

Upper Gastrointestinal Cancers in Rwanda: Epidemiological, Clinical and Histopathological Features in Patients Presenting to a Tertiary Referral Hospital

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Abstract

Background: Scant data on upper gastrointestinal cancers in Rwanda exist to guide potential prevention efforts. We evaluated the epidemiological, clinical and histopathological data among patients with gastric and esophageal tumors at a tertiary Referral Hospital in Rwanda. **Methodology:** We performed a retrospective review of histologically-confirmed esophageal and gastric cancers in adults age ≥ 18 yrs. old presenting to a university teaching hospital (Centre Hospitalier Universitaire de Butare) from 2014-2019. Variables included age at diagnosis, sex, clinical presentation, tumor location and histopathological type. **Results:** There were 149 upper gastrointestinal cancers, of which 137 (92%) were gastric and 12 (8%) were esophageal. Gastric cancer patients had a mean age at presentation of 56.9 ± 12.3 years (range 21 - 87). Presenting symptoms were epigastric pain (78.8%), weight loss (53.3%), post-prandial vomiting (52.6%), early satiety (29.9%), epigastric mass (24.8%), hematemesis (19.7%) and melena (16.8%). The location was antrum 50.3%, corpus 21.8%, fundus 8%, and cardia 8%. Tumor type was adenocarcinoma in 94.1%. *Helicobacter*



pylori infection was present in 108 (78.8%). Esophageal cancer patients had a mean age of 54.4 ± 9.5 years (range 35 - 72). Presenting symptoms were dysphagia (100%) and weight loss (83%). The most common site was lower third esophagus (9/12), and adenocarcinoma cancer subtype accounted for 5/12 (41.6%) cases. **Conclusion:** Gastric adenocarcinoma was the most commonly diagnosed upper gastrointestinal cancers and was associated with a high prevalence of *H. pylori* infection. This study lays the foundation for future work to improve cancer outcomes in Rwanda.

Keywords

Epidemiology, Upper Gastrointestinal Cancer, *H. pylori*, Rwanda

1. Introduction

Upper gastrointestinal (GI) malignancies remain a major global public health issue in both developed and developing countries [1]. Data from Globocan 2018 indicates that gastric cancer remains prevalent worldwide with over 1,000,000 new cases and an estimated 783,000 deaths in 2018 [2]. Adenocarcinoma of the gastric body is highly aggressive, representing one of the leading causes of deaths in the world. It is the fifth most frequently diagnosed cancer and the third leading cause of death worldwide [2] [3] but declining rapidly in the Western world. GISTs (gastrointestinal stromal tumors) are a rare form of gastric neoplasms and account for <1% of gastrointestinal tumors [4]. Esophageal cancer is the eighth most common cancer worldwide and the sixth most common cause of cancer-related death, ranking seventh in incidence (572,000 new cases) and sixth in overall mortality (509,000 deaths) in 2018 [2]. The majority of esophageal malignancies are squamous cell carcinoma (~70%), whereas esophageal adenocarcinoma counts for ~30%. Gastroesophageal reflux disease (GERD) and Barrett's esophagus are risk factors for esophageal adenocarcinoma [5].

Data on the incidence of gastric and esophageal cancers in Africa are as yet limited. Mali has the highest known incidence of gastric cancer with 9.5 cases per 100,000 inhabitants [6]. Burundi (East Africa), Rwanda's neighboring country, registered 395 cancers of all types over a one-year period. Gastric cancer comprised 14% of all cancers and 38.5% of all gastrointestinal cancers [7]. Studies of East African cancer registries and cancer genomics showed that gastric cancer ranks in the top ten malignancies in Rwanda's other neighboring countries of Uganda and Kenya [8]. The highest incidence of esophageal squamous cell carcinoma (SCC) in Sub-Saharan Africa is found in the southern and eastern regions [9]. Malawi exhibits the highest incidence rate globally, in both men and women. Esophageal SCC was reported in 2018 to be the leading cause of mortality in Kenyan men [2]. Kenya has one of the highest incidence rates of esophageal cancer in the continent with a rate of 17.6 per 100,000 [10].

Little is known about gastric and esophageal cancer in Rwanda [11]. In this

retrospective study, we aimed to assess the epidemiological, clinical and pathological features of gastric and esophageal malignancies among patients presenting to a tertiary referral center in Rwanda.

2. Methodology

Study design: This was a retrospective study of all patients presenting for consultation for potential upper GI cancer between June 2014 and June 2019, and for whom adequate information was available from the endoscopy unit, medical records, and pathology laboratory.

