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Gastric outlet obstruction among adult patients at two Rwandan referral hospitals: Etiology, *H. pylori* infection and outcomes

M.K. Kabuyaya[1], R. Ssebuufu[2,3], B. Asiimwe-Kateera[3], M. Nyundo[1,3], J. Rickard[1,4].
[1]University Teaching Hospital of Kigali, 1024 Rue de la Paix, Kigali, Rwanda
[2]University Teaching Hospital of Butare, PO Box 254Huye, Southern Province, Rwanda
[3]University of Rwanda, College of Medicine and Health Sciences, PO Box 3286, Kigali, Rwanda
[4]RwandaHumanResources for Health Program, PO Box 84, Kigali, Rwanda
***Correspondence to**:* Kabuyaya K. Médard, Email: jeakkame@gmail.com

Background: ***Gastric outlet obstruction (GOO) is characterized by persistent non-bilious vomiting due to obstruction at the pylorus. GOO is associated with Helicobacter pylori through both malignant and benign processes. The objective of this study was to determine the epidemiology of gastric outlet obstruction in Rwanda.***
Methods: ***A cross-sectional descriptive study was undertaken on patients with GOO seen over a 12-month period. Patients' demographics, histopathology, H.pylori infection and mortality, were analyzed using Chi-square (χ2) test and logistic regression. Mortality was assessed with a minimum follow up of 3 months.***
Results: ***A total of 82 patients presenting with GOO were studied. The rate of H.pyloriinfection was 61%. Malignant histopathology was found in 67% of patients. Bivariate analysis showed that pylori infection was associated with a benign histopathology (X^2 =4.77, p=0.029). Logistic regression showed that malignant histopathology was associated with decreased survival (Odds Ratio = 0.072, 95% Confidence Interval = 0.018-0.289, p< 0.001). There was no statistically significant difference in mortality between surgical and non-surgical patients with malignant histopathology (X^2=1.41, p= 0.495).***
Conclusions: ***Malignancy is a common cause of GOO in Rwanda and is associated with increased mortality whether treated surgically or non-surgically. Over 50% of patients with GOO in Rwanda were infected with H pylori.***

Introduction

Gastric outlet obstruction (GOO) describes a clinical condition represented by any disease process causing mechanical obstruction to gastric emptying, including both benign or malignant conditions[1].The incidence of GOO is not precisely known but in developed countries it has been estimated at 5% among patients with benign conditions and in peripancreatic malignancy it has been reported at 15-20%[2]. GOO in developed countries is predominantly associated with malignancy[3]. However, in developing countries such as Ethiopia, the majority of studies report a benign aetiology[4]. *Helicobacter pylori* infect the stomach and produce an inflammation that may contribute to complete or incomplete obstruction of the distal stomach, pylorus or proximal duodenum[5]. The prevalence of *H. pylori* infection among patients with GOO in developed countries is approximately 69%[6]. In Rwanda the prevalence of *H.pylori* among patients undergoing endoscopy was 75%[7].

The majority of patients with GOO often seek medical care late when the patient is dehydrated and nutritional status is compromised(4). A study conducted in Netherlandson patients with advanced malignant GOO reported a post-operative mortality rate of 95%(8). GOO in Rwanda is a common medical condition. However, the causes of GOO and short-term outcomes of surgery have not been adequately studied. Further information is needed to address this public health
The aim of this study was to identify the etiology of GOO, the rate of *H.pylori* infection in patients with GOO and the short-term outcomes for those undergoing surgery at the University Teaching Hospitals of Kigali and Butare.

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Patients and Methods

This was a descriptive cross-sectional study involving patients with a clinical diagnosis of GOO conducted at the University Teaching Hospitals of Kigali and Butare over a twelve-month period (April 2013 to March 2014). All patients with a diagnosis of GOO confirmed by endoscopy or laparotomy were included. Pediatric patients (<15 years old) and those without biopsy results were excluded from the study. The University Teaching Hospitals of Kigali (CHUK) and Butare (CHUB) are national referral and teaching hospitals in Rwanda. CHUK has a bed capacity of 586 with a catchment area of more than 11 million people. CHUB has a bed capacity of 329 and a catchment area of more than 2 million people.

A trained physician performed all endoscopic procedures. GOO was suggested by the inability to progress the endoscope through the pylorus or intubate the duodenal bulb. For patients who underwent laparotomy, the diagnosis of GOO was made by the surgeon noting a protruding mass in the antrum, a cicatrized first part of duodenum, or a pylorus with a dilated and thick-walled stomach. To identify the underlying cause of GOO two biopsies were taken from the antral mass and two more away from the lesion. Biopsy specimens were immediately fixed in 20% formalin and sent for histopathological analysis. Specimens were analyzed at the King Faisal Hospital, University of Rwanda Pharmaceutical Research Laboratories in Rwanda and/or and the Brigham and Women's Hospital USA.

H.pylori infection was diagnosed immediately at endoscopy by performing a modified rapid urease test (MRUT) to fresh biopsies taken from the mucosa of the stomach, distant from the antral mass. The MRUT test materials were freshly made following the description of Katelaris et al, who found a test sensitivity of 97% and specificity of 95%(9). After endoscopy, patients were either placed on the theatre waiting list or underwent immediate laparotomy.

