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Causes and outcomes of upper gastrointestinal bleeding in referral hospitals in Rwanda: a prospective study

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ABSTRACT

INTRODUCTION: Upper gastrointestinal (GI) bleeding is a common emergency that results in significant morbidity and mortality. In Rwanda, data on causes and outcomes are lacking. The aim of this study was to identify the causes and outcomes of upper gastrointestinal bleeding in patients referred to tertiary referral centers.

METHODS: This is an observational prospective study for which we enrolled all patients who presented with presumed upper gastrointestinal bleeding and underwent upper gastrointestinal endoscopy. We studied causes and outcomes during 3 months of follow-up after initial presentation from February 2019 to September 2019.

RESULTS: We enrolled 194 participants. The mean age was 49.6 ± 17.66 years. The common causes of upper GI bleeding were peptic ulcer disease in 82 (43.3%) patients, esophageal varices 32 (16.5%), gastric malignancies 22 (11.3%), and gastritis 21 (10.8%). The upper GI endoscopy was reported to be normal in only 20 cases (10.3%). The mortality and rebleeding rates after 3 months were 37 (19.07%) and 70 (36%) respectively. The esophageal varices were associated with increased rebleeding (OR: 10.791, P value <0.001), while gastric cancer was associated with increased mortality (OR: 4.405, P value 0.008).

CONCLUSION: Upper gastrointestinal bleeding is a considerable problem in Rwandan teaching hospitals. Our findings are in agreement with the reported causes of upper GI bleeding worldwide. From this study, we consider that variceal hemorrhage and peptic ulcer may have the potential to be better managed.

Keywords: Upper Gastrointestinal Tract, Hemorrhage, Endoscopy, Rwanda

INTRODUCTION

Bleeding from the gastrointestinal tract proximal to the Treitz ligament is referred to as upper gastrointestinal (GI) bleeding and can be subdivided into non-variceal and variceal bleeding [1]. Acute significant bleeding may present as melena, hematemesis, hematochezia, or bloody

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aspiration from a gastric lavage [2]. Chronic blood loss may not be clinically apparent to the patient, and the diagnosis is suggested by a positive fecal test for occult blood or features of iron deficiency anemia such as shortness of breath or dyspnea on exertion [3].

Upper gastrointestinal bleeding constitutes a considerable clinical and economic burden. Barkun et al. reported an incidence of 48 to 160 patients per 100,000 adult persons per year, with a mortality of 10% to 14% worldwide [4]. In the USA, 250,000 - 300,000 patients are admitted annually for presumed upper gastrointestinal bleeding, with 15,000 to 30,000 dying from the condition. Gastrointestinal bleeding-related 30-day mortality was reported to be around 14%, and some studies reported a mortality rate of 6% to 10% per year. This rate increases with age and the number of comorbidities. Upper GI bleeding may result in mortality similar to that of an acute myocardial infarction [5].

Wilcox et al. found that the overall 30-day mortality rate in the USA was 8.8% among 796 admitted patients with upper gastrointestinal bleeding. Mortality rates varied from 2.4% for a Mallory Weiss tear patient to 4.3 % for peptic ulcer-related bleeding, and portal hypertension-related hemorrhage (gastric and esophageal varices) was 32%. Upper GI bleed-related mortality was found to increase by a further 35% between the 30th day and 90th day post the date of the index bleeding [5].

Data are emerging from low- and middle-income countries. A retrospective study done by Haidaret al. in Yemen from 2009-2012 reported that esophageal varices were found in 90% of 350 cases who sustained 400 acute GI bleeding episodes. Young Yemenis are affected because of a high incidence of hepatitis B viral infection, autoimmune hepatitis, hepatitis C infection, and schistosomiasis. Alcoholism and related cirrhosis are uncommon in Yemenis due to social and religious taboos. Of note, peptic ulcer disease was uncommonly reported as a cause of acute upper GI bleeding, and the same applies to gastric cancer[1]. In total 20 deaths were reported (5.72%), and the distribution was from variceal bleeding 17 (85%) and 3 (15%) from the non-variceal group [1].

