

Histomorphology Spectrum of Gastrointestinal Lesions in A Tertiary Care Centre

Sunita Bamanikar^{1*}, Dayanand Sankawade², Arvind Bamanikar³, Charusheela Gore¹, Shirish Chandanwale¹ and Archana Buch¹

¹Professor, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra, India

²Resident Pathologist, Department of Pathology, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra, India

³Professor, Department of Medicine, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra, India

***Corresponding Author:** Sunita Bamanikar, Professor, Dr.D.Y.Patil Medical College, Hospital and Research Centre, Dr.D.Y.Patil Vidyapeeth, Pimpri, Pune, Maharashtra, India.

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Abstract

Introduction: Today gastrointestinal (GI) pathology is accepted as one of the largest sub-specialties in pathology. Histopathological evaluation of GI lesions is the gold standard for providing essential diagnostic and prognostic information to clinicians for the best and timely management of each patient.

Aims and Objectives: To study the pattern of gastrointestinal non-neoplastic and neoplastic lesions and the correlation between age, sex and site distribution of various lesions.

Material and Methods: This is a unicentre retrospective and prospective study of 2941 patients with GI lesions over a period of four years from January 2015 to December 2018. Biopsies and resected specimens of gastrointestinal tract were fixed in 10% Formalin. These specimens were then; processed in automatic tissue processor. Routine Hematoxylin and Eosin stain and special stains, including immunohistochemical stains were done; wherever indicated. The slides were examined and the data generated from observations was used for statistical analysis.

Results: Out of a total 21831 histopathology specimens received in the four years, over 17 % specimens were GIT lesions. Of the 3738 GI specimens, appendix was the most common specimen received (26.9%) followed by gastric specimens (23.2%) and small intestine specimens (18.9%). Non-neoplastic GI lesions (94.5%) were most common followed by neoplastic lesions (5.5%). Males outnumbered female patients having M: F ratio of 1.2:1. The peak incidence for non-neoplastic lesions was found in the age group of 21-40 years and that for neoplastic lesions found in the age group of 50-70 years. Appendicitis was the most common GI pathology (26.8%) followed by gastritis (21.1%). Adenocarcinoma was the most common histological malignancy (65.4%) followed by Squamous cell carcinoma (26.7%). Most common lesion of the esophagus was squamous cell carcinoma whereas adenocarcinoma was common in the colo-rectum.

Conclusion: Apart from an overview of the spectrum of histopathological lesions encountered in the surgical pathology department, this study reiterates that histopathological evaluation is a valuable diagnostic tool for definitive, early diagnosis of GI lesions, which has impact on management of the neoplasia.

Keywords: Adenocarcinoma; Gastrointestinal Lesion; Inflammation; Squamous Carcinoma

Introduction

Gastrointestinal tract (GIT) diseases are one of the most common entities we come across in day to-day practice. Given its sheer length and extent, there is a possibility of various pathologies affecting individual segments of the entire tract. Ranging from congenital anomalies, inflammatory conditions to neoplastic conditions including both, benign as well as malignant lesions, the spectrum of diseases which can occur individually or in combination with various segments is wide [1].

Minimally invasive procedures such as gastroduodenoscopy and colonoscopy are used to obtain biopsies, which are subjected to histological and immunohistochemical examination. This method is the gold standard for diagnosis of GI lesions. Histopathology provides crucial information from the biopsy specimen for definitive diagnosis. However, histopathological study detects mucosal lesions at an early stage especially various metaplasia and dysplasia, which can help to prevent further progression to invasive cancer or to treat it at an early stage, thus; increasing the chances of cure. India is harboring 0.31% of cancerous conditions worldwide, where colorectal carcinomas account for 4th most common cancer affecting 0.03% population of the world while gastric cancers comes 8th in rank affecting 0.01% of the world population [2]. Hence histopathological confirmation is always necessary for planning appropriate treatment regimen followed by immunohistochemistry whenever indicated. With advancement in medical technology, the minimal invasive procedure such as gastroduodenoscopy and colonoscopy, or endoscopic ultrasound guided biopsies play important role in making definitive diagnosis.

Aims and Objectives

To study the spectrum of histopathological lesions of gastrointestinal tract and to correlate with age, sex and other clinico-pathologic parameters.

