Profile and outcome of adult patients presenting to the emergency medicine department with upper gastrointestinal bleeding

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PROFILE AND OUTCOME OF ADULT PATIENTS PRESENTING TO THE EMERGENCY MEDICINE DEPARTMENT WITH UPPER GASTROINTESTINAL BLEEDING

By

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A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Medicine (Emergency Medicine) of

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CERTIFICATION

The undersigned certifies that he has read and hereby recommended for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled: **‘‘Profile and Outcome of Adult Patients Presenting To The Emergency Medicine Department With Upper Gastrointestinal Bleeding’’**, in (partial) fulfillment of the requirements for the degree of Master of Medicine (Emergency Medicine) of the Muhimbili University of Health and Allied Sciences.

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Dr. Hendry Sawe

Supervisor

_____

Date

DECLARATION AND COPYRIGHT

I, **Shaffin S. Rajan**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature…….. **Date**……..

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DEDICATION

To my parents and my partner Nancy.

ABSTRACT

Background: Upper Gastrointestinal Bleeding (UGIB) is a common Emergency Department (ED**)** presentation with high morbidity and mortality. There is a paucity of data on the profile and outcome of patients who present with UGIB in emergency situations, especially within limited resource settings. We aimed to determine the profile and outcome of adult patients who present to the emergency department of a national referral hospital in a limited resource setting with UGIB.

Methods: This was a prospective cohort study of adult (≥18 years) patients presenting to the Emergency Departments of Muhimbili National Hospital (EMD-MNH) and MUHAS Academic Medical Centre (EMD-MAMC), in Dar-es-Salaam, Tanzania with non-traumatic upper gastrointestinal bleeding (UGIB) from July to December 2018. Patient demographic data, clinical presentation, severity and ED management provided were recorded. We used the clinical Rockall score to assess disease severity. The primary outcome of mortality was summarized using descriptive statistics. Regression analysis was performed to identify predictors of 7-day mortality.

Results: We screened 31987 patients, and included 123 (0.4%) patients with UGIB. Overall the median age was 42 years (IQR 32-64 years), and 87 (70.7%) were male. Hematemesis with melena was the most frequently encountered ED complaint 39 (31.7%). PUD was the most frequently reported comorbidity 39 (40.2%). A median Clinical Rockall score of 3 was observed with most patients ranging between scores of 3-4 (51.2%). Mortality occurred in 23 (18.7%). Age >40 years was a significant predictor of mortality (OR=7.00(1.9-26.4), p=0.004). Receiving UGI endoscopy significantly reduced the risk of mortality (OR= 0.273(0.08-0.9), p=0.047).

Conclusion: In this urban ED in Sub-Saharan Africa over half of patients with UGIB did not receive endoscopy during the current presentation. UGIB carried a high mortality rate among these patients, and age above 40 years, and endoscopic evaluation at any point during the hospital are independent predictor of mortality. Future studies should focus on evaluating how to improve access to UGI endoscopy so as to improve outcomes.

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LIST OF ABBREVIATIONS

BP	Blood Pressure
ED	Emergency Department
EMD	Emergency Medicine Department
GBS	Glasgow-Blatchford score
HB	Hemoglobin
HIC	High income countries
HR	Heart rate
HVPG	Hepatic Venous Pressure Gradient
MAMC	MUHAS Academic Medical Center
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Science
NVUGIB	Non-Variceal Upper Gastrointestinal Bleeding
POC	Point of Care investigations
PPI	Proton Pump Inhibitor
PUB	Peptic Ulcer Bleed
RS	Rockall score
SBP	Systolic blood pressure
UGIB	Upper Gastrointestinal Bleeding
VUGIB	Variceal Upper Gastrointestinal bleeding.

OPERATIONAL DEFINITION OF KEY TERMS

Acute Intake Areas: A space within the hospital where undifferentiated new patients are seen and either admitted or treated as outpatients.

Emergent Upper GI Endoscopy: Upper GI endoscopic evaluation (examination of esophagus and stomach using a fiberoptic scope) carried out either directly from the ED or within 12 hours of ED presentation.

Hematemesis: Vomiting either fresh blood or coffee ground liquid as either reported by the patient and or relative or witnessed by medical personnel in the ED.

Hematochezia: Passage of fresh blood per rectum, usually mixed with stool as a result of massive UGIB with rapid GI transit time.

Liver disease: Known history of chronic liver disease or newly diagnosed by clinical criteria or ultrasonographic findings in the ED.

Malignancy: Any known or new diagnosed cancer, both metastasized and non-metastasized.

Melena: Passage of black tarry stool which is either reported by the patient or his/her relative and/or witnessed by a medical personnel during physical examination.

Renal disease: Known history of renal disease either reported by the patient/relative or as evident by previous medical records or new diagnosed by standard criteria during the ED visit.

Rockall score (Clinical) staging:

- **Scores <3:** Low risk for adverse outcome i.e. mortality, re-bleeding or need for surgery.
- **Scores 3-4:** Moderate risk for adverse outcome i.e. mortality, re-bleeding or need for surgery.
- **Scores >4:** High risk for adverse outcome i.e. mortality, re-bleeding or need for surgery.

