Review Article

Histopathology of Endoscopic Biopsies of Gastrointestinal Tract Lesions with Clinical Correlation

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Abstract

Introduction: Because of limited anatomical space and certain unusual clinicopathological features, gastrointestinal tract lesions causes problem in their diagnosis, prognosis, and management. The primary objective of the study is to know the utility of endoscopic biopsy in diagnosing gastrointestinal lesions, and the secondary objective is to correlate the histopathological findings with the clinical symptoms and endoscopic appearance of the lesions. **Materials and Methods:** The present study is a simple retrospective observational study. Upper and lower gastrointestinal lesions in the form of ulcer, polyp, and growth were biopsied by biopsy forceps using flexible fiberoptic endoscopes. Only adequate biopsies were included in the study. The exact site of the biopsy with clinical data was provided by the endoscopist. Routine histopathological examination was done on the specimens submitted in 10% formalin. The use of special stains was done wherever needed. **Results:** A total of 100 cases were categorized as nonneoplastic and neoplastic. Friedman and Osborn classification was used for nonneoplastic lesions. The maximum number of cases was seen in 5th–6th decade with male predominance with equal distribution of cases as far as anatomical site is concerned. **Conclusion:** Targeted biopsies are possible with definitive diagnosis in 90% of cases with safe use of endoscopy. 17% of cases diagnosed on endoscopy were confirmed on histopathology. In 73% of cases, histopathology was essential for further subtyping. Histopathology was mandatory in 8% of the cases. Recommended combined use of endoscopy and histopathology can offer a definitive diagnosis in 98% of cases.

Keywords: Endoscopic biopsy, gastrointestinal tract lesions, histopathology

Introduction

Endoscopy, meaning "peering within" has evolved much in the past thirty years. In 1957, fiberoptic endoscopes were introduced by Basil Hirschowitz and Lawrence Curtiss. Endoscopy is an extremely safe and minimally invasive procedure with minor risks with definitive diagnosis in 90% of the cases. Using a flexible fiberoptic gastroscope and colonoscope, great improvements in the accuracy of diagnosis of gastrointestinal tract lesions are achieved. Direct look and directed biopsy help in diagnosing all pathological lesions of the upper and lower gastrointestinal tract.[1-3] However, the lesions should be biopsied only when there is a potential change in the future approach of the patient, and in few cases, the cost-benefit of biopsies solely depends on the decision-making of the gastroenterologist.[4]

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Materials and Methods

The present study comprises endoscopic mucosal biopsies procured from 100 cases from tertiary care institute and super specialty hospital that was carried out in the pathology department. Patients with upper and lower gastrointestinal symptoms who underwent endoscopy and were having gastrointestinal lesions in the form of ulcer, polyp, and growth were biopsied. Only adequate biopsies were studied. The use of fiberoptic endoscopes was done. Mucosal biopsies were obtained by FUJINON MODEL No.-"EG-250 WR5" in upper gastrointestinal tract lesions and for lower gastrointestinal tract lesions biopsies were obtained by FUJINON MODEL NO. "EC-250 WRIS." The biopsies were taken through biopsy forceps. Detailed endoscopic appearance of the lesion was

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provided by the endoscopist along with the exact site of the biopsy with complete clinical data and informed consent. The present study was approved by the institutional ethics committee.

Handling of mucosal biopsies

A wet filter paper was used for keeping the biopsies with mucosal surface on the upper side to prevent the curling of the biopsy. Ten percent formalin was used as a fixative. The tissue was processed for paraffin embedding. The specimens were oriented at the time of embedding for obtaining vertical sections. Approximately 4–5 serial sections of 5 microns were prepared from each block. Routine hematoxylin and eosin (H and E) staining and special stains such as PAS, Masson's Trichome, and Giemsa were done as and when required.

Results

This is a retrospective study of 100 adequate gastrointestinal mucosal biopsies procured using fiberoptic endoscopes from 100 cases. In the present study, males outnumbered females. Maximum cases were seen in 41–60 years of age range and one in 2nd to 3rd decade. The minimum age in the present study was 8 years, and the oldest was 85 years. We almost have an equal distribution of cases as far as anatomical site is concerned. In the present study, intestinal lesions were 41% followed by those from esophagus and stomach. Age incidence in gastrointestinal tract epithelial malignancies is from 4th to 5th decade. Males were more than double the number of females suffering from epithelial malignancies. Out of 24 endoscopic biopsies, 62.5% of cases were having squamous cell carcinoma. 43.4% of the cases were of gastric carcinoma followed by 26% of chronic gastritis. All the cases from small intestine were of celiac disease. The majority of the cases from the large intestine were of ulcerative colitis (51.20%). Cases of carcinoma were more than rest of the lesions [Table 1].

Discussion

In this retrospective study of 100 adequate gastrointestinal mucosal biopsies, we studied 49 and 51 biopsies of upper and lower gastrointestinal tract lesions, respectively. Twenty-four cases from esophagus, 22 cases from the stomach, and 3 cases from small intestine were noted in the upper gastrointestinal tract. In the lower gastrointestinal tract lesions, 41 cases were from large intestine and 10 cases from rectum [Table 2]. Hirachand *et al*. stated that a histopathological study of endoscopic biopsy specimens confirmed the diagnosis of suspected malignancy or benign condition that allows an early therapeutic decision without unnecessary delay.[5] Siddiqui *et al*. mentioned that advancing age increases the risk of gastrointestinal malignancies; hence for early detection of these lesions, increased use of endoscopic biopsies could be helpful.[6]

Esophageal candidiasis

We had 3 cases of esophageal candidiasis in the age range from 29 to 36 years. Two were female and one was male. All of them were immunocompromised patients (HIV patients). Laine and Bonacini, Wilcox and Karowe found that the most common causative organism for esophageal infection in HIV patients was candida.[7-9] These patients presented with symptoms of odynophagia and dysphagia. According to Mathieson and Dutta, odynophagia and dysphagia are salient clinical features of candida esophagitis.[10] Hiese *et al*. emphasize that endoscopies are necessary for early histological diagnosis of gastrointestinal pathogens in symptomatic AIDS patients.[11] All 3 cases showed discrete whitish plaques on endoscopy, as observed by Brown *et al*. in esophageal candidiasis[12] [Figure 1]. On histopathology, oval spores with budding and pseudo hyphae were seen in the mucosa [Figure 2]. Goldman *et al*. also noticed oval spores with small buds and prominent elongation leading to the appearance of nonseptate pseudohyphae.[12]

Reflux esophagitis

We had a single case of reflux esophagitis, a 45 years male who presented with symptoms of heartburn and dysphagia. According to Crawford, reflux esophagitis is accompanied by regurgitation, heartburn, pain, and dysphagia and is largely limited to adults older than 40 years of age.[13,14] We had a narrowing in the lower end of esophagus on endoscopy. Marks and Richter observed that the chronic effects of reflux esophagitis are fibrosis leading to stricture formation.[15] According to Goldman *et al*., histopathological features of basal cell hyperplasia, elongation of papillae, and intraepithelial eosinophils are the prototype features of reflux esophagitis.[12] Brown *et al*., Janisch *et al*., and Tummala gave significance to intraepithelial eosinophils for histological diagnosis of reflux esophagitis.[12,16,17] Mohan *et al*. suggested that a biopsy recommendation is done only when a mucosal irregularity is visible in cases of gastroesophageal reflux disease. No mucosal change, but only the presence of inflammatory signs does not warrant a biopsy.[18]

Barrett's esophagus

Barrett's esophagus is noted in 3 cases in the age range of 40–55 years. Out of which two were male and one female.

