



**ETIOLOGICAL PROFILE OF CHRONIC LARGE BOWEL DIARRHOEA- A TERTIARY CENTRE EXPERIENCE**

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**ABSTRACT**

**Objective:** Colonoscopy is often considered in the complete evaluation of chronic unexplained diarrhoea. However, the exact yield of colonoscopy with and without biopsy and the additional yield from ileal intubation is largely unknown.

**Methods:** We performed cross-sectional study of 403 patients with chronic diarrhoea evaluated by colonoscopy between October 2016 and January 2019. Chronic diarrhoea was defined as a variable combination of loose, frequent bowel movements for a minimum period of 4 wk. Patients were not included in study if biopsies were not performed during normal colonoscopy, history of previous bowel surgery, a history of IBD, HIV, or an inadequate colonoscopy due to poor preparation.

**Results:** Four hundred and three patients were included in the analysis, of whom 334 (83%) had ileal intubation and biopsy done. Ileocolonoscopy and biopsy yielded a specific diagnosis in 114 (28%) patients. These included Ulcerated colitis (28), Colorectal malignancy (21), Microscopic colitis (20), Crohn's disease (15), intestinal tuberculosis (13), radiation enteritis/proctitis (7), ischemic colitis (3), Amoebic colitis (3), Eosinophilic colitis (3) and NSAID colitis (1). Ileoscopy yielded significant findings in 2.5% of patients (four with Crohn's disease, two each with Ileal TB and Ileal adenocarcinoma, one each with Eosinophilic enteritis, ischemic enteritis and radiation enteritis).

**Conclusions:** Colonoscopy with biopsy is useful in the evaluation of patients with chronic diarrhoea leading to a histological diagnosis in 28% of patients without a previous diagnosis. Ileoscopy complemented colonoscopy findings in a significant minority of patients with chronic diarrhoea and was exclusively useful for a diagnosis in around ten patients.

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**INTRODUCTION**

Chronic diarrhoea is clinically a difficult condition to diagnose. Although colonoscopy invariably performed among them, the usefulness of colonoscopy with biopsy in this scenario is largely unknown. Colonoscopy is very useful in evaluation of chronic diarrhoea in the setting of HIV<sup>1</sup>. However, the decision to use Colonoscopy in the evaluation of general population with chronic diarrhoea is based on limited data. Ileocolonoscopy may be preferred to sigmoidoscopy for the detection of right-sided colitis, isolated ileitis, microscopic colitis or in the case of pancolitis to distinguish Crohn's disease from ulcerative colitis<sup>(2-3)</sup>. However, this finding has not been prospectively evaluated (9). Presently available studies of colonoscopy in chronic diarrhoea have had different inclusion criteria and multiple biases. Some of them include the duration of the diarrhoea (e.g., acute vs chronic),

the extent of lower GI scopy, and in the case of microscopic colitis whether random colonic biopsies were performed or not<sup>4</sup>. The incidence of Microscopic colitis ranges from 5% to 8.5% of patients undergoing an investigation for chronic diarrhoea<sup>5</sup>. Such information supports the idea of performing biopsies of normal colonic mucosa when evaluating chronic diarrhoea<sup>6</sup>. Although, contrary view is that biopsies of normal colonic mucosa may be unnecessary, especially for patients who fit criteria for the irritable bowel syndrome (IBS) according to ROME definition<sup>5-7</sup>. The objective of this study was to evaluate the diagnostic yield of total ileo-colonoscopy and biopsy in non-HIV patients referred for unexplained chronic diarrhoea.

**MATERIALS AND METHODS**

This is a Cross-sectional study of patients conducted at a tertiary care centre in south India between October 2016 and January 2019 for investigation of chronic diarrhoea. Chronic diarrhoea was defined as a variable combination of loose, frequent bowel movements for a minimum period of 4 weeks.