Upper Gastrointestinal Bleeding: Any bleeding from the gastrointestinal tract occurring proximal to the ligament of Treitz.

Urgent Upper GI Endoscopy: Upper GI endoscopic evaluation carried out within 24 hours of ED presentation.

CHAPTER ONE

1.0 BACKGROUND

Upper Gastrointestinal bleeding (UGIB) is a medico-surgical emergency, defined by any gastro intestinal (GI) bleeding occurring proximal to the ligament of Treitz (1). It is a common condition seen at the emergency department (ED) which presents with a variety of esophageal, gastro-duodenal symptoms, including hematemesis, melena, and or hematochezia(2).

In developed countries, like the United States of America, UGIB accounts for 300,000 admissions per year (3), though a global decline in the annual incidence is noted (4,5). Overall mortality ranges from 6-10% (6), and it is suggested that the overall rate of mortality from acute upper GI bleed has remained relatively unchanged over the past 50 years.(7) UGIB is found to have significant impact on the cost of care per patient with inpatient bed stay, endoscopy and RBC transfusion being the main cost drivers, as reported from a study in the United Kingdoms (UK) (8).

From the developing country perspective, a mortality range of 10-30% has been reported across the African continent. A mortality of 13.6% in a Nigerian ED study(9), 23.5% in a Malawian study(10), 10-12% in a Northern Tanzanian study(11,12) and an astonishingly high mortality of 33.5% in Dar-es-Salaam Tanzania, in a study conducted in Muhimbili National Hospital (13).

Considering the disease's significant morbidity and mortality, the emergency physician and personnel are challenged to quickly and appropriately resuscitate, stabilize and diagnose these patients presenting with UGIB (14). Not all patients presenting with UGIB need admission, thus the ED physician and personnel are obligated to appropriately risk stratify these patients and decide on the appropriate disposition, which includes also both admissions and safely discharging patients with outpatient management.

In Tanzania, a standard treatment guideline (STG) aids physicians in managing patients with UGIB. The standard management proposed according to the 2013 STG is more or less similar to the internationally proposed guidelines for the management of UGIB, with emphasis being paid on early and aggressive stabilization of hemodynamic status and urgent UGI endoscopy within 24 hours of patient presentation (15). The presence of full capacity Emergency department at Muhimbili National Hospital and MUHAS Academic Medical Centre (MAMC) has provided the opportunity for early stabilization and management of patients presenting with UGIB. However there is paucity of data on profile and outcome of these patients, thus limiting our knowledge on the patient-set we see, their response to ED care and whether the ED interventions performed are in-line with recognized UGIB management guidelines.

1.1 Literature Review

Pathophysiology of UGIB

UGIB can be divided into variceal and non-variceal causes. Variceal UGIB (VUGIB) is attributed to gastric and esophageal varices whereas Non-Variceal UGIB (NVUGIB) is commonly due to peptic ulcer disease (PUD). With regards to Variceal UGIB (VUGIB), it is preceded by portal hypertension. There are a number of causes that lead to portal hypertension (HTN) in the developing world,; the commonest cause is liver diseases and Schistosoma infection (11). Portal hypertension is initially caused by distortion of the hepatic vascular bed, which leads to increased resistance to portal blood flow. This is coupled with splanchnic vasodilation and subsequent sodium and water retention. This results in plasma expansion and a reduction in peripheral resistance, thus a hyperdynamic circulation develops. Consequently there is significant blood flow through the portal vein which further contributes to portal hypertension. Esophageal varices then appear and may bleed when the Hepatic venous pressure gradient (HPVG) exceeds 12mmHg (16).

Causes of NVUGIB include erosive gastritis, Mallory-Weiss tear, arteriovenous malformations and malignancies (1,17). Pathophysiology of UGIB is dependent on the underlying etiology of UGIB. The commonest etiology of Non-variceal UGIB (NVUGIB) is Peptic Ulcer disease (PUD). Helicobacter pylori (H.pylori) is known to have a strong association with PUD, though current literature suggests declining incidence of H.pylori associated PUD. In ulcer-associated UGIB, as the ulcer burrows deeper into the gastro-duodenal mucosa, the process causes necrosis and weakening of arterial wall, leading to development of a pseudo-aneurysm. The weakened wall ruptures, producing hemorrhage (18). A small increase in vessel size leads to a significantly larger amount of blood flow and bleeding. Mallory-Weiss tear occurs during the process of vomiting, whereby the lower esophagus and the upper stomach are forcibly inverted, leading to mucosal tear of the esophagus and stomach. The depth of tear determines the severity of bleed (18).

Risk factors

Some of the noted risk factors for UGIB include advanced age, history of liver disease or liver cirrhosis; which predisposes patients more to VUGIB. History of smoking, NSAID or alcohol use; are risk factor for NVUGIB.

History of vomiting or persistent retching will predispose patient to Mallory-Weiss tear (17).

