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ORIGINAL ARTICLE

Frequency of microscopic colitis in patients presenting with chronic diarrhea.

Naik Muhammad[1], Mansoor-Ul-Haq[2], Adeel Rahat[3], Asad Abbas Jafri[4]

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ABSTRACT… Objective: To evaluate frequency of microscopic colitis in patients presenting with chronic diarrhea at a tertiary care hospital in Karachi, Pakistan. **Study Design:** Descriptive Cross-sectional study. **Setting:** Department of Gastroenterology, Liaquat National Hospital, Karachi, Pakistan. **Period:** January, 2022 to June, 2022. **Methods:** Patients presenting in out-patient department of age >18 years of any gender with history of diarrhea >1 month, normal thyroid tests, negative serology for Celiac disease (Anti TTG IgA and IgG), and normal colonoscopy findings including terminal ileum were enrolled in the study after written informed consent. MC diagnosis was established using clinical diarrhea history and colonic biopsy findings. **Results:** Total 130 patients were analyzed with median age of 38 (IQR= 28-55) years. Nearly half were females (n=67, 51.5%). All patients had normal colonoscopy findings. Out of 130 patients, microscopic colitis was seen among 7(5.4%) cases out of which 5(3.8%) had lymphocytic colitis and 2(1.5%) had collagenous colitis. Patients with and without MC shared the same characteristics. **Conclusion:** A lower microscopic colitis frequency was found in the studied sample. Lymphocytic microscopic colitis is predominant than collagenous microscopic colitis.

Key words: Chronic Diarrhea, Colonoscopy, Collagenous Colitis, Lymphocytic Colitis, Microscopic Colitis.

INTRODUCTION

A chronic inflammatory bowel illness called microscopic colitis (MC) is defined by non-bloody diarrhea in the presence of normal-appearing colonic mucosa and specific histopathologic characteristics.[1] Collagenous colitis (CC) and lymphocytic colitis (LC) are subclasses of MC. When crypt architecture is unaltered and intraepithelial lymphocytes are raised to at least >20 lymphocytes per 100 cells, LC is identified. CCs differ histologically, revealing a more than 10-m collagen band in the subepithelial layer, lacking in LC. Since the two variations have similarities in clinical presentation, assumed pathogenesis, and clinical course, they were subsequently combined into one disease entity, MC.[2,3]

In 1980, Read et al. made the first mention of MC as a potential cause of persistent diarrhea with an undetermined origin.[4] The frequency of the diarrhea has been observed to range up to 15 bowel movements per day and might occur suddenly or gradually. Watery diarrhea is frequently accompanied by nocturnal symptoms such as urgency, incontinence, weight loss and/or abdominal pain.[5] Fatigue has been—seen frequently in MC.[6,7] Irritable bowel syndrome symptoms, such as abdominal discomfort and/or alterations in bowel habits may occur in one in three patients with MC, according to a pooled analysis, but the prevalence of symptoms was comparable to that of the common population, although latest case-control studies reported the conflicting findings.[8]

According to a recent pooled analysis, overall annual incidence of CC and LC is 4.14 per 10^5 person-years and 4.85 per 10^5 person-years respectively. The industrialized Western nations of Canada, Netherlands, Spain, Denmark and USA account for the majority of data on the MC incidence and prevalence. There is a shortage of data from the developing world.[9]

1. MBBS, FCPS-I, Post-graduate Resident Gastroenterology, Liaquat National Hospital, Karachi.
2. MBBS, FCPS (Medicine), FCPS (Gastroenterology), Professor & Head Gastroenterology, Liaquat National Hospital, Karachi.
3. MBBS, FCPS (Gastroenterology), Senior Registrar Gastroenterology, Liaquat National Hospital, Karachi.
4. MBBS, FCPS (Histopathology), Assistant Professor Histopathology, Liaquat National Hospital, Karachi.

Correspondence Address:
Dr. Naik Muhammad
Department of Gastroenterology
Liaquat National Hospital, Karachi.
naikbugti007@gmail.com

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Thoughts on the precise pathophysiology and progression of MC are still lacking. Middle-aged women are particularly susceptible to MC. Beta-blockers, proton pump inhibitors, statins, and NSAIDs are commonly used medications that are linked to an increased risk of MC.[10] The MC differential diagnosis is broad and includes inflammatory bowel disease, drug-induced diarrhea, a variety of malabsorptive disorders, and irritable bowel syndrome with diarrhea. This is because the diagnosis is frequently challenging to make because of overlap with several other gastrointestinal illnesses. Due to these reasons, the diagnosis rate may vary physician to physician. Hence, we intended to evaluate frequency of MC among patients presenting with chronic diarrhea at tertiary care hospital in our settings in Karachi.

