

High rates of gastroesophageal cancers in patients with dyspepsia undergoing upper gastrointestinal endoscopy in Uganda

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ABSTRACT

Background and study aims Dyspepsia is the most common presenting symptom in the gastrointestinal clinic of

Mulago National Referral hospital. The etiology is essentially not fully described in our patient population. This study was therefore conducted to establish the causes of dyspepsia based on endoscopic diagnosis among patients with dyspepsia seeking care at the National Referral hospital of Uganda.

Patients and methods This retrospective study conducted in the endoscopy unit of Mulago hospital reviewed 356 patient endoscopy reports spanning January 2018 to July 2020 with a focus on those with a referral indication of dyspepsia. Age and sex were the independent variables of interest while the endoscopy findings as reported by the endoscopist were the outcome variable of interest.

Results Of the 356 endoscopy reports reviewed, 159 met the inclusion criterion of dyspepsia as the indication. Participant mean age was 47.7 years (± 16.53) with the majority (25.79%) in the fifth decade while the male to female ratio was 1. The majority of patients had organic dyspepsia (90.57%) while the commonest finding was gastritis 69 (43.4%). Gastroesophageal cancers represented (18) 11.32% of all findings. There was a positive association between age >50 years with gastroesophageal cancers (7.639) as well as age <50 years and functional dyspepsia (2.794); however, all these were not statistically significant ($P=0.006$ and $P=0.095$, respectively).

Conclusions Organic/structural dyspepsia comprises over 90% of investigated dyspepsia with 11% comprising cancer among patients seeking endoscopy at the National Referral Hospital of Uganda.

Introduction

Dyspepsia, which by definition is the presence of one or more of the symptoms of epigastric pain, bloating, post-prandial fullness, early satiation, and retrosternal pain [1], is estimated to affect up to 50% of individuals globally [2] with an estimated higher prevalence in low and middle income countries, particularly Africa with the highest prevalence of uninvestigated dyspepsia [3]. In one community study conducted in rural Uganda, more than 50% of the respondents reported having had symptoms of dyspepsia [4]. The majority of dyspepsia in Africa is un-

investigated with patients often treated symptomatically. This creates a challenge as treatable diseases including malignancies are often missed only to present in very advanced stages. The paucity of information on dyspepsia in sub-Saharan Africa (SSA) also affects development of clinical and policy strategies of mitigating causes including cancer of the stomach which is the most prevalent gastrointestinal malignancy in SSA. SSA is projected to have a more than 73% increase in gastrointestinal cancers by 2030, way more than the 59% global estimate [5]. With uninvestigated dyspepsia masking this growing burden, there is a need to fully understand the characteristics of dys-

peptic symptoms in our population seeking care for dyspepsia. In one study in western Uganda, the majority of dyspeptic patients had gastritis [6] while in a study done in Kenya a significant majority had functional dyspepsia [7], contrasting with a study in Nigeria where only 8% of the participants had functional dyspepsia [8]. Other studies conducted in Uganda are representative of specific regions [9] and therefore non-generalizable. This variability in findings, therefore, warrants a characterization of dyspepsia in Uganda at a national referral center that receives a more diverse patient population from all regions in Uganda. This research, therefore, characterizes the etiology of dyspepsia as seen on upper gastrointestinal endoscopy of patients seeking care at the National Referral Hospital of Uganda.

Patients and methods

This was a retrospective study conducted in the Endoscopy Unit of Mulago National Referral Hospital of Uganda. This hospital has a bed capacity 1500 at any given time and has 100% occupancy consisting of primarily referrals from other hospitals around the country. The gastrointestinal outpatient clinics comprise one medical and one surgical outpatient unit, which are attended by patients referred from other hospitals with an average attendance of 2500 to 3000 patients per year. It is from this population that patients referred for upper gastrointestinal endoscopy are sent to the endoscopy unit. The endoscopy unit also directly receives referrals from other hospitals in the region.

Despite receiving patients from all over the country, the majority of patients seeking care at the endoscopy unit are from the surrounding central region of Uganda. Endoscopy services are provided by experienced physicians and surgeons in the unit and the diagnoses made are based on their observation of the clinical characteristics of the disease entity. Where necessary, biopsies are performed on suspicious tissues for further evaluation. For gastritis, “endoscopic gastritis,” which refers to the diagnosis of gastritis based on observations seen on endoscopy, was the primary method of diagnosis and in severe forms, biopsy with histological diagnosis of gastritis would be performed. Diagnosis of gastritis is occasionally further classified into superficial, hemorrhagic, erosive, atrophic, and metaplastic.

