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PROFILE OF ANALYSIS OF COLONIC BIOPSIES IN CHRONIC COLITIS IN TERTIARY CARE HOSPITAL OF CENTRAL INDIA

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Abstract
Background: Chronic colitis, regardless of type, is defined histologically by chronic inflammation, mainly plasmacytosis, in the lamina propria. Specific diagnosis of chronic colitides in biopsies can be challenging for practicing pathologists. The present research was undertaken to study complete clinico-pathology of chronic colitis, pathological pattern and spectrum of colitis, also study correlation of colonoscopy and histopathology of these lesions.Method:This study was a retrospective and prospective analysis of 187 cases ofhistopathologicallyproven colitis on colonic biopsies over a period of 5 years from June 2015 to May 2020. Results:Majority of specimen were rectal biopsies (57.22%) followed by mapping biopsies (34.22%). Of 85 cases where both colonoscopy and histopathology diagnosis was available, 61 (71.76%) colonoscopy diagnosis were consistent with histopathology. Among 187 cases, 107 were inflammatory bowel disease (57.22%), they were further sub classified as ulcerative colitis (UC) (96.26%), Crohn's (0.93%) and indeterminate colitis (2.8%). Cases of UC had features of basal plasmacytosis (97.19%), crypt distortion (93.45%), crypt loss (70.09%) and goblet cell depletion.48cases diagnosed as non-specific colitis. Infectious colitis comprised 8.56% of total colitis cases. It included tuberculosis 4 (2.14%), CMV colitis 2(1.07%) and 5.35% cases of acute self-limiting colitis. 5(2.67%) cases were diagnosed as lymphocytic colitis and 2 cases showed focal active colitis. Also, found single case of eosinophilic colitis and radiation proctitis each.Conclusion:Good clinico-pathological correlation helps to reduce number of cases diagnosed as non-specific colitis. To improve the detection rate of microscopic colitis, it is important to take multiple biopsies from normal looking colon on colonoscopy.
Keywords: Colitis, Colonoscopy, Histopathology, Biopsy, Inflammation, Plasmacytosis

Introduction

Colitis includes various inflammatory lesion of large bowel. Various type of colitis affects large number of people all over the world. It includes inflammatory bowel disease (IBD),

microscopic colitis, CMV colitis, solitary rectal ulcer syndrome (SRUS), infective colitis, non-specific colitis etc. [1]. Chronic colitis usually implies IBD. However, it also includes mimics of IBD like ischemic colitis, SRUS, diversion colitis, colitis associated with diverticular disease etc. these entities have similar clinical features but histopathology contributes to differentiate them from each other [1, 2].

Patients with different types of colitis usually present with diarrhea, blood and mucous in stools, abdominal pain etc. Colonoscopy examination is important in the diagnosis and treatment of suspected colonic diseases. It has replaced radiology as initial test of choice in many clinical situations [3]. However, the value of colonoscopy combined with biopsy frequently is not realized. Macroscopic evaluation alone cannot always detect mucosal disease. Hence, colonoscopy and colonoscopy guided biopsy is investigation of choice to diagnose specific type of colitis and asses its severity [4].

The colorectal mucosa has a limited repertoire of responses to injury and the similarity of pathological changes in ulcerative colitis, Crohn's disease and other intestinal inflammation is there, however examination of colorectal biopsy specimen is a reliable method for diagnosing inflammatory bowel disease and different types of colitis. As management depends on accurate clinicopathological classification, it is important to diagnose specific colitis on biopsy [5]. The biopsy number for non-neoplastic lesions of colon is gradually increasing. Of these, majority are reported as ulcerative colitis. Considering the fact that non-neoplastic colonic lesion [colitis] form significant burden of GI diseases and important cause of morbidity in our population, we decided to review and analyze "COLITIS" with respect to clinical data and histopathology features in colonic biopsies.

Materials and Methods

This is a retrospective and prospective study conducted during a period of 2years, from June 2018 to May 2020 in pathology department of Indira Gandhi Government Medical College, Nagpur. During this period, colonic biopsies were studiedfrom June2015 toMay 2020 in cases of different types of inflammatory diseases of large intestine (colitis).

