Histopathological Diagnosis Of Gastrointestinal Malignancies - A Retrospective Study

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Abstract Objective: Worldwide gastrointestinal malignancies are a leading cause of both mortality and morbidity with marked epidemiological differences in various geographic and ethnic populations. The objective of current study was to study the prevalence, age and sex distribution and to analyze variations in histopathological lesions of gastrointestinal malignancies. Method: The entire specimens were fixed overnight in 10% formalin, processed using automatic tissue processor and stained with routine Haematoxylin and Eosin stain. Results and conclusion: Total 98 cases of gastrointestinal malignancies were analyzed; out of these, total 61 were male patients while 37 were female patients with overall male to female ratio of 1.65:1. The commonest affected age group was 46-60 years with more than 50% cases of gastrointestinal malignancies in this age group. The youngest patient was 14 years of age while the oldest was 92 years old. Adenocarcinoma was the commonest histopathological diagnosis with 70 cases followed by 15 cases of squamous cell carcinoma. We also found cases of malignant gastrointestinal stromal tumour, non-Hodgkin's lymphoma, carcinoid tumour and malignant melanoma at different anatomical location of gastrointestinal tract. [Purohit M et al NJIRM 2013; 4(2) : 107-112]

Key Words: Adenocarcinoma, Gastrointestinal malignancies, Non Hodgkin's Lymphoma, Squamous cell carcinoma.

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Introduction: Gastrointestinal malignancies are a leading cause of mortality and morbidity. Although adenocarcinomas are the predominant histopathological variant, there are wide histopathological variations in gastrointestinal malignancies. There is variation in age distribution, sex distribution, etiology, and histopathological patterns from one ethnic group to other and one geographic area to other. There are variation in the age incidence, sex incidence, etiology and histopathological typing as per their anatomical location. The most common carcinoma of the esophagus is squamous cell carcinoma.

Most Squamous cell carcinomas occur in adults over the age of 50 years[1]. Adenocarcinoma predominantly arises from Barrett's esophagus[2]. Gastric cancer was the second commonest cancer in the World in 1990 and 60% of them occurred in developing countries[3]. Helicobacter pylori infection, nitrate level in diet and a high dietary salt intake are the risk factors for the development of gastric adenocarcinoma[4]. Lymphoma constitute up to 10 % of all gastric malignancies[5]. Most gastrointestinal mesenchymal neoplasms are gastrointestinal stromal tumours (GISTs). GISTs account for 2.2% of malignant gastric tumors[6]. Tumours larger than 5 cm in diameter with signs of necrosis are parameters of malignant nature of GIST[7]. Although the small bowel represents 75 % of the length of the alimentary tract, tumours account for only 3-6% with slight predominance of benign tumors[1,8]. Virtually 98 % of all cancers in the large intestine are adenocarcinomas. They arise as polyps and produce symptoms relatively early and at a stage generally curable by resection[1].

Objectives : 1. To study the incidence of GIT malignancy in study group 2. To study the age, sex and location distribution of GIT malignancy in study group. 3. To find out the histopathological patterns of GIT malignancies in study group.

Material and Methods: This was a two year retrospective study done at Pathology Department, P.D.U. Medical College, Rajkot, during August 2010 to July 2012. Total 6060 specimen were received for histopathological examination during these period, out of these 98 specimens were of gastrointestinal malignancy. The specimens were either a radical specimen or a laparoscopic biopsy. The specimens were bisected and fixed overnight in 10% formalin. They were processed using Microm STP-120 automatic tissue processor.

Ascending grade of acetone (LR Grade) was used for dehydration of tissue, Xylene (LR Grade) as clearing agent and Paraffin wax (melting point 54-56degree) was used for block preparation. The sections were prepared with Microm HM-325 microtome. Routine haematoxylin and eosin stain was done, as and when required special stains like PAS (Periodic acid Schiff) stain were employed. Sections were examined under the light microscope and analysed.