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Detailed history regarding duration and severity of diabetes mellitus, any feature suggestive of hyperthyroidism; complete drug history including over the counter drugs, herbal and dietary supplements, complementary and alternative medications with main emphasis on PPI, H2RA, multivitamin supplements, antibiotic usage, coffee/tea usage and alcohol consumption. All patients had blood tests such as RFT, LFT, FBS/PPBS, HbA1c, serum electrolytes, HIV, CRP, IgA anti-TTG, TSH; Chest X-ray (to look for associated pulmonary TB); stool examination for ova/parasite, WBC, culture and sensitivity, occult blood. Selective patients underwent Stool GDH assay when clinical suspicion of *Clostridium difficile* is high. If any explainable cause of diarrhoea could be found, then patients were not included in the study. Only patients with unexplained chronic diarrhoea in spite of detailed history, physical examination (with main emphasis on DRE to rule out spurious diarrhoea and Faecal incontinence) and laboratory tests were included. Colonoscopy was performed after split dose bowel preparation with clear liquids the day before. For the purposes of this study, colonoscopic findings of polyps that were less than 3 cm and without villous features were not considered causes of diarrhoea. During colonoscopy, any erosions, ulcerations, increased friability, loss of vascular pattern, bleeding, any proliferative growth were noted down and if normal colonoscopy macroscopically, multiple random biopsies were taken from Ascending, transverse, descending, sigmoid colon and rectum were taken. Every attempt was made to intubate the Ileum and if successful, biopsy of it was done. All biopsies taken from different segments of colon were labelled separately and sent to pathologist. A single expert GI pathologist reviewed all abnormal histology in a blinded fashion. All biopsy reports were categorized as specific (leading to a histological diagnosis), non-specific and normal histology. Patients were excluded if they had 1) a prior diagnosis of IBD; 2) prior intestinal surgery; 3) HIV positive; 4) no random biopsies performed in a grossly normal colon; 5) an incomplete colonoscopy or inadequate prep; and 6) prior colonoscopy for diarrhoea. The term non-specific colitis is used to indicate chronic inflammation of the lamina propria for which an etiology cannot be determined by histological examination.

The usefulness of colonoscopy as a whole (with biopsies in normal appearing colon) in establishing diagnosis in patients with chronic diarrhoea was evaluated. Additional usefulness of Ileal intubation in identifying terminal ileal conditions causing chronic diarrhoea was also evaluated.

## RESULTS

Between October 2016 and January 2019, a total of 454 patients underwent colonoscopy at the Institute of Medical gastroenterology, Madras Medical college, for an evaluation of chronic diarrhoea. 51 patients were excluded for the following reasons: 17 patients had HIV, 13 patients had normal colonoscopy without random biopsies being taken, 10 patients had prior intestinal surgery, four patients had incomplete examinations, three patients had a known diagnosis of inflammatory bowel disease, two patients had unavailable pathology results, one patient did not have chronic diarrhoea (as defined above), and one patient had repeat examination.

The final study group consisted of 403 patients with age ranging from 19-81 year, with a mean age of 54 year. Two hundred and five patients (51%) were women. Ileoscopy and

biopsy was done in 334 patients (83%). Two hundred and eighty-nine patients (72%) also underwent upper endoscopy with distal duodenal biopsy. In the 403 study patients, 114 patients (28%) had a specific histological diagnosis; 37 patients (9%) had a histological diagnosis of nonspecific colitis, and the remaining 252 patients (62.5%) had normal colon histology. The list of specific histological diagnoses is in Table 1.

**Table 1** Specific Histological Diagnoses by Colonoscopy With biopsy and Ileoscopy with biopsy

Diagnosis	Number of patients
Ulcerative colitis	28
Malignancy	21
Microscopic colitis	20
Crohn's disease	15
Tuberculosis-Ileocolonic	13
Radiation	7
enteritis/colitis/proctitis	7
Amoebic colitis	3
Ischemic enteritis/colitis	3
Eosinophilic enteritis/colitis	3
NSAID colopathy	1
<b>Total</b>	<b>114</b>

Histology of ileal biopsy was helpful in sixteen patients (4% of overall patients or 5% of patients who had ileoscopy with biopsy). Nine patients had Crohn's disease by biopsy of the ileum, but only three had isolated ileitis. Two each had Ileal tuberculosis and Ileal adenocarcinoma. One patient each had Eosinophilic enteritis, Ischemic enteritis and Radiation enteritis.

Out of 28 patients with Ulcerative colitis, 13 had Proctitis, 9 had Left sided colitis, 6 had Extensive colitis while 2 of them had Pancolitis. None of our patients had Backwash ileitis. Out of 21 patients with Malignancy as the cause of chronic diarrhoea, 19 had colorectal adenocarcinoma while only 2 had Ileal adenocarcinoma. Out of 20 patients with Microscopic colitis, 12 had Lymphocytic colitis and 8 had Collagenous colitis. Among 15 patients with Crohn's disease, 6 had Ileocolonic crohn's, 3 had only Ileitis and 2 had isolated Crohn's colitis. 11 patients had colonic TB while 2 had Ileal TB. 5 had Radiation proctitis, one each had Radiation colitis and Radiation enteritis. Among 3 patients with Eosinophilic disorders, 2 had colitis while one had enteritis.

Two hundred and eighty-nine patients (72%) also underwent upper endoscopy with distal duodenal biopsy. All patients with either non-specific colitis or normal colonic histology underwent OGD scopy. Many of them were diagnosed with celiac disease, but majority of them had non-specific duodenitis.

