

Research Article

Clinico-pathological study of colonoscopic biopsies in patients with chronic diarrhea

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ABSTRACT

Background: Colonoscopic biopsy is important in the diagnosis and treatment of suspected colonic diseases as it is a diagnostic procedure of choice for patients with chronic diarrhea lasting for several weeks to months. Main objective of the study were to establish colonoscopic biopsy as an effective tool in the diagnosis of chronic diarrhea and to evaluate normal and abnormal mucosal colonoscopic biopsy in the contribution of differential diagnosis in chronic diarrhea patients.

Methods: The present study was conducted over a period of 2 years from November 2013 to October 2015 in the Department of Pathology, Andhra medical college, Visakhapatnam. This study included 104 colonoscopic biopsies with clinical history of chronic diarrhea.

Results: Out of 104 biopsies evaluated, specific diagnoses were 41 (39.42%) and nonspecific diagnoses were 63 (60.57%). This study showed male preponderance (67% of cases) with average age of 40.5 years (6-84years), remaining 33% female cases had average age 45 years (16-65 years). Out of 41 specific histological diagnoses made, majority of them were malignancies seen in the age group of 51-60 years and inflammatory bowel disease seen in the age group of 30-40 years.

Conclusions: The importance of colonoscopic biopsies lies especially in some chronic diarrhea patients with normal colonoscopy as in present study which contributed the more specific diagnosis like lymphocytic colitis, eosinophilic colitis, ulcerative colitis and pseudo membranous colitis and nonspecific cases to be followed up regularly.

Keywords: Chronic diarrhea, Colonoscopic biopsy, Lymphocytic colitis

INTRODUCTION

With passing generations and the accompanying lifestyle changes is associated an increased incidence of gastrointestinal diseases. Chronic diarrhea defined as changes in intestinal transit lasting four or more weeks characterized by reduced stool consistency, increased daily evacuation frequency and a daily stool weight of >200 g.

The cause may be infectious, endocrine-metabolic, neoplastic, functional or drug related.^{1,2} Thus, the diagnosis of chronic diarrhea is ample and complex. In

patients with chronic diarrhea multiple examinations are required to follow the course of the disease and to detect and correct any complications at an early stage. Utilizing colonoscopy and biopsy, it is possible to identify the location and type of colon disease. The histological identification of each lesion help in appropriate specific treatment.⁸

To put the interpretation of the biopsy findings into more rational and comprehensible content, we aim to provide herein an understanding of normal and abnormal histology and describe commonly encountered abnormal histological patterns.³

METHODS

The present study was conducted over a period of 2 years from November 2013 to October 2015 in the Department of Pathology, Andhra medical college, Visakhapatnam. This study included 104 colonoscopic biopsies from the patients those attended the outpatient department of Gastroenterology, King George Hospital, Visakhapatnam, India with clinical history of chronic diarrhea. The histological diagnosis was given after studying the H and E stained sections and assessing the collagenous layer (On Masson trichrome stained sections) as well.

Inclusion criteria

Cases of chronic diarrhea of the large bowel type (high frequency with low quantity stools), Duration of diarrhea longer than 4 weeks.

Exclusion criteria

Post-operative diarrhea, uncontrolled diabetes, HIV patients, untreated hyperthyroidism, inadequate biopsy. The following clinical data was documented in each case; age of the patient, duration of lesion, site of lesion, personal history, family history, occupational history and socio-economic status.

RESULTS

Out of the 104 colonoscopic biopsies evaluated specific histological diagnosis made were 41 (39.42%) and nonspecific diagnosis were 63 (60.57%) (Table 1).

Table 1: Total number of cases (n=104).

Histological diagnosis	Number
Total no cases	104
Specific diagnosis	41 (39.42%)
Nonspecific diagnosis	63 (60.57%)

Table 2: Sex incidence.

Sex	Number
Male	70 (67%)
Female	34 (33%)
Total	104



Figure 1: Colonoscopic view-normal mucosa.

Out of the 104 cases studied 67% of cases showed male preponderance with average age of 40.5 years (6-84 years), remaining 33% female cases had average age 45 years (16 -65 years) (Table 2).

Table 3: Gross colonoscopic findings.