Result: Total 6060 specimen were received for histopathological examination during August 2010 to July 2012. Out of these 98(1.62%) were specimens of gastrointestinal malignancy. The histopathological diagnosis of these gastrointestinal malignancies were as per Table No.1

Table 1: Histopathological diagnosis of GI malignancies

Histopathological Diagnosis	No. of cases
Adenocarcinoma	70(71.4%)
Squamous cell carcinoma	15(15.30%)
Non Hodgkin's Lymphoma	6(6.12%)
Carcinoid tumour	3(3.06%)
Malignant GIST*	2(2.04%)
Malignant Melanoma	2(2.04%)

*Gastrointestinal stromal tumour

Only malignant GIST were considered for present study with size more than 5cm, geographical necrosis and mitotic count of 5 per 50hpf. Both the malignant GIST in current study were friable grossly, larger than 8cm in size with necrosis and high mitotic index. The sex ratio of each histopathological pattern was as per the Table No.2.

Table No.2: Male: Female ratio of various histopathological diagnosis

Diagnosis	Male	Female	M:F Ratio
Adenocarcinoma	40	30	1.33:1
Squamous cell carcinoma	13	2	6.5:1
Non Hodgkin's Lymphoma	5	1	5:1
Carcinoid tumour	1	2	1:2
Malignant GIST	1	1	1:1
Malignant Melanoma	1	1	1:1
Total	61	37	1.65:1

Overall M: F ratio was 1.65:1 for all gastrointestinal malignancies. Except carcinoid tumour all other types of GI malignancies show male preponderance or equal M: F ratio. The age incidence of each histopathological diagnosis was as per Table No.3

Table No. 3 Age group distribution of various histopathological diagnosis

Age Group	Adenocarcinoma	Squamous cell carcinoma	Non Hodgkin's Lymphoma	Carcinoid tumour	Malignant GIST	Malignant Melanoma
1-15	00	00	01	00	00	00
16-30	00	00	02	00	00	00
31-45	15	04	01	00	00	00
46-60	37	07	01	03	00	02
61-75	15	04	00	00	02	00
>75	03	00	01	00	00	00
Total	70	15	06	03	02	02

Overall most no. of GI malignancies were seen in the age group of 46-60 years with total 50 cases(51.02%), the youngest patient was 14 year old boy with Non Hodgkin's Lymphoma of small intestine while the oldest patient was a 92 year female with mucinous adenocarcinoma of large intestine(rectum). The anatomical location wise distribution of various histopathological diagnosis was as per Table No.4

Esophagus: Among 19 cases of esophageal carcinoma, 14(73.68%) were squamous cell carcinoma while 5(26.32%) were adenocarcinoma, all 5 adenocarcinoma were located in lower esophagus.

Table No.4 Anatomical Location And Histopathological Diagnosis

Location	Adenoca.	SCC	NHL	Carcinoid	GIST	MM	Total
Esophagus	05	14	00	00	00	00	19
Stomach	08	00	01	00	02	00	11
Small Intestine	08	00	05	03	00	00	16
Large Intestine	48	00	00	00	00	00	48
Peri-Anal region	01	01	00	00	00	02	04
Total	70	15	06	03	02	02	98

Esophagus: Among 19 cases of esophageal carcinoma, 14(73.68%) were squamous cell carcinoma while 5(26.32%) were adenocarcinoma, all 5 adenocarcinoma were located in lower esophagus.

Stomach: Among 11 cases of stomach carcinoma 8(72.72%) were adenocarcinoma, 2(18.18%) were malignant GIST (Fig.1) and 1(9.09%) was NHL. Out of 8 adenocarcinoma 6 showed signet ring cell carcinoma (Fig.2 and Fig.3) and 2 were intestinal type adenocarcinoma. 5 of this adenocarcinoma showed diffuse infiltrating pattern (Linitus Plastica).

Small Intestine: Among 16 cases of small intestinal carcinoma, 8(50%) were adenocarcinoma, 5(31.25%) were NHL(Fig.4) and 3(18.75%) were carcinoid tumour(Fig.5).All 8 adenocarcinoma were around the opening of Ampulla of Vater and Whipple's procedure was performed. Out of 5 cases of NHL, 3 patients were seropositive. All 3 carcinoid were located in ileum.