Endoscopy reports of all patients that underwent an upper gastrointestinal endoscopy procedure between January 2019 and January 2020 were reviewed. The referring doctor’s diagnosis or reason for recommending an endoscopy as written on the referral note was reviewed for inclusion in the study.

Inclusion criteria

Referral reports with the diagnosis or reason for referral registered as either dyspepsia or uninvestigated dyspepsia by the referring doctor were included in the study. For referral notes that had a different diagnosis besides dyspepsia, the diagnosis or reason for referral was compared to the definition of dyspepsia based on the ROME IV criteria [10] of having any of the following: epigastric pain, epigastric fullness, early satiety, or burning epigastric pain. When the referral reason or diagnosis met the

► **Table 1** Participant demographic characteristics.

Parameter	Frequency	Percentage or $\pm$ SD
Age		
<30	29	18.24
31–40	27	16.98
41–50	28	17.61
51–60	41	25.79
60–70	17	10.69
>70	17	10.69
Mean age	47.698	$\pm$ 16.53
Sex		
Male	79	49.69
Female	80	50.31

ROME IV criteria, the patient was included in the study. Reports whose reason for referral was reported that did not meet the inclusion criteria, including some listed as dysphagia, odynophagia, gastrointestinal bleeding, or screening endoscopy, all were excluded from the study. For referral notes in which more than one reason was included, such as dysphagia with dyspepsia, these were also included as long as the indication of dyspepsia was included in the referral note/endoscopy request. The endoscopies were performed by qualified endoscopists in the unit.

The primary outcome variable of interest was the endoscopic diagnosis as reported on the endoscopy report by the endoscopist. The findings were classified as organic/structural if a physical lesion was observed on endoscopy while the presence of normal findings was classified as functional dyspepsia. Other variables included the participant demographics including the age, sex, tribe, and region.

Variables were captured in an Epi-data database and later exported to Stata 16 software for analysis. Statistical analysis took on a descriptive approach. All variables were categorical and therefore described using proportions along with their percentages.

Results

In total, 356 patient endoscopy reports were evaluated and of these, 159 met the inclusion criteria.

The male to female ratio of the study population was one while the mean age was 47.70 years ($\pm$ 16.53) with the majority (25.79%) in the fifth decade of life (► **Table 1**). On the primary outcome variables of the endoscopic diagnosis, 90.57% of patients had organic dyspepsia, meaning that there was a diagnosis of a structural disease while 9.43% of the participants had normal findings despite the dyspeptic symptoms (► **Table 2**), a condition referred to as functional dyspepsia.

The most common findings on endoscopy were gastritis followed by gastroesophageal reflux disease. Gastroesophageal

► **Table 2** Endoscopic findings.

Diagnosis	Frequency	Percentage
Normal findings	15	9.43
Gastritis	69	43.4
Gastric ulcers	3	1.89
Duodenal ulcers	5	3.14
Hiatal hernia	4	2.52
GERD	31	19.5
Gastric cancer	11	6.92
Esophageal cancer	7	4.40
Esophagitis	2	1.26
Others	12	7.55

GERD, gastroesophageal reflux disease.

► **Table 3** Dyspepsia classification.

Dyspepsia classification	Frequency	Percentage
Functional dyspepsia	15	9.43
Organic dyspepsia	144	90.57

cancers (gastric and esophageal cancer) comprised 11.32% of all diagnoses (► **Table 3**). Of the 18 patients who had a diagnosis of gastrointestinal cancer, 61 % had gastric cancer while the rest had esophageal cancer (► **Table 4**).

On evaluation for the association between the two independent variables of age and sex with the primary outcome variable, age was stratified into two categories: <50 years and >50 years. We found no association between age and gastritis with a chi square coefficient of 0.612 while the presence of gastroesophageal cancers was strongly associated with age >50 years with a positive coefficient of 7.639 ($P=0.006$) while that of functional dyspepsia was 2.794 ($P=0.095$). However, these variables were not statistically significant in our study population. In regard to the location of the cancer, there was no association with age or sex. Similarly, there was no association between sex and the overall endoscopy diagnosis.