Material and Methods

This unicentric study over a period of four years was conducted; retrospectively from January 2015 to August 2017 and prospectively; from September 2017- December 2018, in department of pathology, Dr.D.Y.Patil Medical College, Hospital and Research Centre, Pimpri, Pune.

Specimens received in 10 % buffered formalin were fixed for 12 hours; followed by grossing and sections were taken from appropriate lesions. Sections were processed in an automated tissue processor in case of prospective specimens. The paraffin embedded blocks were retrieved from the records of department in case of retrospective samples; multiple sections of approximately 5µm thick were cut with microtome and stained with routine Hematoxylin and Eosin stain (H and E). Further, the lesions were cat-

egorized as inflammatory, premalignant, neoplastic and miscellaneous. Special stains including immunohistochemical stains were applied whenever required. Results were then tabulated and statistically analyzed.

Results

Total 3738 specimens from 2941 patients were included in this study with 2116 (55.6%) surgically excised specimens and 1622 endoscopic biopsies (43.3%). The age wise distribution shows maximum number of cases belong to age group of 21 - 30 years (24.7%), least common was in the age of less than one year (0.7%), and the mean age of the cases in this study was of 32.4 years (Table 1). There was male preponderance in our study with 1615 males (55%) in gastrointestinal lesions. The lesions of gall bladder had female number in excess of males.

Age (in years)	No. of Cases (n)	Percentage
< 1	22	0.7
1-10	46	1.5
11-20	441	14.9
21-30	722	24.7
31-40	571	19.4
41-50	415	14.3
51-60	342	11.6
61-70	260	8.8
>70	122	4.1
Total	2941	100

Table 1: Age Group Distribution of GIT Cases.

Of the 3738 specimens, Appendix was found to be the most common tissue (26.9%). This was followed by gastric (23.2%) and small intestine tissues (18.9%). Gall bladder specimens comprised of 14.5% followed by large intestine with anorectum 9.4% and esophagus specimens 7.1 % (Chart 1).

Chart 1: Pie Diagram Showing Organ-Wise Distribution of GIT Specimens.

On histopathological evaluation, non-neoplastic lesions in various GI sites were the most common (94.5%) finding; followed by neoplastic pathology (5.4%). The premalignant histopathological findings and dysplasia accounted for 0.7%, Appendix was the commonest site for non-neoplastic lesion (26.8 %), followed by gastric lesions (21.8 %) whereas neoplastic lesions were most commonly detected in large intestine and ano-rectal region (2.4%) followed by stomach and esophagus (1.4%) each (Table 2). *H. Pylori*-associated chronic active gastritis (5.9%) was detected by IHC stains using Biogenex Anti-Helicobacter Pylori polyclonal marker for *H. Pylori* (Figure 1).

Site	Neoplastic (%)	Non-neoplastic (%)	Total (%)
Esophagus	51 (1.4%)	217 (5.8%)	7.1
Stomach	53 (1.4%)	810 (21.8%)	23.2
Gall Bladder	7 (0.1%)	538 (14.4%)	14.5
Small intestine	4 (0.1%)	703 (18.8%)	18.9
Appendix	1 (0.1%)	1004 (26.8%)	26.9
Large intestine and ano-rectum	89 (2.4%)	261 (7%)	9.4
Total	205(5.5%)	3533(94.5%)	100

Table 2: Distribution of GIT Lesions According to Site and Type (n= 3738).

Figure 1: Microphotograph of gastric antral biopsy with strong immunoreactivity for H.Pylori in glandular lumina (IHC for H.Pylori, x400)

Of the total 205 neoplastic lesions, malignant lesions were of 93.2% and benign 6.8%. Large intestine and ano- rectum (43.4%) was the most common organ involved in malignant lesions followed by stomach (25.8%) and esophageal carcinoma (24.9%) (Figure 2).

Figure 2: Microphotograph of well differentiated squamous cell carcinoma of esophagus with keratin pearl (H and E, x400).

In the present study, 101(53.6%) males had neoplastic lesions; as compared to 95 (46.4%) females having M: F ratio of 1.1:1. Most common age group having neoplastic histopathology was 51 - 60 years; having 61 cases (29.7%); followed by the age group 41-50 years with 47 cases (23%). The anorectal lesions were most common in age group of 41-70 years.