Large Intestine: All 48 cases were adenocarcinoma. Rectum was the commonest site with 24(50%) cases, followed by ascending colon and caecum 11(22.91%) cases, sigmoid colon 9(18.75%) cases and transverse colon 4(8.33%) cases. Most of the adenocarcinoma of sigmoid colon and rectum showed infiltrating pattern with stricture formation, whereas ascending colon and caecum showed fungating growth pattern. Microscopically mucinous adenocarcinoma with large areas of extracellular mucin pools was the commonest pattern (Fig.6), adenocarcinoma without any intracellular or extracellular mucin secretion was the second common pattern (Fig.7). One case of intracellular mucin (Signet ring cell carcinoma) was seen.

Peri-anal region: Out of 4 cases of peri-anal location 2(50%) were malignant melanoma (Fig.8), 1(25%) case each of squamous cell carcinoma and adenocarcinoma was observed.

Fig.1 Malignant GIST showing geographical necrosis and high mitotic index,H&E 10 X

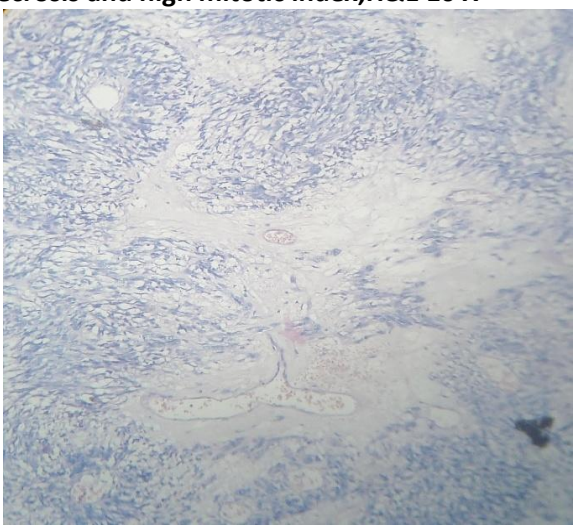


Fig.2. Infiltrating signet ring cell Carcinoma, H&E 40 X

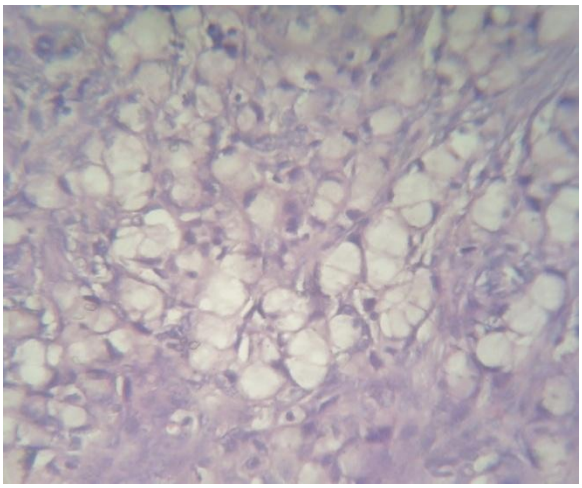