Study Setting: The study was conducted at Centre Hospitalier Universitaire de Butare (CHUB), a tertiary level hospital serving the Southern Province of Rwanda. This hospital has 400 beds and sees 120,000 patients annually with a catchment area of 140 km in Western and 120 km in Southern Province of Rwanda.

This is the main referral hospital which serves the Southern Province's population and others from some Districts of Western Province. The total population to be served by CHUB is more than 3,772,230 peoples according to the National Institute of Statistics of Rwanda (2012). The Gastrointestinal Endoscopy Unit performs 1600 - 1800 endoscopies annually.

Study Participants: Patients age 18 and older (consulting as in- and outpatient) during the study period with a final pathologic diagnosis of primary gastric or esophageal malignancy.

Data collection: Using the hospital electronic medical record database, we collected demographic (age of presentation, sex and district of origin), and clinical data (signs and symptoms and their duration), risk factors (*Helicobacter pylori* (*H. pylori*) infection with modified rapid urease test on biopsy specimens, chronic gastritis, gastric ulcer, smoking and alcohol and family history of gastric or esophageal cancer) and histological type of upper gastrointestinal cancer. A standardized data abstraction form was used to ensure consistency of data collection.

Inclusion Criteria: Age 18 or older, pathological diagnosis of primary cancers of the esophagus or the stomach.

Exclusion criteria: Lack of tissue diagnosis; patients with oral or pharyngeal cancers, small bowel or ampullary tumors or metastatic disease to the esophagus and/or stomach.

Data Analysis: Descriptive statistics were performed to evaluate frequency, percentages and means. All analyses were conducted using SPSS 16.0 software.

Human Subjects Protection: This study was approved by the Institutional Review Board and Ethical Committee of Butare University Teaching Hospital on 10/6/2019.

3. Results

Between 2014-2019, there were 149 cases of histologically confirmed upper GI cancers. Most patients were >50 years old (77%), with only a minority < 50 years old (23%). The peak incidence (36%) was between 51 and 60 years of age. *H. py-*

lori infection was present in 114 (76.5%) patients.

Gastric cancer

Of the 149 upper GI cancer, 137 (92%) were gastric tumors. The mean age was 56.9 ± 12.3 years (range 21 to 87 years). The 108 of 137 patients (78.8%) had *H. pylori* infection (Table 1) with an even distribution by sex (male: female ratio was 1.2:1). The most common symptoms were epigastric pain (78.8%), weight loss (53.3%), postprandial vomiting (52.6%), early satiety (29.9%), epigastric mass (24.8.8%) and hematemesis (19.7%) (Figure 1). The mean time from the

Table 1. Characteristics of the 149 patients found to have upper gastrointestinal cancers at a tertiary hospital in Rwanda.

	Gastric cancer (n = 137)	Esophageal cancer (n = 12)	Total (N = 149) (%)
Sex distribution			
Male	74 (54.0%)	9 (75.0%)	83 (53.0%)
Female	63 (45.9%)	3 (25.0%)	66 (47.0%)
Province of Origin			
West	22 (16%)	2 (16.0%)	24 (16.1%)
South	113 (82.5%)	9 (75.0%)	122 (81.8%)
Northern	0 (0%)	0 (0%)	0.0%
East	2 (1.4%)	1 (8.0%)	3 (2.0%)
<i>Helicobacter Pylori</i> status			
Positive	108 (78.8%)	6 (50.0%)	114 (76.5%)
Negative	16 (11.6%)	3 (25.0%)	19 (12.7%)
Not known	13 (9.4%)	3 (25.0%)	16 (10.7%)

