

## Original Article

# Frequency of Microscopic Colitis among Clinically Suspected Diarrhea Predominant IBS Patients

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### Abstract:

**Background:** Microscopic Colitis (MC) and diarrhea predominant irritable bowel syndrome (IBS-D) has almost same clinical feature. Every day, new cases are diagnosed as IBS-D but how many of them are a case of MC is not usually determined and very few studies are found. This study will help to assess the frequency of MC in clinically suspected IBS-D.

**Materials & Methods:** A cross-sectional observational study was conducted in department of medicine and gastroenterology in Faridpur Medical College Hospital over a period of 6 months from July '15 to December '15. Total 100 clinically suspected IBS-D patients were selected by purposive sampling technique. Then full colonoscopy was done and biopsy was taken from colonic mucosa for histopathology.

**Results:** Out of total 100 patients, 38 had lymphocytic Colitis (LC), 39 had nonspecific microscopic colitis (NSMC), 14 had irritable bowel syndrome non-inflamed (IBSNI) and 9 had others (macroscopically colon had hyperaemia, ulcer).

**Conclusion:** Clinical symptom-based criteria for IBS-D are not specific enough to rule out the diagnosis of MC. Therefore, patients with IBS-D should undergo colonoscopy and biopsies of the colon for histopathology to investigate for possible MC.

**Keywords:** Irritable bowel syndrome, Microscopic colitis, Colonoscopy, Biopsy, Diarrhea.

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### Introduction:

Irritable bowel syndrome (IBS) is a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or a change in bowel habit.

Bloating, distension and disordered defecation are commonly associated features. IBS is defined by symptom-based diagnostic criteria, in the absence of detectable organic causes. The symptomatic array is not specific for IBS, as such symptoms may be experienced occasionally by almost every individual. To distinguish IBS from transient gut symptoms, experts have underscored the chronic and relapsing nature of IBS and have proposed diagnostic criteria based on the occurrence rate of symptoms. There are some characteristics of IBS that can be depicted as 1) It is not known to be associated with an increased risk for the development of cancer or inflammatory bowel disease, or with increased mortality. 2) It generates significant direct and indirect health-care costs. 3) No pathophysiological substrate has been demonstrated in IBS. 4) A transition of IBS to, and overlap with, other symptomatic gastrointestinal disorders (e.g., gastroesophageal reflux disease, dyspepsia, and functional constipation) may occur. 5) The condition usually causes long-term symptoms: may occur in episodes, symptoms vary and may be meal-related, symptoms interfere with daily life and social functioning in many patients, symptoms sometimes seem to develop as a consequence of a severe intestinal infection or to be precipitated by major life events, or in a period of considerable stress.<sup>1</sup>

On the contrary, Microscopic Colitis (MC) is an inflammatory condition of the colon in which the colonic mucosa appears normal endoscopically and radiologically, while histological examination of the colonic mucosa reveals specific histopathological features. This entity of inflammatory bowel disease is composed of two separate but related diseases—Collagenous Colitis (CC) and Lymphocytic Colitis (LC). The two entities are similar in their presentation and natural history but differ in their histological appearances. In both the conditions, there is inflammation in the lamina propria of the colonic mucosa, with increased intraepithelial lymphocytes. Specifically in CC and not in LC, there is, in addition, marked thickening of the sub-epithelial collagen layer, which is the hallmark of this disease. This disease entity has attracted a lot of attention recently as an important and relatively common cause of chronic diarrhea. The initial description of MC was first published in 1976 and since that time, it has been increasingly recognized as a relatively common cause of chronic diarrhea.<sup>1</sup>

MC is a disorder of unknown etiology but several hypotheses on its etiology have been postulated:

Gastrointestinal infections, autoimmune diseases, bile acid malabsorption, and various drugs.<sup>2</sup> Studies comparing the prevalence of the disease in developing countries as compared to developed countries may shed more light on the possibility of a post-infectious etiology.<sup>2</sup>

Patient with IBS are classified into diarrhea predominant (IBS-D), constipation predominant (IBS-C) and mixed type (IBS-M). Community based data indicate that IBS-D is more prevalent than IBS-C& IBS-M. Colonoscopy and biopsies were thought to be unremarkable in patients with IBS. Microscopic Colitis (MC) is a new form of idiopathic inflammatory bowel disease. Clinical features are almost same to D-IBS like abdominal pain or discomfort, chronic diarrhea. Colonoscopic findings also normal. The diagnosis of MC is dependent on well-defined histologic criteria. It is possible that many of the patients labeled as IBS-D has actually microscopic abnormality in the colorectum. Without colonoscopic biopsy, possibility of MC cannot be excluded in patients with IBS-D and it can be said that clinical symptom-based criteria for irritable bowel syndrome are not sufficient enough to rule out the diagnosis of microscopic colitis.