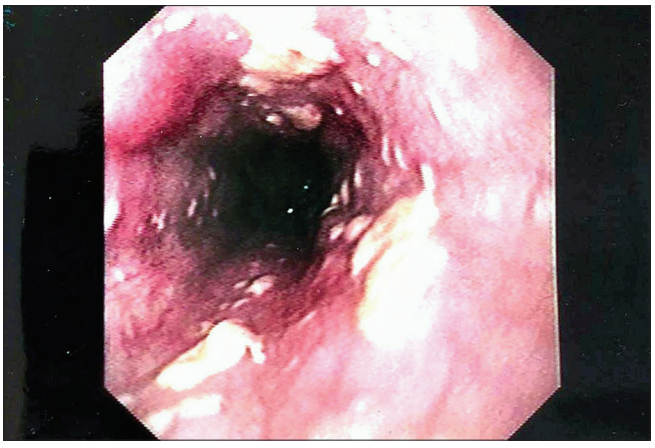

Figure 1: Endoscopic view of esophageal candidiasis

Table 1: Correlation of endoscopic findings with histopathological diagnosis of gastrointestinal lesions

Histopathological diagnosis	Number of cases	Endoscopic appearance
Candida esophagitis	3	Cream coloured discrete plaques in esophagus
Reflux esophagus	1	Narrowing in lower end of esophagus
Barrett's esophagus	3	Ulcer seen in lower esophagus other 2 cases showed velvety mucosa in lower esophagus
GIST (esophagus)	2	Smooth surface polypoidal swelling in upper esophagus
Squamous cell carcinoma	15	46% of the cases had exophytic growth 33% of cases had ulcerative growth 20% of the cases had ulcero-infiltrative growth 73% of cases in mid esophagus. 20% of cases in lower esophagus 7% of cases in upper esophagus
Chronic peptic ulcer	1	Ulcer in body of stomach with regular margins
Chronic gastritis	6	50% of the cases had diffuse gastritis 33% of cases had antral gastritis 17% of cases had superficial ulceration in antrum
Granulomatous gastritis	2	Large prepyloric ulcer with ragged margins and necrotic base
Gastric polyp	1	Small polyp seen in antrum
Pseudo lymphoma	1	Antral nodularity
Gastric lymphoma	1	Prepyloric ulcer with nodular borders
Gastric carcinoma	10	80% of cases had ulcerative growth 10% of cases had ulceroinfiltrative growth 10% of the cases had polypoidal growth 40% of the cases seen in body of the stomach 30 of the cases seen in body and antrum 30% cases seen in antrum
Celiac disease	3	Loss of mucosal folds of duodenum and jejunum
Ulcerative colitis	21	Most of the cases had feature of pancolitis. Rest were having ulcers in sigmoid colon and recturm
Crohn's disease	6	Most cases had ulcers in caecum and ascending colon
Nonspecific colitis	1	Congested mucosa
Indeterminate colitis	3	33% had features of pancolitis. 33% ulcer in descending colon 33% had stenotic stricture in sigmoid colon
Large intestinal polyp	3	50% of the polyp located in sigmoid colon and other 50% in ascending colon
Carcinomas	5	40% of the cases had exophytic growth. 40% had ulcerated growth. 20% had ulcero-infiltrative growth 80% of the case located in sigmoid colon
Lymphoma	2	Ulcer seen in ascending colon and another case had features of pancolitis
Rectal polyp	2	Small polyp
Solitary rectal ulcer	1	Rectal ulcer
Rectal carcinoma	5	40% had ulcerated growth. 40% had exophytic growth 20% have ulcero infiltrative growth
No specific diagnosis	2	One case had small rectal ulcer with smooth margins, while remaining one case had congested mucosa
Total	100	

GIST: Gastrointestinal stromal tumor

Table 2: Organ wise distribution of mucosal biopsies

Biopsy site	Number of cases (%)
Esophagus	24 (24)
Stomach	22 (22)
Small intestine	3 (3)
Large intestine	41 (41)
Rectum	10 (10)
Total	100 (100)

All of them had long-standing gastroesophageal reflux disease. According to Crawford, up to 11% of cases with symptomatic reflux disease causes Barrett's esophagus, which is a complication of long-standing gastroesophageal reflux.[13,14]

Two cases on endoscopy showed red velvety mucosa and other cases showed ulcer in the lower end of esophagus. Crawford also mentioned that mucosa appeared red velvety in between the smooth pale esophageal squamous mucosa on endoscopy in Barrett's esophagus.[13,14] On histopathology, columnar epithelium replaced squamous epithelium where goblet cells were not seen. According to Goldman *et al*. and Morson, Barrett's esophagus has three histological patterns. They are (a) Columnar epithelium with intestinal goblet cells, (b) cardiac or junctional type of epithelium, and (c) atrophic fundic type of epithelium.[12,19] Lagergren *et al*. stated that the main complications of Barrett's esophagus are peptic ulcer, stricture, and development of dysplasia and adenocarcinoma.[20] According to Crawford mentioned 30–40-fold increased rate of

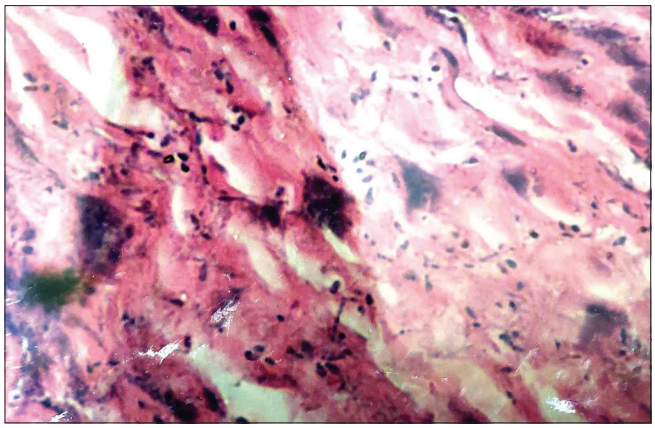

Figure 2: Microphotograph showing oval spores with small buds and pseudohyphae in case of esophageal candidiasis. (H and E, ×40)

adenocarcinoma over general population.[13,14] Hence, it is very important to diagnose and treat Barrett's esophagus earlier.