This study dealt with spectrum of colitis in adults so patients with age less than 14 years were excluded from the study. All biopsies bearing a diagnosis of chronic colitis were selected. In many patients suspected to have IBD-rectal biopsy or mapping biopsies was taken, however in few of them single colonic biopsy from particular site (example: caecal) was taken and sent for histopathological examination. All the above mentioned biopsies and their repeat biopsies (if any) were included in the study.

Data was obtained regarding clinical presentation, duration of symptoms, other coexisting illness and colonoscopy findings from pathology requisition forms. The relevant blocks and slides were retrieved and reviewed. All biopsies were stained with haematoxylin and eosin stain. Special stains like Zheil nelson, Periodic Acid Schiff, Masson trichrome etc. were performed whenever required. In current study, clinical details were correlated with histopathological findings.

Observations and Results

Total numbers of colonic biopsies received in our Pathology section during study period of 5 years were 360, out of which 187cases were histopathologicalydiagnosed as colitis and comprised in study group.Among 187 cases, 107 (57.22%) were males and 80 (42.78%) were

females. The peak incidence of colitis was between 21-40 years of age (57%) with mean age of 37.8 years, (Table 1).

Table 1: Distribution of cases according to age group

Age group	No. of cases	Percentage
14—20	15	8.02
21-30	55	29.41
31-40	54	28.88
41-50	29	15.51
51-60	15	8.02
61-70	14	7.49
71-80	05	2.67

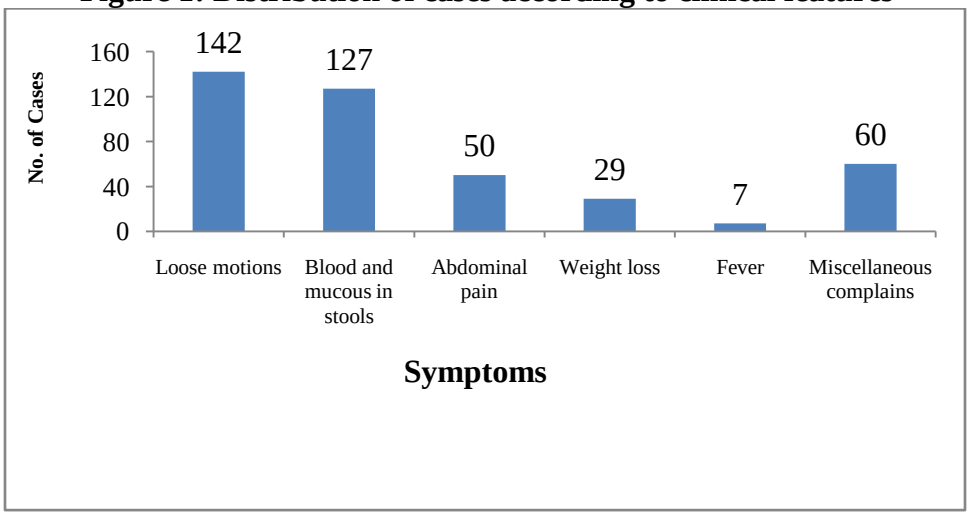
Most common specimen received was rectal biopsy (107; 57.22%) followed by mapping biopsy in approximately 34.22% of cases (64 cases), then caecum biopsy in 3.21% (6 cases), descending colon in 3; (1.60%), ascending colon and cecum, colon in 1.07% each (2 cases), and rectum ,caecum, transverse colon, rectal and descending colon biopsy in 1 (0.53%) case each. There were four repeat biopsies as shown in table 2.

Table 2: Repeat biopsies

No. of cases	Number of times biopsy done	Previous diagnosis	Final diagnosis
1	3	Non-specific colitis	CMV colitis
1	2	Focal active colitis	Non-specific colitis
2	2	Infectious colitis	Non-specific colitis

The loose motions was most common complaint seen in 142 (75.94%) of cases followed by blood and/or mucous in stool (67.91%) as depicted in figure 1.