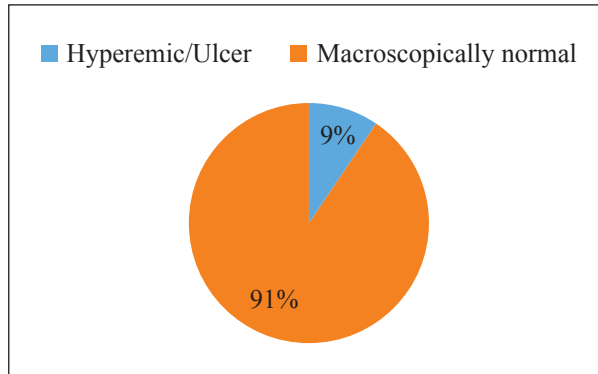
So, aim of this study was to determine the frequency of microscopic colitis in diarrhea predominant IBS in our perspective.

## Materials and Methods:

This cross-sectional observational study was conducted into the Medicine and Gastroenterology departments of Faridpur Medical College Hospital from July'15 to December'15. A total of 100 clinically suspected IBS-D patients were selected by purposive sampling technique. Patients presented with chronic non-bloody diarrhea, abdominal pain or discomfort, above 18 years of both sexes were initially selected for the study from inpatient and OPD of Medicine and Gastroenterology departments. Those patients who had met Rome-III criteria were finally included. After written and verbal consent full colonoscopy was done and biopsy was taken from colonic mucosa for histopathology. After histopathological examination, the information was collected in a preformed data collection sheet and analyzed accordingly with appropriate statistical tests Z test of proportion was done to analyze the data. Level of significance was 0.05. The result was presented in tables in proportion.

### Results:

A total of 100 subjects were studied with colonoscopy on the basis of their symptoms suggestive IBS-D according to Rome III criteria. Out of 100 patients nine patients were found to be have abnormality like hyperemia, ulcer and remaining ninety-one were macroscopically normal (Figure 1).



**Figure 1:** Distribution of patients according to colonoscopic findings (N=100)

Colonoscopic biopsies were taken from ninety-one patients who had macroscopically normal colonoscopic finding and were studied for evidence of mucosal inflammatory cell infiltration. Intraepithelial lymphocytes (IEL) were studied. Thirty-eight (41.76%) of study subjects had  $\geq 20$  IEL/100EC and 53 (58.24%) had  $< 20$  IEL/100EC. None shows total absence of intraepithelial lymphocytes (Table 1).

**Table 1:** Distribution of patients according to pattern of IEL of colonic mucosa (n= 91)

Number of IEL	No. of patients (%)
$\geq 20/100$ epithelial cell (EC)	38 (41.76%)
$< 20/100$ epithelial cell (EC)	53 (58.24%)

Chronic inflammatory cells in the lamina propria were studied including lymphocytes and plasma cell, shows all patients who had IEL  $\geq 20/100$  EC also had increased chronic inflammatory cells infiltration in the lamina propria. Whereas in patients those with IEL  $< 20/100$  EC, out of 53 patients; 39 showed increased chronic inflammatory cells infiltration and remaining 14 had no chronic inflammatory cell infiltration in the lamina propria (Table 2).

**Table 2:** Distribution of patients according to pattern of chronic inflammatory cell (lymphocytes, plasma cell) in the lamina propria (n=91)

	IEL $\geq 20/100$ EC group (n=38)	IEL $< 20/100$ EC group (n=53)
Increased	38	39
Decreased	0	14

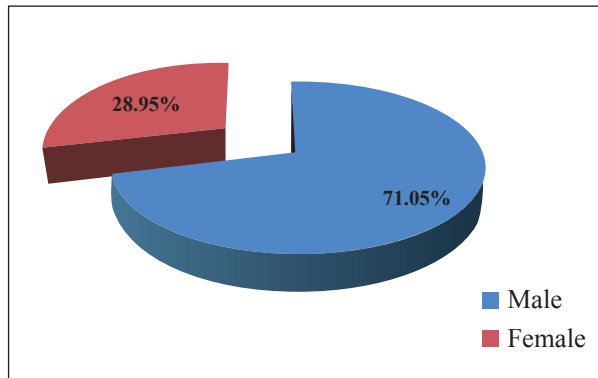
Mean thickness of the sub epithelial collagen band was studied, which was  $< 10 \mu\text{m}$  in all patients of both groups.