The choice of surgical procedure was at the discretion of the operating surgeon. The most common surgical procedure was gastrojejunostomy with one patient undergoing antrectomy and gastrojejunostomy (Billroth II).All patients were telephoned at least once per month for a minimum of three months for follow up and document the patient's status.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 16.0 for Windows. Frequencies and percentages were reported for categorical variables. Age was evaluated as a categorical variable. Factors associated with benign or malignant etiologies of GOO were assessed using the Chi-squared test. Bivariate analysis of factors associated with mortality was performed using the Chi-squared test. A p value <0.05 was considered to be statistically significant. For those patients who survived, data from the date of last contact was used.

Ethical approval was obtained from the School of Medicine, College of Medicine and Health Sciences at the University of Rwanda as well as from the Ethical Review Board at the University Teaching Hospital of Kigali. Informed consent was obtained from all patients or the witness of patients enrolled in the study.

Results

Eighty-two (82) patients were diagnosed with GOO. The majority (76%) were farmers. 54 (66%) patients were older than 50 years of age and 58% were male (Table 1). 50% completed primary school education. Most patients (98.8%) reported epigastric pain, intermittent non–bilious postprandial vomiting, and weight loss. The mean duration of epigastric pain was 27.5 months (SD: 36.8).Sixty-seven percent (67%) of patients reported using a combination of modern (antibiotics and proton-pump inhibitors) and traditional medicine prior to presentation.

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Table 1. Characteristics of patients presenting with gastric outlet obstruction

	Frequency	Percentage
Demographics		
Age		
<50 years	28	34.1
>50 years	54	65.9
Gender		
Male	48	58.5
Female	34	41.5
Aetiology		
Malignant	55	67.1
Intestine	48	58.5
Diffuse	7	8.5
Benign	27	32.9
Chronic gastritis	21	25.6
Erosive gastritis	3	3.7
Other	3	3.6
H. pylori		
Positive	50	60.9
Negative	32	39.1
Management		
Non operative	47	57.3
Benign	15	18.3
Malignancy	32	39.0
Surgery	35	42.7
Benign	12	14.6
Malignancy	23	28.0
Outcomes		
Survival	41	55.4
Mortality	33	44.6

Table 2. Factors associated with etiology of GOO

	Benign	Malignant	X^2	P value
Age				
<50 years	12 (14.7%)	17 (20.7%)	1.89	0.168
>50 years	15 (18.3%)	38 (46.3%)		
Gender				
Male	18 (21.9%)	30 (36.5%)	1.09	0.295
Female	9 (10.9%)	25 (30.5%)		
H.pylori				
Positive	21 (25.6%)	29 (35.4%)	4.77	0.029
Negative	6 (7.3%)	26 (31.7%)		

Overall, 55(67.1%) cases of GOO were associated with malignancy, while 27(32.9%) cases had a benign etiology. Chronic gastritis was the most common diagnosis in benign disease, accounting for 21(25.6%) cases of GOO. Intestinal type accounted for the most common malignant etiology

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with 48(58.5%) cases of GOO. *H.pylori* was detected in 50 (61%) patients. Bivariate analysis showed *H.pylori* infection to be significantly associated with a benign etiology of GOO ($\chi 2$ =4.77, p=0.029) (Table2).

A total of 35 (43%) patients underwent surgical treatment for GOO. Of these, 23 (66%) had a malignant etiology while the remainder were benign. Most patients (97%) underwent gastrojejunostomy with only one patient undergoing antrectomy and gastrojejunostomy (Billroth II).

Table 3. Outcomes and relationship to epidemiologic and clinical characteristics

	Survival	Mortality	OR	95% CI	P value
Age					
< 50 years	19 (25.6%)	8 (10.8%)	2.633	0.833-8.318	0.050
> 50 years	22 (29.7)	25 (33.7%)			
Gender					
Male	23 (31.1%)	19 (25.6%)	0.94	0.34-2.64	0.898
Female	18 (24.3)	14 (18.9)			
Aetiology					
Malignant	17 (20.2%)	30 (49.5%)	0.072	0.018-0.279	<0.001
Benign	24 (32.4%)	3 (3.85%)			
Management					
Non operative	23 (31.1%)	16 (21.6%)	1.36	0.49-3.78	0.495
Surgery	18 (24.3%)	17 (22.9%)			

A follow up period of at least three months was possible in 74 of 82 (90%) patients with GOO. The eight patients (10%) lost to follow up all had malignant disease. The overall mortality rate at three months of follow up was 44.5% (Table 1).Bivariate analysis showed that age greater than 50 years ($\chi 2$=3.85, p= 0.050) and malignant etiology of disease ($\chi 2$= 19.29, p<0.001) were associated with increased mortality. Multivariate logistic regression revealed that a malignant aetiology of GOO was associated with decreased survival compared to benign causes (OR= 0.072, 95%CI=0.018-0.279, p<0.001) (Table 3).In patients with malignancy, the 3-month survival was not statistically different between those operated on and those not ($\chi 2$=1.41, p=0.495) (Table 3).