Adenocarcinoma (65.4%) was the most common pathological finding in 191 cases of malignancy followed by squamous cell carcinoma (26.7%); least common was malignant lymphoma and leiomyosarcoma with 0.5% each (Chart 2). The most common type of histological differentiation seen was moderately differentiated grade in both adenocarcinoma and squamous cell carcinoma (52.4%) with 16.2% being poorly differentiated.

Chart 2: Bar Diagram Depicts Distribution of Malignant Lesions According to Histopathological Type.

Discussion

Gastrointestinal (GI) diseases are highly prevalent in population in India and carry heavy economic and social consequences. Current demographic data shows India is harboring more than 65% population below 35 years [3]. In present study, most commonly affected age group was in thirties (24.7%) which signifies the burden of GIT diseases on economical aspect.

Preponderance of males with M: F ratio of 1.2:1 was noted in our study, the results reported by Patel., *et al.* [7] and Prasaad., *et al.* [10] also suggest similar trend (Table 3).

Authors	Total number of cases	Males	Females	M: F
Aried., <i>et al.</i> [4]	100	66	34	1.94:1
John Berry., <i>et al.</i> [5]	246	148	60	2.47:1
Crabbe., <i>et al.</i> [6]	205	140	65	2.15:1
Patel., <i>et al.</i> [7]	461	234	227	1.03:1
Present study	1005	616	389	1.58:1

Table 3: Comparison of sex distribution of Appendicitis.

Most common form of GI pathology was inflammatory followed by neoplastic lesions [4]. In the present study, of the total 3738 GI specimens, there were 93.5% inflammatory and 5.4% neoplastic lesions on histopathological examination. Amongst the inflammatory lesions, appendicitis was the most common (26.8%) with a high incidence in males as compared to females with a ratio of 1.5:1 which is comparable with previous study done by Aried., *et al.* [4]. Of the 5.4 % neoplastic lesions in our study, 5.1 % were malignant and 0.3 % benign lesions. Ours was a larger study with 3738 specimens in which the incidence of inflammatory and neoplastic lesion is comparable with the results reported by Patel., *et al.* [7] and Thakur., *et al.* [8] (Table 4).

Author	Total no of specimens		
		Inflammatory lesions	Neoplastic lesions
Khatib., <i>et al.</i> [1]	263	198 (75.2%)	65 (24.8%)
Thakur., <i>et al.</i> [8]	800	740 (92.5%)	40 (7.5%)
Patel., <i>et al.</i> [7]	969	953 (98.3%)	16 (1.7%)
Ekta., <i>et al.</i> [9]	159	124 (77.9%)	35 (22.1%)
Present study	3738	3533 (93.5%)	205 (5.4%)

Table 4: Comparison of GIT histopathology lesions with various studies.

Our study also revealed dysplastic lesions (0.5%), miscellaneous (0.4%) and premalignant lesions (0.2%). Hyperplastic polyp was the most common benign lesion found in histopathology from the specimen of the upper GI and large intestine in our study.

Esophagus

According to National Cancer registry, esophageal malignancies are 6th most common cancer in India and 4th leading cause of cancer related mortality in both sexes [12]. In present study, 268 (7.1%) specimens were from esophagus of which 52.2% cases were chronic inflammatory lesions, 8 (2.9%) cases of Barrett’s esophagus and 51 cases (18.2%) were malignant, of which squamous cell carcinoma was most common (Figure 3) followed by one case of malignant GIST.

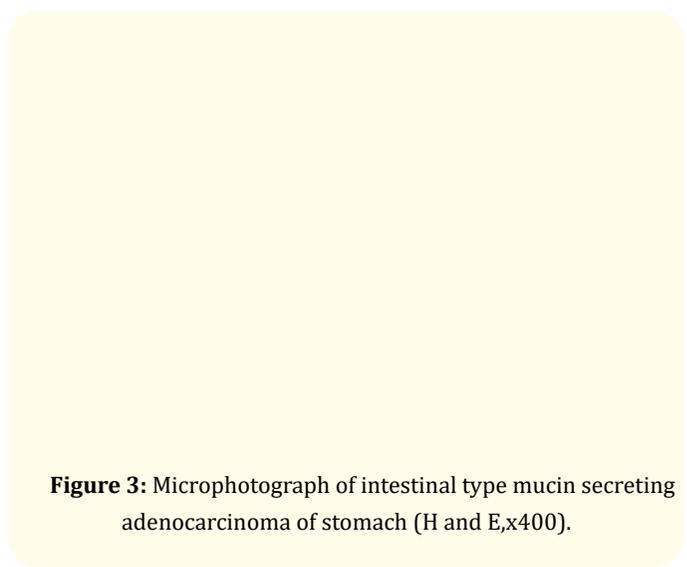


Figure 3: Microphotograph of intestinal type mucin secreting adenocarcinoma of stomach (H and E,x400).

