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Inflammatory Bowel Disease: A Clinicopathological Study at a Tertiary Care Centre in India

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Abstract

Objective: Colonoscopy and histopathology are essential tools for diagnostic work up of inflammatory bowel diseases. The present prospective study was conducted with the aim to study the spectrum of lesions, to find age and sex distribution of these lesions, anatomical site and to study the various colonoscopic and histopathological features which helps to make correct diagnosis and categorize IBD.

Material and Methods: The present prospective study was conducted in department of pathology in collaboration with department of Gastroenterology, Pt. B.D. Sharma, PGIMS, Rohtak. A total of 100 consecutive colonic mucosal biopsies from clinically suspected patients of inflammatory bowel disease were taken along with clinical and colonoscopic findings.. Biopsies were fixed and processed by routine histological technique for paraffin embedding and staining with hematoxylin and eosin. A histopathological diagnosis was made on basis of certain histopathological features represented by crypt architectural abnormalities, mucosal epithelial changes and inflammatory features.

Results: Maximum number of patients were in the age group of 31-40 years (30%). Males were more commonly affected (55%) with a male: female ratio of 1.2:1. The main clinical manifestations were pain abdomen, bleeding per rectum, diarrhea, blood in stools which were present alone or in combination. The common endoscopic findings observed in our study were distal colitis, erosion/ulceration and loss of vascular pattern with erythema and granularity. Anatomical location of diseases included pancolitis (36%), left sided colitis (33%), proctitis (16%) and ileocaecal region (07%). In our study common histopathological findings were chronic lymphoplasmacytic infiltrate (97%), acute inflammatory cells in lamina propria (76%), cryptitis (48%), crypt abscess with crypt destruction (36%), ulceration (15%), and transmural inflammation (02%).

Conclusion: A wide range of inflammatory conditions affect the GIT. Among IBD ulcerative colitis is more common in this part of India. The clinical presentation and colonoscopy can suspect the cases as IBD but endoscopic biopsies are the gold standard for the diagnosis of IBD and to distinguish the various form of colitis from IBD.

Keywords: Colonoscopy, Histopathology, IBD, UC, CD.

Introduction

India is a vast country with a multi-linguistic population of differing race, genetic setup, culture and dietary habits.[1]

A variety of inflammatory and neoplastic disorders affect the lower gastrointestinal tract, with differing clinical outcomes and management. These conditions encompass a spectrum of acute and chronic conditions.[2]

Inflammatory bowel disease (IBD) is a chronic condition resulting from inappropriate mucosal immune activation. The two disorders that comprise IBD are Ulcerative Colitis (UC) and Crohn's Disease (CD). Indeterminate colitis is used for cases of IBD without definitive features of either UC or CD.[3]

Ulcerative colitis and Crohn's disease frequently present in the teens and early 20s, with the former being slightly more common in females. IBD incidence worldwide is on the rise, and it is becoming more common in regions such as Africa, South America, and Asia where its prevalence was historically low.[3]

IBD results from the combined effects of alterations in host interactions with intestinal microbiota, intestinal epithelial dysfunction, aberrant mucosal immune responses and altered composition of the gut microbiome.[3]

Ulcerative colitis involves the rectum and variable length of proximal colon in continuity. According to the extent of disease, ulcerative colitis may be divided into ulcerative proctitis, left side colitis, subtotal colitis and pancolitis. The small intestine is normal, although mild mucosal inflammation of the distal ileum, termed backwash ileitis, may be present in severe cases of pancolitis.[4]

Grossly, ulcerative colitis is characterized by diffuse and continuous chronic inflammation of colonic mucosa with edema, erythema, diffuse mucosal granularity and superficial ulcers. The transition between the involved and normal mucosa is sharp. Inflammatory pseudopolyps, mucosal bridges , mucosal atrophy and toxic megacolon are also seen.[4]

Ulcerative colitis exhibits histological pattern of chronic active colitis which refers to the presence of active inflammation accompanied by features of chronic mucosal injury. Activity is defined as neutrophil mediated epithelial injury including cryptitis, crypt abscesses or infiltration of surface epithelium with mucosal ulceration. Chronicity is defined by crypt architectural distortion including shortening and branching of crypts, basal lymphoplasmacytosis or paneth cell metaplasia in the left colon. The inflammatory process is diffuse and generally limited to the mucosa and superficial submucosa.[4]