Fig.3. Infiltrating signet ring cell Carcinoma, PAS Stain 40 X

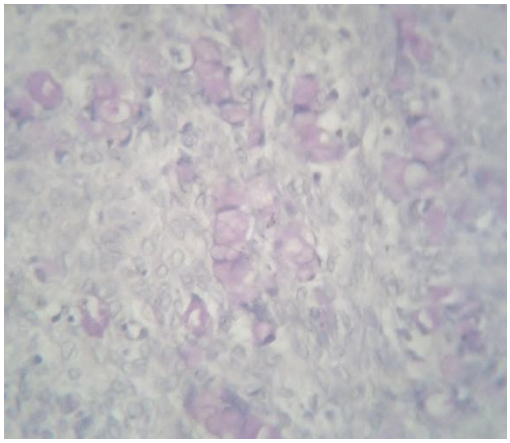


Fig.4 Non Hodgkin's Lymphoma of Small intestine, H&E Stain 10 X

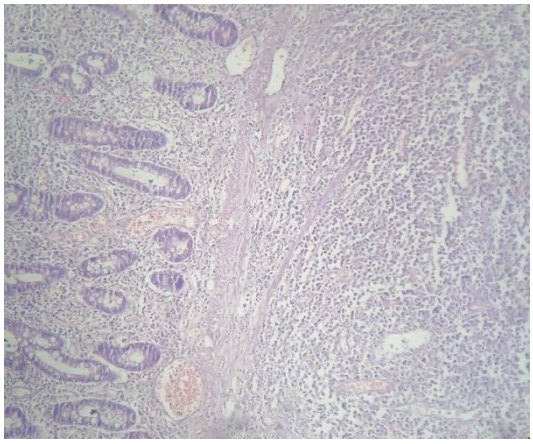


Fig.5 Infiltrating Carcinoid Tumour showing Perineural invasion, H&E Stain 10 X

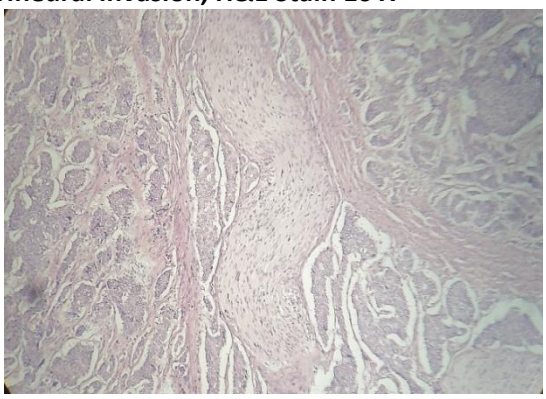


Fig.6 Malignant mucinous adenocarcinoma with large extracellular mucin pools, H&E Stain 40 X

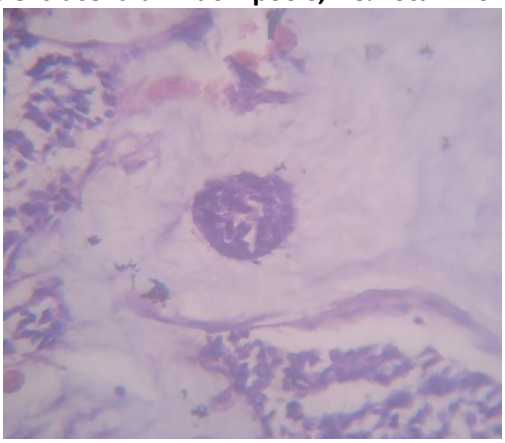


Fig.7 Invasive Malignant adenocarcinoma, H&E Stain 40 X

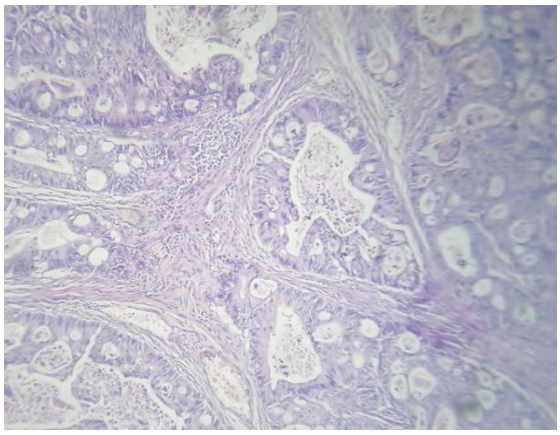
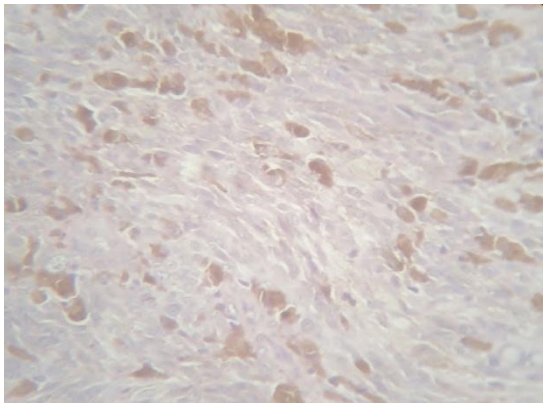


Fig.8 Invasive Malignant Melanoma, H&E Stain 40 X



Discussion: The current study done at Pathology department, P.D.U. Medical college, Rajkot shows 98 cases (1.62%) of gastrointestinal malignancies from 6060 received specimen. Similar study conducted by Basnet et al shows 171 cases (1.54%) of gastrointestinal malignancies from 11,127 received specimen[9]. The anatomic location wise distribution of gastrointestinal malignancies of current study and study of Basnet et al are tabulated below[9].