A retrospective study done in a tertiary hospital in Nigeria to assess the clinical characteristics and outcome of patients who had upper GI bleeding from January 2011 to December 2012 found that among 169 patients who presented as an emergency with features of upper gastrointestinal hemorrhage, the most common presenting symptom was hematemesis (34.9%) followed by melena (16.6%). Twenty-three patients (13.6%) died, and the most frequent cause of upper GI bleeding was esophageal varices [6].

At Lacor Hospital in northern Uganda, among 224 patients who had endoscopy for upper GI bleeding, the commonest cause of upper GI bleeding was esophageal varices (40.6%), then esophagitis (14.7%) followed by gastritis (12.6%), and peptic ulcer disease (6.2%). Malignancy (gastric and esophageal) contributed to only 2.6% of cases. The endoscopy report was normal in 16.1% of patients [7].

The paucity of published data about outcomes and causes of upper gastrointestinal bleeding in Rwanda was the trigger to pursue a study on causes and outcomes of upper GI bleeding in two of the few referral centers where upper GI hemorrhage can be evaluated. The data from this study could help to improve upper gastrointestinal bleeding outcomes and related mortality through better understanding, early referral, and intervention where needed.

METHODS

This was a prospective cohort study. From February 1, 2019 to September 30, 2019, inpatients and outpatients in the endoscopy units of two main public referral hospitals of Rwanda, Kigali University Teaching Hospital (CHUK) and Butare University Teaching Hospital (CHUB) were assessed by trained data collectors (nurses or doctors in the endoscopy unit) to determine if they had features suggestive of upper GI bleeding. The purpose of the study was explained to the patient or relative, and they signed consent to participate in the study and then completed a questionnaire with the support of data collectors. Demographic characteristics, symptoms, risk factors for upper GI bleeding, vital signs, available laboratory results, and esophagogastroduodenoscopy findings were recorded for every recruited patient. Patients were followed directly or through a relative for a period of three months to assess mortality and rebleeding rate. The mortality rate in this study reflects the case fatality rate as it expresses the percentage of patients who died among the patients who suffered the same condition (upper GI bleeding).

Ethical approval was obtained from the University of Rwanda/College of Medicine and Health Sciences Institutional Review Board and from the CHUK and CHUB research departments (Approval 364/ CMHS IRB/2018). We included adult patients ≥ 18 years old who consented to the study and had evidence of hematemesis, melena, coffee ground emesis, or other stigmata of upper gastrointestinal bleeding. Trauma cases were excluded.

Descriptive statistics were summarized for demographics, comorbidities, presenting symptoms, findings at endoscopy, intervention done, admission status (inpatient or outpatient), status at discharge, and outcomes after three months (death, rebleeding, improvement). Pearson's chi-square test was performed to compare variables, and a p-value < 0.05 was considered statistically significant. Bivariate and multivariable logistic regression analyses were done to determine variables related to upper gastrointestinal bleeding associated with increased risk of mortality and rebleeding. Statistical analysis was performed in SPSS version 21.0.

RESULTS

Baseline characteristics: One hundred ninety-four participants were enrolled in this study, with 132 from CHUK and 62 from CHUB. The mean age was 49.6 (SD = 17.7) years. One hundred four participants (53.6%) were male (Table 1).

Hematemesis alone was the presenting symptom in 95 cases (49%), both hematemesis and melena in 55 (28.4%), melena alone in 41 (21.1%), hematochezia alone in three (1.5%) and 17 patients (8.8%) reported other additional symptoms including epigastric pain, symptomatic anemia, dizziness, and syncope. The symptoms were less than one week in 48 cases (24.7%), 1-2 weeks in 65 (33.5%), 2-4 weeks in 37(19.1%) and > 4 weeks in 44 (22.7%) cases. No patient presented within 24 hours of symptom onset (Table 1).

On presentation, the systolic blood pressure was greater than or equal to 100 mmHg in 152 cases (78.4%). The pulse rate was less or equal to 100 beats per minute in 167 (86.1%) cases. Orthostasis was present in 19 (9.8%), but it was not checked in 98 (50.5%) cases (Table 1).