Gastrointestinal stromal tumor

We have 2 cases of gastrointestinal stromal tumor (GIST) occurring in 62-year-old male and 43-year-old female. Both cases were found in the esophagus. According to Miettinen *et al*., GISTs are rare mesenchymal tumors majority of which originating from stomach and small intestine. Majority of the GIST are found in adults mainly in middle age, with peak in the fifth to seventh decade.[21,22] According to Sundaram the incidence of GIST was 50%–60% in the stomach, 33% in small intestine, 5%–15% in recto-colon and 1%–5% in esophagus.[23] In the present study, we encountered two esophageal GIST. Both patients presented with dysphagia. Ludwig and Traverso stated that symptoms such as abdominal pain, hematemesis, weight loss, and obstruction were common in such cases.[24] On endoscopy, both patients have smooth surface polypoidal swelling projecting into the lumen. The mucosa was intact. As the lesions were polypoidal, endoscopic sampling was an easier task. Jhala noted that GISTs were detected as submucosal, often polypoidal lesions with mucosa appearing normal to ulcerated.[25] On histopathology, the stratified squamous epithelium was seen with an ill-defined mass made up of cells arranged in a fascicular pattern. Individual cells had ill-defined eosinophilic cytoplasm with spindly and wavy nuclei. No atypical mitosis or necrosis was seen. Nirag Jhala stated that GISTs showed many histological patterns of growth such as solid sheets of cells, cells with fascicular or storiform pattern, nuclear palisading reminiscent of nerve sheath tumors, or organoid or alveolar pattern reminiscent of neuroendocrine tumors. The cells were spindled to epithelioid. Often benign GIST shows whorled extracellular collagen fibers designed as skenoid fibers. Aggressive tumors show infiltrating pattern, increased mitosis, hemorrhage, and necrosis.[25]

Squamous cell carcinoma of the esophagus

Fifteen cases of squamous cell carcinoma are studied in the esophagus in the age range of 50-80 years. Out of which 14 cases were above 50 years of age. Out of 15 cases, 12 cases were males and 3 cases were females. According to Schottenfeld and Mannell and Murray *et al*., the occurrence of squamous cell carcinoma of the esophagus was more in males aged more than 50 years of age.[26,27] Most of the patients had complaints of dysphagia and weight loss. Impaired nutrition and the effects of the tumor resulted in dysphagia, huge weight loss, and debility. On endoscopy, 73% of cases were found in mid esophagus, 20% of cases in lower esophagus and 7% of cases were in upper esophagus. Exophytic growth was seen in 46% of cases followed by ulcerative growth in 33% and ulceroinfiltrative in 20%. According to Crawford, squamous cell carcinoma was located in 50%, 30%, and 20% of cases in middle third, lower third, and upper third of esophagus, respectively. Approximately 60% of the cases had polypoid exophytic growth, 15% of the cases had diffuse infiltrative growth, and remaining 25% of cases had ulcerated growth.[13,14] In a study by Ahamed *et al*., middle-third of esophagus was the most common site, followed by lower third and upper third. On histology, the most frequently reported grade was moderately differentiated squamous cell carcinoma.[28] All esophageal biopsies on histopathology showed features of either well to moderate to poorly differentiated squamous cells carcinoma.

Chronic gastritis

We had 6 cases of chronic gastritis in the age range from 18 to 60 years. Out of 6 cases, 4 were females and 2 were males. These patients presented with pain and burning sensation in the upper abdomen. According to Crawford, chronic gastritis frequently presented with symptoms such as discomfort in upper abdomen, nausea, and vomiting.[13,14] On endoscopy, most of the cases had diffuse gastritis, one case had congested mucosa in the antral region suggestive of antral gastritis, and other showed superficial ulcerations in antrum. According to Rosai, chronic superficial gastritis on endoscopy showed diffuse gastric mucosal erythema with tiny red dots of reddened mucosa, while chronic atrophic gastritis showed thin, smooth mucosa with undue prominence of submucosal vessels.[29] On histopathology, features of chronic superficial gastritis were seen in 2 cases with chronic inflammatory cells in supraglandular layer of the mucosa. According to Morson, there was a greater number of plasma cells, lymphocytes and variable numbers of polymorphs seen in the lamina propria in between the foveolae and the surface epithelium, but not extending into the glandular layer.[19] Three cases showed features of chronic atrophic gastritis where a deep mucosal layer infiltrated by cells of chronic inflammation resulting in destruction and glandular atrophy. According to Stemmermann, in chronic atrophic gastritis, inflammation involved the deeper layer of the mucosa resulting in destruction and glandular atrophy. Pyloric and intestinal types of metaplasia can be noted.[30] One case showed features of chronic follicular gastritis in which lymphoid follicles were seen in lamina propria. According to Morson, follicular gastritis was a variant of chronic gastritis in which lamina propria showed lymphoid follicles. These follicles may be seen in the submucosa as well.[19]

Eidt *et al*. and Genta *et al*. found that *Helicobacter pylori* (*H. pylori*) infection was strongly associated with the prevalence of lymphoid follicles.[31-34] We also did Giemsa stain but could not find *H. pylori* in both Giemsa and H and E stain.

Gastric hyperplastic polyp

We had 2 cases of hyperplastic polyp noted in male patients aged 50 years and 62 years. Both of these patients were suffering from acid peptic disease. According to Haruma *et al*. and Abraham *et al*., gastric hyperplastic polyps had a tendency to occur in conditions such as chronic gastritis, gastric atrophy, hypergastrinemia, hypochlorhydria, and low levels of pepsinogen I.[35,36] On endoscopy, both cases showed a small polyp in the Antrum.