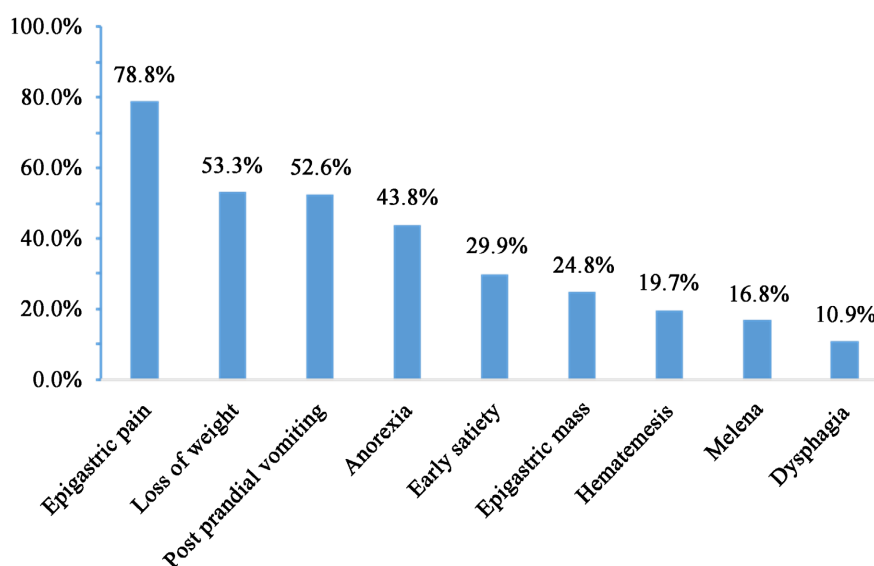


Figure 1. Presenting signs and symptoms among the 137 patients with gastric cancer.

onset of symptoms to diagnosis was 4 months.

Tumors localized to the gastric antrum (50.3%), corpus (21.8%), fundus (8%) and cardia (8%) (**Figure 2(a)**). Adenocarcinoma was the predominant histology (94.1%); gastrointestinal stromal tumors (GISTs) and mucosa-associated lymphoid tissue (MALT) lymphoma accounted for 1.4% and 1.4% of cases, respectively (**Table 2**). Intestinal, diffuse and mixed subtypes were 60.4%, 24.0% and 6.9% respectively based on Lauren classification that provides 2 major histological

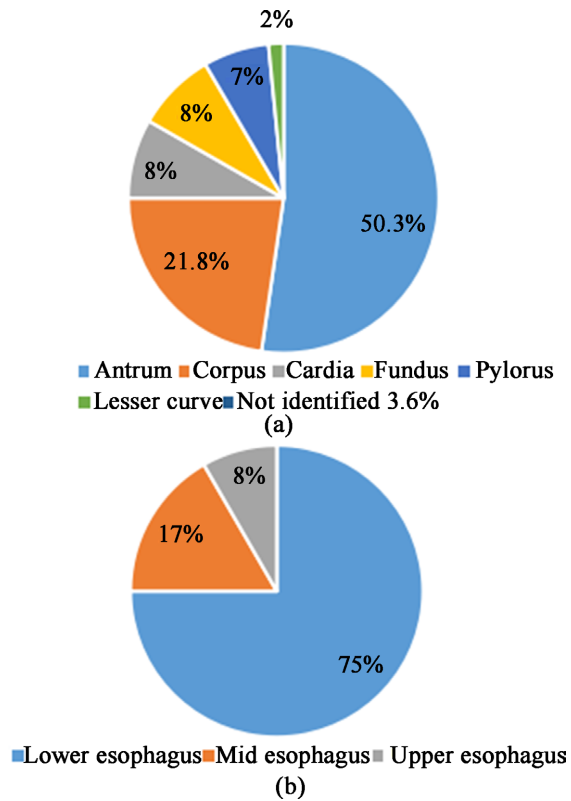


Figure 2. (a) Anatomic location of gastric cancers (N = 137); (b) Anatomic location of esophageal cancers (N = 12).

Table 2. Histological subtype of upper gastrointestinal cancer among the 149 patients found to have upper gastrointestinal cancers at a tertiary hospital in Rwanda (CHUB).

Gastric (n = 137)	No. of patient	Percentage (%)
Adenocarcinoma	129	94.1
MALT lymphoma	2	1.4
Squamous Cell Carcinoma	1	0.7
GIST tumor	2	1.4
Other	4	2.9
Esophageal (n = 12)		
Squamous Cell Carcinoma	7	58.4
Adenocarcinoma	5	41.6

subtypes (intestinal and diffuse) [12].

Esophageal cancer

Of the 149 upper GI cancers, 12 (8%) were esophageal cancers. The mean patient age was 54.4 ± 9.5 years with a range of 35 to 72. The male to female ratio was 3:1 (Table 1). Patients uniformly presented with progressive dysphagia (100%) and most had associated weight loss (83%). The mean time from the start of symptoms to diagnosis was 6 months. The distribution by anatomical location was 1/12 (8.3%) in the upper third, 2/12 (16.6%) in middle third and 9/12 (75%) in distal third of esophagus (Figure 2(b)). Seven (58.4%) were SCC and 5 (41.6%) were adenocarcinoma (Table 2).