Underlying comorbidities and medication history

Comorbid conditions included cirrhosis in 35 (18%) patients, malignancy 7 with confirmed underlying malignancy, five (2.6%) with chronic renal failure, and 25 (12.8%) had other conditions which include recurrent anemia, hypertension, diabetes, ischemic heart disease, human immunodeficiency virus and portal vein thrombosis, and 122 (62.8%) did not have any underlying disease (Table 2).

Use of medications associated with GI bleeding was found in 44 (22.7%) cases: non-steroidal anti-inflammatory drugs (NSAIDs) in 22 (11%), low dose aspirin in 2 (1%), anticoagulants in 2 (1%), and other medications in 18 (9.3%) (Table 3).

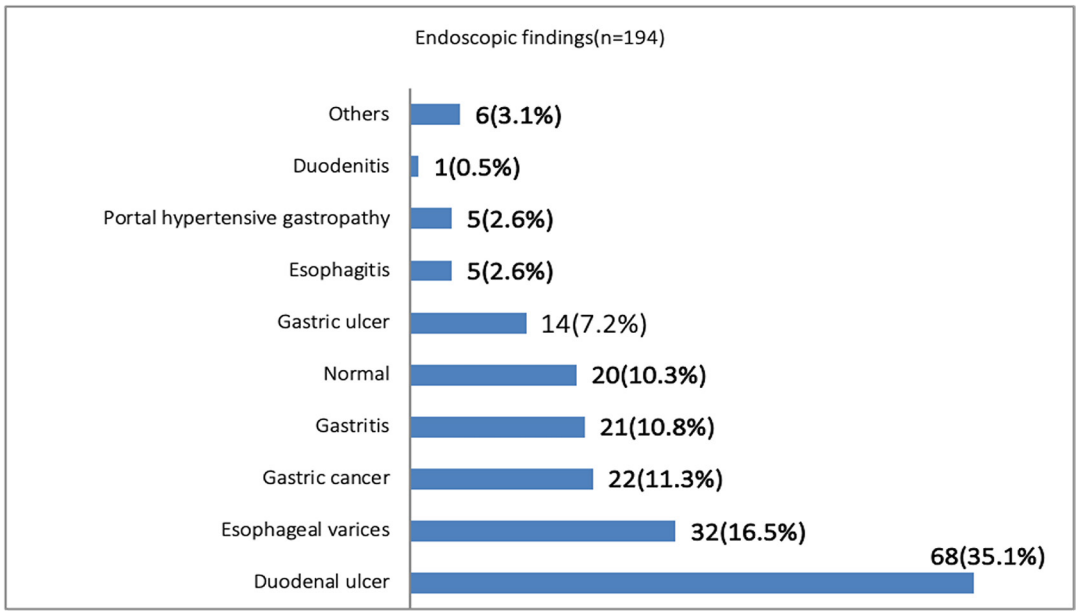

Figure 1: Endoscopic diagnosis in 194 patients with suspected upper GI hemorrhage

Table 1: Clinicodemographic characteristics of upper GI bleeding among study participants

Characteristics	Frequency	(%)
Age (Mean ± SD) in years	49.6±17.7	
Gender		
Male	104	53.6
Female	90	46.4
Chief complaints		
Hematemesis only	95	49
Hematemesis + Melena	55	28.4
Melena alone	41	21.1
Hematochezia only	3	1.5
Symptoms duration before endoscopy		
Less than 24 hours	0	0
>24hrs but < 1 week	48	24.7
1-2 weeks	65	33.5
2-4 weeks	37	19.1
>4 weeks	44	22.7
Systolic blood pressure		
< 100mmHg	42	21.6
≥ 100mmHg	152	78.4
Pulse rate		
≤ 100bpm	167	86.1
> 100bpm	27	13.9
Orthostasis		
Yes	19	9.8
No	77	39.7
Not checked	98	50.5

