome IV [15]:

Recurrent abdominal pain on average at least 1 day per week during the previous 3 months that is associated with two or more of the following: (related to defecation, associated with a change in stool frequency and associated with a change in stool form or appearance).

Supporting symptoms include the following: (altered stool frequency, altered stool form, altered stool passage (straining and/or urgency), mucorrhea, abdominal bloating or subjective distention).

Exclusion criteria:

1. Patients with bloody diarrhea.
2. Patients with any abnormal colonoscopic findings other than that suggesting MC (as described before) as: (mass, polyp, diverticulae and fistula).
3. Patients with endoscopic findings suggesting inflammatory bowel disease (IBD):

- Typical ulcerative colitis (UC) features (diffuse superficial colonic inflammation, involvement of rectum, but this can be patchy, shallow erosions and ulcers and spontaneous bleeding) [16].

-Typical Crohn's disease (CD) features (discontinuous transmural asymmetric lesions mainly involving ileum and right-sided colon, cobblestone appearance, longitudinal ulcer and deep fissures) [16].

All participants were subjected to thorough history taking with special emphasis on history of smoking, any associated illness, history of drug intake (PPIs, NSAIDs, beta-blockers, statins and SSRIs) and lower gastrointestinal symptoms (watery non-bloody diarrhea, fecal urgency, abdominal pain, weight loss and bloating), full clinical examination, laboratory investigations including (complete blood count, serum creatinine level and viral markers), pelvi-abdominal ultrasound and complete colonoscopy examination with ileal intubation. Midazolam or propofol was used for sedation then colonoscopy was done. Most procedures done using Olympus 180 and FUJI EC 720 endoscopy units. Endoscopic biopsies were done in a well-equipped place under complete aseptic condition by highly qualified professors and a standard sheet was filled for every patient. Endoscopic biopsies from at least the right and left side of the colon were taken for all patients for histopathological diagnosis. All biopsy samples were evaluated and categorized as follows:

(1) A diagnosis of lymphocytic colitis requires an increase in intraepithelial lymphocytes to more than 20 lymphocytes/100 surface epithelial cells combined with an increased inflammatory infiltrate in the lamina propria and a not significantly thickened collagenous band (< 10 μm) [17].

(2) For a diagnosis of collagenous colitis, an increase/irregularity in subepithelial collagen (>10 μm) combined with an increased inflammatory infiltrate in the lamina propria is required (17).

In borderline cases, if additional studies needed (supplementary special stain as Masson or Trichrome stain for CC and immunohistochemical staining for CD3 for LC), they were applied [18, 19].

(3) Nonspecific colitis (NSC): When there are <5 intraepithelial lymphocytes per 100 surface epithelial cells and the collagen layer is <5 μm or inflammatory changes not specific to particular diseases but exceeding the limits of the normal mucosa [20].

(4)Chronic active colitis: pattern of injury characterized by cryptitis, crypt abscesses, basal lymphoplasmocytic infiltrates, Paneth cell metaplasia and crypt architectural distortion [21].

STATISTICAL ANALYSIS:

The collected data were summarized in terms of median and Inter Quartile Range (IQR) as appropriate for nonparametric data and mean ± Standard Deviation (SD) as appropriate for parametric data and frequency and distribution for qualitative data. The statistical significance of the difference between the studied groups was evaluated using Mann Whitney test for comparison between two groups as appropriate for parametric data and Student *t* test for comparison between two groups as appropriate for parametric data. Univariate logistic

regression analysis was done to detect the significant predictors of microscopic colitis. All tests were two sided. A P value less than .05 was considered significant. A P value less than .01 was considered highly significant. A P value more than .05 was considered non significant. Statistical Package for the Social Sciences (SPSS) 25.0 for windows SPSS Inc., Chicago, IL, USA) was used.

RESULTS:

The studied patients included 89 males (51.7%) and 83 females (48.3%), their median age was 42 years. Most patients (67.4%) were from rural areas. Thirty-six cases (20.9%) were smokers **Table (1)**. One hundred nineteen patients (69.2%) had history of drug intake **Table (1)**. Twenty-one patients (12.2%) were diabetics and 26 patients (15.2%) had hypertension **Table (1)**. Twenty-seven patients (15.7%) had history of concomitant diseases **Table (1)**. Most patients (90.1%) had no abnormality detected (NAD) on colonoscopy, 14 patients had erythema, 2 patients had edema, and only 1 patient had irregular vascular pattern **Figure (1)**. Nine cases (5.2%) had microscopic colitis {lymphocytic type (6 cases), collagenous type (3 cases)}. One hundred twenty-one cases (70.3%) were diagnosed as chronic non-specific colitis, 19 cases were diagnosed as chronic active colitis (11.1%) while 23 cases (13.3%) were normal **Table (2) and Figure (2)**. There was no statistically significant differences between patients with MC and patients without MC regarding personal history except for sex. Most patients with MC were females (8 patients) (88.9%) compared to patients without MC (75 patients) (46%) **(p = .01) Table (3).** There was a statistically significant difference between patients with MC and patients without MC regarding history of drug intake. All patients with MC (100%) had history of drug intake compared to 110 patients without MC (67.5%) **(p = .04) Table (3).**

Nonsteroidal anti-inflammatory drugs (NSAIDs) intake constituted a significant variable between the studied patients **(p= .02)**. Seven patients with MC (77.8%) used NSAIDs compared to 64 patients without MC (39.3%) **Table (3)**. Proton pump inhibitors (PPIs) intake constituted a significant variable between the studied patients **(p= .01)**. All patients with MC used PPIs compared to 92 patients without MC (56.4%) **Table (3)**. No significant differences were detected between the studied patients regarding utilization of the other drugs (SSRIs, Beta blockers and Statins).

There was a highly statistical significant difference between the studied patients regarding history of concomitant diseases **(p = .000) Table (3)**. Two patients with MC had thyroid disease, 4 patients had IHD and 3 patients were asthmatic compared to patients without MC (one patient had thyroid disease, 5 patients had IHD, 2 patients were asthmatic) **Table (3)**. Seven patients without MC had rheumatoid arthritis and 3 patients had allergy compared to none of patients with MC **Table (3)**. Chronic diarrhea was highly significantly more frequent in patients with MC; 6 patients (66.7%) compared to patients without MC; 21 patients (12.9%) **(p = .000) Table (3).** There was a highly statistical significant difference between the studied patients regarding chronic diarrhea duration **Table (3)**. Patients with MC complained from chronic diarrhea for longer duration (Median (IQR) 24 (11.75-36) months) compared to patients without MC (Median (IQR) 3 (2-6) months) **(p = .000) Table (3).** There was no significant difference between the studied patients regarding laboratory investigations **Table (3)**. Univariate logistic regression analysis of predictors for developing microscopic colitis showed that chronic diarrhea and chronic diarrhea duration are highly significant

independent predictors for microscopic colitis **(p=.000)** and NSAIDs drug use is a significant independent predictors for microscopic colitis **(p=.03) Table (4).** Multivariate logistic regression analysis of predictors for developing microscopic colitis showed that chronic diarrhea, chronic diarrhea duration, recurrent abdominal pain, concomitant diseases, drug history and gross colonoscopy findings are insignificant independent predictors for microscopic colitis **Table (5)**.

DISCUSSION:

Microscopic colitis 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 [(5)].

The aim of the current study was estimation of microscopic colitis among patients with normal or nonspecific colonoscopic findings. In order to achieve this goal, this cross-sectional study was performed at the Hepatology, Gastroenterology and Infectious diseases Department at Benha University Hospitals including 172 subjects with normal or nonspecific colonoscopic findings. Endoscopic biopsies from the right and left side of the colon were taken for all patients for histopathological diagnosis. Of all the studied cases, 9 cases (5.2%) had microscopic colitis {lymphocytic type (6), collagenous type (3)}. One hundred twenty-one cases were diagnosed as chronic non-specific colitis (70.3%), 19 cases were diagnosed as chronic active colitis (11.1%) while 23 cases (13.3%) were normal. The results in this study come in accordance with a similar study in which the prevalence approached 4.5% of MC among the studied group of cases [(22)], also another study conducted on 184 patients revealed a prevalence of MC of 7% in the studied group [(23)]. The MC global prevalence was noted at 103.0 per 100,000 subjects with 63.7 per 100,000 subjects for LC and 39.3 per 100,000 subjects for CC [(24)].

On the other hand, a study revealed that the prevalence of MC is 29.3% in patients with chronic diarrhea [(25)]. Another study found that the prevalence of MC was 40% [(26)]. There was a large difference between results of locally performed studies regarding estimation of MC. Two studies reported prevalence of MC among patients with chronic watery diarrhea about 50 % and 29.5 %, respectively [(27, 28)], while other studies reported prevalence of MC about 10 % and 14 %, respectively [(29,30)].This difference may be due to small sample size, selection bias and population characteristics of included patients.

