

Original Article

Histological Evaluation of Patients with Chronic Nonbloody Large Bowel Diarrhea and Normal Colonoscopy

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ABSTRACT

Introduction: Chronic diarrhea is defined as the passage of soft or watery stool more than three times per day with or without blood and/or mucous or the passage of stool of more than 200 g per day and lasts for more than 4 weeks. Studies exploring the causes of chronic diarrhea in the developing countries are scarce and might not be generalizable from one setting to another. **Aim:** The aim of the study is to study the colonic and terminal ileal macroscopic and mucosal histopathological findings in chronic large bowel diarrhea patients. **Methods:** Eighty-six patients with chronic large bowel diarrhea were included after negative HIV status, stool analysis, and stool culture. A full-length colonoscopy with terminal ileoscopy was done. When the colon was within normal limits, randomly four biopsies each were taken from terminal ileum, ascending colon, transverse colon, and rectosigmoid region, respectively. **Results:** In a total of 86 patients, most of the patients (48%) were in the age group of 41–60 years. Females predominated in the present study in the ratio of 3:2. Ileal intubation was possible in all (100%) cases. Histology is normal in 35 patients. Fifty-one patients had histological changes of which 22 were diagnostic for specific disease which altered the treatment. Among 22 patients, 21 (95.4%) had histological changes in ascending colon and only 9 (40.9%) had changes in biopsy from rectosigmoid. In our study, definite diagnostic histology was obtained in 25.5% of cases. **Conclusion:** The yield of colonoscopy and biopsy in chronic large bowel diarrhea is moderate. Colonoscopy and biopsy have higher diagnostic yield than sigmoidoscopic biopsies.

KEYWORDS: Biopsy, chronic large bowel diarrhea, colonoscopy, histology

INTRODUCTION

Chronic diarrhea is defined as the passage of soft or watery stool more than three times per day with or without blood and/or mucus or the passage of stool of more than 200 g per day and lasting for more than 4 weeks.^[1] Studies exploring the causes of chronic diarrhea in the developing countries are scarce and might not be generalizable from one setting to another. Chronic disorders that can be diagnosed by visualization of the colonic mucosa include pseudomelanosis coli, polyps, tumors, Crohn's disease, ulcerative colitis, Amebic colitis, and nonspecific ulceration.^[2] Diseases in which the colonic mucosa appears normal endoscopically but which can be diagnosed histologically include microscopic colitis, amyloidosis, and granulomatous

infections.^[2] The evaluation of chronic nonbloody large bowel diarrhea by colonoscopy and biopsy is not well explored in the Asian subcontinent and the data published as on date is insufficient to draw conclusions to provide guidelines for the management of such patients.

The present study aims to study the colonic and terminal ileal mucosal histopathological findings in patients with chronic nonbloody large bowel diarrhea and normal colonoscopy.

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METHODS

Study participants prospectively evaluated were patients with chronic nonbloody large bowel diarrhea (small volume stools, more than four times a day and loose to semisoft for more than 4 weeks) and normal colonoscopy findings. Biopsies were taken from terminal ileum, ascending colon transverse colon, and rectosigmoid region (four from each segment). Inclusion criteria were (1) diarrhea for over 4 weeks and normal mucosa without macroscopic changes on colonoscopy, (2) negative HIV status, and (3) normal stool analysis (three times) and culture. Patients with bloody diarrhea, drug-induced diarrhea, and postsurgical (gastrectomy) were excluded, as the presence of blood in stools usually denotes abnormalities that would be seen on colonoscopy.

The study protocol was approved by the Institutional Ethics Review Board. All the patients consented to the study after having received oral and written information.

The pathology slides corresponding to each patient's biopsies were anonymously reported by a single experienced gastrointestinal pathologist using standardized pathological criteria. The histological diagnosis was given after studying the H and E-stained sections and assessing the collagenous layer (Masson Trichrome-stained sections) as well.

Histopathology and diagnostic criteria

The presence of a low-grade inflammatory infiltration, with plasma cells, lymphocytes, and rare eosinophils distributed over the superficial colonic mucosa was interpreted as normal.

Nonspecific colitis was defined by the presence of chronic cellular infiltrate, with the absence of architectural distortion and multiple basal lymphoid aggregates or plasma cells immediately above the muscularis mucosae.

Collagenous colitis was defined by a subepithelial collagen layer reaching or exceeding 10 µm thickness and lymphocytic colitis by an increased intraepithelial lymphocyte count reaching or exceeding 20 lymphocytes per 100 epithelial cells.

Eosinophilic colitis was diagnosed by the following features

1. More than twice the normal number of eosinophils in the lamina propria per high-power field (HPF): more than 100 per HPF in the right colon, more than 84 per HPF in transverse and descending colon, and more than 64 per HPF in rectosigmoid colon
2. Altered eosinophil behavior manifest as lamina propria sheets, eosinophilic cryptitis, eosinophilic crypt abscesses.