SD: Standard deviation

Endoscopic diagnosis: During endoscopy, some patients were diagnosed with more than one condition, but the research team retained one diagnosis per patient as the leading cause of upper GI Bleeding based on the endoscopist's description of the likely diagnosis linked to upper GI bleeding. Among our study population we found 68 (35.1%) with duodenal ulcers, 32 (16.5%) with esophageal varices, 22 (11.3%) with gastric malignancy, 21 (10.8%) with gastritis, 14 (7.2%) who had gastric ulcers, esophagitis in 5 cases (2.6%), 5 (2.6%) with portal hypertensive gastropathy, 1 case (0.5%) of duodenitis, and 6 (3.1%) had other diagnoses including Cameron lesions, severe caustic burn, esophageal malignancy, cloverleaf deformity and pyloric stenosis. The upper GI endoscopy was normal in 20 (10.3 %) participants, and no source of bleeding was identified (Figure 1). Of 194 study participants, 22 (11.3%) had an endoscopic biopsy, 8 (4.1%) of esophageal varices had band ligation, and one case (0.5%) was sent to surgery for bleeding control.

Table 2: Underlying diseases

Underlying disease	Frequency	%
Renal failure	5	2.6
Current malignancy	7	3.6
Cirrhosis	35	18
None	122	62.9
Others	25	12.8

Outcomes of patients after 3 months: Of 194 participants, 86 (44.3%) were admitted, among whom 15 patients (17.4%) died in-hospital and 71 patients were discharged.

Table 3: Current medications

Current medications	Frequency	%
Low dose aspirin	2	1
Anticoagulant	2	1
NSAIDs	22	11.3
None	150	77.3
Others	18	9.3

NSAIDs: Non-steroidal anti-inflammatory diseases

One hundred study participants (51.6%) were treated and showed improvement. However, among them, 21 rebled in the first month of follow-up. At three months of follow-up, 40 (20.6%) patients had stigmata of upper GI rebleeding by reporting dark stool and were recommended to consult their nearest health facility urgently.

At the end of the study period, the case fatality rate was 19.1% (37 deaths) and included 9 who had another bleeding episode. Rebleeding was observed in 70 (36%) participants and 17 (8.8%) were lost to follow-up (Table 4).

Outcome-based subgroup analysis: In 32 patients with esophageal varices, 24 (75%) rebled, and 8 (25%) died after three months. The rebleeding

Table 4: Outcomes at the end of the study

Outcomes	N (%)	Rebleeding: N (%)
Death	37 (19.07)	9 (4.6)
Died in first month	15 (7.73)	
Died after the first month	22 (11.34)	
Survival	140 (72.2)	61 (31.4)
Lost to follow-up	17 (8.8)	
Total	194	70 (36)

Table 5: Outcomes-based on subgroups analysis

Diagnosis	Mortality rate	Rebleeding rate
Peptic ulcer disease (n=82)	10.90%	9.70%
Esophageal varices (n-32)	25%	62.5
Gastric cancer (n=22)	59%	22.70%

rate for peptic ulcer (n = 82) was 23 (28%) and 10 died (12.2%). In patients with a diagnosis of gastric cancer (n = 22), rebleeding occurred in nine (40.9%) and 13 (59%) died (Table 5).

Bivariate analysis: Bivariate analysis was done, and variables with a p-value less than 0.05 were considered statistically significant and were identified as independent risk factors for upper GI bleeding outcomes. The Systolic blood pressure on admission < 100 mmHg (OR: 2.423, p: 0.021, 95%CI: 1.124-5.223) and esophageal varices as diagnosis (OR: 11.833, p < 0.001, 95% CI: 5.032-27.829) were associated with rebleeding risk. The presence of