METHODS

This cross-sectional study was performed at Gastroenterology Department, Liaquat National Hospital Karachi, Pakistan. The study was conducted during January, 2022 to June, 2022. The Hospital Ethics Committee (IRB: App 0689-2021 LNH-ERC) first evaluated and approved the study protocol. With their written informed consent, study participants were enlisted

Inclusion Criteria

Patients presenting in out-patient department of age >18 years of any gender with history of diarrhea >1 month, normal thyroid tests, negative serology for celiac disease (Anti TTG IgA and IgG), and normal colonoscopy findings including terminal ileum were enlisted in the study.

Exclusion Criteria

Patients presenting with fever, bloody or mucous stools, gastrointestinal carcinoma and inflammatory bowel diseases were excluded from this study.

Sample size was calculated using MC prevalence of 11.5% in patients with chronic diarrhea[11], 95% confidence interval and margin of error is 5.5%. A sample size of 130 patients was computed through Open-Epi with proportion option.

Study subjects were registered in the study with their written informed consent. MC diagnosis was established using clinical diarrhea history and colonic biopsy findings. Increased intraepithelial lymphocytes (more than 20/100 enterocytes), modest mononuclear growth of the lamina propria, surface degradation, and normal subepithelial collagen were all indicators of lymphocytic colitis. The presence of thickened and irregular subepithelial collagen that frequently contains inflammatory cells and small vessels, mild lamina propria enlargement (often with eosinophils), surface degeneration frequently accompanied by epithelial detachment, and elevated intraepithelial lymphocytes are all indicators of collagenous colitis. The treating physician documented the history taken in patient's medical record file. The assigned data collectors documented patient's data including their demographic features age, gender, clinical features, disease duration, frequency of stools and findings of colonoscopy and histopathology in a pre-designed study proforma.

The collected data was put up in statistical software SPSS version 21 for statistical analysis. Categorical patients' features were outlined as frequency and percentage. Numerical characteristics like age was expressed as median with inter-quartile range as it was non-normally distributed. Shaprio-Wilk test was applied to check normality assumption. Categorical variables were compared among patients with and without MC applying Chi-square/Fisher-exact test. Statistical significance was defined based on two tail p-value less than or equal to 0.05.

RESULTS

Total 130 patients were enlisted with median age of 38 (IQR= 28-55) years. Nearly half were females (n=67, 51.5%). Table-I shows the descriptive statistics of disease presentation.

Colonoscopy findings were normal in all patients. The frequency of microscopic colitis is depicted in Figure-1. Out of total 7 (5.4%) cases of microscopic colitis, 5(3.8%) had lymphocytic colitis and 2(1.5%) had collagenous colitis. Table-II compares the patients' features among those

who had non-specific colitis and microscopic colitis. Patients with and without MC shared the same characteristics.

Variables	Frequency (%)
Frequency of Stools Per Day	
<3	42 (32.3)
3-5	74 (56.9)
6-8	11 (8.5)
>8	3 (2.3)
Duration of Illness	
≤1 month	38 (29.2)
2-3 months	45 (34.6)
>3 months	47 (36.2)