Ulcerative colitis is a relapsing disorder characterized by attacks of bloody diarrhoea with stringy mucoid material, lower abdominal pain and cramps that are temporarily relieved by defecation, urgency, incontinence. Generalised clinical manifestations include fever, weight loss, fatigue, loss of appetite and growth retardation. Extraintesinal manifestations include arthropathy, erythema nodosum, pyoderma gangrenosum, uvetis and primary sclerosing cholangitis.[5]

Crohn's disease may affect any part of the gastrointestinal tract from the mouth to anus, but the most common sites involved at presentation are the terminal ileum, ileocaecal valve and caecum. Grossly crohn's disease shows a discontinuous pattern of transmural inflammation, edema and loss of mucosal texture, skip lesions, perianal pathology including skin tags, deep ulcers, fissures, fistulae, abscesses, blind sinus tract and strictures. Fat wrapping has a high predictive value for diagnosis of crohns disease. Cobble stone appearance of mucosa is seen[6].

Focal chronic inflammation, focal crypt irregularity and granulomas (not related to crypt injury) are microscopic features of crohn's disease. In addition an irregular villous architecture, pyloric gland metaplasia, focal cryptitis,

aphthoid ulcers, disproportionate submucosal inflammation, increased intraepithelial lymphocytes, submucosal fibrosis and hypertrophy of musularis propria are seen. . Noncaseating granulomas a hallmark of Crohn's disease, are found in approximately 35% of cases.[6]

The clinical manifestations of Crohn's disease are diarrhoea, fever, and abdominal pain. Later on iron-deficiency anemia may develop in individuals with colonic disease, while extensive small bowel disease may result in serum protein loss and hypoalbuminemia, generalized nutrient malabsorption, or malabsorption of vitamin B12 and bile salts. Fibrosing strictures, fistulae, perforations and peritoneal abscesses are common. Extraintestinal manifestations of Crohn's disease include uveitis, migratory polyarthritis, sacroiliitis, ankylosing spondylitis, erythema nodosum, and clubbing of the fingertips.[5]

The other conditions which mimic IBD are infectious colitis, diversion colitis, microscopic colitis including collagenous colitis and lymphocytic colitis, graft versus host disease, sigmoid diverticular disease.[3]

Colo-rectal cancer (CRC) has been recognized as a leading cause of long-term mortality in patients with IBD and causes 8% of all deaths in patients with UC.[4]

Colonoscopic examination is important in the diagnosis and treatment of suspected colonic disease. It is a diagnostic procedure of choice for patients with diarrhoea lasting several weeks to months or for any bloody diarrhea.[7] Endoscopic features suggestive of UC include diffuse and continuous inflammation proximal to the anal canal, granularity, loss of the normal vascular pattern friability, superficial ulcerations, and a line of demarcation, which is described as an abrupt transition between normal and abnormal mucosa at the proximal extent of the colitis. The most useful endoscopic features consistent with CD are skip lesions (segmental colitis), rectal sparing, involvement of the terminal ileum, identification of the internal opening of a fistula tract, and anal or perianal disease. Other endoscopic features suggestive of CD include aphthous ulcers, deep ulcers, serpiginous ulcers, and cobblestoning.[8] Endoscopists do not always appreciate that a macroscopically normal colonic mucosa may be pathologically inflamed; thus, without biopsy, significant inflammatory bowel disease may go unrecognized or be mistaken for a functional disorder.[9]

Fibreoptic colonoscopy is gaining an increasingly important role in the evaluation of the patients with colonic diseases as direct visualization and biopsy of entire length of the colon is now possible. Utilizing colonoscopy and biopsy it is possible to identify the location and type of colonic disease. The histological identification of colonic lesion help in appropriate specific treatment.[10]