Table 6: Bivariate analysis for UGIB rebleeding rate

	Bivariate		
Variable	**OR**	**95%CI**	**P* value**
Hematemesis	0.982	0.488-1.975	0.959
Melena	0.917	0.386-2.177	0.845
Hematemesis and melena	0.948	0.436-2.063	0.894
Hematochezia	1.949	0.172-22.049	0.586
less than 1 week	0.369	0.136-1.003	0.044
1-2 weeks	1.632	0.800-3.332	0.178
2-4 weeks	1.078	0.450-2.582	0.868
Greater than 4 weeks	1.176	0.523-2.646	0.696
SBP< 100 mmHg	2.423	1.124-5.223	0.021*
SBP ≥ 100 mmHg	0.413	0.191-0.890	0.021*
PR≤ 100bpm	0.895	0.335-2.390	0.825
PR >100bpm	1.118	0.418-2.985	0.825
Orthostasis	1.03	0.322-3.292	0.961
Admission	1.719	0.853-3.463	0.129
Transfusion	0.673	0.260-1.742	0.415
Esophageal varices	11.83	5.032-27.829	<0.001*
Duodenal ulcer	0.392	0.169-0.907	0.025*
Gastric ulcer	0.623	0.134-2.903	0.546
Gastric cancer	1.151	0.397-3.336	0.796

*OR: Odd ratio; CI: Confidence interval; *Statistically significant*

Table 7: Bivariate analysis of UGIB mortality rate

	Bivariate analysis		
Variable	**OR**	**95%CI**	**P * value**
Hematemesis	0.27	0.114-0.617	0.001*
Melena	2.5	1.134-5.493	0.02*
Hematemesis and melena	1.99	0.944-4.214	0.068
Hematochezia	1.99	0.752-0.864	0.399
less than 1 week	1.99	0.738-3.528	0.23
1-2 weeks	1.99	0.256-1.315	0.19
2-4 weeks	1.99	0.220-1.692	0.341
Greater than 4 weeks	1.59	0.712-3.548	0.257
SBP< 100 mmHg	3.84	1.769-8.330	<0.001*
SBP ≥ 100 mmHg	0.26	0.120-0.565	<0.001*
PR≤ 100bpm	0.22	0.092-0.525	<0.001*
PR >100bpm	4.54	1.904-10.846	<0.001*
Orthostasis	3.66	1.355-9.894	0.007*
Admission	5.31	2.344-12.033	<0.001*
Transfusion	2.42	1.079-5.419	0.029*
Esophageal varices	1.53	0.624-3.743	0.353
Duodenal ulcer	0.3	0.117-0.752	0.007*
Gastric ulcer	1.17	0.310-4.428	0.817
Gastric cancer	8.91	3.434-23.103	<0.001*

*OR: Odd ratio; CI: Confidence interval; *Statistically significant*

melena (OR: 2.496, p: 0.02, 95% CI:1.134-5.493), a systolic blood pressure < 100 mmHg on admission (OR:3 .839, p-value < 0.001,95% CI: 1.769-8.330), pulse rate >100bpm (OR: 4.544, p< 0.001, 95% CI:1.904-10.846), orthostasis (OR: 3.661, p: 0.007, 95% CI:1.355-9.894), admission (OR: 5.31, p-value < 0.001, 95% CI: 2.344-12.033), being transfused (OR:2.418, p: 0.029, 95% CI:1.079-5.419), and gastric cancer as endoscopic diagnosis (OR: 8.907, p <0.001, 95% CI:3.434-23.103) were associated with mortality risk (Table 6 and 7).

DISCUSSION

This study showed that hematemesis alone was the most common presenting symptom of upper GI bleeding and was reported in 49% of participants. A similar finding was reported in a study done in

Table 8. Multivariate analysis for UGIB rebleeding rate

		Multivariate analysis	
Variable	**OR**	**95%CI**	**P * value**
SPB < 100mmHg	1.194	0.471-3.027	0.708
Duodenal ulcer	0.919	0.353-2.391	0.863
Esophageal varices	10.791	4.067-28.629	<0.001*