Colonoscopic diagnosis	Number of cases (%)
Normal	58 (55.76%)
Polyps	3 (2.88%)
Nonspecific	12 (11.53%)
Diverticulum	2 (1.92%)
Stricture	1 (0.96%)
Nodules	1 (0.96%)
Ulcers	14 (13.46%)
Growth	13 (12.5%)
Total	104 (100%)

The gross colonoscopic findings were normal in the majority of cases (Figure 1) (58 cases-55.76%). Specific changes like ulcers, strictures, nodules and proliferating growths were seen in 27.88% (29 cases); whereas 11.53% of cases showed nonspecific findings such as mild mucosal edema and hyperemia. Incidental findings, such as small polyps (smaller than 0.6 cm 3 cases), and diverticula (2 cases) were revealed in routine colonoscopic examinations (Table 3).

Table 4: Histological abnormalities in colorectal biopsies.

Histological diagnosis	Number of cases (%)
Malignancy	13 (12.5%)
Ulcerative colitis	13 (12.5%)
Crohn disease	4 (3.84%)
Tuberculosis	2 (1.92%)
Polyp	3 (2.88%)
Lymphocytic colitis	4 (3.84%)
Eosinophilic colitis	1 (0.96%)
Pseudomembranous colitis	1 (0.96%)
Nonspecific inflammation	63 (60.57%)
Total	104 (100%)

Table 5: Sex distribution in specific diagnosis showing male predominance.

Histopathological diagnosis	Male cases	Female cases
Malignancies	9	4
Ulcerative colitis	9	4
Crohn disease	3	1
Tuberculosis	1	1
Lymphocytic colitis	2	2
Eosinophilic colitis	1	0
Pseudo membranous colitis	1	0
Polyp	2	1
Total	28	13

Colonoscopic biopsy yielded specific diagnoses in 41 cases (39.42%). Out of 41 specific histological diagnosis majorities of them were malignancies and inflammatory bowel disease followed by lymphocytic colitis, Tubercular colitis, polyps, eosinophilic colitis, and pseudo membranous colitis (Table 4). Inflammatory bowel disease usually common in females, contrary to this present study had male predominance possibly due to lesser sample size, whereas tuberculosis and lymphocytic colitis were equally distributed. Eosinophilic colitis and

pseudo membranous colitis were seen in males. Most common affected age group in specific diagnosis seen was in between 31-60 years (Table 5).

Out of specific diagnosis malignancies were more common in the age group of 51-60years; whereas inflammatory bowel disease seen in the age group between 30-40years (Table 6). Most common affected bowel segment was rectosigmoid (Table 7).

Table 6: Age distribution in specific diagnoses.

Age	0-10	11-20	21-30	31-40	41-50	51- 60	61-70
Malignancies	-	1	-	3	2	4	3
Ulcerative colitis	1	-	3	4	2	3	-
Crohn disease	-	-	1	-	3	-	-
Tuberculosis	-	1	1	-	-	-	-
Lymphocytic colitis	-	1	-	1	1	1	-
Eosinophilic colitis	-	-	-	-	1	-	-
Pseudomembranous colitis	-	-	-	1	-	-	-
Polyp	1	-	-	-	1	1	-
Total	2	3	5	9	10	9	3

Table 7: Most commonly affected bowel segment in specific diagnosis.

Histopathological diagnosis	Ileo-cecum	Ascending colon	Rectosigmoid colon	Total cases
Malignancy	1	8	4	13 (12.5%)
Ulcerative colitis	-	4	9	13 (12.5%)
Crohn disease	3	1	-	4 (3.84%)
Tuberculosis	2	-	-	2 (1.92%)
Polyp	-	1	2	3 (2.88%)
Lymphocytic colitis	2	2	-	4 (3.84%)
Eosinophilic colitis	-	-	1	1 (0.96%)
Psuedomembranous colitis	-	-	1	1 (0.96%)
Total	8	16	17	41

DISCUSSION

The present study is a hospital based study, majority of the patients studied were natives of in and around Visakhapatnam which cannot be regarded as representative of any community or population.

Present study aims to establish colonoscopic biopsy as an effective tool in the diagnosis of chronic diarrhea.

Table 8: Comparison of sex incidence with other studies study.

	Male	No of cases
Joon Hyoek at al ⁵	79 (66.94%)	118
Soudhamini S et al ⁶	136 (68%)	200
Present study	70 (67.30%)	104

Present study showed high prevalence of chronic diarrhea with male preponderance in concordance with Joon hyoek et al, Soudhamini et al studies.

Table 9: Comparison of specific diagnosis with other studies.