Tuberculosis was diagnosed when any of caseation, confluent granulomas, a lymphoid cuff around granulomas, granulomas larger than 400 µm in diameter, five or more granulomas in biopsies from one segment were present.

Crohn's disease was diagnosed when infrequent (<5) and small (<200 µm in size) granulomas that are poorly organized, microgranulomas, crypt-centered inflammation such as pericryptal granulomas and focally enhanced colitis were seen.

Ulcerative colitis was diagnosed when crypt branching, crypt distortion, crypt atrophy, Paneth cell metaplasia, and basal plasmacytosis were observed.

RESULTS

Of 182 patients with chronic diarrhea, 86 patients who met the inclusion criteria were studied. Forty-eight percent of the patients were in the age group of 41–60 years. Females predominated in the ratio of 3:2. Ileal intubation was possible in all (100%) cases. Incidental findings such as diverticula (2) and angioectasia (2) were observed in four cases. Histology was normal in 35 (40.7%) patients. The other 51 (59.3%) patients had some histologic alterations [Table 1].

The most common abnormality reported was nonspecific inflammation [Figure 1] which was found in 29 patients. In addition, lymphocytic colitis was found in 12 patients, eosinophilic colitis [Figure 2] was found in three patients, and tuberculosis [Figure 3] in three patients. Inflammatory bowel disease was found in four patients (ulcerative colitis – 2 [Figure 4], Crohn's disease – 2 [Figure 5]).

After excluding patients with nonspecific colitis, among the 22 patients (25.5%) with diagnostic histology, 21 (95.4%) patients had diagnostic histological changes from right colon whereas only 9 (40.9%) patients had diagnostic histological changes from rectosigmoid colon. Of 12 patients

Table 1: Histological findings in patients with chronic nonbloody large bowel diarrhea

| Histologic finding | Number | Percentage |
|--------------------------|--------|------------|
| Normal | 35 | 40.7 |
| Histologic abnormalities | 51 | 59.3 |
| Non Specific Colitis | 29 | 33.7 |
| Lymphocytic Colitis | 12 | 14 |
| Eosinophilic Colitis | 3 | 3.5 |
| Tuberculosis | 3 | 3.5 |
| Ulcerative Colitis | 2 | 2.3 |
| Crohns disease | 2 | 2.3 |

with lymphocytic colitis, left colon biopsies fulfilled diagnostic criteria in only 4 patients whereas right colon biopsies were diagnostic in all 12 patients emphasizing the importance of right colon biopsies if only distal colon was examined the diagnosis would have been missed in 8 patients. In patients with eosinophilic colitis, diagnostic criteria were fulfilled in both left and right colonic biopsies. Of 2 patients of ulcerative colitis, one patient had pancolitis and one patient had left-sided colitis. In 2 patients with Crohn's disease, both had ileal involvement. Of all the positive histological diagnoses, ileoscopy added to the diagnosis only in Crohn's disease. All patients with tuberculosis had only cecal involvement.

DISCUSSION

In the 86 patients who had chronic diarrhea, in this study, histologic aspects of diagnostic importance were found in 22 (25.5%) patients with lymphocytic colitis,

eosinophilic colitis, tuberculosis, ulcerative colitis, and Crohn's disease.

Our results were comparable to the findings of da Silva *et al.*^[3] who concluded that the observed changes had diagnostic implications for 32.1% of their patients. In a study by Sanderson *et al.*,^[4] diagnostic histologic changes were seen in 15.3% of patients but sample size of this study was small. In a study by Shah *et al.*,^[5] the yield of specific histological diagnosis is 31%. In a study by Khanna *et al.*,^[6] definitive diagnostic histology was found in 31.5% of patients.

There are no specific guidelines regarding when to take biopsy in chronic large bowel diarrhea and how many biopsies should be taken.^[7] In our study, abnormal histology was found in 59.3% of patients, and definitive diagnosis could be established in 25.5% of patients. When compared with biopsies from the rectosigmoid

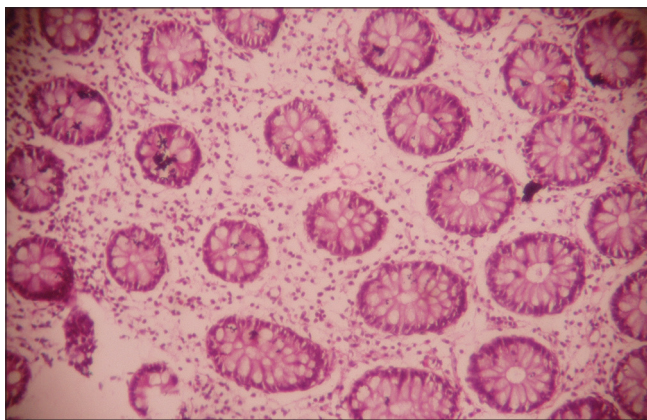


Figure 1: Studied section shows normal intestinal glands and stroma. Stroma shows mild inflammatory infiltrate composed mostly of lymphocytes along with few eosinophils