Clinical presentation

As mentioned earlier, UGIB can present itself in a variety of ways including hematemesis, coffee-ground vomitus, melena or hematochezia. The color of the vomitus may serve as an indicator of the onset of bleeding. Bright red or red vomitus may suggest recent onset of bleed, whilst dark red, brown or even black vomitus suggests bleed that has been in the stomach there for a while. Coffee-ground vomitus suggests precipitation of blood clots in the vomitus (19). The redder the stool color in hematochezia, the severer is the UGIB, thus signifying a very rapid transit time of blood through the GI tract, with less time for it to be digested to form melena (6). In the ED setting, these patients may present either as hemodynamically stable or unstable depending on the amount, duration and frequency of bleeding. Patients may present with symptoms of anemia including weakness, dizziness and syncope as a result of the bleeding episode(s) (18).

Clinical severity

In the ED setting, early identification of patients who are at high risk of re-bleeding and death is crucial to the effective management of UGIB. An ideal scoring system for clinical severity will serve to timely and effectively assess the patient's condition and risk of an adverse outcome and will serve as a basis for the establishment of treatment procedures to improve patient prognosis and reduce medical costs (19,20).

Several scoring systems have been used to stratify these UGIB patients based on their disease severity and risk of adverse outcomes. The two commonly used scoring systems are the Rockall score (RS) and the Glasgow-Blatchford score (GBS). The GBS stratifies UGIB patients who are "Low-risk" and candidates for out-patient management. It determines which patients with UGIB can safely be discharged from the emergency department. Its use in the in-

patient setting remains controversial (21). Scores >2 can be termed as “High risk”, and it can accurately predict urgent need for interventions such as BT and endoscopic interventions (22).

The clinical or pre-endoscopic RS is used for the prediction of clinical outcome of patients presenting with UGIB. The use of pre-endoscopic findings answers a key question which faces most EM physicians, i.e. “*does the patient require urgent endoscopy*?”(19). The pre-endoscopic RS and the GBS is particularly useful in the ED setting as it quickly addresses the question whether the UGIB patient warrants an urgent endoscopy or not (20). Both the scores predict adverse outcomes i.e. mortality, re-bleeding and need for surgery in patients with UGIB. The pre-endoscopic Rockall score is calculated based on clinical bleeding (i.e. without endoscopy results) and uses parameters such as age, presence of shock and comorbidity status to calculate the total points which then correlated with the severity of risk i.e. Low risk, moderate risk and high risk patient. The Glasgow-Blatchford score is also a pre-endoscopic score that identifies UGIB patients who are “low-risk” and candidates for outpatient management. It helps to identify patients with UGIB who may be safely discharged from the ED. It consists of 9 variables, presence of each variable increases the priority for admission and likelihood for interventions such as UGI endoscopy. A score of ≥3 categorizes patients as high risk (22). GBS was found to be better at predicting mortality, need for hospitalization or need for interventions when compared to pre-endoscopic Rockall score (23). The Charlson’s Comorbidity index is a method of categorizing patient comorbidities with each comorbidity category having an associated weight (from 1 to 6). The sum of weights result in single comorbidity score for the patient. The higher the score, the more likely the predicted outcome will result in mortality or higher use of resources.

Diagnosis of UGIB

A thorough history can often provide a significant lead to the underlying cause of UGIB. The definitive diagnosis is best made via endoscopic evaluation. Current literature suggests that endoscopic evaluation and treatment of patients with UGIB be done within 24 hours of ED presentation, i.e. early/urgent endoscopy. Early endoscopic evaluation and treatment allows

for safe and prompt discharge of patients classified as low risk, improves patient outcomes, and reduces morbidity and length of stay amongst those classified as high risk patients (24).

Nasogastric tube (NG tube) lavage may be diagnostic and therapeutic. Although a negative NG tube aspirate does not conclusively exclude UGI source of bleed, a positive aspirate provides a strong evidence of UGI source of bleeding. NG tube aspirate can also be used as a way of risk stratification (1,18). While it adds a prognostic value in some selected cases of patients, NG tube placement and aspirate though are not routinely recommended (24,25). Controversies still exist regarding placement of NG tube, with some studies calling it an obsolete practice, since no statistically significant difference has been observed in the diagnosis and need for OGD for UGIB between clinicians' evaluation and NG findings (26). Moreover it was argued that almost all patients in will eventually undergo endoscopic evaluation for their UGIB.

Management of UGIB

The primary goal of the ED physician involves stabilization of the UGIB patient. Early airway management in selected cases, placement of large bore IV cannulas, aggressive fluid resuscitation and provision of blood and blood products to patients in hemorrhagic shock and anticipation and activation of massive transfusion protocol (1).