Figure 1: Distribution of cases according to clinical features



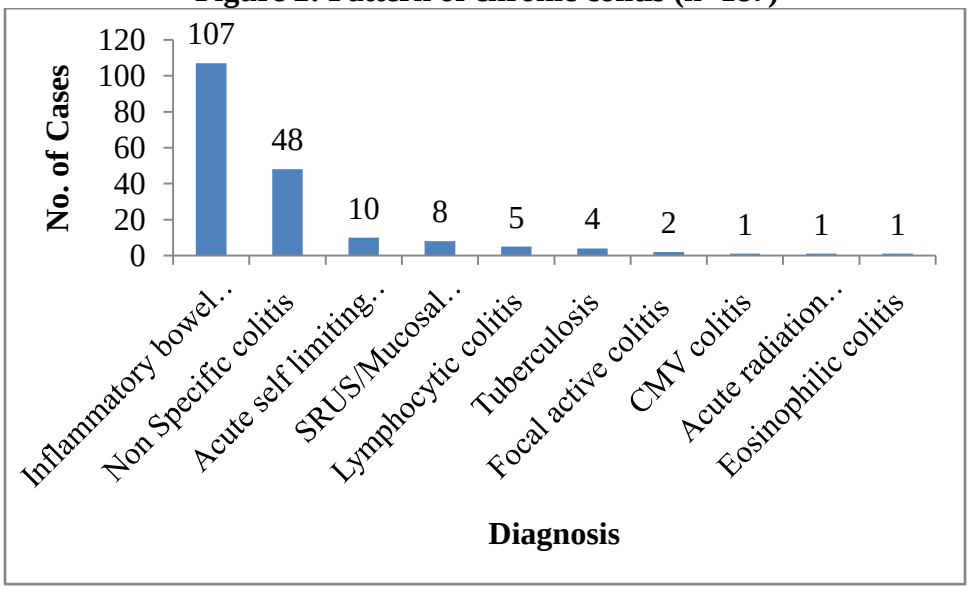
Colonoscopy was not done in 39 of cases where only proctoscopic rectal biopsy was taken and sent for examination. In 8 cases no definitive diagnosis was given on colonoscopy. Out of 148 cases of colonoscopy, descriptive reports were given in 63 cases. The most common definitive diagnosis was UC given in 45 cases (30.40%) and other commonly diagnosed conditions are shown in table 3.

Table 3: Colonoscopy findings (n=148)

Colonoscopy impression	No. of Cases	Percentage
Descriptive	63	42.56
Ulcerative colitis (UC)	45	30.40
Normal	16	10.81
IBD	6	4.05
SRUS	4	2.70
Colonic growth	3	2.02
Rectal ulcer	2	1.35
Proctitis	1	0.67
No definitive diagnosis	8	5.40
Total	148	100

Out of total 187 cases, 107 (57.22%) were diagnosed as inflammatory bowel disease followed by 48 cases (25.67%) were diagnosed as non-specific colitis and other pattern of chronic colitis areshown in figure 2.