In the current study, the median age of the included cases was 42 years**,** the median age of patients with MC was 45 years. These findings agreed with a study which showed that the mean age of cases diagnosed with MC was about 45.9 years [(31)]. In this study, there was no significant difference between patients with MC and patients without MC regarding age. Another study also confirmed our findings regarding age, there was no significant difference between microscopic colitis and controls regarding age and in that study, the mean age of the included cases was 50.2 and 48.6 years for microscopic colitis and controls respectively [(32)]. But these results are different from other studies, one of them revealed that the peak incidence for LC and CC was around 65 years, Other report stated that increasing age is an

established risk factor, with 75% of the people affected being over 50 years old [33]. Another study reported that MC is typically a disease of the elderly, with an average age at diagnosis of 65 years [34]. The variability in the peak age for MC might be related to the nonspecificity of the symptoms that can be missed or misdiagnosed as functional bowel disorder.

This study was carried out on 172 cases; including 89 males and 83 females. Most patients with MC were females (88.9%) compared to patients without MC (46%)**.** Likewise, it was reported that the females have higher possibility of development of CC. The causes for this are unrecognized and potential influences of the hormonal changes [35]. Similarly, another study showed that MC was associated with female sex (6.1% women vs. 5% men in LC) [36]. On the other hand, another study reported that there was no significant difference between the two groups regarding patient gender [32].

In the current study, only one patient with MC (11.1%) had history of smoking. There was no statistically significant difference between patients with MC and patients without MC regarding history of smoking**.** According to these results smoking is not a risk factor for MC which disagree with the results of a study which found that of the 116 patients with CC, 37% were smokers compared with 17% of controls, and the conclusion was smoking is a risk factor for CC which is against result of our study [37].

The major clinical manifestations in the MC patients were abdominal pain, abdominal distension and diarrhea. In this study, chronic diarrhea was highly significantly more frequent in patients with MC (66.7%) with median duration of 24 months compared to patients without MC (12.9%) with median duration of 3 months.

A study showed that the duration of symptoms before diagnosis were between 3 to 30 months with average duration 24 months [38], which comes in line with the results of this study. Mean durations of diarrhea in patients with MC were 21.6 months in a study [29] and 12 months in another study [39]. Another study showed 286 patients out of 540 (53.0%) presents with diarrhea more than 1 month duration [40].

In this study, abdominal pain was found in all cases with MC. Another study found that 1 in 3 cases suffering from MC can complain of symptoms of IBS, namely abdominal pain and changes in the bowel habits [41].

Although the MC cause remains unrecognized, variable risk factors, approximately involving tobacco, medications, and autoimmune disorders, have been known that are concerned in MC occurrence and flaring [10]. In this study, all patients with MC had history of drug intake. The commonly used drugs in patients with MC were PPIs followed by NSAIDs. NSAIDs intake constituted a significant variable between patients with MC and patients without MC. Seven patients with MC (77.8%) used NSAIDs compared to 64 patients without MC (39.3%)**.** In agreement with this study, a systematic review has reported that the use of NSAIDs was associated with a slightly increased risk of microscopic colitis [7]. The histologic alterations and symptoms enhance with cessation of NSAIDs and reappear with reusing suggesting that these agents are of great importance in the MC pathophysiology [42]. But on the contrary, other authors reported that NSAIDs intake was not a significant risk factor for microscopic colitis [32]. As regard PPIs intake in this study, all patients with MC used PPIs compared to 56.4% of patients without MC. This comes in agreement with a systematic review which has

stated that there was a substantially increased risk of MC with the use of PPIs [7]. Also, a study detected a strong correlation of PPIs with both LC and CC [43]. But conversely, another study reported that PPI intake was not a significant risk factor for microscopic colitis [32]. It is important to clarify that this study and previous all studies lack information about appearance of clinical symptoms after drug exposure and if symptoms disappear after stopping of drugs in order to establish a causal relationship.

In this study, the incidence of concomitant diseases in MC patients was significantly higher than patients without MC. In agreement with this study, other studies reported that a history of autoimmune disease, including diabetes mellitus, thyroid disorders, rheumatoid arthritis, and celiac sprue, is associated with MC [6, 44].

The present study revealed that level of hemoglobin, total leucocytic count, and platelets counts were within normal values in patients with MC. This agreed with two studies which showed the same findings in patients with MC [45, 46]. In this study, there was no significant difference between patients with MC and patients without MC regarding HBs Ag and Anti HCV Abs. Neither of the previous studies handling microscopic colitis has detected an association between the incidence of MC and patient's hepatitis markers status [7, 32].

