



Original Article

Metabolic Comorbidities as Independent Predictors of Microscopic Colitis in Diarrhoea-Predominant Irritable Bowel Syndrome Patients

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Abstract

Background: Microscopic colitis (MC) is frequently misdiagnosed as diarrhoea-predominant irritable bowel syndrome (IBS-D) due to overlapping symptoms and normal endoscopic appearance. The role of metabolic comorbidities such as diabetes mellitus (DM) and hypertension (HTN) as independent predictors of MC remains underexplored, particularly in the people of South Asia. This study aimed to determine the frequency of MC in IBS-D patients and specifically evaluate metabolic comorbidities. **Materials and Methods:** A cross-sectional observational study was conducted at the Department of Gastroenterology, Bangladesh Medical University (BMU), from July 2023 to December 2024. A total of 223 IBS-D patients fulfilling Rome IV criteria underwent full colonoscopy with multi-segment biopsies. Histological examination was carried out using H&E and Masson's trichrome staining techniques. Multivariate logistic regression was used to identify independent predictors of MC. **Results:** MC was identified in 51 (22.87%) of IBS-D patients in which 34 (66.7%) lymphocytic colitis and 17 (33.3%) collagenous colitis. Diabetes mellitus (50.99% vs 12.8%; $p<0.05$) and hypertension (54.9% vs 14.5%; $p<0.05$) were significantly more prevalent in MC patients. On multivariate regression, hypertension (AOR: 1.91, 95% CI: 1.50-2.42, $p=0.001$), DM (AOR: 1.65, 95% CI: 1.23-2.22, $p=0.001$), thyroid disorder (AOR: 1.80, $p=0.015$), statin use (AOR: 2.04, 95% CI: 1.54-2.68, $p=0.001$), and PPI use (AOR: 1.35, $p=0.002$) were independent predictors of MC. **Conclusion:** Metabolic comorbidities, particularly DM and HTN, are significant independent predictors of MC in IBS-D patients. Routine histopathological evaluation should be prioritized in IBS-D patients with metabolic comorbidities or prolonged statin and PPI use.

Keywords: Microscopic colitis, IBS-D, Metabolic syndrome, Diabetes, Hypertension, Bangladesh, Histopathology.

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Introduction

Microscopic colitis (MC) is a chronic immune-mediated inflammatory disorder of the colon characterized by chronic, watery, non-bloody diarrhea with a grossly normal colonoscopic appearance, requiring histopathological confirmation for diagnosis¹. It is classified into two principal subtypes: lymphocytic colitis (LC), defined by ≥ 20 intraepithelial lymphocytes (IELs) per 100 epithelial cells, and collagenous colitis (CC), characterized by a subepithelial collagen band

exceeding $10 \mu\text{m}^2$. The incidence of MC in Europe ranges from 10.5 to 25.8 per 100,000 person-years, with a prevalence of approximately 197.9 to 246.2 per 100,000, disproportionately affecting older women^{3,4}.

Diarrhoea-predominant IBS (IBS-D) is a functional gastrointestinal disorder diagnosed using Rome IV criteria, affecting 9-23% of the global population and 7.7-12.9% of Bangladeshis^{5,6}. Because both MC

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and IBS-D present with chronic watery diarrhoea, abdominal pain, and normal colonoscopy, the clinical differentiation between them is challenging⁷. Studies suggest that 10-22% of patients labelled as IBS-D may actually harbor undiagnosed MC, leading to diagnostic delay and inappropriate management^{8,9}.

Established risk factors for MC include older age, female sex, smoking, prolonged use of proton pump inhibitors (PPIs), non-steroidal anti-inflammatory drugs (NSAIDs), selective serotonin reuptake inhibitors (SSRIs), and statins^{4,5,10}. Emerging evidence also implicates systemic metabolic conditions - particularly diabetes mellitus and hypertension - in the pathogenesis of MC, possibly through shared immune-inflammatory pathways^{2,6}. However, data from South Asian populations, where metabolic comorbidities are highly prevalent, remain limited.

Previous Bangladeshi studies by Rahman et al. (2012) and Rahman et al. (2016) reported MC prevalence of 36.7% and 24.0% respectively among IBS-D patients, yet neither systematically evaluated metabolic comorbidities as independent predictors using multivariate analysis^{11,12}. This study aimed to determine the frequency of MC in IBS-D patients and specifically evaluate metabolic comorbidities like diabetes, hypertension, and thyroid disorders - as independent predictors of MC using logistic regression modelling.