Discussion

We conducted this study with the intention of describing endoscopy findings among patients who underwent upper gastrointestinal endoscopy for dyspepsia as it is the most common presenting symptom and indication for upper gastrointestinal endoscopy at the Gastrointestinal Surgery Clinic in Mulago National Referral hospital in Uganda.

We found that the majority of patients who presented for upper gastrointestinal endoscopy were aged 51 to 60 years. In Uganda, it is recommended but not mandatory that the presence of dyspeptic symptoms should be investigated with

► **Table 4** Location of gastroesophageal malignancies.

Tumor type and location	Frequency (N)	Percentage (%)
Esophagus (7)		
Proximal third	1	5.56
Mid third	5	27.78
Distal third	1	5.56
Stomach (11)		
Upper stomach (cardia and upper body)	3	16.67
Middle stomach (angle, middle body)	3	16.67
Lower stomach (lower body, antrum, pylorus)	5	27.78

endoscopy in patients aged >50 years. The public health training and awareness campaigns about gastric cancer could explain the higher proportion in this age group. Globally screening for gastroesophageal cancers is recommended in dyspeptic patients aged >40 years [11, 12] and this is in keeping with our findings.

Our study reveals a very high prevalence of organic dyspepsia of >90% which could imply that by the nature of our study setting being a national referral hospital, the most severe and persistent symptomatic patients could possibly be the ones seeking care at the national referral hospital, and hence, likely to have more organic causes. This, therefore, is a potential source of bias. Second the majority of referrals often come late, due to either financial constraints associated with the procedure or perceptions such as disease progression after biopsy. All these could explain the high rate of organic dyspeptic findings being representative of late presentation. However, when the prevalence of organic dyspepsia among patients with dyspepsia is compared with studies conducted in the African region, there is a striking similarity. In Kenya, the prevalence was slightly lower at 8% [7], implying a 92% prevalence of organic dyspepsia. while in a similar study in Ibadan, Nigeria, the prevalence of functional dyspepsia among dyspeptic patients was lower at 6% [13], implying a prevalence of organic dyspepsia of 94%. Overall, the global prevalence of functional dyspepsia is approximately 11% to 29.2% [3]. Our findings along with the studies in SSA demonstrate that the majority of dyspepsia is due to an organic cause.

The finding that gastritis was the most prevalent condition in our study population was not surprising as it is similar to the described findings in other regions of Uganda [6] and SSA [14, 15]. Not surprisingly, there was no association between the age and sex in gastritis or any other endoscopic findings among the study population.

Gastroesophageal cancer presentation, especially in early stages, mimics any other benign causes of dyspepsia [16], hence increasing the likelihood of missed early diagnosis [17] in patients with dyspepsia. In our study population, the preval-

ence of gastroesophageal cancers among patients with dyspepsia was rather strikingly high at 11.32% when compared to larger studies in Hong Kong [18] and Canada [19], in which the prevalence was less than 1%. However, it should be noted that the above studies had a significantly larger sample size. Nevertheless, these findings raise a red flag for a potentially higher prevalence of gastroesophageal malignancies among dyspeptic patients in Uganda. This further emphasizes the need for more purposeful investigation for gastroesophageal malignancies in patients in SSA who present with dyspepsia, especially in the fourth decades and above.

It is projected that SSA will have the highest burden of gastroesophageal cancers globally by 2030 [5] and this is a red flag our results seem to agree with. Typically esophageal cancer presents with dysphagia and patients with dysphagia were excluded; however, it's important to recognize that dyspepsia, especially retrosternal pain, may point towards early esophageal cancer, hence requiring early screening [20].

Conclusions

More than 90% of dyspepsia in patients seeking care in Mulago hospital is associated with a structural/organic lesion, including gastritis, among other causes. There is a higher prevalence of gastroesophageal cancer among patients with dyspepsia who are aged >50 years. We recommend that patients aged >50 years who have dyspepsia that has not been investigated undertake a mandatory endoscopic evaluation as the likelihood of having a gastroesophageal malignancy in this population is very high.

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Competing interests

The authors declare that they have no conflict of interest.

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