A restrictive strategy for blood transfusion (BT) is recommended with a trigger Hb of <7g/dl. For elderly patients with comorbidities, a trigger Hb of <9g/dl is recommended in view of their poor tolerability of acute anemia (1,24). Management of NVUIB involves; administration of Proton pump inhibitors (PPI). A high bolus dose followed by IV infusion has been shown to reduce the need for surgery, length of in-hospital stay, re-bleeding rates and mortality amongst those classified as high-risk. PPI may also be used to downstage the endoscopic lesion and reduce the need for endoscopic intervention, although this should not delay endoscopy (1,24). Endoscopic evaluation and treatment as discussed earlier should be provided to all patients within 24 hours. (Urgent/early endoscopy). A second look endoscopy is warranted for those patients who re-bleed. Re-bleeding is defined as the presence of hematemesis or melena with signs of hemodynamic instability or decrease in hemoglobin level by >2g/dl in a previously

stable patient (27). Surgical management should be sought for those patients in whom endoscopic intervention has failed (7,24). H2-receptor antagonist, somatostatin and Octreotide are not routinely recommended for acute ulcer bleed (24).

For VUGIB, somatostain analogue/Octreotide plays a key role in the management. These agents tend to work by causing splanchnic vasoconstriction to reduce blood flow to the gastro-duodenal mucosa. Despite this fact, Octreotide does not offer benefit in mortality reduction. Only terlipressin has been found to have a mortality reduction benefit (1,7). Antibiotics should be administered to all patients with suspected or confirmed variceal bleed (7). The use of antibiotics in this patient population is aimed at reducing the risk of bleeding, infections and mortality (27). Moreover the use of erythromycin prior to OGD has been show to improve endoscopic visualization, reduced need for second look endoscopy, decreased blood transfusion requirement and reduced hospital length of stay (25).

Pro-kinetic/pro-motility agents may improve diagnostic yield during endoscopy, are not routinely recommended for use in all patients in UGIB.(24) However, they may be indicated for patients going for endoscopy from the ED with suspected large amount of blood or clot in the stomach (1).

Trends of epidemiology of UGIB

It is reported that UGIB accounts for 300,000 annual admissions in the US and 70000 admissions in the UK (18). Despite these large figures, a global decline in UGIB cases, especially non-variceal GI bleed (NVUGIB) is noted. *Tielleman et al* found a declining trend in the incidence of non-variceal bleeding from 108 to 78 cases per 100000 person between 1994 and 2009 in the US (3). This trend was not only observed in the US, but other parts of the world as well (3). For instance, a decline in incidence rate from 162.9/100000 persons in 1995 to 108.3/100000 persons in 2005 was observed in Greece (4).

Looking at other areas of the world, the incidence of UGIB in the west of Scotland was found to be 172/100000 adult person whereas in Denmark and the Netherlands it was found to be 37 and 48/100000 adults respectively (28). Iceland was found to have a crude incidence rate of 87/100000 inhabitants per year with UGIB in the year 2013 (29). In the same year in the EDs of France, an incidence rate of 122/100000 inhabitants was seen. In the Nigerian ED, of the 8281 medical cases attended to, 169 patients had UGIB, which accounted for 2% of ED presentation (9). Other African data to note is the retrospective chart review conducted in 2010 in Malawi which found that of the 5000 patient charts reviewed, 187 (3.7%) patients were found to have UGIB (30).

Mortality and re-bleed are adverse outcomes associated with UGIB. Looking at prior studies, *Teilman et al* showed an overall mortality from UGIB to be 5%, with a 55.8% decline in mortality risk from 1979 to 2009 (3). A similar trend was noted in France where a decline in mortality rate is observed from 11% to 7% (6). However *Leerdam et al* in 2008 showed the mortality associated with UGIB ranges from 3-14% had not changed significantly in the Netherlands for past 10 years. The re-bleeding rate with UGIB was found to be 7-16% despite endoscopic interventions (28). In Greece the overall mortality was noted to be 6.5%, with re-bleeding being at 5.9% (4). Similarly *Sostres and Lana*, in their systematic review showed a mortality of 3-14% and moreover found little change in the rate over the past years (5). In this systematic review re-bleeding which was observed in 6-10% of patients was shown to be an important predictor of morality.

Nable and Graham in the US, noted a very high mortality rate approaching 30-37% with a re-bleed rates varying from 25-30% in VUGIB and 20% in PUB (14). From the ED point of view, the study done in EDs of France showed an overall ED-mortality of 11% (2). Mortality was higher in the hypotensive patients, those with exteriorized bleeding in the ED and those with altered mental status and marbling.

Looking at the ED study done in Nigeria, 13.6% patients with UGIB died. An association was noted between mortality and diastolic blood pressure. A high diastolic blood pressure was noted as a risk factor for mortality (9).

Some of the other African studies conducted on UGIB include the following;

- In Malawi, in a retrospective review of charts in 2010, an in-hospital mortality of 23.5% was attributed to UGIB with the commonest cause of UGIB being esophageal varices. Re-bleeding rate were not assessed in this chart review (30).

- In Mwanza Tanzania, two studies concerning UGIB could be identified. A study conducted by *Chofle et al,* 10% in-hospital mortality was observed whereas in the study conducted by *Jaka et al,* a 11% in-hospital mortality and 3.3% re-bleed rate was seen (11,12).
- In the Kilimanjaro region of Tanzania, the in-hospital mortality was noted to be 17%. Re-bleeding rate was not reported in this study (31).