Materials and Methods

This cross-sectional observational study was conducted at the Department of Gastroenterology, Bangladesh Medical University (BMU), Dhaka, from July 2023 to December 2024. Ethical approval was obtained from the BMU Institutional Review Board (IRB), and informed written consent was obtained from all participants. Patients aged ≥ 18 years presenting to the outpatient, inpatient, and endoscopy units with symptoms fulfilling Rome IV criteria for IBS-D were enrolled consecutively. IBS-D was defined as loose/watery stools $\geq 25\%$ of the time with hard/lumpy stools $<25\%$ of the time^{5,6}. Exclusion criteria included per-rectal bleeding, anaemia, abdominal mass, infectious colitis, inflammatory bowel disease (IBD), pancreatic insufficiency, bile acid malabsorption, and lactose intolerance. Sample size was calculated using the formula $n = z^2pq/d^2$, yielding a minimum of 222 participants ($p=17.5\%$ based on Sheeladevi et al.⁸ study).

All enrolled patients underwent a full colonoscopy using a high-resolution colonoscope (CF-HQ190L, Olympus). Multiple biopsies were obtained from the caecum, ascending, transverse, and descending

colon. Tissue sections were stained using H&E and Masson's trichrome staining techniques. LC was diagnosed when IELs exceeded 20/100 epithelial cells; CC was diagnosed when the subepithelial collagen band exceeded 10 μm , per UEG/EMCG diagnostic criteria¹³.

Data was entered and analysed using SPSS v26.0 (IBM). Continuous variables were expressed as mean $\pm$ SD; categorical variables as frequency and percentage. Comparisons between groups were conducted using the chi-square test or Fisher's exact test. Multivariate logistic regression was performed to identify independent predictors of MC, expressed as adjusted odds ratios (AOR) with 95% confidence intervals (CI). Statistical significance was set at $p < 0.05$.

Results

Among 223 IBS-D patients (mean age 45.4 ± 13.4 years; 51.6% male), MC was confirmed histopathologically in 51 patients (22.87%): 34 with lymphocytic colitis (LC; 66.7%) and 17 with collagenous colitis (CC; 33.3%). Table-I summarizes the comparative demographic characteristics. MC patients were significantly older, with 58.8% aged >57 years compared to 11.1% in IBS-D patients ($p < 0.05$). Female predominance was observed in MC (58.8% vs 45.4%), though not statistically significant. Widowhood was significantly higher in the MC group (19.6% vs 0.6%; $p < 0.05$), likely to reflect the older age cohort. Educational level also differed significantly, with higher rates of illiteracy in MC patients (35.3% vs 6.9%; $p < 0.05$).

Table-II and III presents the distribution of comorbidities and drug history between IBS-D and MC patients, along with multivariate regression findings. Diabetes mellitus was present in 51.0% of MC patients versus 12.8% of IBS-D patients ($p < 0.05$), and hypertension in 54.9% versus 14.5% ($p < 0.05$). Statin use was significantly higher in the MC group (39.2% vs 7.6%; $p < 0.05$), as was PPI use (68.6% vs 41.8%; $p < 0.05$). On multivariate logistic regression, hypertension (AOR: 1.91, 95% CI: 1.50-2.42, $p=0.001$), diabetes mellitus (AOR: 1.65, 95% CI: 1.23-2.22, $p=0.001$), thyroid disorder (AOR: 1.80, 95% CI: 1.12-2.89, $p=0.015$), statin use (AOR: 2.04, 95% CI: 1.54-2.68, $p=0.001$), and PPI use (AOR: 1.35, 95% CI: 1.12-1.63, $p=0.002$) were independently associated with MC.

Figure-1 illustrates the frequency and subtype distribution of MC among study participants. Figure-2 demonstrates the gender distribution across MC subtypes, showing female predominance in both LC (35.3%) and CC (23.5%).