Material And Methods

The present prospective study was conducted in department of pathology in collaboration with department of Gastroenterology, Pt. B.D. Sharma, PGIMS, Rohtak. Hundred cases of consecutive colonic mucosal biopsies from clinically suspected patients of inflammatory bowel diseases formed the study group. A complete information including age, gender, address and a detailed clinical history was taken from clinically suspected patients of IBD. Informed and written consent for fibreoptic colonoscopy was obtained from the patients. The colonoscopic findings were recorded and representative colonoscopic mucosal biopsies were taken. Biopsies were fixed and processed by routine histological technique for

paraffin embedding and staining with hematoxylin and eosin.[11]

A diagnosis was made on basis of certain histopathological features represented by crypt architectural abnormalities, mucosal-epithelial changes, inflammatory features and any associated dysplasia/carcinoma .[12,13]

Statistical Analysis

The collected data was compiled, tabulated and entered into Microsoft excel, transferred and expressed as percentage of categorical variables, mean for a continuous variable using SPSS 20.0 software.

Results

In our study maximum number of the patients (30%) lied in the age group 31-40 years followed by age group 21-30 years (27%). Male patients constituted 55% of the study group. Minimum and maximum age of male patients was 11 years and 74 year respectively. Female patients constituted 45% of the study group. Minimum and maximum age of female patient was 17 year and 65 year respectively. Our study shows male preponderance with M:F ratio of 1.2:1. The main clinical manifestations were pain abdomen, bleeding per rectum, diarrhea, blood in stools which were present alone or in combination. Most common presenting feature was diarrohea alone or in combination with other features (45%) followed by pain abdomen alone or in combination with other features (36%) and bleeding per rectum alone or with other features (27%). The common endoscopic findings observed in our study were distal colitis, erosion/ulceration and loss of vascular pattern with erythema and granularity. Most common endoscopic finding was ulceration alone or in combination with other features (40%) followed by distal colitis (32%) and loss of vascular pattern along with erythema and granularity (28%). In our study endoscopic biopsies were taken from multiple sites in colon (36% cases), rectosigmoid (19% cases), rectum (16% cases), sigmoid colon (14% cases) and ileocaecal (07% cases). Anatomical location of diseases included pancolitis (36%), left sided colitis (33%), proctitis (16%) and ileocaecal region (07%).

In our study, out of 100 cases, 90 cases were of IBD and 10 cases were of non IBD. Among IBD cases, Ulcerative colitis –active disease (49%) and ulcerative colitis – inactive disease (49%) together constituted 98% whereas Crohn's disease was present in 02% of cases. In our study common histopathological findings were chronic lymphoplasmacytic infiltrate (97%), acute inflammatory cells in lamina propria (76%), cryptitis (48%), crypt abscess with crypt destruction (36%), ulceration (15%), and transmural inflammation (02%). To accurately monitor intestinal inflammation, a combination of clinical findings, endoscopy and histology are needed for patients with UC.

Table 1: Case Distribution According To Clinical Features (N=100)

Sex		Age Group	No.of Cases	Clinical Manifestations	No.of Cases
Male	Female				
55	45	11-20	12	Pain Abdomen	21
		21-30	27	Diarrhoea	11
		31-40	30	Bleeding Per Rectum	20

		41-50	17	Blood In Stools	11
		51-60	09	Pain Abdomen+Blood In Stools	03
		61-70	04	Pain Abdomen+Diarrhoea	11
		71-80	01	Diarrhoea+Bleeding Per Rectum	06
				Diarrhoea+ Blood In Stools	16
				Pain Abdomen+ Diarrhoea+Bleeding Per Rectum	01

Table 2: Spectrum of All Cases (N=100)

IBD		**Non-IBD**	
Disease	No.of Cases	Disease	No.of Cases
Ulcerative Colitis –Active Disease	44	Eosinophilic Colitis	01
Ulcerative Colitis-Inactive Disease	44	Lymphocytic Colitis	01
Crohns Disease	02	Infective Colitis	01
		Drug Induced Colitis	01
		Granulomatous Inflammation	05
		NHL	01
Total	90	Total	10
Total	**100**		

Table 3: Case Distribution According To Endoscopic Findings (N=100)

Endoscopy Findings	**No. Of Cases**	**Percentage**
Distal Colitis	32	32%
Diffuse Colitis	05	05%
Erythema	02	02%
Ulceration	26	26%
Loss Of Vascular Pattern	05	05%
Diffuse Colitis +Uclceration	03	03%
Ulceration+ Erythema	01	01%
Ulceration+Loss Of Vascular Pattern	05	05%
Loss Of Vascular Pattern+Erythema	07	07%
Loss Of Vascular Patern+Granularity	01	01%
Loss Of Vasular Pattern+Erythema+Granularity	08	08%