Colonoscopy examination of all MC patients in this study was normal with no obvious pathological mucosal findings. In consistent with these results, a study which was conducted on 247 patients with no detected any mucosal pathological lesions during colonoscopy examination and had been previously diagnosed IBS with diarrhea [31]. In contrast, another study reported endoscopic mucosal abnormalities as oedema, erythema, or abnormal vessel pattern in 37% of collagenous colitis patients and 25% of lymphocytic colitis patients [47]. Similarly, another study showed there are macroscopic endoscopic abnormalities in 20 - 30% of patients with MC [48].

This difference between studies could be due to endoscopy related factors which can influence the detection of subtle endoscopic pathological mucosal abnormalities [49].

LIMITATIONS OF THE STUDY:

This study has some limitations; the main limitation that this was a single-center study. This study was conducted with a small sample size of patients, It did not enable us to find possible associations and differences between subtypes of MC. Patients with lymphocytic colitis and collagenous colitis were considered as a one group in this study as the number of both were small to be compared.

CONCLUSION:

This study confirms the importance of colonoscopy and biopsies from normal colonic mucosa in selected patients with certain factors making them at risk for developing specific colonic pathology. Microscopic colitis was found in 5.2% of the studied patients (3.5% lymphocytic colitis and 1.8% collagenous colitis). MC is more common among females. Abdominal pain, chronic diarrhea and abdominal distension were the most common clinical manifestations of MC. Patients with microscopic colitis suffered from diarrhea for longer durations. There was a significant correlation between using NSAIDs with cases proved to have MC.

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AUTHOR CONTRIBUTION:

Authors contributed equally in the study.

CONFLICTS OF INTEREST:

No conflicts of interest.

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Table (1): Sociodemographic characteristics, history of concomitant diseases and history of drug intake of all the studied patients.

Variable \ Studied patients		(N.=172)	
		N.	%
Sex	**Female**	83	48.3
	Male	89	51.7
Age (years) Median (IQR*)	42 (33-54)		
Residence	**Rural**	116	67.4
	Urban	56	32.6
Special habits	**No**	121	70.4
	Smoking	36	20.9
	Alcohol	0	0
History of drug intake**	**Yes**	119	69.2
	No	53	30.8
NSAIDs	**Yes**	71	41.3
	No	101	58.7
PPIs	**Yes**	101	58.7
	No	71	41.3
SSRIs	**Yes**	13	7.6
	No	159	92.4
Beta blockers	**Yes**	22	12.7
	No	150	87.3
Statins	**Yes**	20	11.6
	No	152	88.4
DM	**Yes**	21	12.2
	No	151	87.8
Hypertension	**Yes**	26	15.2
	No	146	84.8
Concomitant diseases	**No**	145	84.3
	Thyroid disease	3	1.7
	Rheumatoid Arthritis	7	4.1
	IHD	9	5.3
	Asthma	5	2.9
	Allergy	3	1.7
	Celiac disease	0	0.0

*IQR= InterQuartile Range, NSAIDs=Nonsteroidal Anti-Inflammatory Drugs, PPIs= Proton Pump Inhibitors, SSRIs= Selective Serotonin Reuptake Inhibitors, DM= Diabetes Mellitus, IHD= Ischemic Heart Disease.

** One patient may have history of more than one of the listed triggering drugs.

Table (2): Distribution of histopathological findings of biopsies among the studied patients:

Variable \ Studied patients	(N.=172)	
	N.	%

Histopathological findings	**Collagenous colitis**	3	1.8
	Lymphocytic colitis	6	3.5
	Chronic nonspecific colitis	121	70.3
	Chronic active colitis	19	11.1
	Normal biopsy	23	13.3

Table (3): Comparison between the studied patients regarding different variables.