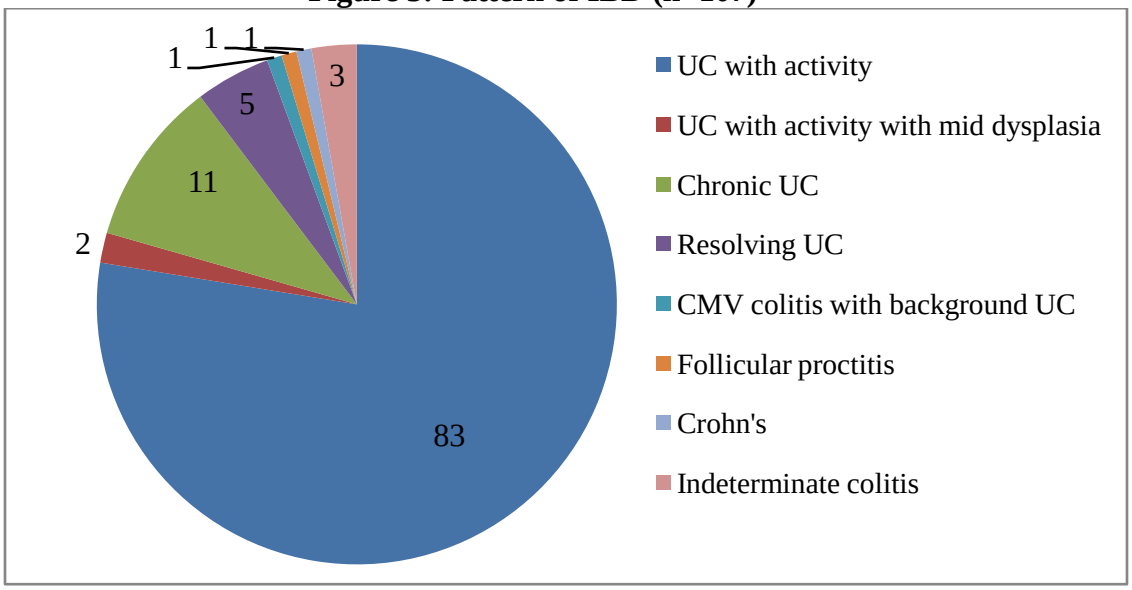
Figure 2: Pattern of chronic colitis (n=187)



Inflammatory bowel disease constituted 107 (57.22%) of total colitis cases, it includes 103 (96.2%) cases of ulcerative colitis. 11 (10.28%) cases showed no activity and were diagnosed as chronic UC. Only 5 (4.67%) cases of UC showed patchy histopathology features with history of treatment were called resolving UC. Diagnosis of Crohn's disease in biopsy was

given in only one case and 3 cases just had features suggestive of IBD and further sub classification could not be done which were called indeterminate colitis, (Figure 3).

Figure 3: Pattern of IBD (n=107)



Of the 85 cases where both colonoscopy and histopathology diagnosis was available. In 61 (71.76%) colonoscopy diagnoses were consistent with histopathology while in 24 (28.24%) cases colonoscopy diagnoses were discrepant with histopathology, (Table 4).

Table 4: Discrepancy in colonoscopy and histopathology diagnosis

Colonoscopy diagnosis	Final histopathology diagnosis	No. of cases
Normal colonoscopy	UC	3
	ASLC	1
	Lymphocytic colitis	3
	Non- specific colitis	8
	Eosinophilic colitis	1
Growth	ASLC	1
	Nonspecific colitis	2
SRUS	UC with activity	1
UC/IBD	SRUS	1
	ASLC	2
	SRUS	1
Total	Total	24

Out of total 187 cases, 102 cases either had descriptive colonoscopy report without impression (63 cases) or proctoscopic rectal biopsy was taken without colonoscopy (39). So these cases were not included while comparing colonoscopic and histopathology diagnosis. Histopathology diagnosis of cases were definite colonoscopic diagnosis was not available in 102 cases, of which 74; 72.54% cases haddefinitive diagnosis of specific colitis while 28; 27.45% had non-specific colitis.

HISTOPATHOLOGICAL FEATURES OF DIFFERENT TYPES OF COLITIS

Out of 107 IBD cases, 103 were UC. Cases of UC had features of basal plasmacytosis (97.19%), crypt distortion (93.45%), crypt loss (70.09%) and goblet cell depletion as shown in table 5.

Table 5:Histopathological features of IBD

Type of IBD	Crypt Abscess	Cryptitis	Crypt distortion	Crypt loss	Goblet cell depletion	Basal plasmacytosis	Dys pl-asia	Inclu si-on	Gran u-loma
All IBD (N=107)	67	87	100	75	48	104	2	1	0
UC (N=103)	64	84	97	73	47	101	2	1	0
UC with activity (N=83)	61	78	78	63	40	83	0	0	0
UC with activity with mid dysplasia (N=2)	2	2	2	2	2	2	2	0	0
CMV colitis with background UC (N=1)	0	0	1	1	1	1	0	1	0
Follicular proctitis (n=1)	0	0	1	0	0	1	0	0	0
Chronic UC (N=11)	0	0	10	6	4	9	0	0	0
Resolving UC (N-=5)	1	3	5	1	0	5	0	0	0
Crohn's (N=1)	0	1	1	0	0	0	0	0	0
Indeterminate colitis (n=3)	3	2	2	2	1	3	0	0	0

