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Assessment of the Outcome of Gastrointestinal Neoplasms Diagnosed at Kigali University Teaching Hospital.

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Abstract
Background: The prevalence and mortality rate of different gastrointestinal malignancies are well studied in most developed nations. However, in the majority of African countries including Rwanda few publications were done in regard to risks, diseases presentations and clinical outcomes. Based on hospital data, gastrointestinal malignancies are deadly and posing a hurdle to manage in most Rwandan health facilities. This study aimed to determine the outcomes of gastrointestinal malignancies at Kigali University Teaching Hospital.
Methods: This was a prospective observational study on patients diagnosed to have a tumour in their alimentary tract at endoscopy unity of CHUK. During 18 months of the study period, 102 patients were found to have gastrointestinal tumours and signed informed consent before enrolment to the study. Patients' characteristics were recorded, and they were followed for 6 months to know which investigations were requested to them, surgical interventions and treatments provided. The overall outcome was measured by the mortality rate at six months of follow up.
Results: Among study participants female were 52% and the prevalence of gastrointestinal neoplasms was more remarkable among patients above 60 years old (47.1%) and rare below the age of 30 years (2.0%). Stomach cancer was more prevalent at 67.5% of all patients diagnosed to have cancers. Colo-rectal and oesophageal cancers represented 20.0% and 11.2%, respectively. The survival rate for oesophageal, gastric and colorectal cancer after that period was 21.4%, 34.4% and 75.0%, respectively.
Conclusion: Gastrointestinal malignancies are deadly among our study population. Even with short periods of follow up, these neoplasms exhibit poor outcomes and treatment options are scarce. Colorectal cancer patients have a better outcome compared to oesophageal and stomach cancers.

Keywords: Gastrointestinal tract, Neoplasms, the Mortality rate

Background

Gastrointestinal Cancers include Anal, Colorectal, Oesophageal, Gallbladder, Gastric, Liver, Pancreatic and Small Intestine Cancers. The oesophageal, gastric and colorectal cancers are the most common causes of cancer-related death worldwide (1). GI cancers are believed to be caused by the complex interactions of genetic and environmental factors (1)(2). It is reported that allelic variations in oncogenes are candidate genetic risk factors that may alter the onset and outcome of GI cancers (3).

Oesophageal cancer is among prevalent cancers with the eighth position in the world, with an estimated 482,300 incidences and a death toll of 406,800 cancer cases per year (1)(4). The survival rate is very low, wherein in the United States, approximately 17,460 patients are diagnosed with oesophageal cancer in 2012, with 15,070 patients died almost 90% of the mortality rate (1). The report of Surveillance, Epidemiology and End Results data has shown that there was slight improvement during the last 30 years on the 5-year survival rates of oesophageal cancer, from 5% between 1975 and 1977 to 19% between 2001 and 2007 respectively (1)(4)(5).
. However, esophagectomy found to be linked to the highest mortality rate compared to other elective gastrointestinal surgeries with rates as high as 23% (4). A review of randomized

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controlled trials evaluating neoadjuvant chemoradiotherapy vs surgery alone demonstrated no major difference in overall survival (7).

Carcinoma of the stomach is the fourth most common and second cancer-causing mortality worldwide and in Africa ranked twelfth most common cancer usually seen more in the low socio-economic group, with 4/100000 and 3.8/100000 respectively for incidence and mortality rate in Africa. (8). According to a Scandinavian study, weight loss, epigastric pain and gastrointestinal haemorrhage were the important symptoms and adenocarcinoma of the lower oesophagus and obesity highlighted as common risk factors (9). In the study conducted in Pakistan, gastric cancer was three times more prevalent among H. pylori seropositive patients than in the H. pylori seronegative population. (9). H. pylori have a strong association with various gastric pathologies such as gastric adenocarcinoma, gastric MALT lymphoma, peptic ulcer and type B antral enteritis (9)(10)(11), and found positive in half of the patients presenting with stomach cancer (12).