Affected age group in our study varies from 21-70 years, however most commonly affected age group for oesophageal malignancy was above 50 years which is similar to studies reported by Khatib., *et al.* [1] and Das., *et al.* [13].

Stomach

Of total GI specimens evaluated, 863 (23.2 %) specimens were from gastric lesions, where affected age group varied from 31 - 70 years and most commonly affected age group was 41-60 years with a mean age of 44.5 years. There was male predominance with an M: F ratio of 1.3:1. In present study, gastritis (90.9%) was the commonest gastric lesion followed by neoplastic lesion (5.9 %). Among inflammatory lesions, *H. pylori* induced gastritis was seen in 5.9 % of cases. Among neoplastic lesions gastric adenocarcinoma accounted

for 44 (5%) of the cases, in literature tubular adenocarcinoma is most common. In our study diffuse variant outnumbered (56.8 %) followed by tubular adenocarcinoma (Figure 3), (43.2 %) which concurs with the study done by Qui., *et al.* [14] with incidence of 49.2 % and 43.7 % respectively. The affected age group of 50 - 60 years with an M: F ratio of 1.3:1 was observed in malignant lesion, similar results have been reported in studies done by Kamal., *et al* [11]. Adenocarcinoma was the most common malignancy seen in stomach followed by Gastric lymphoma which accounted for 3% - 5% of all malignant tumors of the stomach, [15] however; there was no case of gastric lymphoma in our study.

In present study, GIST (gastrointestinal stromal tumor) ranked 3rd in the neoplastic lesions (4.7%), where most common organ affected was stomach with 4 cases which were CD117 positive (Figure 4). This incidence was slightly higher than reports in literature where GISTs account for approximately 2% of all malignant gastric tumors with the incidence of 11 cases per 1 million [16].

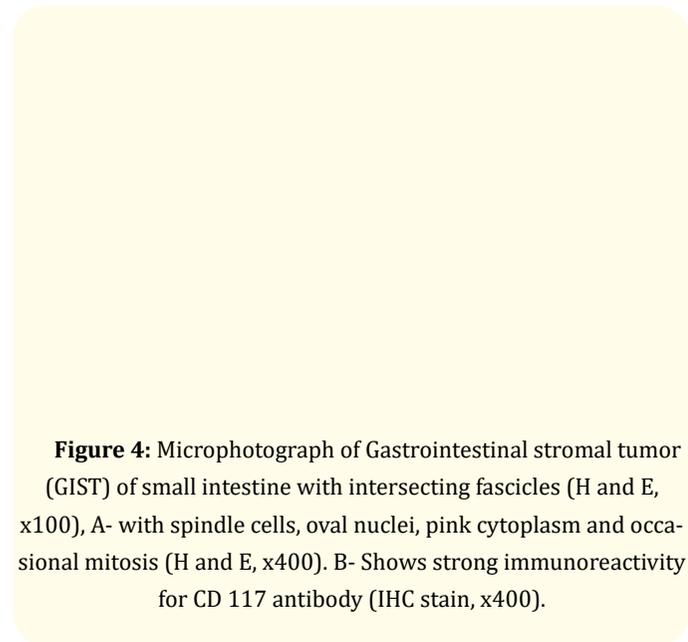


Figure 4: Microphotograph of Gastrointestinal stromal tumor (GIST) of small intestine with intersecting fascicles (H and E, x100), A- with spindle cells, oval nuclei, pink cytoplasm and occasional mitosis (H and E, x400). B- Shows strong immunoreactivity for CD 117 antibody (IHC stain, x400).

Small intestine

There were 707 (18.9%) specimens from small intestine. In present study, chronic inflammation was most common lesion seen in 654 specimens (27.5%). There were very few neoplastic lesions (0.6%).