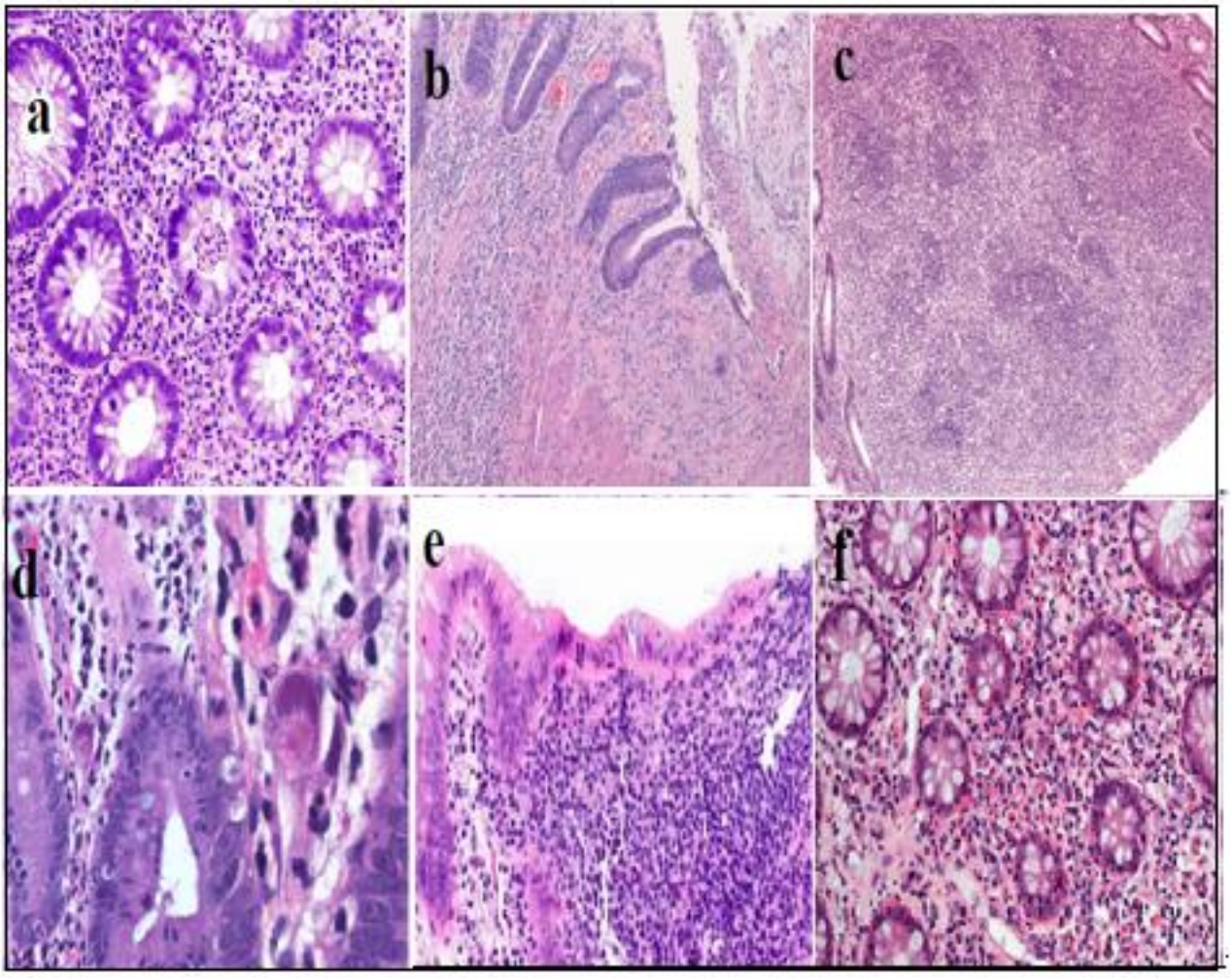
48 cases had significant chronic inflammatory infiltrate without features of any specific colitis and hence diagnosed as nonspecific colitis. We found 10 cases of acute self-limiting colitis and 8 cases of SRUS. The histopathological features of all these colitis are shown in table 6 and Fig 4.