Morson stated that gastric hyperplastic polyps had frequently eroded smooth surface or somewhat lobulated, oval or hemispherical in shape, and larger than 1.5 cm in diameter in rare cases. The sessile polyps were common but larger one may be pedunculated. Single or multiple polyps may be occurred anywhere in the stomach, but antrum is the commonest site.[19] On histopathology, variable-sized gland lined by tall columnar epithelium were seen. Many glands showed cystic dilatation, and stroma was loose oedematous and infiltrated by chronic inflammatory cells. According to Morson and Rosai, their surface was composed of elongated crypts in which intraluminal infolding and frequent branching seen with cystic dilatation present in the deeper parts. The lining epithelium showed a single layer of hypertrophied superficial (foveolar) type epithelium having ample amount of neutral mucin. The edematous lamina propria infiltrated by plasma cells and lymphocytes were variably noted. Sometimes, lymphoid collection with germinal centers might be conspicuous.[19,29]

Granulomatous gastritis

We had only 1 case of granulomatous gastritis, which is a rare entity. A 30-year-old man had complaints of pain in upper abdomen, vomiting, weight loss, and fever. The patient was a known case of pulmonary tuberculosis. Enlarged cervical nodes were noted on general examination, which showed features of tuberculous lymphadenitis by Fine needle aspiration cytology (FNAC). Acid-Fast Bacillus (AFB) stain showed acid-fast bacilli. On endoscopy, a large prepyloric ulcer with ragged margins and necrotic base was seen. On histopathology, gastric mucosa was showing ulceration and noncaseating histiocytic and epithelioid granulomas with Langhan's type giant cells. We suspected a diagnosis of Gastric tuberculosis, so polymerase chain reaction (PCR) of the gastric lavage was done, which confirmed mycobacterium tuberculosis. Hence, the diagnosis of granulomatous gastritis due to tuberculosis was made. According to Morson, gastric tuberculosis was rare and was usually but not always associated with pulmonary tuberculosis.[19] On endoscopy, the lesions were noted in the lesser curvature of the antrum and prepylorus, having the same clinical picture as that of peptic ulcer. Morson also stated that granulomas were necrotizing and confluent, but early forms could not be distinguished from lesions in Crohn's disease or sarcoid. AFB Stain was often negative, and diagnosis might depend on culture or the presence of tuberculosis in other organs.[19]

Chronic peptic ulcer

A single patient with chronic peptic ulcer having symptoms such as epigastric pain, nausea, and vomiting was studied. According to Crawford, remitting and relapsing lesions are seen in peptic ulcers that were frequently diagnosed in middle age and thereafter, but they may be seen first in young adults also.[14] Crawford and Goldman and Hayek mentioned burning or aching pain in epigastrium in peptic ulcers. Nausea, vomiting, bloating, and belching can occur. Few patients can develop anemia, frank hemorrhage, or perforation.[14,37] On endoscopy, an approximately 2 cm size ulcer with smooth margins and sloping edges was seen in the antrum. According to Crawford and Rosai, peptic ulcers had a diameter up to 2 cm in more than 50% cases; however, 10% of cases of benign ulcers had diameter more than 4 cm. Ulcers with a diameter <4 cm may be malignant; hence, a benign ulcer from a malignant one cannot be differentiated.[14,29] On histopathology, all 4 zones were seen which according to Morson are: (a) The base and margins show a superficial thin layer of fibrinoid necrosis. (b) The zone of non-specific inflammatory infiltrate mostly neutrophils is present below superficial layer (c) An active granulation tissue infiltrated by mononuclear cells present in the deeper layers. (d) A zone of extra solid fibrous or collagenous scar with granulation tissue.[19]

Benign lymphoid hyperplasia of the stomach (pseudolymphoma of the stomach)

In the present study, there was a 26-year-old woman known case of acid peptic disease with symptoms of epigastric pain and vomiting. According to Faris and Saltzstein and Ranchod *et al*., pseudolymphoma was a reactive condition, thought to arise in most cases as an exaggerated inflammatory reaction to peptic ulcer, and was problematic to discriminate grossly, microscopically and radiographically from lymphoma.[38,39] On endoscopic examination, there was antral nodularity, and the rest of the stomach appeared normal. According to Morson, pseudolymphoma presented as an ulcer with overhanging margins, but nodularity and an infiltrative appearance of surrounding tissue may be present.[19] On histopathology, the mucosa was mildly atrophic. Lamina propria showed dense infiltration of lymphocytes with the presence of lymphoid follicles. No lymphoepithelial lesion or disruption of glands was seen. Submucosa showed fibrosis. Morson and Saraga *et al*. stated that lymphocytes were the predominant cells, other cell types including eosinophils, polymorphs, and plasma cell may be encountered. Prominent reactive follicle centers are seen amidst the lymphoid infiltrate, and the latter is frequently dissected and separated by bands of fibrous tissue.[19,40,41] Although the most marked changes are limited to the mucosa and submucosa, it is not uncommon for transmural and serosal involvement to occur. In the latter case, muscle fibers are separated and not destroyed by the

infiltrate. Ulceration of overlying mucosa is common, and there may be evidence of previous peptic ulceration in the form of dense scar tissue replacing muscle. The lesions are not clearly demarcated and tend to fade gradually into adjacent fibromuscular tissue. Chronic follicular gastritis is frequently present in adjacent mucosa.

Gastric lymphoma

We have only 1 case of Gastric lymphoma. A 32-year-old male complained of pain in upper abdomen and vomiting. According to Rosai, the clinical symptoms of gastric lymphoma often simulated those of gastritis or peptic ulcer.[29] On endoscopy, an approximately 2.5 cm-sized ulcer with nodular borders was seen in the prepyloric region. According to Rosai, low grade lymphomas were seen as an ulcerated mass, usually in the half of the stomach distally. Rare involvement of pylorus is seen.[29] Yokoi *et al*. stated that progressive cases can mimic hypertrophic gastritis or gastric polyps and can be seen as massive obstructions.[42] High-grade lymphomas usually appear as a large lobulated mass in the half of the stomach distally sparing the pylorus. Superficial or deep ulceration is common. Distinction from carcinoma may be very difficult on endoscopy.[29] On histopathology, mucosa shows ulceration. There was diffuse and intense infiltration by atypical lymphocytes; however, classical lymphoepithelial lesions were not seen. The infiltrate was seen in lamina propria extending up to submucosa. According to Rosai, low-grade lymphomas can exhibit focal or extensive plasmacytoid differentiation. Dutcher bodies (true intranuclear eosinophilic inclusions made up of immunoglobulin) can be encountered in these lymphomas, and they are of great diagnostic significance.[29] Zamboni *et al*. mentioned an important diagnostic sign is the presence of neoplastic lymphocytes in the glandular epithelium, resulting in so-called ”lymphoepithelial lesion.” Few cases have signet ring configuration because of intracellular accumulation of immunoglobulin, thus simulating a signet sing carcinoma.[43]