Table No.5 Comparative Study with Basnet et al

Anatomical location	Current study	Basnet et al[9]
Esophagus	19	11
Stomach	11	73
Small intestine	16	09
Large intestine	48	73
Peri-anal region	04	00
Total	98	171

There is considerable variation in the distribution of anatomical location of gastrointestinal malignancies from various geographic and ethnic populations. However large intestine was the most common site for gastrointestinal malignancies in both studies. Mohandas K.M, Desai DC study of epidemiology of digestive tract also found large intestine as the leading site of gastrointestinal malignancies[8]. To further evaluate distribution of age, sex and histopathological diagnosis we have divided gastrointestinal malignancies as per their anatomical location.

Esophagus: The commonest age group for esophageal carcinoma was 46-60 years in current study which is comparable to the study of Basnet et al. James M. Crawford also found the common age above 50 years[1]. Of all the esophageal malignancies 14 (73.68%), were squamous cell carcinoma, the study of Basnet et al also found 11(72.72%) squamous cell carcinoma[9]. We also found 5(26.32%) cases of adenocarcinoma; the increasing incidence of esophageal adenocarcinoma is associated with increase in the incidence of reflux esophagitis and Barrett's esophagus[10].

Stomach: The commonest age group for stomach malignancies was 46-60 years in current study, which is comparable with the study of Basnet et al[9]. Adenocarcinoma with 8(72.72%) cases was the commonest histopathological diagnosis followed by malignant GIST 2(18.18%) and NHL 1(9.09%). Basnet et al found 88.4% adenocarcinoma[9] while James M. Crawford found 90-95% cases of adenocarcinoma[1]. The incidence of malignant GIST with 18.18% was higher than the studies of Basnet et al (8.98%)[9] and M. Mettinen(2.2%)[6]. The incidence of NHL in a study by A. Wothersoon was 10%[5] while it was 9.09% in current study. H. Pylori infection, alcohol, smoking and amount of nitrous compound in the water are some of the known etiological factors for various malignant stomach lesions.

Small intestine: The commonest age group was 46-60 years for adenocarcinoma and carcinoid tumour in the current study which is comparable with the study of Basnet et al[9]. However the age group for NHL was younger in current study (14-42 years) as compared to the study of Basnet et al (61-75 years)[9]. We found 5 cases (31.25%) cases of NHL, Lee W.J et al found 41.6%[11] and Domizio P et al found 20-40% cases of small intestinal NHL[12]. In this study 8cases(50%) were adenocarcinoma, Lee W.J.et al found 29.7%[11] and Basnet et al found 22.22% cases of adenocarcinoma[9]. In current study 3 out of 5 cases of intestinal NHL were seropositive. In HIV-associated non-Hodgkin's lymphoma, gastrointestinal lesions are the most frequent extra nodal location[13].

Large intestine: In current study large intestine was the commonest site of all GI malignancies with 48cases (48.97%). All our cases were adenocarcinoma (100%), common age group was 46-60 years followed by 61-75 years, and male to female ratio was 1.52:1. Basnet et al found 90.42% adenocarcinoma with the same age group incidence and male to female ratio of 1.86:1[9]. James M. Crawford found 90% adenocarcinoma and common age group was 60-70 years, male to female ratio was 2:1[1]. Mohandas KM, Desai DC also found large intestine as the commonest site for GI malignancies[8]. Among large intestine rectum was the commonest site in the study of Mohandas KM, Desai DC which is comparable with current study having 24 cases (50%) of rectal adenocarcinoma[8]. However compared to the worldwide data the incidence of large intestine carcinoma is lower in India, the low incidence can be attributed to high intake of starch and the presence of natural antioxidants such as curcumin in Indian cooking[8].