Histologic assessment of biopsy specimens was categorized into three groups. Lymphocytic colitis (LC) was considered when IEL were found to be  $\geq 20/100$  EC and chronic inflammatory cell infiltration in the lamina propria. Collagenous colitis was considered if, IEL  $\geq 20/100$  EC and chronic inflammatory cell infiltration in the lamina propria with sub epithelial collagen band thickening  $\geq 10 \mu\text{m}$ . Nonspecific microscopic colitis (NSMC) was considered if IEL were found to be  $< 20/100$  EC but lamina propria shows focal neutrophil infiltration and apparent increase in lamina propria cellularity. Irritable bowel syndrome non inflamed (IBSNI) were considered when IEL were found to be  $< 20/100$  EC and lamina propria revealed no chronic inflammatory cell infiltration. Out of 91 patients, 38 (41.76%) were LC, 39 (42.86%) NSMC, 14 (15.38%) patients were considered as IBSNI and none was found to have CC (Table 3).

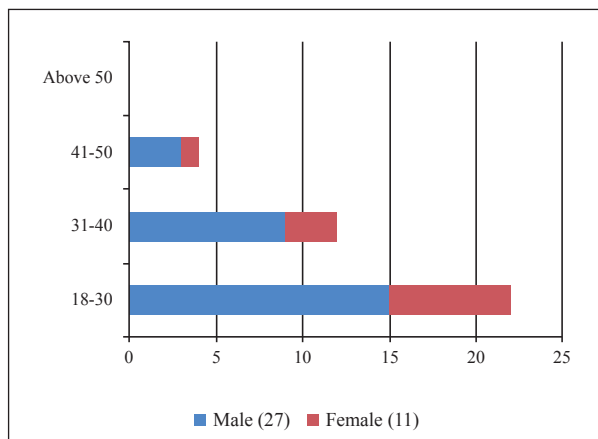
**Table 3:** Classification of inflammatory change in colonic mucosa on the basis of histologic assessment (n=91)

Diagnosis	No. of patient (%)
Lymphocytic colitis	38 (41.76%)
NSMC	39 (42.86%)
IBSNI	14 (15.38%)

Among 38 cases of microscopic colitis 27 (71.05%) were male whereas rest 11 (28.95%) were female (Figure 2). Male patients were more among different age groups also (Figure 3).



**Figure 2:** Distribution of Microscopic Colitis according to sex (n=38)



**Figure 3:** Sex distribution of Microscopic Colitis patients among different age group (n=38)

### Discussion:

In this study patients with chronic non bloody diarrhea who were initially considered as IBS-D under Rome III definition, histopathological study of colonic mucosa demonstrates considerable overlap with the features of MC in a significant number of patients. In this study out of 100 patients, who were initially diagnosed as IBS-D, 38 (38%) patients (71.05% male and 28.95% female) fulfilled the histologic criteria of MC.

A prospective study of 77 patients meeting Rome criteria, by Chadwick VS found that 10% fulfilled histologic criteria for microscopic colitis.<sup>3</sup> David Limsui et al. in their study identified one hundred thirty-one cases of microscopic colitis. Sixty-nine (53%) and 73 (56%) of these patients met Rome and Rome II criteria for IBS, respectively. Fifty-four (41%) had three or more Manning criteria.<sup>4</sup> Study by Hamid Tavakkoli et al.

included a total of 138 patients of IBS with mean age of 34.7 years (female 55.1% and male 44.9%) after meeting Rome-II criteria. All underwent colonoscopy and biopsy. The histologic findings revealed MC in 13 (9.42%) patients.<sup>5</sup> A Turkish study of 129 patient with non-bloody diarrhea revealed LC in 12 (9%) patients (Mean age: 45 year, range: 27-63) and CC was diagnosed in only 3 (2.5%) patients (mean age: 60 years, range: 54-65).<sup>6</sup> In Sweden, MC was reported in 4% of patients with non-bloody chronic diarrhea in 1993, but this rate was reported as 10% in 1998.<sup>7-9</sup> In our country, a study of BSMMU found that 36.7% fulfilled histological criteria for microscopic colitis.<sup>10</sup> Patients fulfilling the criteria of LC is found to be high (38%) in this study comparing to other studies done in different countries but nearer to BSMMU study. This may be due to referral bias as the study was done in a tertiary center or prevalence of MC may be truly high in our country.