Gastric carcinoma

We had nine cases of stomach cancer, 6 of which were male and 3 of which were female, with ages ranging from 23 to 50 years. According to Islam SM, Dupant *et al.*, Grabiec and Theuer *et al*., maximum patients were above 50 years of age, but some cases recorded in younger population and in children also.[44-47] In classification by Lauren, gastric carcinoma of intestinal type shows the mean age of 55 years with male predominance, while in diffuse type, the mean age is 48 years with male and females are equally affected.[13] Most of the patients had symptoms such as vomiting, weight loss, and abdominal pain. Crawford stated that the symptoms such as pain in the abdomen, weight loss, vomiting, loss of appetite, and changes in bowel habits were noted in gastric carcinoma, as observed in our cases also.[14] In the present study, on endoscopy, 80% of cases had ulcerative growth, 10% of cases had ulceroinfiltrative growth and remaining 10% of cases had polypoidal growth. According to Morson, three types of growth are seen: (a) exophytic, tumor growth protruding into the lumen, (b) in an ulcerative type, the surrounding tissue is firm, seems swollen, uneven, and infiltrated, and the margin is irregular with elevated edges. The base of the ulcer is lumpy, shaggy, and necrotic. As opposed to benign ulcers, the mucosal folds radiating from the ulcer crater typically exhibit club-like thickening and fusing. c) Infiltrative cancer-The rugal folds may flatten, and the mucosa may seem opaque as it spreads superficially in the mucosa and submucosa, producing plaque-like lesions.[19] On histopathology, 4 cases showed features of well to moderately differentiated intestinal type adenocarcinoma while the remaining 5 cases showed features of diffuse type of carcinoma. Three cases were poorly differentiated adenocarcinoma and 2 cases were signet ring adenocarcinoma. The intestinal variant of gastric carcinoma, according to Morson and Crawford, was made up of neoplastic intestinal glands similar to those found in adenocarcinoma of colon that permeate the gastric wall but typically grow along broad cohesive fronts as an “expanding” pattern of growth. Ample mucin may be found in the gland lumina, and apical mucin vacuoles are frequently found in malignant cells. In most cases, the diffuse variant does not produce glands; instead, it penetrates the mucosa and wall as scattered single cells or tiny clusters of cells with an infiltrative growth pattern. In this variant, mucin production causes the malignant cells to enlarge and push their nuclei toward periphery, resulting in “signet ring” appearance. On the other hand, excessive mucin formation can result in enormous mucinous lakes that cut across tissue planes, making it difficult to find individual tumor cells or glands there.[14,19]

Celiac disease

We had 3 cases of celiac disease in the age range from 14 to 27 years, 2 of them were females, and 1 was male. Goldman *et al*. stated that although celiac disease is more common in young children and newborns, it can also affect adults and the elderly.[37] All 3 patients had complaints of diarrhea, weight loss, and fatigue suffering from malabsorption syndrome. According to Crawford, diarrhea, flatulence, weight loss, and lethargy were the traditional symptoms of celiac disease.[14] On endoscopy, the mucosal folds of Duodenum and Jejunum were lost. McIntyre *et al*. also states that in celiac disease, the mucosal folds appear to be reduced or absent.[48] On histopathology, the villi were showing partial to complete atrophy. There were more intraepithelial lymphocytes to be seen. Lymphocytes and plasma cells with hyperplastic crypts were also visible in the lamina propria [Figure 3]. Rosai also stated that the villi either significantly reduce or completely disappear in celiac disease. Vacuolar degeneration, loss of the microvillus brush borders, and a rise in intraepithelial lymphocytes are all visible in the surface epithelium. The overall mucosal thickness is unchanged, and the crypts have enhanced mitotic activity and are elongated, hyperplastic, and tortuous. The number of plasma cells, lymphocytes, macrophages, eosinophils, and mast cells in the lamina propria has increased overall. Given that the duodenum and proximal jejunum are exposed to the highest concentration of dietary gluten, all these structural changes are often more pronounced

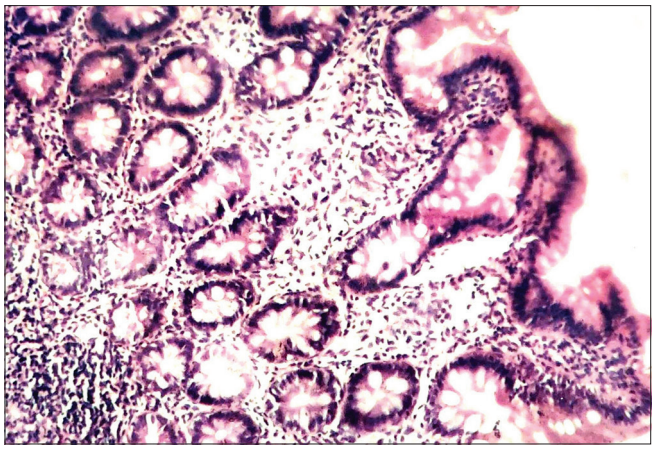

Figure 3: Microphotograph showing blunting of villi and increased mononuclear infiltrate in lamina propria in case of celiac disease. (H and E, ×10)

in the proximal small intestine than in the distal.[29] The villous/crypt ratio, which is 2.5 or greater in the normal mucosa, has been proposed by Drut and Rua as a way to grade the severity of the changes. These were the grades' definitions: 2–2.5 in Grade 1, 1–2 in Grade 2, 1–0.5 in Grade 3, and <0.4 in Grade 4.[49] Accordingly, we graded the mucosal atrophy depending on the villous-to-crypt ratio. In the present study, the grades varied between 2 and 3.

Ulcerative colitis

Out of 100 cases studied, we have 21 cases of ulcerative colitis in the age range from 29 to 62 years, of which 16 cases were found in male and remaining 5 cases in female. According to Garland *et al*., Mayberry and Gryboski, both sexes have ulcerative colitis on an equally frequent basis. Although it can happen at any age, including children, it arises most frequently in patients between the ages of 20 and 30, with a second surge occurring between the ages of 70 and 80.[50-52] All the patients complained of bloody diarrhea on and off. Crawford stated that attacks of bloody mucoid diarrhea, which may last for days, weeks, or months before going away and returning after an asymptomatic period of months, years, or even decades, characterize ulcerative colitis, a recurrent condition.[14] On endoscopy, most of the cases showed features of pancolitis, while the remaining cases showed multiple ulcers in the sigmoid colon and rectum. Lennard-Jones *et al*. and Kelly *et al*. stated that the endoscopic appearance varies with the stage of the disease. In the acute type, petechial hemorrhages are frequently observed, and the mucosal surface of the gut is wet and shining from blood and mucus. Ulcers of varying sizes and shapes start to form. Some of these ulcers cause the mucosa to weaken, leading to the development of mucosal bridges with an underlying inflammatory infiltrate. Pseudopolyps, elevated sessile reddish nodules, are frequently observed on otherwise flat surfaces. They are frequently small and numerous. They do not often grow to enormous sizes, which increases the clinical and radiological suspicion of cancer. In the quiescent stage, the ulceration is absent, the mucosa is atrophic, and there may be extensive submucosal fat deposition. The mucosa may seem normal in some of these situations. The entire gut becomes fibrotic, shorter, and narrowed in the latter stages.[53,54] On histopathology, 10 cases showed features of active phase, 8 cases showed features of resolving phase, and the remaining 3 cases showed features of remission phase on the biopsy provided by endoscopist. These 3 phases were classified following the Morson's criteria of different phases of ulcerative colitis. Salient features of various phases of ulcerative colitis according to Morson were as follows: (I) Active phase: (a) a mucosal surface with irregular contour and luminal pus, (b) epithelium loss coupled with ulceration, (c) the lamina propria shows increased chronic inflammatory cell content, (d) focal neutrophil infiltration accompanied by edema and crypt abscesses, (e) vascular congestion, (f) goblet cell mucin depletion; (II) Resolving Phase: (a) vascular congestion is reduced, (b) the gradual eradication of cryptic and polymorphic abscesses, (c) the population of goblet cells is restored, (d) reactive epithelial hyperplasia and epithelial continuity restoration, (e) a declining plasma cell and lymphocyte population; and (III) Remission phase: (a) loss of parallelism, uneven spacing, and crypt branching, (b) mucosal atrophy, which is the separation of short tubules of various lengths, (c) muscularis mucosae thickening, (d) metaplasia of paneth cells, (e) hyperplasia of endocrine cells, (f) lamina propria fat deposition.[19]