- At the Muhimbili National Hospital, in Dar-es-Salaam Tanzania a 2007 dissertation study showed a mortality rate of 15.6% among patients hospitalized with UGIB (32). However, a study by *Moledina et al,* also conducted at MNH in the Internal Medicine Department, published in 2017 showed a much higher mortality, with mortality rates being 33.5% at 60-days and nearly quarter of those dying within the first 24-hours of admission. The re-bleeding rate was found to be 7.1% (13).

The clinical characteristics of patients presenting with UGIB, the severity and risk factors for poor outcome has been reported in several studies. Some of these studies include;
A prospective, observational, multicenter study in France by *Thiebaud et al,* found that the patients who presented with UGIB were mostly in their 6^{th} decade of life, with male sex being predominant. Hematemesis was the commonest presenting complaint, whereas melena was the second most common presenting complaint. Externalization of bleeding (Visible blood from

mouth or rectum) during the ED stay was observed in 52% of patients. With regards to the cause of UGIB, it was found that gastro-duodenal ulcer was the most frequent etiology of the bleed (30%) followed by varices (20%) and gastritis (11%) (2). Though no validated scoring system to assess for clinical severity was used, the investigators assessed clinical severity signs including systolic blood pressure, heart rate, mental status and hemoglobin level. At least 35% of the patients had one severity sign, with tachycardia being the most frequently noted. The risk factors for mortality noted in the study included hypotension with altered mental status, exteriorization of bleeding in the ED and vasopressor and catecholamine administration.

In a prospective study conducted by *Hreinsson et al* in Iceland, of 1731 patients enrolled, 5% of these patients had originally presented to ED with UGIB. The incidence of UGIB dramatically rose with increasing age. Similar to the French study a male predominance was seen. Hematemesis was the most common presenting complaint followed by melena (29). Less than a quarter of the patients had a prior h/o UGIB. In the Iceland study, Rockall score was used to measure the clinical severity. The majority (78%) of patients had a Rockall score of 3-7 suggesting moderate risk for re-bleeding, mortality or the need for urgent intervention such as urgent OGD or surgery. 8% of the patients had a high risk score, and of these high risk patients, the majority required blood transfusion and had a clinically significant bleed. Risk factors for clinically significant bleeding included testing positive for *H.pylori* infection, use of NSAIDS, low dose aspirin and/or combination of both. The independent predictors of clinically significant bleed were gastric ulcer and NSAID use (29).

Teilleman et al in their systematic review of studies related to UGIB from developed world found that the most common etiology of UGIB is PUD (3). Though there has been a declining incidence of PUD related bleeds, it still accounts for 37% of NVUGIB, with the incidence increasing with increasing age, especially in the elderly male population. *H.pylori* infection and NSAID use have been shown to be the most common cause of PUD related NVUGIB. With the declining overall incidence of PUD related NVUGIB, the incidence of *H.pylori* negative PUD NVUGIB seems to be increasing. *Teilleman et al,* observed an incidence of 20-

67% for PUD related UGIB whereas the incidence of UGIB related to esophageal varices was 4-20% in the developed world.

When examining some of the African literature carried out on UGIB; a study carried out in a Nigerian ED, observed that hematemesis was the most common presenting symptom (34.9%) followed by melena (16.6%). Similar to studies in the developed world, there was a male predominance, but the median age of the patient population was younger than 44 years. The risk factors noted for UGIB were NSAID ingestion and alcohol use (16.8% and 12% respectively). An association between diastolic B.P of >90mmHg and increase rate of mortality was observed in the study. (14.3% vs. 7.1% for Diastolic BP <90mHg). Provision of blood transfusion (BT) was found to improve mortality rate (5.4% vs. 10% amongst those who did not receive BT). Though this study did not look at the etiology of the bleed, it was discovered that 15% of the patient population were known to have PUD as a comorbidity (9).

In a Malawian study, the mean age of patient presentation was 40 years, with no gender predilection noted for overall UGIB cases. The most common presenting complaint was not studied in this literature. Bleeding esophageal varices was the most frequently noted etiology of UGIB (42.8%) with a male predominance noted (63.1%). The patient population in this study had a relatively favorable Rockall score (mean score of 1.87 pre-endoscopically and 3.23 post-endoscopically). Risk factors for mortality observed in the study include; tachycardia, pre and post-endoscopy Rockall score, lower systolic BP, lower pre-transfusion Hb, though statistical significant difference was noted in only two factors, i.e. systolic BP and pre-endoscopic Rockall score (30).

In a Ugandan cohort study, published in 2016, among 107 enrolled participants, there was a lifetime total of 323 episodes of UGIB, with 57% of the participants experiencing ≥2 lifetime episodes of UGIB. Female predominance was observed in this study. 94% of the participants had severe chronic hepatic schistosomiasis and 80% of them had esophageal varices. Unlike patients with UGIB in high income countries, alcohol use was infrequent amongst the study participants. Factors noted to be associated with two or more lifetime bleeding episodes

include; Age≥ 40 years, female sex, history of BT, abdominal collaterals, esophageal varices, anemia and thrombocytopenia (33).