Neoplasms of small intestine are rare accounting 1 - 2% of all GI neoplasms in spite of larger surface area. Adenocarcinoma of the small intestine is rare. The most common site is the periampullary portion of the duodenum; jejunum and ileum [17]. In present study, 4 cases of neoplastic lesions of which 3 were periampullary

adenocarcinoma and one case of malignant GIST (0.1%). Present study shows lowest incidence of small intestine malignancy and the common affected age group was 41 - 60 years which is comparable to studies reported by Sabharwal., *et al.* [18] and Prabhakar., *et al* [19].

Gall bladder

There were 545 (14.5%) specimens from gall bladder with most common pathology being chronic cholecystitis (51.7%) followed by associated cholelithiasis (44.5%) and 1.2% were neoplastic lesions. Our study observed a female preponderance with reversal of M: F ratio (0.6:1). These findings are in concordance with studies reported by Prasad., *et al.* [10] (Table 5).

Author	Total number of specimens	M:F ratio
Thakur., <i>et al.</i> [8]	800	1.7:1
Patel., <i>et al.</i> [7]	969	1.12:1
Kamal., <i>et al.</i> [11]	344	1.3:1
Prasad., <i>et al.</i> [10]	194	1.2:1
Ekta., <i>et al.</i> [9]	159	1.12:1
Present study	2941	1.2:1

Table 5: Comparison of sex distribution of GIT specimens with various studies.

Incidence of xanthogranulomatous cholecystitis is 9% in India; we encountered one case (0.5%) of xanthogranulomatous cholecystitis in the present study. Adenocarcinoma is the most commonly seen malignant lesion in gall bladder, in our study there were 6 cases (1.1%) of adenocarcinoma with female predominance. One case of adenosquamous carcinoma is also seen, it is a rare histological subtype accounting for 1 - 5% of gall bladder carcinomas [20]. The incidence of gall bladder carcinoma in our study correlates well with studies done by Shreshtha., *et al.* [21] and Sharma., *et al.* [22] (Table 6).

Author	Carcinoma	No of cholecystectomy specimens	Incidence
Sharma., <i>et al.</i> [22]	17	863	1.97%
Dipti., <i>et al.</i> [23]	18	4115	0.44%
Mittal., <i>et al.</i> [24]	13	1305	0.9%
Shreshtha., <i>et al.</i> [21]	9	570	1.4%
Present study	7	538	1.3%

Table 6: Comparison of incidence of gall bladder carcinoma with various studies.

Appendix

Appendix was the most commonly affected organ in present study with 1005 cases (26.9%), male preponderance with M: F ratio of 1.6:1; this trend is supported by Aried., *et al.* [4] in literature (Table 3). Acute appendicitis (50.2%) was the most common finding followed by chronic appendicitis (19.3%). Complicated cases such as appendicitis with peritonitis (3.3%), mucocele (0.2%) and obstructive appendicitis (0.5%) were also detected, and there was one case (0.1%) of adenocarcinoma. Neoplastic lesions of appendix are rare which can be incidental finding following appendectomy for appendicitis. While most of the tumors are carcinoid, lymphoma and adenoma, incidence of adenocarcinoma of appendix is 0.08% of all cancers and accounting for 0.5% of all gastrointestinal cancers [12].

Colo-rectum

In present study, 350 (9.4%) cases were from colorectal region and the most common pathology was that of chronic inflammatory lesions (66.3%) followed by 25% neoplastic lesions, of which benign polyps (Figure 5) accounted for 2.6% and malignant lesions of 22.4 %. Inflammatory bowel disease was previously called as disease of the West; but its incidence has increased in Indian population, the reason for this trend may be migration and westernization of food habits. Ulcerative colitis is more common than Crohn's disease. In present study, 12 cases (3.5%) of inflammatory bowel disease were seen where ulcerative colitis (2%) (Figure 6) was the most common entity.

Figure 5: Microphotograph of hyperplastic polyp of rectum (H and E, x400).

Figure 6: Microphotograph of Ulcerative colitis of sigmoid biopsy with crypt abscess, eosinophilic and lymphocytic inflammatory infiltrate (H and E, x400).

