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Anatomic categorization of gastrointestinal malignancies using haematoxylin and eosin stains: A 10-year retrospective histopathological study at the Korle-Bu Teaching Hospital Accra

Der EM[1,3,*], Naaeder SB[2], Clegg-Lamptey JNA[2], Dakubo JCB[2], Edusei L[1], Tettey Y[1] and Gyasi RK[1]

[1] Department of Pathology, University of Ghana Medical School, PO Box 4236, Korle-Bu, Accra, Ghana
[2] Department of Surgery, Korle-Bu Teaching Hospital, PO Box 77, Korle-BU, Accra, Ghana
[3] Department of Pathology, Tamale Teaching Hospital, PO Box BL1883, Tamale, Ghana

Abstract

Background: Data on gastrointestinal (GI) malignancies in Ghana are relatively uncommon and are mostly on colorectal cancers. The aim of this descriptive study was to categorize gastrointestinal tract malignancies according to anatomic location and to evaluate the clinico-pathological characteristics of these malignancies. *Material and methods:* This was a retrospective study in the Department of Pathology from January 2002 to December 2011. *Results:* A total of 971 gastrointestinal (GI) malignancies were diagnosed in our institution with an annual incidence of 97.1 cases. The mean age of patients was 55.2 years (SD=16.1). The common GI malignancies were colorectal 458(47.2%), and gastric 315(32.4%) cancers. Those of the esophagus 91(9.4%), small bowel 41(4.2%), anus 47(4.8%) and the appendix 8(0.8%). The mean ages of the patients with oesophageal, gastric and large bowel cancer were 58.3 (SD=12.7), 58.39(SD=14.69), and 53.6(SD=16.0) years respectively, while those with cancers of the appendix, and small bowel were 37.6 (SD=10.9), and 44.5 years (SD=18.0). Malignancies of the colorectum 242(52.8%) and anus 26(55.3%), were common in females. The commonest malignancy of the small bowel was lymphoma 14(34.1%). A total of 38(3.8%) of the GI malignancies were gastrointestinal stromal tumours. *Conclusion:* The distribution of malignant tumors in the gastrointestinal tract of Ghanaians has been described and it has been found to be similar to that in western nations. The majority of patients were young. Males were the commoner victims. Many of our patients presented with late stage disease with poor prognosis.

Keywords: gastrointestinal stromal tumour; lymphoma; colorectal; gastric; esophagus; cancer

Introduction

The global burden of cancer continues to increase in both developed (high income) and developing (low-middle income) countries largely because of increasing life expectancy and growth of the world population as well as the adoption of cancer-causing behaviors, in the low-middle income countries, particularly smoking [1–6]. The population of Ghana is aging and this has led to an increased morbidity and mortality [6, 7]. Malignancies of the gastrointestinal (GI) tract are more common in the elderly (65 years and above) [8 -10], but are rare in infancy, childhood and adolescence [11–12]. Some studies have shown that gastrointestinal (GI) malignancies are commoner in males than females [13–14] and depending on the anatomic location, majority of gastrointestinal cancers are diagnosed from the colon and rectum [11, 14]. Clinical presentation is usually late, with symptoms such as abdominal mass, ascites, bleeding per rectum, epigastric and abdominal pain as well as significant weight loss.

Specimens of the gastrointestinal system account for a significant portion of the day-to-day surgical

*Corresponding author: Dr. Edmund Muonir Der, Department of pathology, University of Ghana Medical School, PO Box 4236, Korle-Bu, Accra, Ghana. Tel.: 0208709807; E-mail: maadelle@yahoo.com

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and endoscopic pathology material received in the department of pathology at the Korle-Bu Teaching Hospital. In 2008, 11.6%, (805/6934) of the surgical specimens received were from the GI tract, yet there has not been any comprehensive histopathological study of the malignancies of the gastrointestinal tract. The aim of this descriptive study is to categorize gastrointestinal tract malignancies according to anatomic location and to evaluate the clinico-pathological characteristics of these malignancies.

Materials and methods

Study design

This is a descriptive retrospective histopathological study.