Loss Of Vascular Pattern+Erythema+Ulceration	04	04%
Ulceration+Erythema+Granularity	01	01%

TABLE 4:Case Distribution According To Site of Colonoscopic Biopsies (N= 100)

Site Of Biopsy	No. Of Cases	Percentage
Ileum	01	01%
Ileocaecal	07	07%
Caecum	05	05%
Ascending Colon	02	02%
Sigmoid Colon	14	14%
Rectum	16	16%
Rectosigmoid	19	19%
Colon Multiple Site	36	36%

TABLE 05: Histopathological Features In Cases Of IBD (n=90)

Histopathological Features	No. Of Cases	Percentage
Lympho Plasmacytic Infiltration	88	97%
N+E In Lamina Propria	67	75%
Cryptitis	44	49%
Crypt Abscess +Crypt Destruction	35	39%
Erosion/Ulceration	15	17%
Granuloma+Transmural Inflammation	02	02%

Discussion

Inflammatory bowel disease (IBD) encompasses a group of diseases, triggered and perpetuated by a variety of diverse genetic, environmental, and immunologic factors that share similar clinical manifestations and which primarily affect the small intestine and colon.[14] The two most common entities of IBD are ulcerative colitis (UC) and Crohn's disease (CD). They are frequently diagnosed in patients in their 20's or 30's, however, there is a second peak later in life and ulcerative colitis is slightly more common in females. IBD incidence worldwide is on the rise and it is becoming more common in regions such as Africa, South America and Asia. In India there appears to be a north south divide with more ulcerative colitis in north and Crohn's in south India.[15]

IBD results from the combined effects of alterations in the host interactions with intestinal microbiota, intestinal epithelial dysfunction, aberrant mucosal immune response and altered composition of gut microbiome.[4] The major symptom of UC are diarrhea, rectal bleeding, tenesemus, passage of mucus and abdominal pain. CD usually presents with ileocolitis or jejunocolitis. The diagnosis of IBD is usually established through a global assessment of the clinical presentation, radiographic, endoscopic and histopathological findings.[16]

Age range of 11 years to 74 years were observed along with mean age being 35.91 years. The mean age was variable in various other studies. Our data was similar to **Khatib et al** (mean age 39.10 years).[14] Mean age was higher in study by **Rangaswamy et al** (47.48 years) and **Rajbhandari** et al (47.5 years). Difference in mean age of our and others study group may be due to variation in selection of the study group.[14,17,18]

Our study shows male preponderance with M:F ratio of 1.2:1. Our findings are concordant with studies by **Rangaswamy et al**, **Pandey et al** , **Raj bhandari et al** , **Sulegaon et al** and **Karve et al** whereas **Khatib et al** noted equal preponderance amongst males and females.[17,19,18,20,2,14]

The main clinical manifestations were pain abdomen, bleeding per rectum, diarrohea, blood in stools which were present alone or in combination. Our study is in concordance with studies by **Hezagy et al** where abdominal pain (50%) and diarrhea (50%) were most common symptoms.[21] **Obaseki et al** also observed abdominal pain (41%) and bloody or non bloody diarrhea (44%) as main complaints while **Agazadeh et al** observed bleeding per rectum (41%), diarrhea (31%) and pain abdomen (46%) presenting as chief complaints.[22,14] **Islam et al, Rajbhandari et al, Pandey et al and Esheba** et al also observed diarrhea, blood in stools, bleeding per rectum and abdominal pain to be the most common presenting clinical features.[16,18,19,23] **Karve et al, Rangaswamy et al and Dhakhawa et** also observed constipation to be the presenting feature in a few cases.[2,17,24]

Most of the studies as described above observed similar manifestations, however clinical features varied in frequency in various studies due to variation in selection of study group.

The common endoscopic findings observed in our study were distal colitis, erosion/ulceration and loss of vascular pattern with erythema and granularity. Most common endoscopic finding was ulceration alone or in combination with other features (40%) followed by distal colitis (32%) and loss of vascular pattern along with erythema and granularity (28%).