In our study, most commonly affected site for neoplastic lesion was colo-rectum (43.7%) and 41 - 70 years age group was most commonly affected, which is in accordance with studies reported by Kamal., *et al* [11] and Ekta., *et al* [9]. Colorectal cancer is the fourth most common malignancy, where adenocarcinoma was most commonly seen, squamous cell carcinoma (SCC) of the colon are rare entity with less than 100 cases reported in the literature [25]. In our study, we detected 71 cases (20.2%) of adenocarcinoma, one case (0.3%) of recto-sigmoid squamous cell carcinoma (Figure 7) and one case (0.3%) of rectal malignant melanoma. Lymphoma can involve any part of the gastrointestinal tract with the most common site being stomach followed by small intestine, ileocecal region in order of its occurrence [15]. We encountered one case (0.3%) of primary non-Hodgkin's lymphoma and one case of leiomyosarcoma and 3 cases (0.8%) of malignant GIST in our study. Primary gastrointestinal sarcomas are very rare entity accounting for 1% - 2% of all GIT malignancies with high malignant potential; leiomyosarcoma is the most common histocyte in it [26], mainly seen in the fifth and sixth decades of life.

In the present study, among the neoplastic lesions the M: F ratio was 1.1:1 signifying male preponderance. A study done by Sabharwal., *et al.* [18] and Kamal., *et al.* [11] support this trend, which is specified by their figures. Gastrointestinal (GI) cancers account for about 20% of estimated new cancer cases and 15% of estimated mortality worldwide [1]. Organ-wise distribution of malignancies in our study signifies the most common organ involved were co-

lon, rectum and anal canal (43.7%) with least common being tumors involving the small intestine (2.2%), which is in accordance with other studies in literature carried out by Kamal., *et al* [11]. In esophageal carcinoma incidence is in accordance with study done by Sabharwal., *et al.* [18] and Prabhakar., *et al.* [19] (Table 7). Malignant lesion of the stomach in our study (26.3%) is fairly comparable to the study reported by Kamal., *et al.* [11] (Table 7). Malignant lesions from gall bladder and appendix were 3.4% and 0.5% respectively in our study.

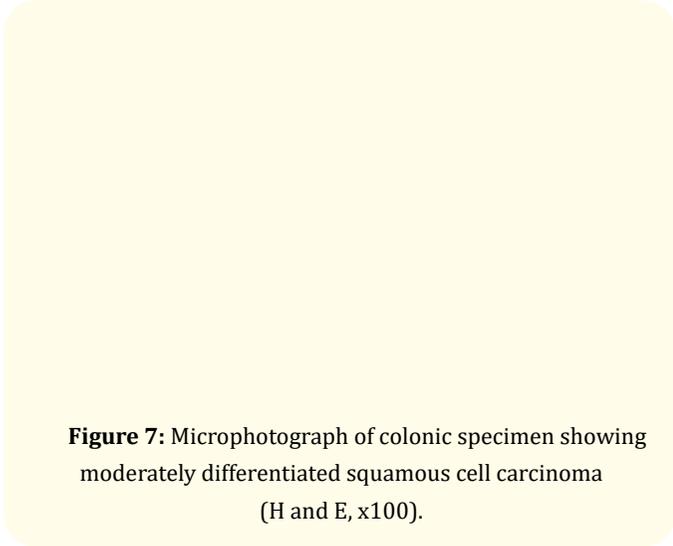


Figure 7: Microphotograph of colonic specimen showing moderately differentiated squamous cell carcinoma (H and E, x100).

Author	Esophagus	Stomach	Small intestine	Colon, Rectum and anal canal
Sabharwal., <i>et al.</i> [18]	25.3%	7%	0.5 %	62.6 %
Prabhakar., <i>et al.</i> [19]	31.4 %	6 %	0.03 %	62.3 %
Kamal., <i>et al.</i> [11]	14.9%	34.2%	6.1%	44.7%
Thakur., <i>et al.</i> [8]	19.23 %	7.6 %	5.7 %	67.3 %
Ekta., <i>et al.</i> [9]	37.14 %	5.7 %	17.14 %	45.71 %
Our study	27.8 %	26.3 %	2.2 %	43.7 %

Table 7: Comparison of organ-wise distribution of GIT malignancies.

Conclusion

Our study summarises the wide variety of GI tract lesions encountered and inflammatory lesions of the GI tract are most common entity on histomorphology. Histopathological evaluations play a crucial role in final diagnosis for appropriate patient management and follow up of cancerous and inflammatory conditions. Thus, GI endoscopic representative biopsy is relatively simple and minimally invasive procedure to obtain the tissue for histopathology and immunohistochemical evaluation. Clinicopathological correlation of these lesions will be of great help in early detection of malignancy, further therapeutic measures, and prognosis.

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