Patients meeting criteria for MC in present study were younger (average:  $31.13 \pm 7.54$  years) because most of the patients selected for the study were under 55 years of age. The proportion of male patient was more in all the age group and this may be a selection bias. In this study we found all patients with MC to have LC, none had CC. Of these 27(71.05%) were male, 11(28.95%) were female.

The reason of absence of CC in our study might be due to that, most of the patients (97%) in our study were younger and only small number of patients (3%) were above 50 years of age and CC may be uncommon in our country. This finding is consistent with the other studies. It was stated in different studies that, LC is more common than CC and CC is more common in elderly people.<sup>11,12</sup> The gender difference for lymphocytic colitis is less striking than for collagenous colitis in some studies. In the present study of the remaining 53 (58.24%) patients, 39 were considered as nonspecific microscopic colitis (NSMC) and 14 patients were considered as irritable bowel syndrome noninflamed (IBSNI), which was supported by the study of Chadwick et al.<sup>3</sup>

### Conclusion:

Microscopic Colitis and diarrhea predominant IBS has almost similar clinical feature but MC is diagnosed by histologic criteria and IBS-D is diagnosed by symptom-based criteria. There is significant symptom overlap between MC and IBS-D. The study was performed in Faridpur Medical College Hospital to assess the frequency of microscopic colitis among

clinically suspected diarrhea predominant IBS patients. This study reveals that microscopic colitis prevalence in this population was 38%, which is very significant. So, we conclude that the clinical symptom-based criteria for IBS-D are not specific enough to rule out the diagnosis of MC. Therefore, patients with IBS-D should undergo colonoscopy and biopsies of the colon for histopathology to investigate for possible MC. Prospective studies with large sample size are needed to validate these findings and to give treatment and follow-up.

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#### Conflict of interest:

There is no conflict of interest.

#### References:

1. Pardi DS, Smyrk TC, Tremaine WJ, Sandborn WJ. Microscopic colitis: 1989;20:18-28. A review. *Am J Gastroenterol* 2002;97:794-802.
2. Otegbayo JA, Otegbeye FM, Rotimi O. Microscopic colitis syndrome. *J Natl Med Assoc* 2005;97:678-82.
3. Chadwick VS, Chen W, Shu D, Paulus B, Bethwaite P. Activation of the mucosal immune system in irritable bowel syndrome, *Gastroenterology*, 2002; 122: 1778–83.
4. Limsui D, Pardi DS, Camilleri M, Loftus EV Symptomatic Overlap between Irritable Bowel Syndrome and Microscopic Colitis. *Inflamm Bowel Disease*. 2007; 13(2): 175-81.
5. Tavakkoli H, Esmaeili FS, Emami MH, mahzouni P, Haghdani S. Is microscopic colitis a missed diagnosis in diarrhea-predominant IBS? *J research in Med Science* 2008; 13: 202-06.
6. Erdem L, Yildirim S, Akbayir N, Yilmaz B, Yenice N, Gültekin S, Prevalence of microscopic colitis in patients with diarrhea of unknown etiology in Turkey, *World J Gastroenterology*, 2008 July 21; 14(27): 4319-32.
7. Olesen M, Eriksson S, Bohr J, Järnerot G, Tysk C. Microscopic colitis: a common diarrhoeal disease. An epidemiological study in Örebro, Sweden, 1993-1998, *Gut*, 2004; 53: 346-50.
8. Olesen M, Eriksson S, Bohr J, Järnerot G, Tysk C. Lymphocytic colitis: a retrospective clinical study of 199 Swedish patients, *Gut*, 2004; 53: 536–41.
9. Bohr J, Tysk C, Eriksson S, Järnerot G. Collagenous colitis in Örebro, Sweden, an epidemiological study 1984-1993, *Gut* 1995; 37: 394-97.
10. Rahman MA, Raihan ASMA, Ahmed DS, Masud H, Safiullah ABM, Khair KB, et al Symptomatic overlap in patients with diarrhea predominant irritable bowel syndrome and microscopic colitis in a sub group of Bangladeshi population, *Bangladesh Med Res Counc Bull* 2012; 38: 33-38.
11. Pardi DS. Microscopic Colitis. *Gastroenterology & Hepatology*, 2009; 5(4): 283-88.
12. Farnandes-Banres F, Salas A, Forne M, Estev M, Espenos J, Viver Jm. Incidence of collagenous and lymphocytic colitis: A 5 year population based study'. *Am J Gastrenerol*, 1999; 94: 418-23.