Crohn's disease

We had 6 Crohn's disease cases, 4 of which were female and the other 2 were male, with ages ranging from 28 to 62. Rubin *et al*., Mayberry and Rhodes, Fabricus *et al*., and Michelassi *et al*. stated that both sexes are equally affected by Crohn's disease. Although the disease can first appear at any age, including childhood and old age, the majority of patients were in their twenties and thirties.[55-58] In a series of 297 Crohn's disease cases evaluated by Morson, 66% of the cases were limited to the small bowel, 17% were restricted to the large bowel, and 17% involved both segments. All 6 cases we studied were from the large intestine, which was an exclusive finding.[19] All the patients had complaints of bloody diarrhea. According to Crawford, in the beginning, Crohn's disease typically manifests as brief episodes of relatively mild diarrhea, fever, and stomach pain, separated by asymptomatic intervals of a few weeks to several months. Although major bleeding is unusual, occult or overt stool blood loss may cause anemia in people with colonic involvement.[14] On endoscopy, ulcers were found in caecum and ascending colon, with normal mucosa seen in between the ulcers. According to Crawford, Morson, and Rosai, in the early stages, the mucosa is reddish-purple, and it may show pinpoint erosions known as aphthoid ulcers. Mucosal ulcers often develop into lengthy, discontinuous, linear ulcers that are positioned along the axis of the colon as the disease progresses. These ulcers are arranged in parallel and connected by short transverse ulcerations giving a cobblestone appearance.[14,19,29] On histopathology, the lamina propria of the mucosa exhibits a well-preserved goblet cell population, lymphocytes, and plasma cells.

Lymphoid hyperplasia was noted in mucosa and submucosa. In one case, Langhan's type giant cells and epithelioid cells made up noncaseating granulomas [Figure 4]. Rotterdam *et al*. stated that granulomas, preservation of the goblet cell population, and the architecture of the glands are the primary characteristics to look for in an endoscopic biopsy.[59] Otto and Gebbers, Dvorak, and Monahan stated that one of the earliest changes is submucosal lymphedema. This is accompanied by a scattering of chronic inflammatory cells, such as mast cells, eosinophils, histiocytes, lymphocytes, and plasma cells, as well as lymphoid hyperplasia in the lamina propria and submucosa.[60,61] Similar changes were noted in 5 cases in the present study. Dourmashkin *et al*. stated that the ulcerations are often seen at the very top of the lymphoid follicles and are preceded by epithelial patchy necrosis.[62] Matson *et al*. and Shephard stated that in 60% of cases, granulomas are seen, which are sarcoid-like and are often seen to arise from within the centers of the lymphoid follicles. They are mostly made up of multinucleated giant cells and epithelioid cells, with necrosis typically being absent or localized to the center of the small area. They can be found at any location of involvement, including the serosa in the intestinal wall, the local lymph nodes, and other places.[63,64] In the present study, only 1 case showed well-formed granulomas.

Indeterminate colitis

In the age range of 25–55 years, we had 3 cases of indeterminate colitis, 2 of which were in men and 1 of which was in women. A diagnosis of indeterminate colitis was recommended because overlapping characteristics of ulcerative colitis and Crohn's disease were observed in some instances on both endoscopy and histology. Lee *et al*. and Odze stated that approximately 15% of patients have characteristics of both Crohn's disease and ulcerative colitis, making a differential diagnosis difficult. Under these circumstances, the name "indeterminate colitis" has been proposed.[65,66] Wells *et al*. stated that very few of these patients finally show features of Crohn's disease throughout long-term follow-up.[67]

Juvenile (retention) polyp

We had 1 case of juvenile polyp, which was found in a 26-year-old male who presented with bleeding per rectum. Morson and Crawford stated that juvenile polyps are focal hamartomatous abnormalities of the mucosal parts most frequently seen in the rectum. They occur most frequently as random lesions in children under the age of five. Adults may have isolated hamartomatous polyps in their colons; these incidental lesions are known as retention polyps. They could manifest as several familial lesions in conjunction with different congenital abnormalities. Both men and women are equally affected. The most common symptom is bleeding; however, some patients may require an arm amputation or prolapse.[14,19] On endoscopy, a small polyp was seen in the sigmoid colon. Morson stated that Juvenile polyps are smooth and spherical with a redhead and a narrow stalk.[19] On histopathology a polypoidal structure lined on all three sides by intestinal epithelium with inflamed and edematous stroma harboring cystically dilated glands. No atypia was noted [Figure 5]. Morson and Rosai stated that the polyp surface is frequently ulcerated and surrounded by granulation tissue. Mucus-filled glands that are cystically dilated, without atypia, and separated by an inflammatory and edematous stroma are present underneath. In 20% of cases, hyperplastic mucosal alterations are evident.[19,29]

Benign lymphoid polyps/benign lymphoid polyposis

We had only 1 case of benign lymphoid polyp/benign lymphoid polyposis found in an 8-year-old male child who complained of bleeding per rectum. Morson stated that in contrast to benign lymphoid polyps, which are more frequent in males than in females and appear in the third or fourth decade of life, benign lymphoid polyposis is a rare condition that typically affects children and causes an overgrowth of the lymphoid follicles normally found in the colon and rectum.[19] On endoscopy, a small, smooth-surfaced polyp was seen in the rectum. Morson stated that the mucosa swells with numerous 0.3–0.6 cm-diameter grey sessile nodules in

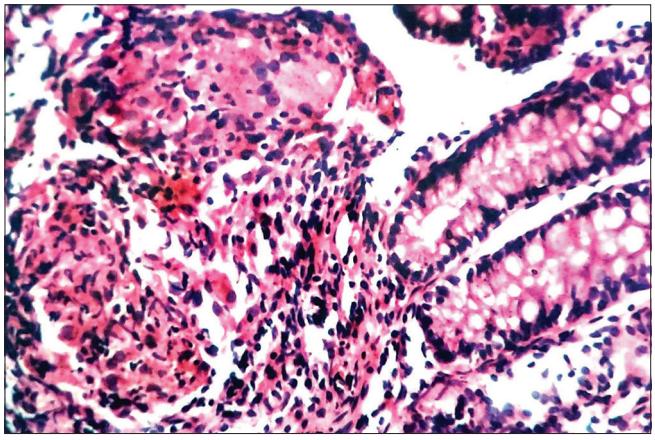

Figure 4: Microphotograph showing granuloma in lamina propria comprising epithelioid cells, Langhan's giant cells and lymphocytes in case of Crohn's disease. (H and E, ×40)