## DISCUSSION

Although colonoscopy is routinely performed, there is insufficient data on the usefulness of total colonoscopy with ileal intubation and biopsy in the evaluation of chronic diarrhoea. In this study, a specific histological diagnosis could be made in 114(28%) out of 403 patients studied.

Twenty of these 114 patients (or 17.5% of patients with a diagnosis made by biopsy) had macroscopically normal-appearing colonic mucosa on endoscopy but on histopathological examination of biopsies were diagnosed with Microscopic colitis. These findings emphasize the importance

of performing random biopsies in grossly normal looking colons. 12 of them had Lymphocytic colitis while 8 had Collagenous colitis. Two of the 12 patients with lymphocytic colitis had mild erythema identified in the left colon. One of the 8 patients with collagenous colitis had mild erythema in the right colon. Whether these endoscopic appearances are attributable to bowel preparation is uncertain<sup>11,12</sup>. Both the types of Microscopic colitis were grossly similar in prevalence and other patient characteristics, although few studies opine symptoms to be more severe in Collagenous colitis<sup>8</sup>.

Histology of ileal biopsy was helpful in sixteen patients, few of them had colonic accompanying lesions as well. Among the 16 people with ileal lesions, Ileal biopsy was essential in making a diagnosis in 10 patients. Ileal intubation and biopsy led to specific diagnosis in 9% of patients with specific histological diagnosis for chronic diarrhoea. Most common diagnosis from ileal intubation was ileal crohn's disease followed by tuberculosis and adenocarcinoma of ileum. Rest of 91% with specific histological diagnosis for chronic diarrhoea, colonoscopy and biopsy led to a diagnosis. As reported earlier, ileal intubation and biopsy may give clinically useful information for patients with chronic diarrhea<sup>9,10</sup>.

Prior *et al*<sup>13</sup> reported on 100 consecutive patients with grossly normal colons and random colonic biopsies and found significant pathology in 22% of them. As only one-half of their patients had diarrhoea, yield was also lower. Patel *et al*<sup>14</sup> reported the use of colonoscopy in non-bloody diarrhoea and found a yield of 18% among 205 patients studied. This figure is lower than our yield of 28%. These two studies differed from our study in that they included patients with both acute and chronic diarrhoea and excluded patients with rectal bleeding. We included not only patients with non-bloody watery diarrhoea but also bloody diarrhoea. In addition, more than 30% of their patients had sigmoidoscopy alone; therefore, right-sided colitis and ileitis may have been missed<sup>2,9,10</sup>. In addition, patients with abdominal pain were not included in an attempt to differentiate organic diarrhoea from IBS. Although nonspecific, abdominal pain may be a significant feature of IBS and rarely in collagenous colitis, therefore these entities should be ruled out before diagnosing a patient with IBS<sup>15</sup>.

Marshall *et al*<sup>6</sup> did not identify any cases of either lymphocytic or collagenous colitis in more than hundred patients with chronic diarrhoea who had macroscopically normal colon with random biopsies. However, almost one-third of their patients had only sigmoidoscopy done. We know that Microscopic colitis can have patchy involvement and that right colon is more involved than left. Given the variable distribution of microscopic colitis, some cases may have been missed with Sigmoidoscopy biopsy alone<sup>16,17</sup>. A high incidence of colitis has been noted in large population based studies<sup>5,7</sup>. As a result of the majority of the colonoscopist performing colonoscopy in this study and placing all specimens into one jar in an attempt to conserve costs, we cannot comment on which specimen (e.g., cecum or sigmoid colon) specifically led to the diagnosis. However, we recommend obtaining two specimens from the cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum.

A significant proportion (42%) of our patients with normal or nonspecific colitis were subsequently diagnosed with IBS-D or Functional diarrhoea. These findings are consistent with those of Read *et al*<sup>18</sup> who after detailed evaluation of 27 patients

reported 8 to have IBS. In our study, 18 additional patients with apparent normal histology had spontaneous resolution of their diarrhoea on subsequent follow up. Six patients with nonspecific colitis had the diagnosis of IBS on follow-up. An intercurrent illness cannot be excluded as the cause for this histological finding of non-specific colitis and later developing into IBS<sup>19</sup>.

Distal duodenal biopsies were not done in a systematic manner, only a proportion of patients underwent distal duodenal biopsy. Thus, any recommendations on its regular usage in evaluating patients with chronic diarrhoea cannot be made from available information. The higher yield for histopathology in our study is mostly due to inclusion of a large population of patients undergoing an initial evaluation for unexplained diarrhoea and our inclusion of patients with associated bloody diarrhoea.