There have been five studies carried out on UGIB in Tanzania. In Mwanza a study conducted by *Chofle et al*, published in 2014, on patients with hematemesis found that of the 124 enrolled patients, 70% had esophageal varices and 48% of the patient population had an active Schistosoma infection. The next two most common etiologies noted were gastric and duodenal ulcers (14% and 12% respectively). Male sex was predominant (60%) and the median age was 38 years. Re-bleeding occured in 50% of the enrolled patients within 2 months of admission and 85% of these patients had an in-hospital re-bleed. Notably four of the participants had severe re-bleed and the etiology was found to be bleeding PUD.
An important correlation was noted in this study suggesting that endoscopic intervention was associated with significantly reduced mortality (7% mortality in the endoscopy group vs. 21% in the non-endoscopy group) (11).

Another study carried out in Mwanza by *Jaka et al*, published in 2012, was a retrospective review of patients undergoing fiberoptic upper GI endoscopy in the management of patients with UGIB. Of the 240 patients included in the study, a male predominance was noted (2.1:1 male: female ratio). The median age of the patient population was 37 years, with 60% of the patient population being aged <40 years. Hematemesis was the commonest presenting complaint (80.4%) followed by melena (9.2%). Esophageal varices was the leading cause of UGIB (51.3%) followed by peptic ulceration (25%). Use of NSAID prior to the bleeding episode was found in 7.9% cases. Re-bleed rate was reported to be 3.3%. Mortality was significantly higher in patients with; variceal bleeding, shock, hepatic decompensation, HIV infection, malignancy, age> 60 years and in patients with higher Rockall score. Early blood transfusion was associated with an improved patient outcome (12).

In Moshi, Tanzania, a study carried out from January 2007 to December 2008 by *Suba et al*, 130 patients with UGIB admitted at the Kilimanjaro Christian Medical Center (KCMC), found 56.2% were male patients; thus reflecting the same male predominance as noted in most other

studies. Esophageal varies accounted for 42.3% of all cause of bleed followed by duodenal ulcer (15.4%) and erosive/hemorrhagic gastritis (7.7%). In 27% of cases no identifiable cause was noted (31).

In Dar-es-Salaam, Tanzania, a dissertation study conducted by *Kimu N.*, conducted at MNH, looking at the profile of patients with acute UGIB in 2007, found a similar picture of male predominance; males being five times more affected then females. Esophageal varices accounted for 48.1% of all bleeding followed by duodenal ulcers (22.1%). The peak age for variceal bleed was between 31-50 years whereas for duodenal ulcer it was >50years. A statistically significant relationship between splenomegaly and VUGIB was noted, whereby a palpable spleen was present in 91.9% of VUGIB patients. Risk factors for mortality and re-bleed were not studied in this case, though it was noted that not receiving UGI endoscopy was linked to higher mortality (32).

A study carried out by *Moledina et al* in the internal medicine ward of MNH from June 2015 to January 2016, recruited 170 patients with UGIB. 71.2% of these were male patients, with a median age of 40 years. Esophageal varices accounted for 57% of cases followed by PUD (18%) and gastritis (10%). Re-bleeding was reported in 7.1% of the patients. 25% of these patients re-bled in the first 96 hours of admission. Mortality was found to be higher in patients with; high white blood cell count, raised serum ALT, raised serum total bilirubin and in those who did not receive an endoscopic procedure. Those who did not have an endoscopic procedure had a 4 times higher 60-days mortality as compared to the group that had (13).

Time to endoscopy and appropriate resuscitative measures crucially impact survival of patients. The recommended time to urgent endoscopy is within 24 hours and it has been shown to have a good patient outcome as compared to delayed (>24hour) or no endoscopy having an increased incidence of poor outcome (24) (25). However, very few patients in sub-Saharan Africa receive urgent endoscopy (11–13,31).

Only half of the participants in the study done by *Moledina et* in 2015-2016 at MNH underwent endoscopy and none of them received the procedure in the first 24 hours, i.e. non-urgent endoscopy (13). In Mwanza, the study conducted by *Chofle et al* in 2014, revealed that, 73% of the participants underwent endoscopy and the median time to endoscopy was 2 days (11). However, an earlier study done in the same setting and hospital in Mwanza by *Jaka et al*, the mean time to endoscopy was 6.8hours (12).

In regards to the above mentioned studies, it is clear that there seems to be an epidemiological difference in the profile of patients with UGIB in the developed/industrialized and the developing world. While most UGIB patients present in their advanced age or in their 6^{th} decade of their lives with bleed in the developed world, the age group seen in the developing world, particularly from the African point of view is much lower, with most patients being in their 4^{th} decade of life. The commonest etiology of UGIB is noted to be PUD in the industrialized nations, particularly due to NSAID use and *H.pylori* infection, whereas variceal bleed is the most common etiology of UGIB in the developing nations, with Schistosoma infections and chronic liver disease being the main culprit. The risk factors for mortality include an advancing age, higher clinical/pre-endoscopic severity score, hypotension at presentation, active bleeding/exteriorizing bleeding at ED. Presence of liver cirrhosis and provision of blood transfusion were also found to be associated with her mortality. Receiving endoscopy has been found to be a protective factor against mortality in both developed and limited income countries, but fewer individuals receive endoscopy in LMIC's and it is often delayed.