Our study is in concordance with the studies by **Hegazy et** al, **Islam et** al, **Esheba et al and Goyal et al** who also observed similar endoscopic findings in patients of IBD.[21,16,23,25]

In our study endoscopic biopsies were taken from multiple sites in colon (36% cases), rectosigmoid (19% cases), rectum (16% cases), sigmoid colon (14% cases) and ileocaecal (07% cases). Anatomical location of diseases included pancolitis (36%), left sided colitis (33%), proctitis (16%) and ileocaecal region (07%). Different population based studies in different part of world also observed similar anatomical locations of disease in cases of IBD.

Goyal et al also observed left sided colitis (39%) and pancolitis (30%) being more common in suspected patients of IBD and right sided colitis (24%) in non IBD patients.[25]

Islam et al observed localization of diseases as pancolitis (44%), left sided colitis (37%) and proctosigmoidits (18%) in suspected cases of UC whereas in suspected cases of Crohn's disease ileal (54%) and ileocolonic (27%) involvement found predominatly as in studies by **Obaseki et al, Hegazy et al, Agazadeh et al** and **Dhawaka et al.**[16,22,21,14,24]

In our study, out of 100 cases, 90 cases were of IBD and 10 cases were of non IBD. Among IBD cases Ulcerative colitis –active disease (49%) and ulcerative colitis –

inactive disease (49%) together constituted 98% whereas Crohn's disease was present in 02% of cases.

Obaseki et al found that, out of 78 suspected cases, 32 cases (41%) were of IBD and remaining 46 cases (59%) were of various non IBD lesions. Among 32 cases of IBD 14 (43%) were cases of CD, while 12 (38%) were cases of UC.[22] **Hegazi et al** conducted a study of 100 suspected cases of IBD. The study revealed 95 cases as IBD and remaining 5 cases were of non IBD. Out of 95 cases of IBD 55 (57%) diagnosed as CD and remaining 45 cases as UC (43%).[21] **Agazadeh et al** conducted a 10 year long study and observed that out of 457 cases, 401 (88%) were of UC and 47 (10%) as CD patients.[14] **Goyal et al** found out of 151 cases, 105 (69%) were of non IBD and 46 (31%) were of IBD. Among IBD, UC was diagnosed in 81% of cases and CD in 19% of cases.[25] **Qayyum et al** studied 477 colonic biopsies and out of these 318 (67%) cases were of IBD and remaining 159 (33%) cases were of non IBD. Among 318 IBD cases, 303 (96%) diagnosed as UC and 15 cases (04%) labeled as CD.[26]

Our study findings are in concordance with **Hegazi et al, Agazadeh et al, Qayyum et al** and show discordance with **Obaseki et al** due to different geographical location and **Goyal et al** due to variation in selection of study group.[21,14,26,22,25]

In our study common histopathological findings were chronic lymphoplasmacytic infiltrate (97%), acute inflammatory cells in lamina propria (76%), cryptitis (48%), crypt abscess with crypt destruction (36%), ulceration (15%), and transmural inflammation (02%). Similar histopathological findings were observed in study by **Islam et al** which showed presence of lymphoplasmacytic infiltration (100%), glandular disarray (92%), cryptitis (88%), crypt abscess (81%) mucosal inflammation (54%) and ulceration (54%).[16] A comparable study by **Hegazi et al** observed crypt abnormalities (100%), erosions (50%), cryptitis and crypt abscess (20% each) and granulomas (10%) on histopathological examination.[21] **Seldenik et al** also observed lymphoplasmacytic infiltrate (92%), acute inflammatory cell in lamina propria (75%), cryptitis (75%), crypt abscess (30%) on histopahology which are in concordance to present study.[27]

Conclusion

To conclude a wide range of inflammatory conditions affect the GIT. Among IBD ulcerative colitis is more common in this part of India. The clinical presentation and colonoscopy can suspect the cases as IBD but endoscopic biopsies are the gold standard for the diagnosis of IBD and to distinguish the various form of colitis from IBD.

Moreover, gastroenterologist and pathologist should work as a team, communicate freely and clearly for accurate diagnosis of disease.