In conclusion, this study reports on the usefulness of colonoscopy with biopsy in the evaluation of non-HIV patients with chronic diarrhoea. Ileoscopy may complement, or less commonly, make the diagnosis for patients with chronic diarrhoea. A significant number of patients (56% of patients with final diagnoses) were determined to have IBS. It could be argued that in cases where IBS is suspected, a normal colonoscopy helps exclude organic pathology. Thus, our report of histological diagnoses is likely an underestimate of the clinically useful information obtained from colonoscopy. Our study is retrospective and the inability to have a uniform selection process for study patients could have influenced the results. Prospective studies may be necessary to assess the yield and cost-effectiveness of colonoscopy versus sigmoidoscopy in non-HIV patients with chronic diarrhoea.

## References

1. Kearney DJ, Steuerwald M, Koch J, *et al*. A prospective study of endoscopy in HIV-associated diarrhea. *Am J Gastroenterol* 1999;94:596–602.
2. Tanaka M, Mazzoleni G, Riddell GH. Distribution of collagenous colitis: Utility of flexible sigmoidoscopy. *Gut* 1992;33: 65–70.
3. Zwas FR, Bonheim NA, Berken CA, *et al*. Diagnostic yield of routine ileoscopy. *Am J Gastroenterol* 1995;90:1441–3.
4. Dickinson RJ, Gilmour HM, McClelland BL. Rectal biopsy in patients presenting to an infectious disease unit with diarrhoeal disease. *Gut* 1979;20:141–8.
5. Fernandez-Banares F, Salas A, Forne M, *et al*. Incidence of collagenous and lymphocytic colitis: A 5-year populationbased study. *Am J Gastroenterol* 1999;94:418–23.
6. Marshall JB, Singh R, Diaz-Arias AA. Chronic, unexplained diarrhea: Are biopsies necessary if colonoscopy is normal? *Am J Gastroenterol* 1995;90:372–6.
7. Alkhatib O, Ferrentino N, Moses PL, *et al*. The incidence of microscopic colitis in patients with chronic unexplained diarrhea. *Am J Gastroenterol* 1998;93:AB294 (abstract)
8. Münch A, Aust D, Bohr J, *et al*. Microscopic colitis: current status, present and future challenges: statements of the European Microscopic Colitis Group. *J Crohns Colitis* 2012;6:932–45.

9. Geboes K, Ectors N, D'Haens G, *et al.* Is ileoscopy with biopsy worthwhile in patients presenting with symptoms of inflammatory bowel disease? *Am J Gastroenterol* 1998;93: 201–5.
10. Coremans G, Rutgeerts P, Geboes K, *et al.* The value of ileoscopy with biopsy in the diagnosis of intestinal Crohn's disease. *GastrointestEndosc*1984;30:167–72.
11. Meisel JL, Bergman D, Graney D, *et al.* Human rectal mucosa: Proctoscopic and morphological changes caused by laxatives. *Gastroenterology* 1977;72:1274–9.
12. Giardiello FM, Lazenby AJ, Bayless TM, *et al.* Lymphocytic (microscopic) colitis—clinicopathological study of 18 patients, and comparison to collagenous colitis. *Dig Dis Sci* 1989;34:1730–8.
13. Prior A, Lessells AM, Whorwell PJ. Is biopsy necessary if colonoscopy is normal? *Dig Dis Sci* 1987;32:673–6.
14. Patel Y, Pettigrew NM, Grahame GR, *et al.* The diagnostic yield of lower endoscopy plus biopsy in nonbloodydiarrhea. *GastrointestEndosc*1997;46:338–43.
15. Palmer KR, Berry H, Wheeler PJ, *et al.* Collagenous colitis—a relapsing and remitting disease. *Gut* 1986;27:578–80.
16. Carpenter HA, Tremaine WJ, Batts KP, *et al.* Sequential histologic evaluations in collagenous colitis: Correlations with disease behavior and sampling strategy. *Dig Dis Sci* 1992;37: 1903–9.
17. Alkhatib O, Fisher JB, Callas P, *et al.* Sensitivity of flexible sigmoidoscopy vs. full colonoscopy for the diagnosis of microscopic colitis (collagenous and lymphocytic colitis): Metaanalysis of all published data. *Am J Gastroenterol* 1998;93: AB295 (abstract).
18. Read NW, Krejs GJ, Read MG, *et al.* Chronic diarrhea of unknown origin. *Gastroenterology* 1980;78:264–71.
19. MacIntosh DG, Thompson WG, Patel DG, *et al.* Is rectal biopsy necessary in irritable bowel syndrome? *Am J Gastroenterol* 1992;87:1407–9.

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