Table-I: Comparative Demographic Distribution of IBS-D and Microscopic Colitis Patients (N=223)

Characteristics	Category	IBS-D (=172) n (%)	MC (N=51) n (%)
Age Groups	Mean $\pm$ SD	45.4 $\pm$ 13.4	45.2 $\pm$ 13.3
	18-27 years	19 (11.1)	08 (15.7)
	28-37 years	36 (20.9)	02 (3.9)
	38-47 years	55 (31.9)	03 (5.9)
	48-57 years	43 (25.0)	08 (15.7)
	>57 years*	19 (11.1)	30 (58.8)
Gender	Male	94 (54.6)	21 (41.2)
	Female	78 (45.4)	30 (58.8)
Residence	Rural	65 (37.8)	23 (45.1)
	Urban	74 (43.1)	23 (45.1)
	Semi-Urban	33 (19.1)	05 (9.8)
Education	Illiterate	12 (6.9)	18 (35.3)
	Primary	33 (19.2)	18 (35.3)
	SSC	46 (26.7)	04 (7.8)
	HSC	46 (26.7)	09 (17.6)
	Graduate & above*	35 (20.3)	02 (3.9)
Marital Status	Unmarried	32 (18.6)	07 (13.7)
	Married	138 (80.2)	34 (66.7)
	Widow*	01 (0.6)	10 (19.6)
Smoking Status	Non-smoker	103 (59.9)	29 (56.9)
	Smoker	62 (36.0)	18 (35.3)
	Ex-smoker	07 (4.1)	04 (7.8)

* $p < 0.05$ in Fisher's exact test; Values in parentheses represent column percentages.

Table-II: Comorbidities and Drug History of Microscopic Colitis in IBS-D Patients (N=223)

Variable	Total (N=223) n (%)	IBS-D (N=172) n (%)	MC (N=51) n (%)	p-value
Comorbidities				
Diabetes Mellitus	48 (21.5)	22 (12.8)	26 (51.0)	<0.05**
Hypertension	53 (23.8)	25 (14.5)	28 (54.9)	<0.05**
Thyroid Disorder	06 (2.7)	01 (0.6)	05 (9.8)	>0.05*
Rheumatoid Arthritis	06 (2.7)	04 (2.3)	02 (3.9)	>0.05*
SLE	03 (1.3)	02 (1.2)	01 (2.0)	>0.05*
No Comorbidity	132 (59.2)	124 (72.1)	08 (15.7)	<0.05**
Drug History				
Proton Pump Inhibitors (PPIs)	107 (47.9)	72 (41.8)	35 (68.6)	<0.05*
Statins	33 (14.8)	13 (7.6)	20 (39.2)	<0.05*
NSAIDs	19 (8.5)	13 (7.6)	06 (11.8)	>0.05*
ACE Inhibitors	14 (6.3)	07 (4.1)	07 (13.7)	>0.05*
SSRIs	03 (1.3)	02 (1.2)	01 (2.0)	>0.05**

* $p < 0.05$ by Chi-square; ** $p < 0.05$ by Fisher's exact test. AOR = Adjusted Odds Ratio; CI = Confidence Interval. Values in parentheses are column percentages.

Table-III: Multivariate Predictors of Microscopic Colitis in IBS-D Patients (N=223)

Variable	AOR	95% CI	P Value
Hypertension	1.91	1.50-2.42	0.001
Diabetes Mellitus	1.65	1.23-2.22	0.001
Thyroid Disorder	1.80	1.12-2.89	0.015
PPI Use	1.35	1.12-1.63	0.002
Statin Use	2.04	1.54-2.68	0.001

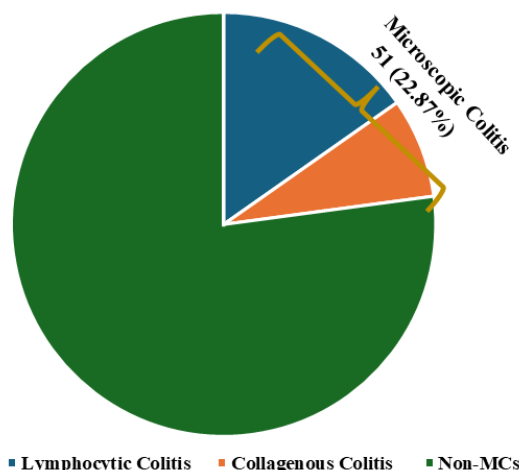


Figure-1: Frequency & subtypes of Microscopic Colitis among IBS-D patients (N=223)