Further studies dealing with biological behavior of IBD disease should be encouraged for better understanding of disease and disease progression to make necessary change in diagnosis, treatment and follow up strategies.

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Legends Figures

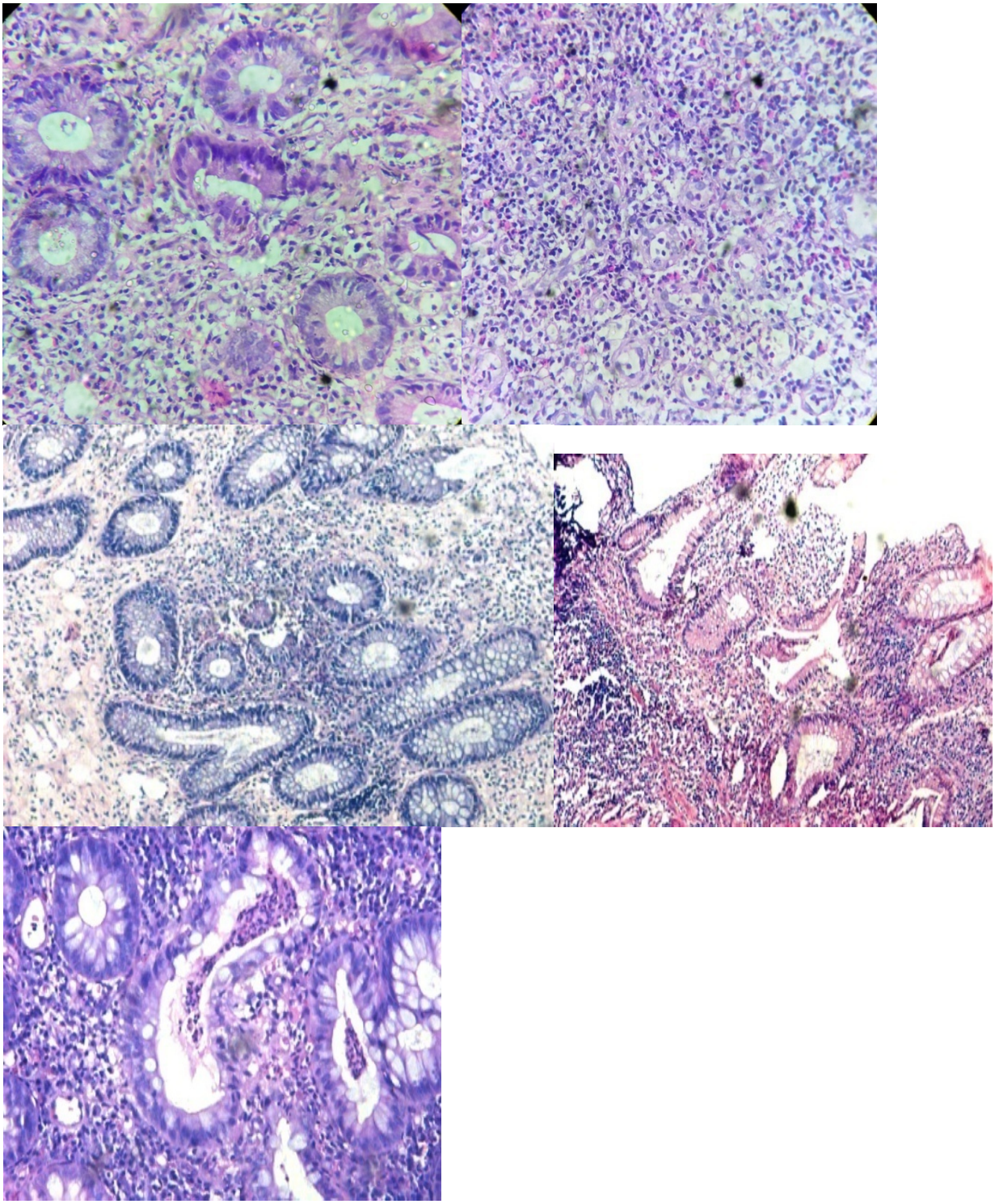

Fig 1: Photomicrograph showing cardinal histological features of UC including crypt architecture distortion, crypt destruction, cryptitis, crypt abscess (H&E, 100X, 200X)