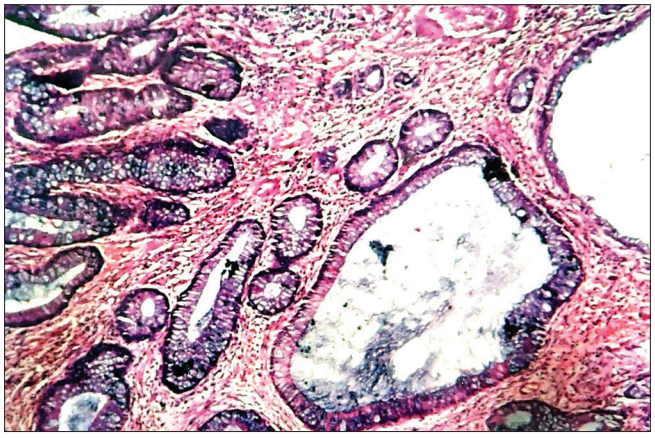

Figure 5: Microphotograph showing cystic dilated glands with mononuclear infiltrate in lamina propria in case of Juvenile polyp. (H and E, ×10)

benign lymphoid polyposis.[19] Smooth, rounded, submucous tumors called benign lymphoid polyps can be found in the lower portion of the rectum. Sessile polyps predominate, while pedunculated polyps can also occur. Although they might be as many as four or five, they are often single. They range in size from a few millimeters to 3 cm in diameter. Ulceration is very rare. On histopathology, the mucosa appeared normal. In the lamina propria, dense lymphoid aggregates consisting of mature lymphocytes were seen. Submucosa was not seen. On histopathology, the normal lymphoid tissue that makes up benign lymphoid polyposis comprising lymphoid follicles with germinal centers. They are mostly covered by attenuated mucosa and are located in the submucosa. It is unusual for the deep muscle layer of the gut wall to be affected. Their small size, follicular pattern, lack of mucosal ulceration, and non-involvement of muscle coat usually allow them to be easily differentiated from malignant lymphomas.[19]

Adenomatous polyps

We had 3 cases of adenomatous polyps in the age range from 32 to 52 years, of which 2 cases were males and one was a female. According to Crawford, the neoplasms known as adenomatous polyps range in size from small, frequently pedunculated lesions to large, mostly sessile neoplasms.[14] Before the age of 40 years, there are 20%–30% more colonic adenomas than beyond the age of 60, when there are 40%–50% more cases. Both men and women were equally affected. All 3 cases had complaints of bleeding per rectum. Sobin stated that most polyps are asymptomatic, but they may result in bleeding from twisting or vascular obstruction.[68] Adenomatous polyps are divided into three kinds based on the structure of the epithelium. (a) Tubular adenomas–Tubular glands, (b) Villous adenomas–Villous Projections, (c) Tubulovillous adenomas-A mixture of tubular glands and villous projections.[14] The endoscopic appearance, histopathology, and malignant potential of these three subtypes are different.The first case was of tubular adenoma which on endoscopy was seen as a small sessile 0.5 cm size polyp in ascending colon. Morson stated that tubular adenomas resemble miniature cauliflowers with an irregular surface that is darker than the surrounding mucosa. Their diameter ranges from <0.1 cm to several centimeters, but the majority are just around 1 cm. Small adenomas, like the one in our case, are sessile, whereas lesions with a diameter of more than 1 cm are typically pedunculated.[19] On histopathology, columnar cells were found lining the closely packed tubular glands, and the nuclei were enlarged and hyperchromatic with a moderate amount of cytoplasm. Eosinophilic goblet cells were also seen. Lamina propria appeared normal. These features were suggested of mild dysplasia. Similar histopathological findings were noted by Morson.[19] The second case was also of tubular adenoma however with carcinoma *in situ* which on endoscopy was seen as multiple sessile polyps of size varying from 0.5 to 1 cm in sigmoid colon. Tubular glands were closely packed and lined by tall columnar cells with little cytoplasm on histopathology. The number of goblet cells decreased. In one area, there were glands with hyperchromatic nuclei and a high N:C ratio. Increased number of mitotic figures were noted. However, there was no stromal invasion. These changes were suggestive of carcinoma *in situ* (severe dysplasia). Some adjacent tubules were showing moderate dysplasia. Similar histopathological findings were noted by Morson stating that in severe dysplasia nuclei assume a more rounded configuration with a prominent nucleolus. There are also notable architectural changes with excessive budding and branching producing in severe dysplasia-a gland within gland pattern.[19] A large area of overt malignant alteration restricted to the mucosa (intramucosal carcinoma) may converge with severe dysplasia (carcinoma *in situ*). Invasive adenocarcinoma is a cancerous invasion into the submucosal stalk of the polyp.[14] According to Gillepsie *et al*., Shinya and Wolff invasive cancer was found in 2% to 3% of Tubular adenomas.[69,70] Third case was villous adenoma with focal carcinoma, which on endoscopy was seen as a pedunculated polyp of 1.5 cm in size in the rectum. According to Morson, villous adenomas were large sessile tumors but may also be pedunculated. The surface is shaggy or velvety, and the neoplastic tissues are soft and fragment easily. Occasionally, villous adenomas may initially be flat, making their endoscopic diagnosis difficult. Multiple villous adenomas are rare, but villous adenomas often co-exist tubular adenoma.[19] On histopathology, a polypoidal structure was seen showing villous-like projection. Individual cells are tall columnar showing moderate to severe dysplasia. At one focus malignant glands were seen infiltrating the stroma. Stalk was not invaded by the tumor cells. Similar histopathological features were noted by Morson.[19] According to Gillepsie *et al*., Shinya and Wolff invasive cancer was found in 10% to 18% of villous adenomas.[69,70]