Study site

All data were collected from the Department of Pathology, University of Ghana Medical School. The department, which reports between 5,000 and 8,000 histopathological cases annually, is the largest in Ghana. It receives surgical and endoscopic specimens mainly from the Korle-Bu Teaching Hospital, the largest referral hospital in Ghana. The department also receives specimens from other health facilities within the Accra metropolis, the Greater Accra region, and other regions southern Ghana. The sample size of 971 is adequate and representative of GI tract malignancies as seen in southern Ghana. It is also adequate for evaluation of the clinical and histologic characteristics of GI tract cancers in this part of the country.

Data collection and analysis

All histopathology request forms and slides of confirmed GI tract malignancies based on haematoxylin and eosin (H&E) stains in the Department of Pathology from January 2002 through December 2011 were reviewed independently (by EM and cross checked by LE), for clinical characteristics (age, main complaints, duration of symptoms, anatomic location, and type of specimen) and histologic features (type of cancer, differentiation, Duke's stage/TNM stage and resection margins). The GI tract included the esophagus, stomach, small bowel, colon and anus.

In this study, the pathological stage of the colorectal cancers was based on modified Dukes system, as recommended by the American Joint Committee on Cancer, which takes into account the depth of invasion, the number of cancerous lymph nodes, and spreading to other pelvic structures. The diagnosis of all the tumors was based on H&E stains. No histochemical studies were conducted. The data were entered into a computerized spreadsheet and analyzed using SPSS version 18 (SPSS, Chicago, IL).

Results

Between 2002 and 2011, 971 gastrointestinal malignancies were diagnosed in our institution giving an annual incidence of 97.1 cases. The ages of patients ranged from 3 to 100 years, with a mean age of 55.18 years (SD=16.08). Two hundred and twenty-three (23.0%) patients were in the 50-59 years age group, with median age of 56 years (Table 1). More than half of the patients were males 544(56.0%). The clinical presentations were varied with a little above one-fifth (23.5%) presenting with abdominal mass (Table 2). The commonest GI malignancy in this study was colorectal carcinoma 458(47.2%) followed by gastric carcinoma 315(32.4%) (Table 3).

Table 1 Age characteristics of major groups of GI malignancies.

Location/ Age(yrs)	*≤29 n/%*	*30-39 n/%*	*40-49 n/%*	*50-59 n/%*	*60-69 n/%*	*≥70 n/%*	*Total*
Age	68(7)	88(9.1)	178(18.4)	224(23)	212(21.8)	201(20.2)	971(100)
Oesophagus	0/0	3(3.3)	27(30)	17(18.9)	24(26.7)	19(21.1)	90(100)
Stomach	8(2.5)	26(8.3)	46(14.6)	76(24.2)	83(26.4)	75(23.9)	315(100)
Small bowel	10(24.4)	4(9.8)	9(22)	8(19.5)	7(17.1)	3(7.3)	41(100)
Colorectal	45(8.9)	53(10.5)	90(17.9)	120(23.8)	93(18.5)	103(20.4)	458(100)
Anus	0(0)	6(12.8)	9(19.1)	12(25.5)	10(21.3)	10(21.3)	47(100)
Appendix	2(28.6)	1(14.3)	3(42.9)	1(14.3)	0(0)	0(0)	7(100)

Oesophageal cancers

Ninety-one (9.9%) patients had cancer of the oesophagus. Patients diagnosed with oesophageal cancer were relatively old, with a mean age of 58.29 years (SD=12.73). Many (30%) were in the 40-49 year age group (Table 1). Majority of the patients were males 62(68.1%). The commonest clinical presentation of oesophageal cancer was dysphasia 72(86.7%) (Table 4). The duration of symptoms at presentation was available for 24 cases, out of which 15 (62.5%) presented within 4-6 months of onset illness. Oesophageal specimens were mostly small endoscopic biopsies 79 (87.8%). The common histologic subtype of oesophageal cancer was invasive squamous cell carcinoma 66 (73.3%) (Table 5).

Gastric malignancies

A total of 315(32.4%) malignancies were observed from the stomach. The youngest with gastric cancer was

Table 2 Symptoms at presentation of gastrointestinal malignancies.

Symptom	*Frequency (n)*	*Percentage (%)*
Abdominal mass/tumour	202	23.5
Bleeding per rectum	194	22.6
Dysphagia	86	10
Intestinal obstruction	64	7.5
Abdominal pain	59	6.9
Epigastric pain	58	6.8
Constipation	44	5.1
Ulcer	42	4.9
GOO/Vomiting	36	4.2
Weight loss	33	3.8
Others	41	4.7
Total	859	100

Table 3 The distribution of malignancies along the gastrointestinal tract.