Studied patients / Variable		**Patients with MC (N.=9)**		**Patients without MC (N.=163)**		**Chi square test**	**P value**
		N.	**%**	**N.**	**%**		
Age (years) Median (IQR)*		**Median (IQR)**		**Median (IQR)**		**Zmann Whittney=**	.30
		45	36.5-63.5	41	33-54	1.03	
Sex	**Female (83)**	8	88.9	75	46	6.28	**.01 (S)**
	Male (89)	1	11.1	88	54		
Special habits	**No (121)**	6	66.7	115	70.6	2.41	.29
	Smoking (36)	1	11.1	35	21.5		
History of drug intake **	**Yes (119)**	9	100	110	67.5	4.23	**.04 (S)**
	No (53)	0	0	53	32.5		
NSAIDs	**Yes (71)**	7	77.8	64	39.3	5.21	**.02 (S)**
	No (101)	2	22.2	99	60.7		
PPIs	**Yes (101)**	9	100	92	56.4	6.67	**.01 (S)**
	No (71)	0	0	71	43.6		
SSRIs	**Yes (13)**	1	11.1	12	7.4	0.17	.67
	No (159)	8	88.9	151	92.6		
Beta blockers	**Yes (22)**	1	11.1	21	12.9	0.02	.87
	No (150)	8	88.9	142	87.1		
Statins	**Yes (20)**	2	22.2	18	11	1.03	.30
	No (152)	7	77.8	145	89		
Concomitant diseases	**No (145)**	0	0.0	145	89.0	FET= 89.5	**.000 (HS)**
	Thyroid disease (3)	2	22.2	1	0.6		
	Rheumatoid arthritis (7)	0	0.0	7	4.3		
	IHD (9)	4	44.4	5	3.1		
	Asthma (5)	3	33.3	2	1.2		

	Allergy (3)	0	0.0	3	1.8		
Chronic diarrhea	**Yes (27)**	6	66.7	21	12.9	18.6	**.000 (HS)**
	No (145)	3	33.3	142	87.1		
Chronic diarrhea duration (Months) Median (IQR)		24	11.75-36	3.0	2.0-6.0	3.41	**.000 (HS)**
Recurrent abdominal pain	**Yes (130)**	9	100	121	74.2	3.06	.08
	No (42)	0	0	42	25.8		
Fecal urgency	**Yes (21)**	1	11.1	20	12.3	0.011	.91
	No (151)	8	88.9	143	87.7		
Constipation	**Yes (72)**	2	22.2	70	42.9	1.50	.22
	No (100)	7	77.8	93	57.1		
Diarrhea alternate with constipation	**Yes (20)**	1	11.1	19	11.7	0.002	.96
	No (152)	8	88.9	144	88.3		
Abdominal distension	**Yes (101)**	7	77.8	94	57.7	1.42	.23
	No (71)	2	22.2	69	42.3		
Mucorrhea	**Yes (32)**	2	22.2	30	18.4	0.08	.77
	No (140)	7	77.8	133	81.6		

	Median	**IQR**	**Median**	**IQR**	**Zmann Whittney test**	**P value**
HB (gm/dl)	13.1	9.1-15.9	12.2	10.2-14.0	0.85	.39
WBCs (x 1000 / cmm)	5.8	4.6-10.6	6.5	5.0-8.4	0.12	.90
Platelet (x10 ^{9}/L) **(Mean±SD)**	252.4	93.0	264.8	86.3	**St-*t* test** =0.41	.67
Serum creatinine (mg/dl)	1.1	0.8-1.4	1.0	0.7-1.2	1.03	.29

		N.	**%**	**N.**	**%**	**Chi square test**	**P value**
HCV Abs	**Positive (8)**	1	11.1	7	4.3	0.89	.34
	Negative(164)	8	88.9	156	95.7		
HBs Ag	**Positive (0)**	0	0.0	0	0.0	-	-
	Negative (172)	9	100	163	100		

*IQR= InterQuartile Range, MC= Microscopic Colitis, NSAIDs=Nonsteroidal Anti-Inflammatory Drugs, PPIs= Proton Pump Inhibitors, SSRIs= Selective Serotonin Reuptake Inhibitors, DM= Diabetes Mellitus, IHD= Ischemic Heart Disease, HB= Haemoglobin, WBCs= White Blood Cells, SD= Standard Deviation, HCV Abs= Hepatitis C Virus Antibodies, HBs Ag= Hepatitis B Surface Antigen, S= Significant, HS = Highly Significant, FET= Fisher Exact Test, St-*t* test= Student *t* test.
** One patient may have history of more than one of the listed triggering drugs.

Table (4): Univariate logistic regression of predictors for developing microscopic colitis.