Innovative advancement of endoscopic technology like Chromo-endoscopy, magnifying endoscopy narrow-band imaging (NBI) have greatly contributed to the better outcome and helped in improving accuracy and reliability for the diagnosis of early gastric cancer (13)(14).

In many countries and especially in the developed world, guidelines and protocols have been elaborated regarding the management of different types of cancers. In Rwanda, subtle or nearly non-existing efforts are put on to improve the clinical condition of patients with different types of cancer.

Gastrointestinal neoplasms are a common finding among patients undergoing endoscopies at the university teaching hospital of Kigali. However, there are neither guidelines nor interdepartmental regulations to help improve the clinical outcome of such patients. This study intended to describe demographic characteristics of patients diagnosed with GI tumours, assess their management plan, and determine the mortality rate with 6 months of follow up after diagnosis.

Methodology

This study was conducted at the Kigali University teaching hospital. It is the main public and largest health facility in Kigali among four national referral and teaching hospitals in Rwanda. It has 17 clinical departments among them the internal medicine department hosts endoscopy service. The service is open Monday to Friday and at least 46 endoscopies are performed every week. Patients who undergo endoscopy may be referred from district hospitals and different inpatients wards with internal referral to endoscopy.

This study was a descriptive longitudinal study conducted on patients who underwent endoscopy at the university teaching hospital of Kigali and diagnosed with gastrointestinal tract neoplasms. The study population was adult patients aged 16 years old and above diagnosed with a tumour throughout the gastrointestinal tract, willing to participate and signed a consent form. All other patients not meeting these criteria like those aged under 16 years old, patients who already started treatments, and those who did not accept to participate in the study or those who declined to consent were excluded in this study.

After the endoscopist has confirmed the diagnosis and a nurse was available to have an informed consent form signed and collects demographic characteristics of the patient. each patient was followed up to assess for further steps in the definite diagnosis of the condition notably laboratory investigations, pathological assessment and imaging and establishment of his management plan. Patients who were assigned to curative or palliative surgery and or chemotherapy were followed up for the outcome. Patients were observed for a minimum period of six months. The general outcome was measured by the mortality rate at the time of completion of the study.

The risk for developing GI cancer in North Africa and the Middle East is less than in the developed countries (18). There is little information on the incidence and prevalence of GI malignancies in the rest of Africa. And various reports from Sudan showed that these tumours were uncommon (20).

The total number of patients consulted during the study period were 151 patients. Then, the study used a simple random sampling technique without repetition and the sample size calculation for this study was calculated using the Yamane1967 formula

Where $n=N/1+N(e)^2$, $e=0.05$

Hence, $n=151/1+151(0.05)^2$

$n=102$

The study obtained ethical approval from the University Teaching Hospital of Kigali research committee and the University of Rwanda ethical committee. (Approval Notice: No 361/CMHS IRB/2016). The purpose of the study was explained to each participant and only participants who consented and signed a consent form were enrolled. The patient's confidentiality was observed as per the questionnaire. Recorded data were depersonalised (no names mentioned) and only the patient's code was used. During the whole process of the study, patients reliably chose themselves to provide information and they were protected from any risk of stigma and marginalization from their condition. Data collected with the questionnaire from each participant were entered and validated into EpiData Version 3.1. Statistical analyses performed with SPSS version 23 and results were presented in tables.

Results

From July 2016 to June 2017 a total of 127 patients were recruited to participate in this study. Every participant was followed for at least six months. After a total period of follow up, only 102 participants had valid data records and were analysed (see figure 3).