Table-I. Descriptive statistics for disease presentation

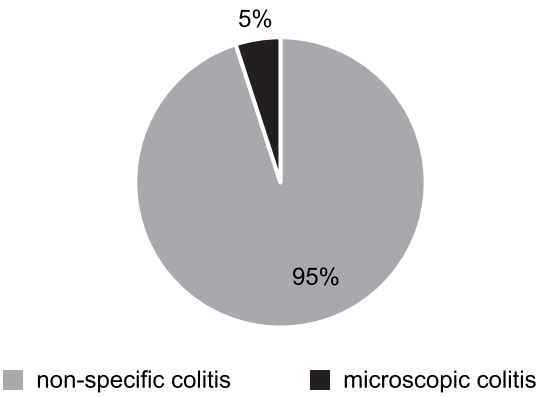

Figure-1. Microscopic colitis frequency among patients having chronic diarrhea

Variable	Microscopic colitis		P-Value
	Yes n(%)	No n(%)	
Age (in years)	29(23-34)	39(28-55)	0.078
Gender			
Male	4(6.3)	59(93.7)	Ɨ0.712
Female	3(4.5)	64(95.5)	
Frequency of stool per day			
<3	3(7.1)	39(92.9)	Ɨ0.869
3-5	4(5.4)	70(94.6)	
6-8	0(0)	11(100)	
>8	0(0)	6(100)	
Duration of illness			
1 month	2(5.3)	36(94.7)	Ɨ1.000
2-3 months	2(4.4)	43(95.6)	
>3 months	3(6.4)	44(93.6)	

Table-II. Differentiation of patients' features among microscopic colitis and non-microscopic colitis cases

+Fisher-exact test is reported

DISCUSSION

Despite being a curable basis of chronic, non-bloody, watery diarrhea, MC is less well-known among physicians (especially in primary care) than other chronic diarrheal diseases.[12] Nocturnal diarrhea, abdominal discomfort, urgency, and fecal incontinence can all be symptoms of the illness. These symptoms result in a lower quality of life and higher medical expenses. Microscopic colitis's clinical manifestations may resemble and confound with functional bowel disorders, such as diarrhea-predominant irritable bowel syndrome, making the diagnosis susceptible to error.[13]

Surprisingly, in our study patients were almost equally distributed among all three classes of disease duration i.e. nearly one third presented during with disease of one month duration, 2-3 months and more than three months. 286 patients out of 540 (53.0%) had diarrhea for more than a month, according to Kane et al., 2017.[14] Another similar investigation from Egypt reported a similar disease duration of 2.5 months.[15] An Indian study also reported a mean disease duration of 3.2±2.5 months.[16] In a study from Eg ypt, Badran and his coauthors analyzed frequency of microscopic colitis among patients of irritable bowel syndrome according to ROME-IV criteria and reported a median disease duration of 8 months. The change in methodology and diagnosis as per the ROME-IV criteria could be the possible because of higher disease duration in this study.[17]

The present study analyzed only 5.4% cases of microscopic colitis among chronic diarrhea patients undergoing colonoscopic evaluation. Further it was observed that, out of 7 cases of MC, 5 were LC and 2 were CC. The higher proportion of LC than CC is consistently reported in the literature.[16-19] The finding of lower MC prevalence is in agreement with an Indian study in which 400 colonoscopy evaluation was performed for patients presenting with chronic diarrhea and only 3.7% of them were found to have microscopic colitis.[16] A low prevalence of microscopic colitis (5.5%) was also reported in another similar study.[18] However, some investigations reported quite a higher MC prevalence than which is in disagreement in our study. MC prevalence of

21.7% among patients with chronic diarrhea was reported from Egypt.[15] Another Egyptian study reported a prevalence of 20% among 100 patients of irritable bowel syndrome.[17] The difference in study findings is possible because of difference in performing colonoscopy, awareness and knowledge of the disease. This difference is also behind the rising incidence rate particularly in the West, better disease knowledge and more frequent investigation through colonoscopy and biopsies is rising the detection rate.[19]

In our study it also noticeable that 5.4% of the patients showing normal colonscopy findings had MC. In people with microscopic colitis, the macroscopic representation of the colon on endoscopy is classically standard, nevertheless in a systematic review, non-specific changes, such as edema, erosions, hyperemic mucosa, mosaic mucosal pattern, patchy erythema or loss of vascular pattern were present in about 39% of total cases.[20]

The existing study is cross-sectional in nature with a limited sample size and is based on a single center experience from Karachi. Generalizing study results to the entire Pakistani population is doubtful due to these constraints. To corroborate the study's findings, a larger sample size study may be done in the future to fill in the study's gaps.

CONCLUSION

A lower microscopic colitis frequency was found in the studied sample. Lymphocytic microscopic colitis is predominant than collagenous microscopic colitis**.**

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Naik Muhammad	Conceptualized the study, designed study protocol initial manuscript writing.	
2	Mansoor-Ul-Haq	Designed the study protocol, Critical review.	
3	Adeel Rahat	Designed the study protocol, Critical review.	
4	Asad Abbas Jafri	Performed data analysis and involved in result writing.	