Location	*Frequency (n)*	*Percentage (%)*
Oesophagus	91	9.4
Stomach	315	32.4
Small bowel	41	4.2
Colorectal	458	47.2
Anus	47	4.8
Appendix	8	0.8
Metastases to GI tract	11	1.1
Total	971	100

Table 4 Distribution of clinical symptoms according to locations.

Symptom/ Location	*Dysph n(%)*	*Abd.M n(%)*	*Bld.PR n(%)*	*E.pain n(%)*	*Abd.pain n(%)*	*Ulcer n(%)*	*GOO n(%)*	*Contp n(%)*	*Int.ob n(%)*
Oesophagus	72(86.7)	2(2.4)	1(1.2)	2(2.4)	0(0)	4(4.8)	0(0)	0(0)	0(0)
Stomach	14(5.6)	40(15.7)	25(9.8)	51(20)	19(7.5)	30(11.8)	33(13.7)	2(0.8)	0(0)
Small bowel	0(0)	11(29.7)	1(2.4)	2	8(21.6)	0(0)	0(0)	1(2.4)	12(32)
Colorectal	0(0)	135(29.2)	167(35.8)	3(0.6)	30(6.4)	8(1.7)	0(0)	40(8.6)	52(11.2)
Anus	0(0)	22(53.5)	12(27.9)	0(0)	1(2.3)	7(16.3)	0(0)	0(0)	0(0)
Appendix	0(0)	3(50)	0(0)	0(0)	1(16.7)	0(0)	0(0)	0(0)	4(100)

Abbreviations: Dysph = Dysphagia, Abd.M = Abdominal mass, Bld.PR = Bleeding per rectum, E.pain = Epigastric pain, GOO = Gastric outlet obstruction, Contp = Constipation, Int.ob = Intestinal obstruction.

Table 5 Common histological subtypes of gastrointestinal malignancies according to location.

Cancer/ Location	*Adeno ca n(%)*	*SCC n(%)*	*Gist n(%)*	*Lymph n(%)*	*Carcin.ca n(%)*	*Metast n(%)*	*Others n(%)*
Oesophagus	23(25.5)	66(73.3)	0(0)	0(0)	0(0)	0(0)	1(1.2)
Stomach	270(86)	0(0)	27(9)	13(4)	2(0.6)	0(0)	3(1)
Small bowel	12(29)	0(0)	6(15)	14(34)	4(10)	5(12)	0(0)
Colorectal	440(87)	25(5)	5(1)	11(2)	5(1)	0(0)	16(3.2)
Anus	25(53.2)	16(34)	0(0)	1(2.1)	0(0)	1(2.1)	4(8.5)
Appendix	5(62.5)	0(0)	0(0)	1(12.5)	1(12.5)	0(0)	1(12.5)

Abbreviations: Adeno ca = Adenocarcinoma; SCC = Squamous cell carcinoma; Gist = Gastrointestinal stromal tumour; Lymph = lymphoma; Carcin.ca = Carcinoid; Metast = metastasis.

3-years-old (diagnosed with lymphoma) and the oldest with 100 years (diagnosed with adenocarcinoma). The mean age was 58.39 years (SD=14.69), with 83(26.4%) within the 60-69 years age group (Table 1). Nearly two-thirds (64.8%) were males. Of the 255(81.0%) patients with symptoms at presentation, only 48 (18.8%) had stated duration ranging from one week to more than two years. Epigastric pain 51(20.0%) was the commonest symptom, followed by abdominal mass 40(15.7%) (Table 4). The common type of gastric specimen in this study was small endoscopic biopsies 189(60.05%), followed by partial gastrectomy 116(37.0%). Of the gastrectomy specimens 80 (69.0%) had tumour infiltrating the full thickness to the gastric wall. A total of 69 (59.4%) out of 116 partial gastrectomy had TNM staging, with 40(57.9%) subjects being stage II (Table 6). Adenocarcinoma was the commonest histological type 270 (86.0%), consisting of intestinal subtype 238 (88.1%) and diffuse subtype 32(11.9%); 102(42.8%) of the intestinal type were poorly differentiated (Table 5).

The second common histological type was gastrointestinal stromal tumour 27(9.0%) followed by lymphoma 13(4.0%), [Consisting of non-Hodgkin lymphoma 10(77.0%), MALTOMA 2(15.3%) and Hodgkin lymphoma 1(7.7%)].