Of the 102 analysed, 64 patients (62.7%) had tumours at different locations of the stomach, 24 (23.6%) tumours were distributed to intestines (one per cent of them was found to ileocecal junction) and 14 (13.7%) patients had tumours at the oesophagus.
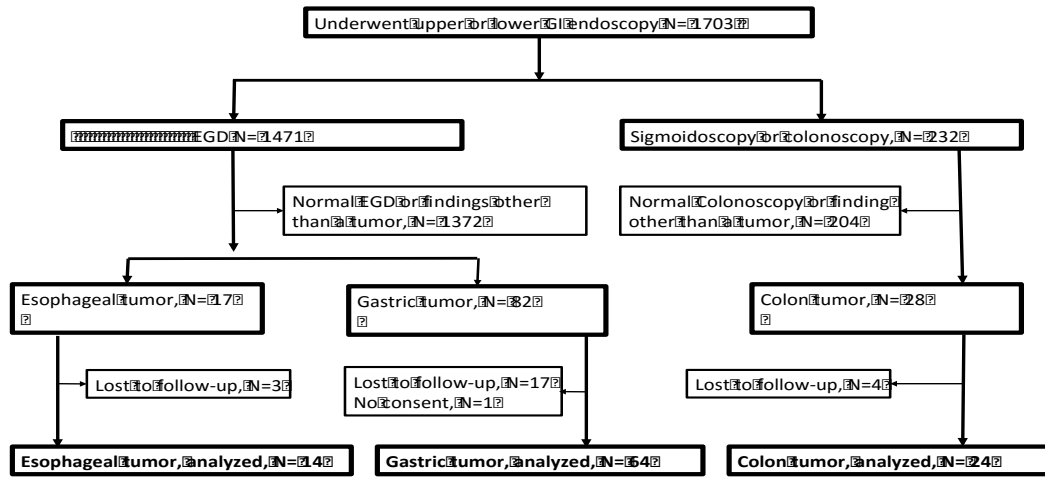
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                    ┌─────────────────────────────────────────┐
                    │  Underwent upper or lower GI endoscopy   │
                    │              N= 1703                     │
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Fig. 1: Flowchart of the recruitment of study participants and follow up.

Socio-demographic Characteristics of the study population.

Table 1: Age and socio-demographic characteristics of study participants.

	Tumour types			Total (N=102)
	Oesophageal (N=14)	Gastric (N=64)	Colon (N=24)	
Gender				
Male	11 (78.6%)	25 (39.1%)	13 (54.2%)	49 (48.0%)
Female	3 (21.4%)	39 (60.9%)	11 (45.8%)	53 (52.0%)
Age range				
<30 years	2 (14.3%)	0 (0.0%)	0 (0.0%)	2 (2.0%)
30-39 years	0 (0.0%)	6 (9.4%)	4 (16.7%)	10 (9.8%)
40-49 years	3 (21.4%)	8 (12.5%)	5 (20.8%)	16 (15.7%)
50-59 years	2 (14.3%)	17 (26.6%)	4 (16.7%)	23 (22.5%)
>60 years	7 (50.0%)	33 (51.6%)	11 (45.8%)	51 (50.0%)
Residence				
Kigali city	2 (14.3%)	14 (21.9%)	11 (45.8%)	27 (26.5%)
South	0 (0.0%)	10 (15.6%)	3 (12.5%)	13 (12.7%)
North	2 (14.3%)	14 (21.9%)	1 (4.2%)	17 (16.7%)
East	7 (50.0%)	21 (32.8%)	3 (12.5%)	31 (30.4%)
West	3 (21.4%)	5 (7.8%)	6 (25.0%)	14 (13.7%)

Among participants, 53 (52%) were female. Most of the participants were above 60-year-old (47.1%). Only a small number were below 30-year-old (2.0%). There was still detection of tumours in the younger population with 15.7 per cent ranging between 40 and 49-year-old, also 9.8 per cent ranging between 30 and 39-year-old.

Demographically, the Eastern Province had a big number of participants (30.4%) followed by Kigali City with 26.5 per cent of participants. Southern and Northern Provinces had the lowest prevalence with 12.7% and 16.7% of study participants, respectively.

Frequent Investigations.

Table 2: Further investigations asked after endoscopy.