Study	Percentage of specific cases	No of cases
Joon Hyoek et al ⁵	21.2% (25)	118
Shah RJ et al ⁴	31% (52)	168
Soudhamini S et al ⁶	50% (95)	200
Present study	39.42% (41)	104

In present study colonoscopic biopsy yielded specific diagnoses in 39.42% (41) cases almost correlating with shah RJ at al study.⁴ But this was a much lower yield

compared to the one obtained by Soudhamini S, et al which was around 50%.⁶ This merely reflects the numerous factors in play, e.g. skill of the gastroenterologist, type of equipment used and sample size.

Table 10: Comparison of most common specific diagnosis with other study.

Studies	Most common diagnosis
Soudhamini S, et al ⁶	Polyps
Kolhe HS et al ⁹	Ulcerative colitis
Present study	Malignancy and ulcerative colitis

Among the specific diagnoses most commonly encountered cases were malignancy and ulcerative colitis in concordance with Kolhe HS et al study.⁹ Whereas soudhamini S, et al study had polyps as most common specific diagnosis followed by malignancy.⁶

In present study out of 13 cases of malignancy 1 case had a previous history of ulcerative colitis. Lack of specific diagnosis was reflected in 60.57% of cases labeled as chronic nonspecific colitis (Figure 2). This might point to the importance of follow-up in such cases.

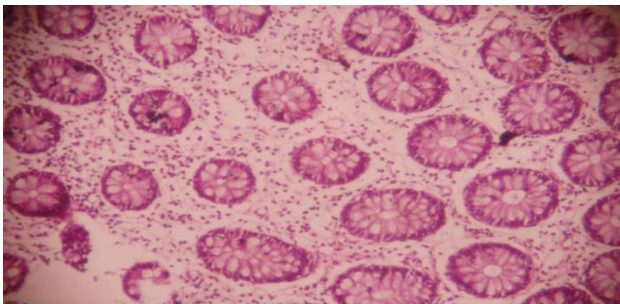


Figure 2: Nonspecific colitis, H and E stain (100X).

Malignancy

In this study ascending colon is most commonly affected bowel segment followed by recto-sigmoid colon. Clinically these cases presented with anemia (average haemoglobin is 7 gm/dl), weight loss and diarrhea which is not a usual symptom in right sided tumors; whereas cases with rectosigmoid tumor presented with occult blood in stool, tenesmus with diarrhea.

Usual presentation of left sided tumors is altered bowel habits but present study included only the tumors presented with diarrhea, excluded cases presented with altered bowel habits.

Present study 13/104 cases (12.5%) is in concordance with Soudhamini S et al study 32/200 cases (16%).⁶ One case had a previous history of ulcerative colitis and biopsy revealed adenocarcinoma, (Figure 3) which

indicates the possibility of premalignant nature of ulcerative colitis.

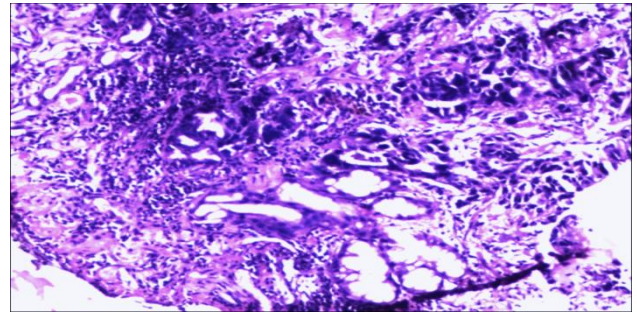


Figure 3: Moderately differentiated adenocarcinoma H and E stain (100x).

Ulcerative colitis

Most commonly affected segment in present study is recto sigmoid which is usual site for ulcerative colitis. 12 out of 13 cases of ulcerative colitis had moderate disease endoscopically with features of erosions, complete loss of vascular pattern, and significant erythema. Remaining case showed only mild mucosal erythema. Histologically all cases showed typical features of ulcerative colitis having marked inflammatory cells in superficial layers and crypt abscesses with neutrophils (Figure 4).

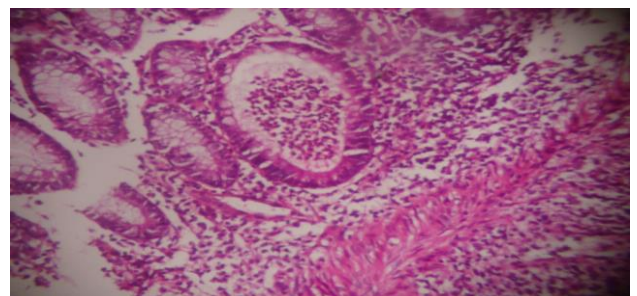


Figure 4: Ulcerative colitis—crypt abscess, H and E stain (100X).