Table 6: Histopathological features of- 1) Nonspecific colitis (n=48), 2) acute self-limiting colitis (n=10) and 3) SRUS (n=8)

Histopathological features of Nonspecific colitis	No. of cases	Percentage
LP infiltrate	46	95.83
Cryptitis	9	18.75
Granulation tissue/exudates	8	16.66
Mucosal ulceration	6	12.5
Goblet cell depletion	2	4.16
Crypt distortion	1	2.08
Crypt abscess	1	2.08
Histopathological features of acute self-limiting colitis	**No. of cases**	**Percentage**
LP infiltrate	10	100
Crypt abscess	7	70
Cryptitis	7	70
Mucosal ulceration	5	50

Fibrinosuppurative exudate	3	30
Crypt loss	0	0
Crypt distortion	0	0
Goblet cell depletion	0	0
Histopathological features of SRUS	**No. of cases**	**Percentage**
Fibromuscular obliteration of lamina propria	8	100
Crypt distortion	6	75
Hypertrophied muscularis mucosae	5	62.5
Mucosal ulceration	3	37.5
Goblet cell depletion	2	25
Crypt loss	1	12.5

Figure 4: a) Ulcerative Colitis showing cryptitis,Crypt abscess(100x); b) Solitory Rectal ulcer syndrome (100x); c) Lymphoid follicular Proctitis(40x); d) CMV colitis; e) Lymphocytic Colitis,(100x); f) Eosinophilic colitis(100x)



Discussion

The colonic biopsies for evaluation of a suspected case of colitis constitute significant number of specimens received in pathology division of our institute. The peak incidence of colitis was between 21-40 years of age with slight male predominance (57.22%) which is comparable with the study done by Al-Quorain et al [6].

Of the total 187 cases analyzed:

1) In 39 cases- Proctoscopic rectal biopsy was taken but colonoscopy was not done,

2) In 63 cases- Specific colonoscopic diagnosis was not forwarded to us with biopsy specimen and only descriptive reports were sent,

3) In 85 cases- Definite colonoscopic diagnosis was provided; hence correlation between colonoscopy and histopathology was possible. Of these: a) 61 colonoscopic diagnoses could be confirmed on biopsy features, b) 24 cases, a discrepancy between colonoscopic diagnosis and histopathology features were noted.

Of the 126 cases, where colonoscopy was not diagnostic, histopathology features on biopsy helped to diagnose particular colitis in 88 cases and non-specific colitis was seen in 38 cases. Indicating that colonoscopy with biopsy played significant role in giving diagnosis of specific colitis in 88 cases (47.05%) of the total study group which is in accordance with the study conducted by Shah et al (27%) [7]. But percentage of such cases was lower as compared to present study. This can be explained as this study included all patients with diarrhea and not specifically colitis, so many of their histopathology reports were normal colonic biopsy. Out of 16 cases: diagnosed as normal colon on scopy, 8 had significant colitis. Shah et al [7] found 14 such cases, emphasizing importance of taking random multiple biopsies in cases with normal colonoscopy.

Inflammatory bowel disease (IBD) was the most common cause of chronic colitis (57.22%) similar to previous studies [6-9] but in all these studies incidence of IBD was lower than current study. Higher prevalence of IBD can be explained in present study depending on clinical criteria to do biopsy. In this set up patients presenting with acute onset diarrhea are usually given trial of antibiotics and only cases with chronic diarrhea or lower GI symptoms non responsive to therapy were taken up for biopsy. Being referral centre we usually get biopsy from patients with chronic colitis. This selection bias could be the reason for having less case of infectious colitis (usually short duration) and more of chronic colitis or IBD. Changing environmental conditions, westernization of life style especially food habits or allergy to food constituents like milk can also explain high prevalence of IBD in this study. There is a possibility that some of our UC cases were early infectious colitis as there are overlapping histological features between the two. In such cases follow up biopsies will resolve the issue. However, we did not have follow up of many of our patients. Study by Thia et al [10] conducted that the previously reported incidence and prevalence rates of IBD in Asia were low compared with the West, but there was a notably rising trend, which supports high prevalence of IBD in current study.