Further investigations	Frequency	Percentage
Pathology	80	78.4
Chest CT-scan	68	66.7
Abdominal CT-scan	62	60.8
MRI	1	1.0
Ultrasound	1	1.0
Pet CT-scan	1	1.0

Investigations that frequently utilized were histopathology (78.4%), chest CT scan (66.7%) and abdominal CT scan (60.8%). One patient went to India for both PET CT-Scan and chemotherapy

Intervention and Management

Table 3: Different Interventions and Management.

	Frequency	Percentage
Time from diagnosis to intervention/surgery		
3-4 weeks	10	9.8
>4 weeks	33	32.4
Not applicable	59	57.8
Management/intervention		
No intervention	58	56.9
Curative surgery	27	26.5
Palliative surgery	16	15.7
Neo-adjuvant chemotherapy	1	1.0
Adjuvant chemotherapy	5	4.9
Palliative chemotherapy	2	2.0
Radiotherapy	2	2.0

Most of the patients 56.9% (58/102) didn't have any intervention done on them. Only 10 (9.8%) patients could be operated on in fewer than 4 weeks. Curative surgery or tumour resection was done on 27 (26.5%) patients.

Palliative surgery applied to 16 (15.7%). Chemotherapy was rarely indicated, 5 (4.9%) patients got adjuvant, 2 (2.0%) had palliative and one patient had chemotherapy before surgery. Only two patient got radiotherapy abroad.

Patients Outcomes

Table 4: General view on the outcome of tumours.

	Oesophageal (N=14)		Gastric (N=64)		Intestinal (N=24)		Overall mortality
	Died	Alive	Died	Alive	Died	Alive	
First month	1 (7.1%)	13 (92.9%)	5 (7.8%)	59 (92.8%)	0 (0.0%)	24 (100%)	6 (5.9%)
Second month	5 (35.7%)	9 (64.3%)	16 (25.0%)	48 (75.0%)	0 (0.0%)	24 (100%)	21 (20.6%)
Third month	10 (71.4%)	4 (28.6%)	30 (46.9%)	34 (53.1%)	1 (4.2%)	23 (95.8%)	41 (40.2%)
Fourth month	10 (71.4%)	4 (28.6%)	31 (48.4%)	33 (51.6%)	2 (8.3%)	22 (91.7%)	43 (42.2%)
Fifth month	11 (78.6%)	3 (21.4%)	38 (59.4%)	26 (40.6%)	6 (25.0%)	18 (75.0%)	55 (53.9%)
Sixth month	11 (78.6%)	3 (21.4%)	42 (65.6%)	22 (34.4%)	6 (25.0%)	18 (75.0%)	59 (57.8%)

The mortality rate was high after 6 months of the period of follow-up. Seventy-eight per cent of patients who were diagnosed to have oesophageal cancer died within the first 6 months of follow up. Among patients who were diagnosed to have gastric tumours, 65.6% died at 6 months and 25% for intestinal tumours, after 6 months of follow up.

Discussion
This study aims at determining the outcome of gastrointestinal malignancies was the first documented to be conducted in Rwandan health facilities. While in Rwanda there is no population-based cancer registry, it is not easy to justify which malignancy is more frequent and deadliest especially in the field of alimentary tract diseases where endoscopy services are not easily accessible throughout the nation and the number of trained personnel in that matter is insubstantial.

In the present study, stomach cancer was by far the most frequent entity among patients undergoing endoscopy at Kigali University Teaching Hospital (62.7%), followed by colorectal and oesophageal cancers with 23.6% and 13.7% respectively. In one review of 714 cases of GI tumours in Nigeria, F. B Abdulkaleem et al demonstrated that colon cancer was more prevalent even if the study included more types of cancer and it didn't intend to highlight the outcome of these tumours (21).

In this study, oesophageal cancer was the deadliest cancer where 78.6% died after a follow-up period of six months. Colon cancer was likely to have a favourable clinical outcome.