4. Discussion

The data from this retrospective study performed at an academic referral hospital in Rwanda, suggest that the incidence of gastric cancer far surpassed that of esophageal cancer and that in most patients it was associated with active *H. pylori* infection. In this small series, there was a male predominance of esophageal cancer, similar to other parts of the world, including the US (78% male 22% female) [13].

Gastric cancer

The rate of *H. pylori* infection in gastric adenocarcinoma was 78.8%, almost the same as the rate of 75% found by Walker *et al.* in the same general population [11]. Given that *H. pylori* infection is a well-defined carcinogen in the development of gastric cancer [14] [15] [16], population-level efforts to eradicate *H. pylori* may be one step to addressing gastric cancer in Rwanda. Liou *et al.* showed that the eradication of *H. Pylori* infection would be effective approach for gastric cancer prevention [17] and similarly Lee *et al.* showed that mass eradication of *H. Pylori* infection has the benefit of gastric cancer prevention and reduced incidence of other gastric diseases [18]. However, Sonnenberg showed that the costs-benefits, including the potential impact on the development of antibiotic resistance and many other factors, may hinder the feasibility and desirability of such an approach [19]. In addition, other factors, including smoking of tobacco, are known to play a role in gastric cancer [20].

In our study, there was inadequate documentation on other risk factors limiting our ability to report on these. The potential role of dietary risk factors (e.g., nitrosamines) and obesity as potential major confounders for various malignancies should be incorporated in future studies.

The sex distribution of gastric cancer in other regions of Africa is slightly different from ours. Ankouane *et al.* showed a male predominance of 3:1 in Yaounde, Cameroon [14] and Fehim *et al.* showed a male predominance of 1.36:1 in Algeria [3]. The lag time from the onset of symptoms to diagnosis was reported in other sub-Saharan countries and low income setting [6] [21] [22] [23] similarly to what we found. The frequency of symptoms is supported by other studies in Africa [3] [7]. Kadende *et al.* found that the most common presentations of gas-

tric cancer were epigastric pain (77.5%), post-prandial vomiting (42.5%), loss of weight (42.5%) and epigastric mass (22%), almost identical to ours [7]. In our study, the most common site of gastric cancer was antrum (50.3%), similar to other reports [3] [7] [24] and in contrast to Western studies, where there is a higher incidence of gastro-esophageal junction tumors [25]. GERD (Gastroesophageal reflux Disease) is a risk factor for both esophageal adenocarcinoma and gastric cardia adenocarcinoma [5] [20], however we were not able to assess for GERD within this retrospective study.

With regard to histological type, we found that adenocarcinoma was the commonest type of gastric cancer (94.1%). This result is similar to the one that Ndamba E. *et al.* found in Cameroon [6], Fehim *et al.* found in Algeria [3] and to the one that Das *et al.* found in Bangladesh [26]. GIST was a rare type of gastric cancer in our cohort (1.4%), similar to the low frequency shown by Smith *et al.* in Morocco, where they found only 3% of 725 cases of gastric tumors [27]. In addition, Patel *et al.* showed in their review in the USA an overall 0.70 per 100,000 people per year (2001-2015) [28] while Fehim *et al.* (Algeria) found that 7.5% of gastric cancers were GIST [3].

Esophageal cancer

Esophageal cancer was less common in our study population. Chbani *et al.* in their retrospective review in Morocco showed similar results with 67 cases of esophageal cancer and 332 cases of gastric cancer [29].

The mean age was 54.4 + 9.5 years, similar to the findings of a retrospective studies in Kenya by Gatei *et al.* [30] and Tettey *et al.* in Ghana [31]. The male to female ratio was 3:1, similar to that reported by Mchembe *et al.* with 2.2:1 in Tanzania [32] and by Okello in Uganda [33]. The lag time from symptoms to diagnosis is similar that reported in other sub-Saharan countries with lower socioeconomic status [31] [32] [34].

H. Pylori was positive in 50% of patients with esophageal adenocarcinoma. Whether the presence of *H. pylori* is coincidental based on high prevalence in Rwanda overall or somehow associated with associated adenocarcinoma is unknown. Two studies have found *H. Pylori* to be a potential indirect cause of the development of esophageal adenocarcinoma [35] [36], though further definitive studies are needed.

Dysphagia and loss of weight were common manifestations of esophageal cancers in our cohort, similar to findings by Mchembe *et al.* in Tanzania [32] and Gibbs [37]. A study of esophageal cancer at a tertiary care teaching college in India found that dysphagia was the most common symptom (86%) [38].