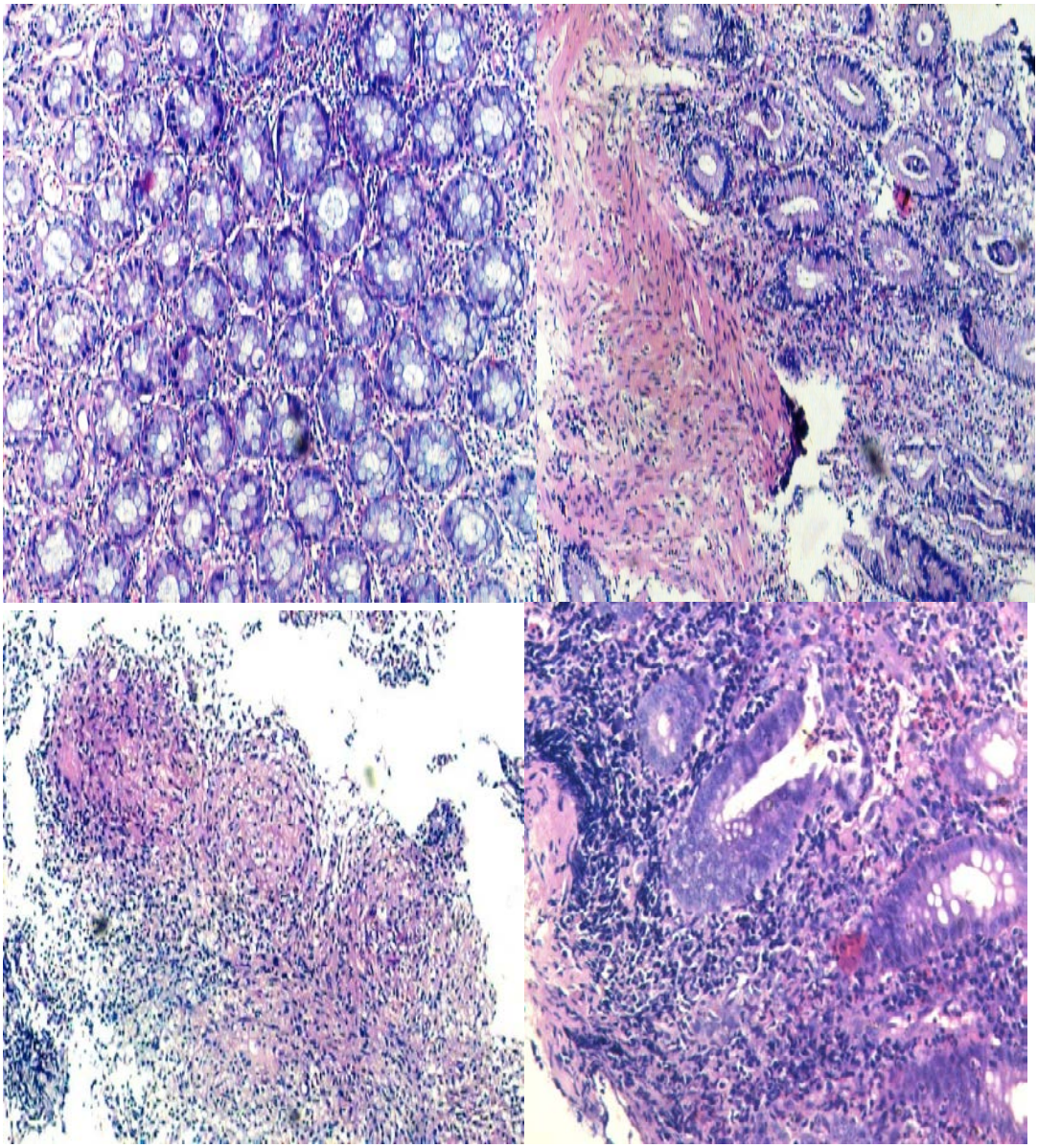

Fig 2: Photomicrograph showing cardinal histological features of Crohn's disease including crypt architecture distortion, transmural inflammation, crypt destruction, cryptitis and non caseating granuloma with giant cells (H&E, 100X, 200X)