Oesophageal cancer is a serious and deadly cancer and is the seventh leading cause of cancer death worldwide (6). Alcohol consumption and tobacco smoking are established risks for oesophageal cancer. Smokers have 5-fold risks and alcohol consumers have 1.8 to 7.4-fold risks depending on weekly volume (22). In our study population, only 2.9% were identified as alcohol consumers and none among patients who developed oesophageal cancer was reported as an active smoker. These findings were contradictory to prior studies. However, we held accountable that till recent passive smoking was significant in the Rwandan community and cannot be ignored.

The goals in the management of oesophageal cancer are not only to treat the underlying disease but also to relieve the obstructive symptoms. Esophagectomy remains the cornerstone in the treatment of early-stage oesophageal cancer, however, surgery alone is rarely curative for tumour invading beyond muscularis propria or loco-regional lymph nodes. The 5-year survival ranges between 15-25% and the best outcomes mainly depend on the early diagnosis (23).

With the above knowledge, multiple trials were conducted and only yielded controversial results. All the patients who presented with oesophageal cancer in our study had Squamous Cell Carcinoma and overall patients were impaired to do their daily activities (Karnofsky Scale 80% and 70%), which would explain a distant disease when patients presented for endoscopy.

Radiotherapy as a single modality has been identified as a treatment option for oesophageal cancer. Shioyama Y et al conducted a small trial of 17 patients with a clinical-stage I oesophageal SCC and the 5-year survival rate was 59%. However, in another trial, Launois et al showed is no difference between surgery alone and neoadjuvant chemotherapy where outcomes were similarly poor with a 5-year survival rate of 11.5% and 9.5% respectively (4).

None of our study participants was operated on. The outcome was mediocre with only 21.4% of patients alive after six months. We assumed our patients had an advanced stage of cancer and since interventions were inexistent in this study the survival rates were likely to be poor.

Incidence and mortality rates of gastric cancer are among the highest in Africa and estimates show that men are more affected than women (8). In Rwanda, Per Globocan, 8.3 in 10000 people are diagnosed to have gastric cancer and 8.0 of them will die of it (8). While we consider this incidence and mortality to be at eminent levels we still hold accountable that African, and more Rwandan, system of reporting is less efficient and diagnostic capacities are limited, though these figures might even be higher (8). Traditionally gastric cancer is rare before the age of 40 and in some reports, the highest prevalence was found between 75-79 years of age (24).

The current study shows that women generally were slightly more prone to contract cancers and we could not have a justification for this. And younger individuals were more diagnosed to have cancers. This is in support of one of the reports that stipulated in Africa some cancers is rising in the younger population notably gastric cancer (8).

Chronic dyspepsia, alcohol intake, smoking and familial history were found to be significant risk factors for gastric cancer among our study population. Walker et al reviewed the H. pylori status of patients presenting for gastroscopy at one of the tertiary level hospitals in Rwanda, and among findings were half of the patients with gastric carcinoma have a positive test (12). This is also evidenced by large studies conducted in different communities where H. pylori eradication has significantly reduced the occurrence of gastric cancer (15). This study didn't aim in testing H. pylori positivity among gastric cancer patients, however, given the frequent complaint of chronic dyspepsia and the burden of the infection in limited-resources nations and its

impact on the variation of clinical presentation, we counted significantly on this risk (24)(25).

The management of the overall of our study participants was short of standards where less than half of patients underwent any kind of surgical intervention. Most patients had a Computed Tomography requested to assess the extent of the tumour; it was reported that patients who had a deferred surgical intervention have presented at a late stage of the disease.

In studies where surgical intervention was performed at an earlier stage of cancer the outcome was favourable (26). However, at the advanced stages of cancer, even if chemotherapy and radiotherapy were added to surgery the survival rates were still not promising (26).

Most of the reports consulted in this review were having a superior time of study compared to a short period of six months we followed our patients. And yet, the outcome was still mediocre in our setting.

Some reviews that were conducted in countries where gastric cancer is much prevalent like China and Japan have shown that mass screening and initiation of improved guidelines for diagnosis and management of gastric cancer yielded to the detection of earlier stages of the disease and extended survival rates (8)(23).