Peri-anal region: In current study only four cases of peri-anal malignancies were seen, out of these 2cases (50%) were malignant melanoma. An article of M. ven't Riet showed sixth and seventh decade as the commonest age for malignant melanoma and female preponderance[14], current study showed both the cases between 50-60 years with equal male to female ratio. The high percentage of malignant melanoma could be an incidental finding, however the sample size is too small to draw any conclusion for malignant melanoma.

Conclusion: Current study shows that 46-60 years was the commonest age group for gastrointestinal malignancies with overall male to female ratio of 1.65:1, large intestine was the commonest site and adenocarcinoma the commonest histopathological diagnosis. However comparisons with other similar studies and data shows there are variations in the age and sex distribution of gastrointestinal malignancies at different demographic and geographic populations. Besides there are variations in incidence of different histopathological diagnosis. The diagnosis also differs from one anatomic location to other.

References:

1. James M. Crawford MD, Ph.D. The gastrointestinal system.Ramji SC, Vinay K. and Stanley (eds). In Robins Pathologic Basis of Diseases. 5th ed. Banglore-India. W.B Sounders Company, 1944: pp 755-829
2. H.E. Gabbert, T. Shimoda, P. Hinaut, Y. Nakamura, T.K. Field, H. Inone. WHO Classification of Tumors. In: Pathology and Genetics of Tumors of the Digestive Systems.. IARC Press, Lyon 2000. pp 11-30
3. C. Feneglio-Preiser, F. Carneiro, P. Corea, P.Guilford, R. Lambert, F. Hegraud. WHO Classification of Tumors. In: Pathology and Genetics of Tumors of the Digestive Systems. IARC Press, Lyon 2000. pp 11-30.
4. John T. Loh, Victor J. Torres and Timothy L. Cover. Molecular Biology, Pathobiology and Genetics. Cancer Res 2007; 67(10): 4709-15.

A. Wothersopoon, A.Chott, R.D. Gascoyne, H.K.Muller-Hermelink. WHO Classification of Tumors. In: Pathology and Genetics of Tumors of the Digestive Systems.. IARC Press, Lyon 2000. pp 11-30.

5. M. Miettinen, J.Y.Blay, H. Sabin. WHO Classification of Tumors. In: Pathology and Genetics of Tumors of the Digestive Systems. IARC Press, Lyon 2000. pp 11-30.
6. Radovanovic D, SteyVanovic D, Pavlovic I, Jasarovic D, Mitovic N, Ilic I. Gastro intestinal stromal tumors of Gaster-case report. Med. Pregl.2008 Jul-Aug; 61(7-8); 409-13.
7. Mohandas KM, Desai DC. Epidemiology of digestive tract cancers in India. V. Large and small bowel. Indian J Gastroenterol.1999 Jul-Sep;18(3):118-21.
8. Basnet R.B, Amartya B., Sibakoti Y.C., Shakya A., Tuladhar A., Malla K. and et al. Histopathological diagnosis of Gastrointestinal malignancies in Bir Hospital. PMJN. 2009 Jan-June ; 8(2): 51-57.
9. Shaheen NJ. Advances in Barrett's esophagus and esophageal adenocarcinoma. Gastroenterology. 2005 May;128(6):1554-66.
10. Lee WJ, Chang KJ, Wang SM, Chen KM, How SW. Primary malignant tumors of the small intestine. J Formos. Med Assoc, 199 Aug; 90(8): 776-81
11. Dimizio P, Owen R. A., Shepherd NA,Talbot I.C., Norton A.J. Primary lymphoma of the small intestine: a clinicopathlogical study of 119 cases. The Journal of Surgical pathology; 1993. vol. 17, no5, pp 429-442(57 refs.)
12. Heise W. GI- lymphomas in immunosuppressed patients (organ transplantation; HIV). Best Pract Res Cli Gastroenterol. 2010 Feb;24(1):57-69.
13. M. van't Riet, R.W.M. Giard,J.H.W. de Wilt and W. Vles. Melanoma of the Anus Disguised as Haemorrhoids: Surgical Management Illustrated by a Case report.Dig Dis Sci.2007 July;52(7):1745-47

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