Small intestine cancers

There were 41(4.2%) small intestinal cancers. The ages of patients ranged from 3 – 76 years with a mean age of 44.4 years (SD=18.00) (Table 1). Ten (24.4%) of the patients were younger than 30 years. Malignancies of the small bowel were commoner in males 32 (78.0%). Twelve (32%) cases presented with intestinal obstruction (Table 4), and 11 (29.7%) with abdominal mass. Small bowel malignancies were commoner in the ileum 33(80.5%). Most of the specimens received were resected segments of bowel 25(61.0%). Lymphoma was the commonest small bowel cancer 14(34.0%), [Consisting of 11 (78.6%) high grade lymphomas and 3(21.4%) maltomas] (Table 5), followed by adenocarcinoma 12 (29.0%). The commonest TNM stage for the 12 adenocarcinoma was stage 3, (41.7%) (Table 6).

Table 6 TNM staging for resected GI malignant specimens.

Location/ TNM Stage	*T1 n(%)*	*T2 n(%)*	*T3 n(%)*	*T4 n(%)*	*Total n(%)*
Oesophagus	0/0	4(33.3)	6(50)	2(16.7)	12(100)
Stomach	2(2.9)	40(57.9)	21(30.4)	6(8.7)	69(100)
Small bowel	3(25)	2(16.7)	5(41.6)	2(16.7)	12(100)
Colorectal	5(4.7)	68(33.2)	128(60.7)	10(6.2)	211(100)
Anus	0(0)	0(0)	0(0)	0(0)	0(0)
Appendix	0(0)	1(50)	1(50)	0(0)	2(100)

Colorectal cancers

Four hundred and fifty-eight (47.2%) of the tumours were colorectal cancers (Table 3). The ages of patients ranged from 4 to 92 years with a mean age of 53.6 years (SD=16.6), many were in the 50-59 years age group 120 (23.8%) (Table 1). A little over 50% were in females accounting for 242(52.8%) cases. Of 425(92.8%), whose symptoms at presentation were available for analysis, bleeding per rectum was the most frequent symptom 156(36.7%) subjects, followed by abdominal mass 102(24.0%) (Table 4). The duration of symptoms was available for 137(30.0%) patients, 51(37.1%) of whom presented within 3 months. The commonest colorectal specimens; were endoscopic biopsies 228(49.8%) followed by 220(48.0%) resected bowel specimens. Majority of the cancers were adenocarcinoma 404(90.4%) (Table 4), followed by 11(2.4%) lymphomas (all high grade non-Hodgkin lymphoma) and 10 (2.2%) squamous cell carcinoma. Most of these cancers were located in the recto-sigmoid region 311(67.9%), with 91 (19.9%) in the caecum. A total of 211 (95.9%) out of the 220 resected specimens were staged by the Astler-Coller modification of Dukes staging system for colorectal carcinoma. Seventy-nine (37.4%) of the resected colorectal specimens were stage C2, followed by B2 50(23.7%) (Table 7). Nine cases could not be staged due to poor preservation. The commonest TNM stage for the resected bowel was stage 3, (60.7%) (Table 6).

Table 7 Stages of 211 resected colorectal specimens by the Astler-Coller modification of Dukes system.

Stage	*Frequency (n)*	*Percentage (%)*
A	12	5.7
B1	47	22.3
B2	50	23.7
C1	23	10.9
C2	79	37.4
Total	211	100

Anal cancers

Forty seven (4.8%) cases were invasive anal carcinomas. Their ages ranged from 32 to 86 years with a mean of 57.4 years (SD=15.34). More than half of the patients were females 26(55.3%). Clinical symptoms were available for 43 cases, of which many presented with anal mass 22 (51.2%), followed by bleeding 12(27.9%). The commonest anal cancer was adenocarcinoma 25(53.2%), (most likely from the low rectal), followed by squamous cell carcinoma 16(34.0%) (Table 5).

Appendiceal malignancies

Eight (0.82%) primary malignancies of the appendix were diagnosed. Ages of patients ranged from 37 to 63 years with a mean age of 37.6 years (SD=10.9). Five (62.5%) out of the eight were males. Cancer of the appendix was commonly diagnosed in appendectomy specimens 6(75.0%). The common clinical presentation of appendiceal malignancy was right iliac fossa mass 3(3/6=50.0%). Adenocarcinoma was the commonest cancer 5(62.5%). There was one case (12.5%) each of carcinoid, lymphoma and spindle cell tumour (Table 7). Two (25%) out of eight of the malignancies of the appendix had modified Dukes staging and both were B2.