Clinical correlates obtained from collected data revealed the association of Ulcerative colitis with frank blood in stool. Contrary to this in our study one patient had occult blood in stool, so it is important to remember that other comparatively less common conditions like Ulcerative Colitis may also present with occult blood in stool.

Here is the clinician’s duty to possess the index of suspicion and order relevant investigations in such cases. It also underlines the importance of yield of colonoscopic biopsy related to specific clinical features. In present study one case of ulcerative colitis presented at the younger age i.e. at 8 years which was a unusual presentation. Present study with 12.5% (13/104 cases) is almost in concordance with Soodet A al 15.6% (23/147cases) and Kolhe HS et al study 16.7% (20/120cases).^{9,10} Whereas Patel Y et al, Shah RJ et al

studies had 1.65% (4/205cases) and 4.92% of cases (7/142cases) respectively.^{4,7}

Tuberculosis

Clinically both the cases presented with ileo-cecal mass. Colonoscopy of two cases revealed ulcers with luminal narrowing; microscopically showed typical features of tuberculosis with granuloma composed of epithelioid cells and caseous necrosis (Figure 5). Present study had 1.92% of cases (2/104 cases) whereas Kolhe HS al study had 7.5% of cases (9/120 cases).⁹

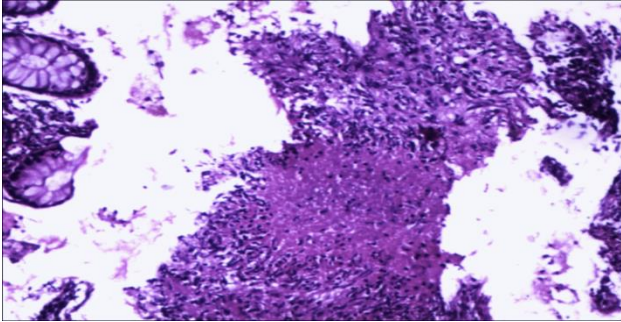


Figure 5: Tuberculosis-caseousnecrosis, adjacent mucosal glands H and E stain (100X).

Crohn disease (granulomatous colitis)

Out of 4 cases, 3 cases involved ileocecal region which is the frequent location of the Crohn disease. Remaining case involved ascending colon which is less common as Colonic Crohn's disease without small bowel involvement. Endoscopically these cases showed aphthous ulcers with average size of 4 mm had various shapes including deep and serpiginous type with characteristic tiny rim of erythema (Figure 6).

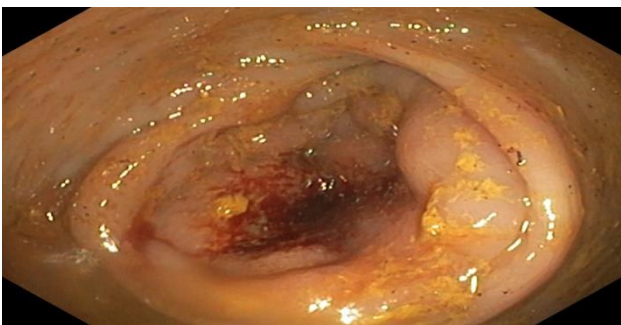


Figure 6: Colonoscopic view- multiple mucosal ulcerations.

Histopathology of all 4 cases showed superficial granulomas with preservation of the goblet cell population and maintenance of the architecture of the glands which are the differentiating features from ulcerative colitis (Figure 8). As present study included superficial biopsies (mucosa and submucosa) transmural granulomas could not be identified. The observations in

present study (3.8% of cases (4/104)) were comparable with studies by Kolhe HS et al (5.8% of cases (7/120)), and Shah RJ et al (6.33% of cases (9/142)).^{4,9} Whereas Patel Y et al study had only 0.96% of cases (2/208 cases).⁷