Discussion

GOO is a common surgical problem in Rwanda and poses many challenges to the general surgeon. A recent study in Rwanda of 961endoscopies found the prevalence of GOO to be relatively high at 10%, compared with other settings[7]. The current study was conducted to identify common etiologies of GOO, the rate of *H.pylori* infection in patients with GOO and the short-term outcomes for those undergoing surgery. To date, these problems have not been adequately studied in Rwanda.

Two thirds of patients were found to have a malignant etiology of GOO. This finding is similar to other studies in developing countries such as Tanzania, Pakistan and India[10, 11, 12]. It contrasts with studies in Nigeria and Ethiopia[13, 14]. Rwanda is situated in the Great Lakes region of Africa where the incidence of gastric cancer is high (3.2 per 100,000) and previous studies have shown that Rwanda has a high incidence of gastric cancer (13 to 15 per 100,000)[14].In developed countries, the predominance of malignancy is theorized to be due to a declining rate of benign etiologies secondary to the early identification and treatment of *H.pylori* and the use of proton

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pump inhibitors[3]. However, it is unknown whether the same principle applies in sub-Saharan Africa.

Of malignant specimens in our study, 87% showed intestinal type disease. This type has been frequently identified in distal gastric biopsies and in populations at high risk for gastric cancer[15]. Similar findings of intestinal type were predominant (62.9%) in a study conducted in Japan[16]. In Uganda, intestinal metaplasia was observed in the majority of Nyarwanda and Nkole tribes[17]. In contrast, in China a study examining the biopsies of gastric carcinoma revealed 47.8% of patients had diffuse-type[18]. The increased rate of intestine -type disease found in Rwanda could be attributed to the high rate of *H. pylori* infection (61%), which is a known risk factor. A meta-analysis conducted in Japan reported that each year, 5% of *H.pylori* positive patients develop gastric cancer[19].

In this study, the prevalence of *H. pylori* among patients with GOO was 61%. Previous endoscopic studies conducted in Rwanda showed a prevalence of *H.pylori* of 75% in all patients (9, 20). In developed countries the variation in prevalence of *H.pylori* infection among patients with GOO ranges from 33 to 69%[6, 21]. The disparity in prevalence rates could be related to variations in the sensitivity of the test used and the underlying cause of GOO. Kate et al found the prevalence of *H.pylori* to be 91% after using multiple testing including serology, histology and rapid urease test among patients with GOO and active ulcers in the duodenum[22]. Our findings are similar to previous data reported in Rwanda and confirm prior reports that *H. pylori* infection is significantly associated with benign etiology of GOO[23].

There was no statistically significant association between malignant etiology of GOO and *H.pylori* infection. *H.pylori* is one of many independent factors in gastric carcinogenesis which has been reported in several case-control studies[24].Others factors such as genetic, dietary, and environmental factors play a major role in development of gastric malignancy among patients with negative *H.pylori* testing[25]. Many of these independent factors were not evaluated in this study.

The lack of statistical difference between *H.pylori* infection and malignant aetiology of GOO could be due to prior medical treatment. *H pylori* infection may also be underestimated because of the laboratory methods used to diagnose *H.pylori*. By combining immunohistologic biopsy specimens with antibodies against *H.pylori*, some studies have detected a prevalence of *H.pylori* in gastric cancer of 98%[26].

In this study, the highest frequency of patients with GOO was in the group age over 50 years. Similar results were reported by Kotisso in Ethiopia[4]. A retrospective study conducted on patients with GOO in developed countries reported a mean age of 61 years[10]. Additionally the majority of deaths (75%) occurred in patients aged greater than50 years. Bivariate analysis revealed that independent factors for mortality were age greater than 50 years and malignancy. Jaka et al[10] found that patients age greater than 60 years and malignant causes of GOO were significantly associated with higher mortality rates[10]. However, on multivariate analysis malignancy alone was associated with mortality. The high mortality in our setting may be due to delayed patient presentation. Most patients had a mean duration of symptoms of 27.5 months (SD=36.8 months) prior to evaluation at a referral hospital. Patients may delay at home while receiving treatment and medicines from traditional healers. There may also be delays within the healthcare system resulting in delayed referral to a tertiary hospital.

This study has several limitations. Many investigations were not routinely available due to financial constraints. The stage of malignancy at time of presentation influences overall mortality results as well as the choice of operation. Also, many patients do not routinely see a physician, so there is limited data on co-morbidities, which could influence mortality. Further studies would be needed to include these factors in the analysis. Despite these limitations, the

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study provides local data that can be used by health care providers to plan for preventive strategies as well as institute management guidelines for these patients.

Conclusion

GOO is a common surgical problem in our setting with malignancy accounting for the majority of cases. Malignant etiology was associated with increased mortality but the mortality rate was similar in surgical and non-surgical patients. *H.pylori* infection is associated with a benign etiology of GOO. Providers at the health center and district hospital should be educated about GOO and refer patients early to optimize outcomes.

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