UC comprised 96.26% of total IBD cases which is slightly higher but comparable to other studies [6, 11]. We did not come across much of Crohn's disease (only 0.93%). This can be explained on the geographic distribution of IBD in our region, probably UC is more prevalent. However, studies on Crohn's colitis are lacking in our region probably because the incidence is

actually low. One possibility is that we have missed diagnosis of Crohn's disease in few cases as mucosal biopsies often show only nonspecific inflammation. 3 cases were diagnosed as indeterminate colitis, where it was difficult to differentiate between UC and Crohn's because of overlap of features. Though, it was believed that IBD is rare in Asian countries. We found significant proportion (57.2%) of colitis due to IBD. Ulcerative colitis (96%) clearly outnumbers cases of Crohn's disease (amongst IBD).

The most common histopathological features in IBD was basal plasmacytosis (97.19%) followed by crypt distortion (93.45%), cryptitis (81.30%) and crypt loss (70.09%). These findings are in accordance with the study done by Selderjink et al [12]. The majority of IBD cases were UC and hence spectrum of biopsy finding quoted above is applicable to cases of UC also. The majority of cases of UC (80.58%) showed activity, 10.67% did not show any activity hence diagnosed as Chronic UC; five cases of UC were under treatment showing patchy histological features, hence diagnosed as Resolving UC. Only single case of UC showed CMV infection and follicular proctitis on pathology. Only two cases showed mild dysplasia (1.86%) which is similar to the finding by Al-Quorain et al [6]. Mild dysplasia does not warrant any surgical intervention. However, it calls for regular follow up for these patients.

We had a case of 14 years male presented with loose motions and abdominal pain. On colonoscopy differential diagnosis of Tuberculosis and Crohn's were suggested. On biopsy, cryptitis was seen locally and crypt distortion was seen suggestive of chronic colitis with activity. Patient was already taking antituberculous treatment and was not responding to the same. In view of correlation with history, colonoscopy and lack of granuloma and caseous necrosis diagnosis of Crohn's disease was suggested. This is quite similar to study done by Al-Quorain et al [6]. In 3 patients, biopsy features suggested diagnosis of IBD, but there were no clear cut pointers towards UC or Crohn's, hence diagnosis of indeterminate colitis was given.

Present study had 25.67% cases of nonspecific colitis which is similar to study by Shah et al [7]. Cases of infectious colitis were 8.56% which is lower than earlier studies [6-8]. Though being a developing country still lower percentage of infectious colitis can be explained by the fact that in our set up patients presenting with short history received antibiotics and respond to therapy, hence are not biopsied. In 4 (2.14%) cases depending on history, colonoscopy and presence of granuloma or langhans giant cell, diagnosis of tuberculosis was given. CMV infection was seen in 2 cases (1.07%). Majority of our infectious colitis cases (5.35% of total) were given histopathological diagnosis of acute self-limiting colitis. Because of lack of microbiological correlation and complete work up of infectious cases, these cases could not be further specified. 5 (2.67%) cases were diagnosed as lymphocytic colitis and 2 cases showed focal active colitis. Single case of radiation proctitis and eosinophilic colitis each were noted in this study. These findings are correlated well with the previous studies [6-8, 11, 13, and 14].

Conclusion

Good clinico-pathological correlation helps to reduce number of cases diagnosed as non-specific colitis. To improve the detection rate of microscopic colitis, it is important to take multiple biopsies from normal looking colon on scopy. The rare entities like radiation proctitis, eosinophilic colitis and follicular proctitis from part of spectrum of chronic colitis should be diagnosed precisely because of their clinical implication.

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