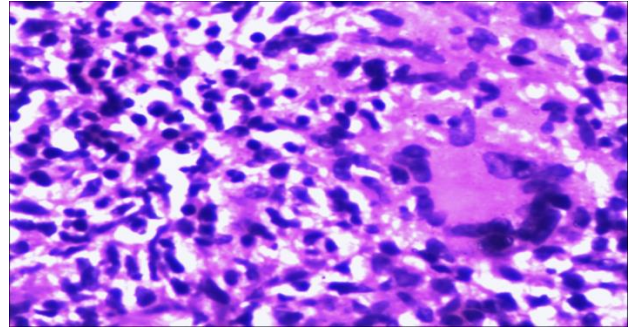


Figure 7: Crohn disease-granuloma with giant cell; H and E stain 400X

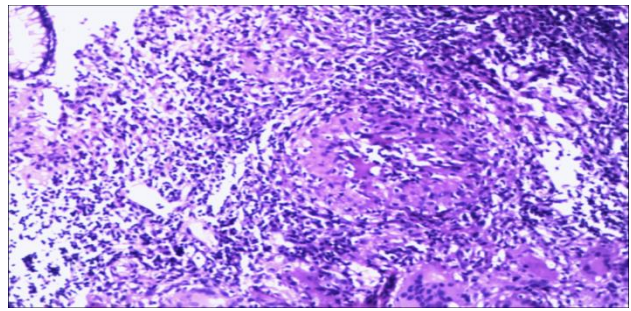


Figure 8: Crohn disease-non caseating granulomas, H and E stain (100X) (block arrow shows mucosal gland).

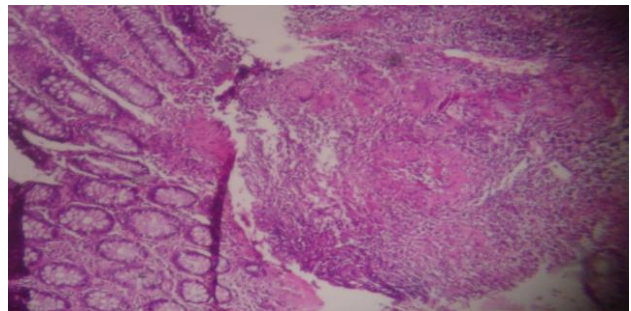


Figure 9: Crohn disease- non caseating -granulomas, H and E stain (40X).

Eosinophilic colitis

Only one case encountered in present study which involved rectosigmoid colon. Clinically patient presented with nausea, vomiting and diarrhea. Colonoscopy - revealed mild inflammatory changes with edema, erythema and loss of vascular patterns. Study histologically revealed eosinophilic infiltration (>20 eosinophils/HPF) of the lamina propria extending towards submucosa. The normal eosinophils at this site are 10/HPF (Figure 10).

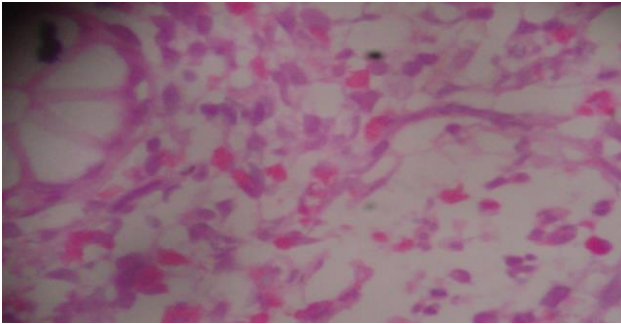


Figure 10: Eosinophilic colitis-more than 20 eosinophils per one high power field, H and E stain (400X).

Peripheral smear of this patient revealed eosinophilia with 35% of eosinophils. The diagnostic criteria of eosinophilic colitis are >20 eosinophils per HPF in biopsy with eosinophilia in peripheral blood.

As eosinophilic colitis in its primary form can be associated with secondary to helminthic infections, inflammatory bowel disease and auto immune diseases, in this case ruled out this differential diagnosis. Incidence of these cases are low as in present study, this may be attributed to no clear consensus exists with regards to the degree of tissue eosinophilia or the presence of distinct pathologic findings.

Presence of more than 15 eosinophils per high-power field in the esophageal squamous mucosa but such consensus does not exist for EC, although most authors have used a diagnostic threshold of 20 eosinophils per high-power field.

Normal values for tissue eosinophils vary widely between different segments of the colon ranging from:

- <10 eosinophils per high-power field in the rectum,
- >30 eosinophils per high-power field in the cecum.

Thus location of colonic biopsy is critically important for proper interpretation of findings and diagnosis of eosinophilic colitis.¹¹ Present study (0.8% of cases (1/104 cases)) is in concordance with Kolhe HS et al study (0.9% of cases (1/120 cases)).⁹

Lymphocytic colitis

Ascending colon and caecum were involved in two cases each. Both Patients presented with pain abdomen and diarrhea. Lymphocytic colitis is associated with autoimmune gastritis, celiac sprue and myasthenia gravis.