MC: Microscopic Colitis; LC: Lymphocytic Colitis; CC: Collagenous Colitis

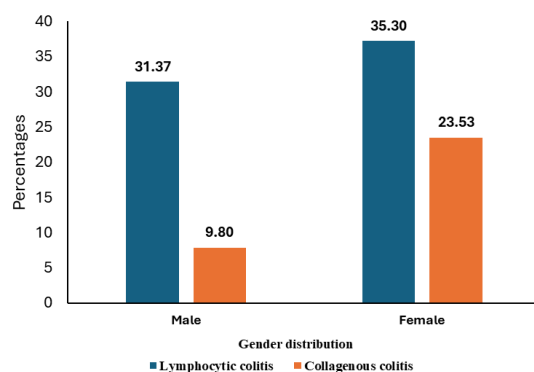


Figure-2: Gender distribution across subtypes of Microscopic Colitis (N=51)

LC: Lymphocytic Colitis; CC: Collagenous Colitis

Discussion

Microscopic Colitis (MC) was observed in 22.87% of IBS-D patients in this study, consistent with reported global prevalence rates of 15%-50% in IBS-D populations^{1,8}. In Bangladeshi context, Rahman et al. (2016)¹¹ and Rahman et al. (2012)¹² reported MC rates of 24% and 36.7% among IBS-D patients, respectively, supporting the notion that MC is significantly underdiagnosed in this population. LC predominated over CC (66.7% vs 33.3%), aligning with international data from Peery et al. (2024)¹⁴ and Weimers et al. (2020)¹⁵.

The most clinically significant finding of this study is the independent association of metabolic comorbidities with MC. Diabetes mellitus and hypertension were present in 51.0% and 54.9% of MC patients respectively, both remaining significant independent predictors on multivariate analysis (AOR: 1.65 and 1.91). This aligns with Fedor et al.⁷, who documented elevated autoimmune and inflammatory comorbidity burdens in MC compared

to IBD, and with Abdel-Razeq et al.², who demonstrated a metabolic risk profile in MC cohorts using a large multicenter database. The proposed mechanism involves chronic low-grade systemic inflammation driven by insulin resistance, adipokine dysregulation, and endothelial dysfunction - conditions central to both metabolic syndrome and colonic mucosal immune activation^{16,17}. Thyroid disorders were also an independent predictor (AOR: 1.80), consistent with the known autoimmune overlap in MC patients mentioned in Weimers et al.¹⁰.

Statin use was the strongest pharmacological predictor (AOR: 2.04), concordant with Weimers et al.¹⁰ and Bonderup et al.³, who demonstrated significant associations between statins and MC risk in Danish nationwide cohorts. PPI use was also independently associated (AOR: 1.35; $p=0.002$), in keeping with Abdel-Razeq et al.² who reported a significant PPI-MC association (population-based study). The high prevalence of statins in MC patients likely also reflects their underlying metabolic comorbidity burden.

Older age (>57 years) was strongly associated with MC (58.8% of MC patients), consistent with the established peak incidence in the sixth to seventh decade¹⁸⁻²⁰. Female predominance in MC (58.8%) aligns with international evidence showing MC is nearly three times more common in women^{21,22}. Importantly, neither smoking status nor NSAIDs showed significant associations in this cohort - potentially reflecting a lower prevalence of these exposures in the Bangladeshi study population²³.

This study has important clinical implications: IBS-D patients harbouring metabolic comorbidities particularly DM and hypertension or receiving long-term statins and PPIs, should be considered for colonoscopic biopsy even when endoscopic mucosa appears normal. Limitations include single-centre design, purposive sampling, and the absence of autoimmune biomarkers or psychological factor assessment. Future multicenter prospective studies with larger samples and biomarker profiling are warranted to validate these findings.

Conclusion

This study confirms that MC occurs in approximately one in four patients clinically diagnosed with IBS-D in Bangladesh. Metabolic comorbidities - particularly diabetes mellitus and hypertension along with statin and PPI use, are significant independent predictors of MC. These findings strongly recommend routine histopathological evaluation via colonoscopic biopsy in IBS-D patients with metabolic comorbidities, even in the presence of a normal endoscopic appearance.

Conflict of Interest and Funding

The authors declare no conflict of interest. No external funding was received for this study.

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