Recent innovations, notably magnifying endoscopy, have increased the diagnostic yield of gastric cancer and sensitivity and specificity are very high. Even if those innovations are not accessible in resource-limited environments, some studies report traditional endoscopy to produce an acceptable diagnostic yield. In our study, 11 patients who were found to have tumours on endoscopy were identified as gastritis. A similar discrepancy might be due to poor biopsy technique and inadequate samples, or ineffective pathological specimen assessment.

Given that in Rwanda chemo-radiotherapy options are very limited, the early diagnosis with a similar approach would increase the outcome of patients with gastric cancer.

In the present study, colorectal cancer was fairly represented among the study participants. We could not find regional epidemiological and prevalence data but some reports have shown colorectal cancer in African subjects can present in the early decades of life and is frequently diagnosed at a very late stage (17)(27).

While in the West screening guidelines and treatment protocols are well designed for colorectal cancer, no standardized guidelines for screening and treatment of colorectal cancer in most African countries and so more in Rwandan health facilities.

In this study, most of the patients had tumours on the left colon and the frequent type was adenocarcinoma. The regional studies investigating the common location of colonic tumours and their types have yielded similar evidence (28) (29). Comparing the outcomes of studies cancers in this review, colorectal cancer patients had a better endpoint even if the study period was limited.

In Rwanda, a possible and easily accessible screening tool would be a flexible colonoscopy. One review that was conducted in economically and medically underserved population has shown that simple protocol and non-invasive tools are effective in detecting colonic benign and malignant lesions (29).

In the United States where modern health services are largely available, it is recommended for the general population to start colorectal cancer screening at the age of 50. With the available evidence, it is controversial whether screening should start earlier in the black population (19) and select population with increased risks and co-morbidities (29).

Overall, colorectal cancer is characterized by earlier presentation in life for our population and most of the patients seek care with an advanced clinical stage that impairs treatment options in resource-limited settings. Tight and improved guidance in screening and management would improve tremendously the outcomes (16) (29)(30).

Limitation of this study
This study was conducted at one endoscopy unit in Rwanda and the duration of follow up was limited to six months. A multicentre and extended study is necessary to verify our findings. Due to the nature and limited diagnostic capacities of hepato-biliary cancers we were unable to include them in our study.

Conclusion
With this study, we can stipulate that gastrointestinal cancers are more prevalent in a population aged above sixty years. Cancer of the stomach was much seen in our study population. All portions of the GI tract were affected but small bowel tumours were extremely rare.

Most of the patients presented for endoscopy were with symptoms of imminent GI disease and the outcome showed that there is a high mortality rate within 6 months Researchers are recommending the Minister of Health and other partners to invest in early diagnosis and treatment for a better outcome.

List of abbreviation

CHUK	Centre Hospitalier Universitaire de Kigali (Kigali University Teaching Hospital)
CT	Computed Tomography
ECCA	Extrahepatic Cholangiocarcinoma
ECF	Epirubicin, Cisplatin, 5-Fluorouracil
EGD	Esophagogastroduodenoscopy
EU	European Union
EUS	Endoscopic Ultrasound
HCC	Hepatocellular Carcinoma
GIT	Gastrointestinal Tract
ICCA	Intrahepatic Cholangiocarcinoma
mCRC	metastatic Colo-Rectal Cancer
MRI	Magnetic Resonance Imaging
NBI	Narrow-Band Imaging
NCCN	National Comprehensive Cancer Network
PET	Positron Emission Tomography
RCT	Randomized Controlled Trial
5-FU/LV	5- Fluorouracil/Leucovorin

Ethical Approval and participants consent.
The ethical approval was obtained from the University of Rwanda Ethics Committee. And the Kigali University Teaching Hospital Research Committee supervised this work. Every participant in this study signed a consent form before enrolment.

Prior Presentation
This work was selected to be presented as a poster during the 10th Consortium of Universities for Global Health conference in Chicago, Illinois.

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