These entities were excluded in all the cases. On colonoscopic examination no significant findings were seen. Histo-pathological examination revealed an increase in intra-epithelial lymphocytes in the mucosal lining. Ratio of lymphocytes per 100 columnar cells was

obtained, which came out to be 25/100 in our case (Figure 11).

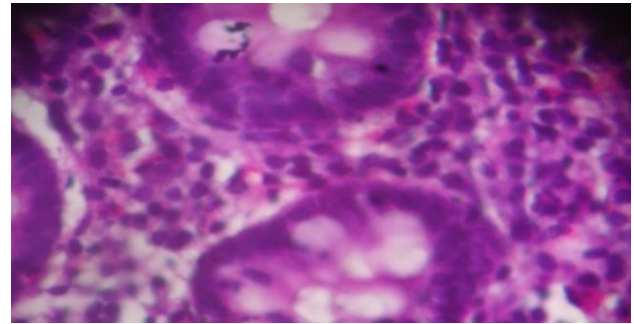


Figure 11: Lymphocytic colitis-more than 2 lymphocytes per 100 epithelial cells, H and E stain (400X).

No other histo-pathological abnormalities were found. These features along with clinical findings combined, supported the diagnosis of lymphocytic colitis. Present study (3.8% of cases (4/104)) is almost in concordance with Kolhe HS et al study (1.7% of cases (2/120 cases)).⁹ "Microscopic colitis" describes collagenous colitis and lymphocytic colitis. In all these cases special stain Masson trichrome was done to rule out the possibility of collagenous colitis, came out to be negative.

Pseudo membranous colitis

Only one case diagnosed in the present study. Clinically patient presented with diarrhea who had the previous history antifungal treatment 3 months back which might be the cause for the colitis. Colonoscopy showed only mild erythema and yellowish patches. Microscopic examination showed denuded epithelium with lamina propria contains dense neutrophils, along with mucopurulent exudate in the crypts formed a mushroom like cloud appearance with karyorrhectic debris (Figure 12).

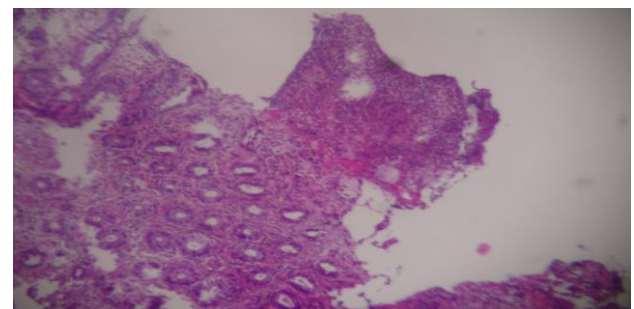


Figure 12: Pseudo membranous colitis– volcano type of ulceration with inflammatory cells H and E stain (40X).

Present study had only 0.96% of cases (1/104 cases) incidence when compared to 5.0% of cases (6/120 cases) incidence in Kolhe HS et al study.

Polyps

Colonoscopy of 3 cases in our study revealed polyps had average size of 0.6cm. Histopathologically two cases showed features of hyperplastic polyps, remaining case had features of inflammatory polyp. Present study had only 6.52% of cases (3/104 cases) which is less when compared to Soudhamini S, et al study about 17% (34/200 cases).⁶ As Soudhamini. S, et al study was conducted only on abnormal colonic mucosa above discordance may be explained.⁶ Lymphocytic colitis is the most common abnormality in normal colonoscopic findings correlating with Shah et al⁴ study. Because of the limited sample study cases of collagenous colitis were not encountered in our study.

Seven out of 41 histological specific diagnosis cases, colonoscopy showed normal mucosa except nonspecific findings like edema and hyperemia. In a case of ulcerative colitis usual colonoscopic findings like irregular ulcers, petechial hemorrhages pseudo polyps were not seen. A case of pseudo membranous colitis with classical histological features showed only mild erythema colonoscopically instead of classical yellowish plaques. Above findings explains the importance of colonoscopic biopsy in chronic diarrhea patients even with normal colonoscopy findings.

CONCLUSION

The importance of colonoscopic biopsies lies especially in some chronic diarrhea patients with normal colonoscopy as in present study which contributed the more specific diagnosis like lymphocytic colitis, eosinophilic colitis, ulcerative colitis and pseudo membranous colitis. Nonspecific cases should be followed up. Therefore all the patients presenting with chronic diarrhea should be evaluated thoroughly with detailed history, clinical examination and colonoscopy with biopsy wherever possible.

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