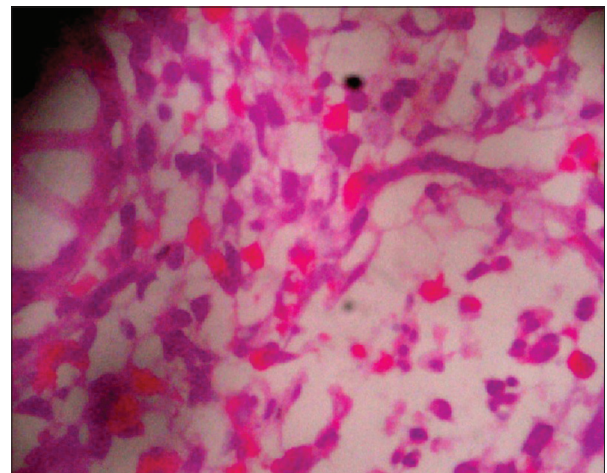


Figure 2: Studied section shows intestinal mucosa with glands showing more than eosinophils infiltrating into the gland with the adjacent stroma showing abundant eosinophils

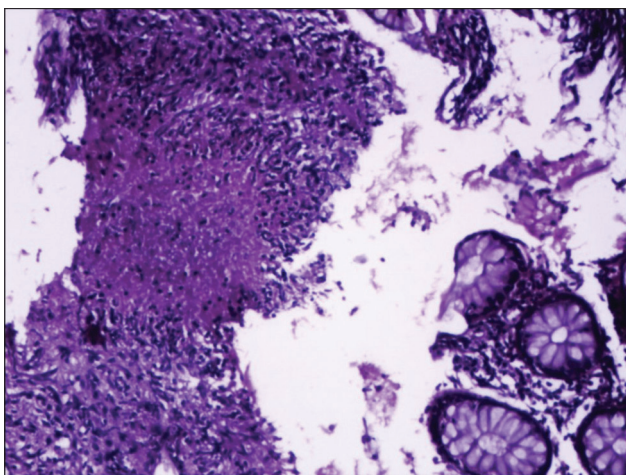


Figure 3: Studied section shows ulcerated intestinal mucosa with large areas of caseous necrosis along with granulomas and Langhans type of giant cells infiltrating the underlying stroma with inflammatory infiltrates

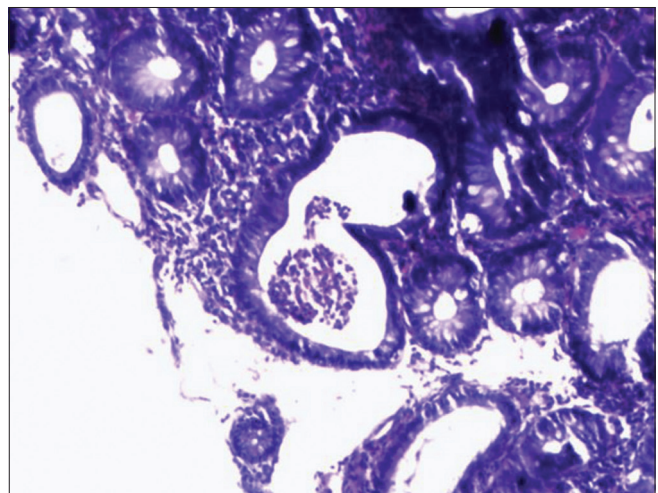


Figure 4: Studied section shows intestinal mucosa with glands showing crypt abscess and irregular branching

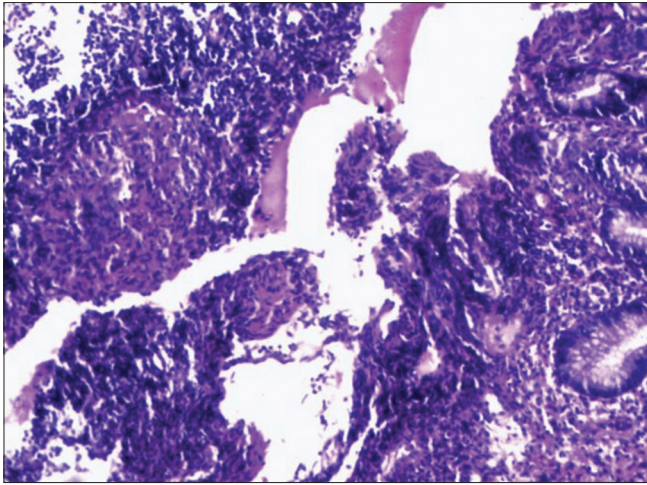


Figure 5: Studied section shows intestinal mucosa showing epithelioid cell granuloma without caseous necrosis and mucus glands

colon, biopsies from right colon yielded better confirmative diagnostic histology.

CONCLUSION

The yield of colonoscopy and biopsy in chronic large bowel diarrhea is moderate but significant. Colonoscopy and biopsy have higher diagnostic yield than sigmoidoscopic biopsies. The most common specific cause of chronic nonbloody large bowel watery diarrhea in the present study was microscopic colitis.

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Conflicts of interest

There are no conflicts of interest.

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