Gastrointestinal stromal tumour (GIST)

Gastrointestinal stromal tumours accounted for 38(3.9%) of the malignancies, the majority arising within the stomach 27(9.0%), with none from the oesophagus (Table 3).

Gastrointestinal lymphomas (Based on H&E Stain)

Lymphomas accounted for 38(3.9%) of the GI malignancies. Of this number 14(36.8%) were in the small bowel (Consisting of 11 (78.6%) high grade NH lymphomas and 3 (21.4%) maltomas), followed by 13 (34.2%) in the stomach, consisting of 8 (61.5%) high grade non-Hodgkin lymphomas, 4 (30.8%) maltomas and 1 (7.7%) Hodgkin lymphoma (Table 1).

Discussion

Gastrointestinal tract tumours contain a wide spectrum of tumours categorized depending on the occurrence

location of GI tract. These tumours often present at late stages at times with distant metastases which are then biopsied and may be difficult to differentiate based on H&E without the aid of immunohistochemical (IHC) stains [1]. Clinical practices in developed countries typically rely on IHC to detect patterns of expression of molecular markers as a strategy to characterize the cancers in newly-diagnosed patients. The role of IHC stains is more important in determining the origin and differentiation of gastrointestinal tract tumours especially in small biopsies [1]. Unfortunately in Ghana, unlike the developed countries, GI tract malignancies are diagnosed based on H&E stains as in this study without the use of IHC stains because the equipment are unavailable.

Malignancies of the gastrointestinal tract are commoner in the aged. In this study we found malignancies of the GI tract in general to be common in the relatively young patients, with a mean age at diagnosis of 55.5 year. This is in contrast to those of studies that found GI tract malignancies to be more common in the elderly, 65 years and above [8–10]. The reason for this disparity may be due to the differences in life expectancy between the developed and developing country such as Ghana. Five children were diagnosed with GI malignancy, the youngest, 3 years, with high grade small intestinal lymphoma and the oldest 12-years, with adenocarcinoma of the colorectum with no stated family history of colorectal carcinoma. GI malignancies are therefore as uncommon in Ghanaian children as found in other studies [11].

Majority of the patients were males. This corroborates studies that found GI malignancies to be commoner in males [13, 14]. The clinical presentations were varied, but many presented with abdominal mass, suggestive of advanced disease. The common sites of GI malignancies in this study, in descending order of frequency were: colorectum, stomach, oesophagus, anus, small bowel, and appendix. Our findings are similar to those of some other studies on GI malignancies [11, 14].

Oesophageal cancer was common in relatively older patients, mean age of 58.3 years. Studies have shown that esophageal cancers are more frequently diagnosed in people over 50 years and in men, a fact our findings support [15–18]. In this study, patients with oesophageal cancer commonly presented with dysphagia. The commonest cancer (73.3%) of the oesophagus was invasive squamous cell carcinoma. This Figure is in accord with most publications on oesophageal cancers [15, 19, 20].

The mean age of patients with malignancies of the stomach was 58.3 years, and the great majority (74.3%) were aged 50 years and above. The study also found that gastric cancer was commoner (64.8%) in males. Possible reasons may include abuse of alcohol and tobacco smoking which is relatively higher in Ghanaian males compared to females. Thus our findings are similar to those of other studies which found that malignancies of the stomach occurred commonly in persons 50 years and older and in males [18, 21–23]. Majority of the patients had symptoms available for the study, (81.0%), one-fifth of which were epigastric pain. The common histological type of gastric cancer was adenocarcinoma, majority (96.0%) of which, were of the intestinal subtype with only 4.0% diffuse subtype. Lauren [24], in his study of histological types of gastric cancer, found that nearly all gastric cancers were adenocarcinoma, and that 53% were intestinal type with 33% diffuse (signet ring) subtypes [24]. *Helicobacter pylori* infection could contribute to gastric mucosal metaplasia. The prevalence of *H. pylori* in the population Lauren studied five decades ago is similar to that of Baako et al. [25] study in Ghana and could explain the near similarity of the two types of cancer [24, 25]. The depth of gastric wall infiltration by the tumour is of great prognostic significance. Approximately, 37.0% of gastric specimens in this study were from partial gastrectomy, and 69.0% of which showed histologically full thickness gastric wall invasion. Also of those that had TNM staging, 57.9% were stage II. These findings seen to suggest poor outcome, and thus support studies that found that, the deeper the penetration of the gastric wall by tumour the greater the chance of metastases and hence the poorer the prognosis [26–28].