In our study population, 9 (75%) of the 12 of esophageal tumors were localized to the distal esophagus, similar to what was found by Tettey *et al.* in Ghana [31] and Chbani *et al.* in Morocco [29]. However, Mchembe *et al.* showed different findings with a predominance localization in the middle third esophagus (58.5%) [32].

Squamous cell carcinoma was the predominant histological type with 58%

(7/12), similar to other studies from Africa by Mchembe *et al.* [32], Ntagirabiri *et al.* (Burundi) [39] and Kachala [40], and from Eastern Africa and Eastern Asia [34] [41] [42] [43]. This finding is in marked contrast to data from the USA where “Barrett’s type” of esophageal adenocarcinoma predominates over squamous cell carcinoma, 67% vs. 33% [13]. However, in our study, we could not determine from endoscopy reports whether adenocarcinoma of lower third of esophagus was believed to be secondary to gastroesophageal reflux disease (Barrett esophagus) or secondary to other risk factors of esophageal cancer.

Strength and Limitations

The strengths of our study include that it is the first clinical epidemiological study of upper GI cancer in Rwanda. All described diagnoses were confirmed by pathology. We acknowledge certain limitations. This study was retrospective so we only could obtain information only from the medical record and relied on the accuracy of data capture within the medical record. Symptoms of esophageal reflux disease (GERD) were neither available, nor other potentially relevant factors such as dietary exposures, family history of cancers, or socioeconomic status. We are uncertain to what extent similar patients may have died at home or in regional medical centers. Because of potential selection bias, we are unable to use data from our study to estimate population level incidence rates.

5. Conclusion

Gastric cancer was diagnosed more frequently than esophageal cancer. There was a high prevalence of *H. pylori* infection among gastric cancer patients. Our patient population was remarkable for its younger age and advanced stage of disease at presentation. Insufficient access to diagnostic centers represents significant barriers to care. Etiologic factors must be addressed: Eradication of *H. pylori* infection at least in symptomatic patients should be considered. Increased and more accessible endoscopic care must follow. By describing the epidemiology of upper gastrointestinal cancers, our study lays the foundation for future prospective studies of outcomes, predictors of treatment response and the resources required to reach community healthcare goals.

Ethics Approval and Consent to Participate

The approval was obtained from Ethical and Research committee of Butare University Teaching Hospital.

Availability of Data and Materials

The datasets used during the current study are available from the corresponding author on reasonable request.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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List of Abbreviations

- AC:** Adenocarcinoma
CHUB: Centre Hospitalier Univesitaire de Butare
EGD: EsophaGogastroDuodenoscopy
GERD: Gastroesophageal Reflux Disease
GI: Gastrointestinal
GIST: GastroIntestinal Stromal Tumor
MALT: Mucosa-Associated Lymphoid Tissue
SCC: Squamous Cell Carcinoma
SPSS: Statistical Package for the Social Sciences

Data Abstraction Form

I. Demographic data

1. Patient ID.....
2. Age group (in years): 1) <20 2) 20 - 30 3) 30 - 40
 4) 40 - 50 5) 50 - 60 6) 60 - 70
 7) >70
3. Sex : Male/Female
4. Province and District of origin:
5. Medical insurance: Yes/No

II. Clinical data

- 1) Epigastric pain
- 2) Post prandial Vomiting (GOO)
- 3) Difficulty swallowing
- 4) Loss of weight
- 5) Hematemesis
- 6) Melena
- 7) Others.....

III. Duration of symptoms

- 1) < 6 months
- 2) > 18 months
- 3) 6 - 12 months
- 4) 12 - 18 months

IV. Anatomical location of the tumor (Endoscopy findings)

1. Esophageal tumor: a) upper third b) Middle third
 c) Lower third
2. Gastric Cancer: a) cardia b) fundus c) Corpus
 d) Antrum e) Pyrolus f) other.....

V. Histological (Biopsy) feature of the cancer

1. Esophageal Cancer: a) SCC b) Adenocarcoma c) other.....
2. Gastric cancer: a) Adenocarcinoma b) MALT lymphoma
 c) SCC d) GIST tumor
 e) Linitus plastic

VI. *H. pylori* status

1. Positive
2. Negative
3. Not Documented

Data Collectors:

Dr. Shikama Felicien (author) or Dr. Ndayisaba Prosper (co-author)

END