1.2 Problem Statement

Though there is a global decline in the mortality associated with UGIB, UGIB still continues to cause significant mortality, particularly in LMICs. In the United States, UGIB accounts for 300,000 admissions per year with approximately 5% mortality rate (3), while previous studies from Tanzania suggest, mortality is much higher, ranging approximately from 10-30% (11–13,31,32). It is unclear why this is the case. Previous studies suggest that this could be due to;

- The underlying etiology of UGIB, where variceal bleeding appears to be more common in SSA.
- High severity of disease at presentation; Few studies in Tanzania characterized the patients by severity using the Rockall score and so it is unclear if the patients in Tanzania are more severely ill.
- Few endoscopies being performed; Endoscopy has been shown to be associated with improved outcome, but endoscopic services aren't readily available in most of the hospitals in SSA, especially Tanzania. Only a handful of patients are fortunate to receive urgent endoscopy i.e. within 24 hour. This may contribute to higher mortality.

Understanding this situation better is important to providing care and improving management of patients in the ED and the hospital in general.

Emergency medicine is a new and growing field in Tanzania and SSA. Prior studies in Tanzania and SSA have not included patients who were treated in a full-service ED and thus had the benefit of early identification and resuscitation. This study will assess the severity of patients with UGIB as a possible reason for differences in mortality using standardized scoring system.

Studies looking at endoscopic services in Tanzania has been conducted several years ago. The likelihood of receiving endoscopy may have changed since then.

To the best of our knowledge we could not identify any study concerning UGIB in Tanzania, conducted in the emergency department. All of the studies carried out have been conducted in an in-patient setting.

1.3 Rationale

This is an observational study to look at the patient profile, the clinical severity and outcomes of the patients who presented with UGIB to the ED. It is not clear if the higher mortality seen in our setting is due to a higher severity on presentation, the etiology of the condition or lack of appropriate care. In this study, we will determine those demographic, clinical and treatment factors that's are associated with higher mortality in our setting. This study will allow us to assess the severity of presentations and compare them with that seen in other studies, including studies conducted in a high income setting. We will be able to determine if appropriate care actions are taken. We will also be able see if there have been improvements in mortality given the presence of full-capacity emergency departments in this setting.

This study will provide a baseline for further studies on the care of patients with UGIB at MNH and SSA. Through this study we will determine how emergency and urgent care provided at the ED can impact outcome in terms of morbidity and mortality and hospital length of stay. The knowledge gained from this study will aid policy makers and concerned personnel find ways to improve patient care to reduce mortality with specific regards to emergency care.

1.4 Research Question

What is the clinical profile and early outcome of adult patients presenting to the EMD- MNH and MAMC with Upper Gastrointestinal Bleeding?

1.5 Objectives

1.5.1 Broad objective

To describe the clinical profile and early outcome of adult patients presenting to the Emergency Medicine Department (EMD) with Upper Gastrointestinal Bleeding (UGIB).

1.5.2 Specific objective

1. To determine the proportion of patients presenting to EMD-MNH and MAMC with Upper Gastrointestinal Bleeding.

2. To describe the clinical characteristics of patients presenting to EMD-MNH and MAMC with Upper Gastrointestinal Bleeding.

3. To describe the ED management strategies and disposition of patients presenting to EMD-MNH and MAMC with Upper Gastrointestinal Bleeding.

4. To determine the in-hospital mortality rates amongst patients presenting with Upper Gastrointestinal bleeding.

5. To determine factors associated with mortality among patients presenting to the EMD-MNH and MAMC with Upper Gastrointestinal Bleeding.

CHAPTER TWO

2.0 METHODOLOGY

2.1 Study Design

This was a prospective cohort study of adult patients above the age of 18 years presenting to the EMD-MNH and MAMC with symptoms of UGIB between July 2018 and December 2018.

2.2 Study Setting

This was a two-centered study, conducted in the emergency departments of Muhimbili National Hospital (MNH) and MUHAS academic medical center (MAMC) in Dar-es-Salaam, Tanzania. MNH is located in the Ilala district, along the United Nations road, Upanga. MNH has a bed capacity of 1500 and serves as top referral hospital in Tanzania. The ED was established in 2010 via a partnership between the Ministry of Health and Social Welfare and the Abbott Fund Tanzania. The ED is the first full capacity public ED in Tanzania and the training site for the only Emergency Medicine (EM) residency program in the country. The department is staffed 24 hours, seven days a week by locally trained specialist emergency physicians, who oversee the care of patients and training of interns, registrars and EM residents. The ED sees an average of 45000 patients annually, with an admission rate of 65%.

MAMC is a recently inaugurated full capacity health facility with a state of the art emergency medicine department, occupying 3800 acres, it is located 3 Km off the Dar-es-Salaam-Morogoro highway, approximately 30Km from MNH.