The mean age of the patients with colorectal cancers was 54.0 years, 62.7% of the patients were 50 years and above. Our findings support studies that found colorectal cancers to be commoner in older individuals' [12].

We found that 37.3% of the study population was younger than 50 years, the youngest being 12 years of age diagnosed with adenocarcinoma. Although this is significant, and may suggest genetic predisposition, there were no stated family history of colorectal carcinoma in this age group, none any previous publication of colon rectal carcinoma in younger age group in Ghana to support our finding. Colorectal carcinoma was relatively commoner (53.0%) in females in this study. This is contrary to studies that found colorectal cancers to be common in males [29, 30]. Colorectal cancer is a disease of older persons. In Ghana women have a higher average life expectancy than men and women also constitute the majority of the population. However this may not explain entirely the slight preponderance of females with colorectal cancer in this study. The common clinical presentation of colorectal cancers was bleeding per rectum, similar to the finding of Dakubo et al. [12]. Majority (61.3%), of the colorectal cancers were located in the recto-sigmoid region. Some studies have reported similar findings [12]. Adenocarcinoma is the commonest histological type of cancer of the large bowel accounting for about 95% of cases [31] which was the case in our study. The pathological stage of the disease assessed by microscopic examination of the resected colon or rectum is the most important prognostic factor [32]. We found that close to half (48.3%) of all resected colorectal specimen that had modified Dukes staging, were C, and therefore of poor

prognosis. In Ghana, many patients with GI symptoms including rectal bleeding tend to seek traditional medical remedies. It is when these have failed that recourse is made to orthodox medicine and even here diagnosis may be delayed as patients may be seen at a peripheral health facility and inappropriately managed without adequate investigation and diagnosis. Many cases of rectal bleeding are often attributed to haemorrhoids and are treated as such. The majority of our patients presented after 3 months, it is therefore not surprising that some of our patients had advanced disease with high Dukes stages. Public education and the introduction of screening for colorectal cancer could lead to early diagnosis and hence an improvement in the prognosis of this disease.

Small bowel cancers were commoner in younger individuals with a mean age of 44.5 years, a significant proportion (24.4%) of the patients were less than 30 years old. Most of the patients were males. These findings differ from studies that found cancers of the small bowel to be most common in the elderly with no sex predilection [33, 34]. The young age of our patients may suggest genetic predisposition and further studies will be required to either confirm or disprove this notion. As elsewhere, intestinal obstruction secondary to intussusceptions was the commonest presentation followed by intra-abdominal mass. Rectal bleeding was less common. Small bowel malignancies are known to be commoner in the proximal segment (duodenum) [35, 36], but we noted a higher frequency (80.5%), in this study to be in the ileum. The reasons for these differences are not clear. Lymphoma was the commonest (34.0%) small bowel cancer in the study, and this is in keeping with the large amount of lymphoid tissue associated with this segment of the bowel.

Cancers of the appendix accounted for 0.8% of all the GI malignancies and were commonly (62.5%) adenocarcinoma. Studies have found adenocarcinoma of the appendix to be uncommon. Our value of 0.8% thus supports these studies [36, 37].

Gastrointestinal stromal tumors (GIST), is a heterogeneous group of tumors frequently located in the stomach. Thirty-eight (3.9%) of all the gastrointestinal malignancies were gastrointestinal stromal tumors, majority (71.1%) were located in the stomach. This finding is in accord with studies that found the stomach to be the commonest location for gastrointestinal stromal tumours [38, 39].

Conclusion

The distribution of malignant tumors in the gastrointestinal tract of Ghanaians has been described and it has been found to be similar to that in western nations. The majority of patients were young. Males were the commoner victims. Many of our patients presented with late stage disease with poor prognosis. Population screening will ensure early diagnosis and treatment with better outcomes but this may be a daunting proposition in resource limited societies.

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Conflict of interest

Authors declare no conflict of interest.

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