Microscopic colitis	EXP (B)	P value	95 % CI	
			Lower	Upper
Chronic diarrhea Yes No (ref)	 .07 -	**.000** **(HS)**	 .017 -	 .318 -
Chronic diarrhea duration	1.17	**.000** **(HS)**	1.08	1.26
Recurrent abdominal pain Yes No(ref)	 .000 -	 .99	 .000 -	 .000 -
Concomitant diseases Thyroid disease Rheumatoid arthritis IHD Asthma Allergy No(ref)	 .000 .000 .000 .75 .40 .000 -	 .99 	 .000 .000 .000 .03 .02 .000 -	 .000 .000 .000 14.9 6.17 .000 -
Drug history Yes No (ref)	 .000 -	 .99	 .000 -	 .000 -
NSAIDs Yes No (ref)	 0.18 -	 **.03** **(S)**	 .03 -	 .91 -
PPIs Yes No (ref)	 .000 -	 .99	 .000 -	 .000 -
Gross colonoscopy findings NAD (ref) Erythema Oedema Irregular vascular pattern	 - 995 1.0 1.0	 - 1.0 	 - .000 .000 .000	 - .000 .000 .000

IHD= Ischemic Heart Disease, NSAIDs=Nonsteroidal Anti-Inflammatory Drugs, PPIs= Proton Pump Inhibitors, CI= Confidence Interval, S= Significant, HS = Highly Significant, NAD= No Abnormality Detected.

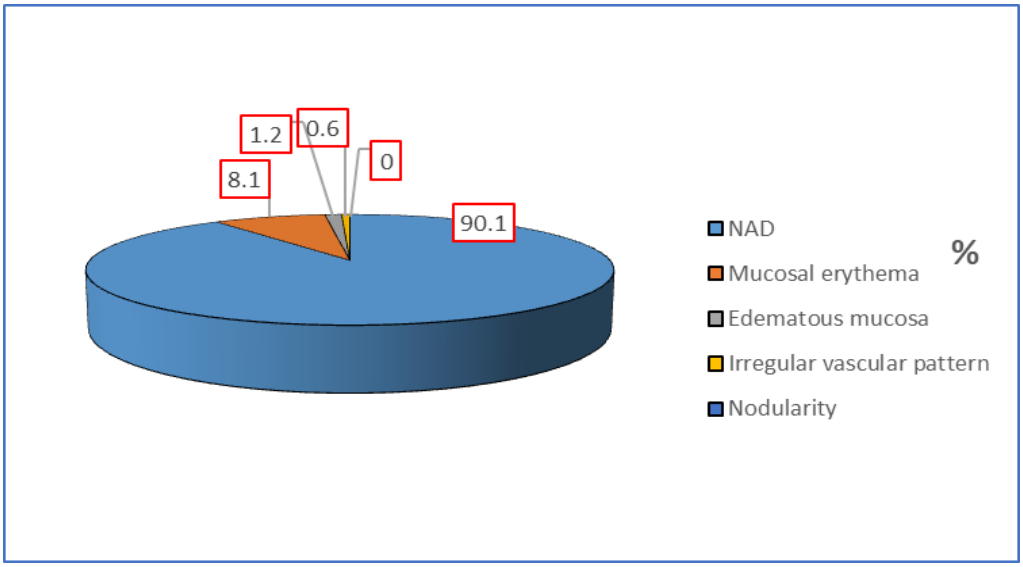
Table (5): Multivariate logistic regression of predictors for developing microscopic colitis.

Microscopic colitis	EXP (B)	P value	95 % CI	
			Lower	Upper
Chronic diarrhea Yes No (ref)	 178 -	 0.99	 .000 -	 .000 -
Chronic diarrhea duration	3.72	0.99	.000	.000

Recurrent abdominal pain Yes No(ref)	 .000 -	 0.99	 .000 -	 .000 -
Concomitant diseases Thyroid disease Rheumatoid arthritis IHD Asthma Allergy No(ref)	 .000 .000 .000 .000 .000 .000 -	 0.99	 .000 .000 .000 .000 .000 .000 -	 .000 .000 .000 .000 .000 .000 -
Drug history Yes No (ref)	 .000 -	 0.99	 .000 -	 .000 -
NSAIDs Yes No (ref)	 0.88 -	 0.99	 .000 -	 .000 -
PPI Yes No (ref)	 .000 -	 1.0	 .000 -	 .000 -
Gross colonoscopy findings NAD (ref) Erythema Oedema Irregular vascular pattern	 - .000 .000 .000	 - 0.99 	 - .000 .000 .000	 - .000 .000 .000

IHD= Ischemic Heart Disease, NSAIDs=Nonsteroidal Anti-Inflammatory Drugs, PPIs= Proton Pump Inhibitors, CI= Confidence Interval, NAD= No Abnormality Detected.

Figure (1): Gross colonoscopy findings of the studied patients.



NAD= No Abnormality Detected.

Figure (2): Histopathological findings of biopsies of the studied patients.