*OR: Odd ratio; CI: Confidence interval; *Statistically significant*

Table 9. Multivariate analysis for UGIB mortality rate

		Multivariate analysis	
Variable	**OR**	**95%CI**	**P * value**
Hematemesis	0.427	0.150-1.220	0.112
Melena	1.573	0.580-4.266	0.373
SPB<100mmHg	1.851	0.707-4.845	0.21
PR ≤ 100bpm	0.611	0.215-1.736	0.355
Orthostasis	1.665	0.509-5.446	0.399
Admission	2.606	0.976-6.957	0.056
Duodenal ulcer	0.493	0.171-1.421	0.19
Gastric cancer	4.405	1.481-13.102	0.008*

*OR: Odd ratio; CI: Confidence interval; PR: Pulse rate; SBP: Systolic blood pressure; *Statistically significant; bpm: beats per minute*

Nigeria by Rukewe et al., who found hematemesis as the most common presenting symptom in 34.9% of participants, followed by melena (16.6%) [8]. In contrast to high-income countries, where 98.4% of patients with upper gastrointestinal bleeding get an endoscopy within 24 hours as recommended, none of our patients presented in the first 24 hours after the presumed onset of the bleeding [9].

The most common diagnoses leading to upper GI bleeding were peptic ulcer disease, esophageal varices, gastritis, and gastric malignancies. These findings are in agreement with the reported overall causes of upper GI bleeding worldwide, where peptic ulcer disease is the most reported cause, followed by variceal bleeding, gastric neoplasm, and Mallory-Weiss tear, but the prevalence of each cause differs by geographical distribution [3]. In developing (or low-income) countries, there are more duodenal ulcers, varices, and gastric malignancies compared to developed countries. This may partly be explained by the high prevalence of chronic infections (Helicobacter pylori, viral hepatitis, and schistosomiasis) in developing countries [1].

At the end of the follow-up period, among 194 study participants, the total case fatality rate was 19.1% (37 deaths among whom nine rebled), and rebleeding was observed in 36% of cases. Of 37 patients who died, 4.12% had esophageal varices, 5.15% had peptic ulcer disease, 6.7% had gastric malignancies, and 3.1% had other diagnoses. The mortality was highest in gastric cancer, and the highest rebleeding rate was observed in esophageal varices.

Our mortality and rebleeding rates were somewhat higher compared to data from high-income countries, where the 30-day mortality rate due to upper gastrointestinal reportedly is 14% (compared with our finding of 19.1%), and the mortality and rebleeding rate 6% and 10% respectively per year [5]. Morbidity and mortality increase with age and the number of associated comorbidities [5]. The differences in outcomes can be explained by more advanced medical services, earlier presentation, availability of intensive care unit support, and availability of interventions done more easily in developed countries compared to our settings. Early endoscopy and endoscopic intervention in patients with bleeding peptic ulcer disease are associated with decreased rebleeding and mortality [10].

Our study showed a total mortality rate of 19.07% (37 cases), which is lower in comparison with some developing countries. A study done in a Malawian tertiary hospital reported that mortality due to upper gastrointestinal bleeding was 23.5% [6]. However, the mortality in our study was higher than in Nigeria, where a mortality rate of 13.6% was recorded [8].

The esophageal varices associated mortality is globally 30% to 50%, and half of these patients die within six weeks after bleeding, similar to our results [11].

Based on our findings, healthcare professionals and population awareness about the severity of upper GI bleeding is recommended, and emergency transfer to a referral hospital where endoscopy can be done may improve outcomes,

in particular, if no concomitant decompensated liver disease is present. A more comprehensive prevention and treatment strategy that includes Helicobacter pylori eradication, treatment and prevention of schistosomiasis, and treatment and prevention of viral hepatitis should help to reduce adverse outcomes of diseases, including upper gastrointestinal bleeding. More recently, variceal band ligation was introduced in our country, and this should improve outcomes if combined with other preventative measures such as administering beta-blocker therapy.

CONCLUSION

Upper gastrointestinal tract bleeding is a challenge for the endoscopy units in our referral hospitals and all hospitals in Rwanda, with a high mortality and rebleeding rate. The commonest causes of upper GI bleeding are Peptic Ulcer Disease, esophageal varices, and gastric malignancies. Further studies to highlight factors contributing to such high mortality and rebleeding rates are recommended.

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