Primary malignant lymphoma of large intestine

We had 2 cases of lymphoma of the large bowel. One case was found in a 19-year-old female, and another in a 52-year-old male. Both patients complained of bloody diarrhea and loss of weight. On endoscopy, one case showed on ulcer in the ascending colon, while the other case showed features of pancolitis. According to O'Briain *et al.*, Schmid *et al.*, and Kohno *et al*., malignant lymphoma of the large intestine can cause noticeable mucosal folds, obvious ulceration, a huge mass, a single giant polyp, or numerous small polyps distributed throughout the colorectum that may extend to the small intestines.[71-73] On histopathology, in both cases, the mucosa was ulcerated, lamina propria, submucosa, and muscularis showed diffuse infiltration by lymphoplasmacytic cells disrupting the glands and infiltrating into the muscle fibers, accordingly diagnosis of MALTOMA (low-grade lymphoplasmacytic lymphoma) was made. Rosai stated that non-Hodgkin lymphomas are type of malignant lymphoma almost always found in colorectal malignancies. It is believed that MALT-type tumors make up the majority of low-grade tumors. They frequently exhibit plasmacytic differentiation; when this is extensive and associated with abundant immunoglobulin production, the designation of plasmacytoma was sometimes used in the past for them.[29]

Solitary rectal ulcer

A 29-year-old male with diarrhea and blood streaks was the only patient of solitary rectal ulcer. Vora *et al*. stated that solitary rectal ulcer is a very benign illness that affects young individuals of either sex.[74] Ford *et al*. stated that the typical symptoms include altered bowel patterns, discomfort, and the flow of blood and mucus through the rectum.[75] On endoscopy, a small 1 cm size ulcer was seen in the rectum. Ford *et al*. stated that a solitary rectal ulcer is green as a solitary ulcerated or polypoid lesions located in the rectum, usually on the anterior wall, frequently associated with mucosal prolapse.[75] On histopathology, hyperplastic mucosal lining with evidence of ulceration was seen. Lamina propria showed an increase in mononuclear cells and the presence of fibromuscular tissue. As per Franzin *et al*., Stuartand Warren *et al*., mucosal ulceration that was very superficial and irregular, hyperplasia of the crypts, a tendency toward villous formation, fibroblasts obliterating the lamina propria, elastin, and smooth muscle cells from the muscularis mucosae, a decrease in the number of lymphocytes and plasma cells, and thickening of the muscularis mucosae with widening of its fibers were all present. In chronic cases, changes analogs to those of colitis cystica profunda may occur.[76-78]

Carcinoma of the large bowel

In the present study, 10 cases of large-bowel carcinoma which affect people between the ages of 30 and 85 years, 5 of the cases involved females and the other 5 involved males. Males and females are equally affected, according to Berg and Howell, Mills and Allen, and Boyle *et al*. The mean incidence age is 62 years old. The majority of these individuals complained of changed bowel habits and rectal bleeding.[79-81] Rosai states that rectal bleeding, bowel habits changes (such as diarrhea followed by constipation), anemia due to ongoing blood loss, and persistent pain in abdomen are all symptoms of large bowel carcinomas. When a tumor is located in the left colon, intestinal obstruction is more common than when it is located in the caecum or ascending colon.[29] On endoscopy, 1 case was found in the transverse colon, 4 cases were found in the sigmoid colon, and remaining 5 cases were found in rectum. 40% of the carcinomas had exophytic growth, 40% had ulcerative growth and the remaining 20% had ulceroinfiltrative growth. Cady *et al*., Netscher and Larson stated that approximately 50% of all carcinomas are found in the rectosigmoid region, although their relative incidence appears to be declining as recent studies have detected a change in location towards the proximal colon.[82,83] Cooper and Slemmer, Iishi *et al*., and Tada *et al*. stated that most colorectal carcinomas are either polypoid, ulcerative, or infiltrating. The former appears as a large mass with clearly defined rolled margins and a distinct boundary from the regular bowel. The latter is centrally ulcerated and has a less raised surface. The term "flat" or "depressed" carcinoma refers to a specific variation of this tumor type that is thought to develop de novo rather than through the malignant transformation of an adenoma. Compared to the more prevalent polypoid forms, these flat carcinomas show a higher tendency for stromal invasion and lymphovascular penetration.[84-86] On histopathology, one case being reported as signet ring carcinoma, the majority of the carcinomas were well to moderately differentiated adenocarcinoma [Figures 6 and 7]. Morson also stated that about 85% of adenocarcinomas of the colorectum are composed of relatively well-differentiated tubules secreting small quantities of mucin, about 20% have well differentiation, 60% have moderate differentiation, and 20% have poor differentiation.[19]

Conclusion and Recommendations

In 90% of cases, flexible fiberoptic endoscopy, a highly helpful and secure noninvasive procedure can provide a conclusive diagnosis. Targeted, sufficient biopsies from nearly all gastrointestinal tract lesions are attainable with the aid of these tools. In the current study, 17% of the cases had endoscopy-based diagnoses that were later confirmed by histopathology. In 73% of cases, histopathology was essential for further subtyping of the lesions, and histopathology was mandatory in 8% of the cases. Despite endoscopic and histopathological evaluation,

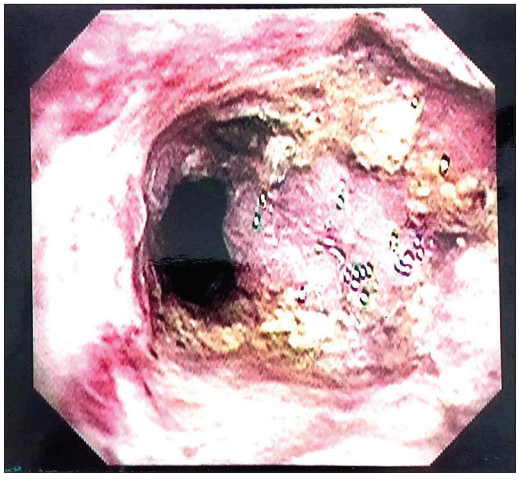

Figure 6: Endoscopic view of ulcerated growth in rectum

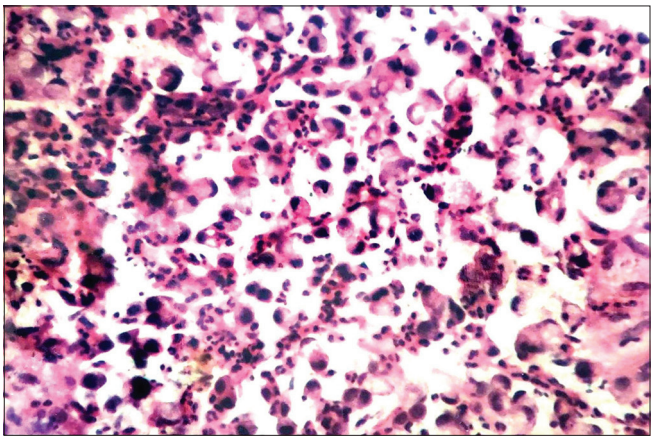

Figure 7: Microphotograph showing sheets of signet ring cells in case of signet ring carcinoma of rectum

no specific diagnosis was offered in 2% of cases. Hence, it is recommended that combined use of endoscopy and histopathology of such biopsies with clinical correlation and endoscopic findings can offer a definitive diagnosis in majority of cases.

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Conflicts of interest

There are no conflicts of interest.

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