Both centers are appropriately equipped to cope with UGIB of any severity. The ED's in both the centers are staffed with highly trained team of medical personnel with 24 hours specialist coverage. Both facilities have a skilled team of surgeons and a gastroenterologist on call on a daily basis. MNH and MAMC both have a fully equipped endoscopy unit which aids in the diagnosis and management of UGIB. To aid in the on-going management of the critically ill UGIB patient, a well-staffed and equipped ICU is available with a blood bank to respond to transfusion requirements.

2.3 Target Population

All adult patients aged 18 years and above who presented to acute intake areas with UGIB.

2.4 Accessible Population

All adult patients aged 18 years and older who presented to EMD-MNH and MAMC with UGIB in Dar-es-salaam Tanzania.

2.5 Study Population

All adult patients with UGIB attended at the EMD-MNH and MAMC-ED at the time the study was being conducted.

2.6 Sampling Design

Consecutive sampling technique was used to enroll adult patients presenting with UGIB, who met the inclusion criteria and an informed consent had been attained either from the patients or their relatives at the time when the researcher or his assistant(s) were scheduled to collect data.

2.7 Subject

2.7.1 Inclusion criteria

a) All adult patients with suspected UGIB with complaint(s) of hematemesis (including coffee-ground vomitus) and/or melena and/or hematochezia as either reported by patient/relative or witnessed or confirmed by EM personnel.

2.7.2 Exclusion criteria

a) Patients with suspected/confirmed traumatic UGIB
b) Patients who had previously been enrolled in the study who presented with recurrent episode of UGIB during the period of the study.

2.8 Variables of Interest

The primary objective of this study was to describe the clinical profile and outcomes of patients presenting with UGIB in the ED. The variable of interests were:

Predictor/Independent variables

a) Demographic data: Age, sex, marital status and occupation
b) Referral status: Self referred/Hospital referred
c) Comorbidities: Prior H/o UGIB, PUD, Liver disease, Esophageal varices, H/o endoscopy and band ligation and Charlson's comorbidity index
d) Drug use within 24-48 Hr: Alcohol, NSAID/Anti-coagulants, Beta Blockers, PPI
e) Prior h/o Hospitalization due to UGIB
f) Active UGI bleed in the ED
g) Clinical severity: Clinical (Pre-endoscopic) Rockall score and Glasgow-Blatchford score
h) ED management strategies
i) Urgent and Non-Urgent endoscopy
j) Disposition status

Outcome/Dependent variables

a) Mortality: ED mortality, 24 Hrs and 7 days
b) ED length of stay
c) In- Hospital Length of stay

2.9 Sample Size Estimation

The primary outcome of this study was In-Hospital Mortality.

Basing on a recent study on UGIB at Muhimbili National Hospital by *Moledina et al* a 60-day mortality of 33.5% was noted.

The sample size for this study was calculated using the following formula:

Sample size: $N = 4Z\alpha^2P(1-P)/(W^2)$

Whereby:

N= Minimum required sample size

Zα= Standard normal deviation for α. A level of confidence of 90% will be chosen for this study.

P= Expected proportion with the characteristic of interest. A value of 33.5% is chosen basing on previous study done at Muhimbili National Hospital, with 60-day mortality being their primary outcome.

W= Total Width of confidence interval. A width of 15% is chosen for this study.

Therefore minimum sample size calculated was:

$N = 4X1.645^2 X\ 0.335(1-0.335)/(0.15^2)$

N= 107 participants.

Following adjustment for 10% non-response rate a minimum sample size of 119 participant was estimated.

2.10 Patient Recruitment

A consecutive patient enrollment scheme was applied. The principle researcher and his assistant(s) were available in the ED 24 hour a day, seven days a week to ensure all eligible patients were captured during the period of study.

All the doctors and nurses at the beginning of the shift were informed to notify either the researcher or his assistants in case they received any patient with suspected UGIB. Additionally research assistant(s) monitored the electronic tracking board for chief complaints related to UGIB (e.g. GI bleeding, hematemesis or melena). Following the triaging process, patients with triage complaint of either vomiting blood, or passing black tarry stool, or passing fresh blood per rectum were approached for eligibility. A standardized data collection checklist were used to assess the eligibility of patients to enroll in the study. An opportunity to participate in the study was offered to all eligible patients/patient relative (proxy) by providing them an informed consent and providing them all the relevant information concerning the study.

A minimum of four (4) research assistants were recruited to facilitate a continuous data collection process on both day and night shifts in both the study centers. Prior to data collection, the research assistant(s) were trained on identification of patients with suspected UGIB, the use of the data collection checklist, and the relevant information to be collected

The principal researcher oversaw the data collection process and data were verified for quality accuracy on a daily basis.

Standardized data collection form/checklist

Data was collected prospectively during the patient's visit using a pre-defined checklist/case-report form, which recorded information with the treating physician and the patient and/or relative(s) and the electronic medical record (EMR).

The standardized data collection checklist/form had the following component:

a) Patient baseline information:

The researcher or his assistant(s) prospectively documented the patient's baseline information including the demographic status, referral status, payment modality.

b) Patient Clinical profile

Patient's presenting symptoms, comorbidities, vital signs and the pre-endoscopic severity scores were prospectively recorded. Clinical severity was measured using the pre-endoscopic Rockall score and the Glasgow-Blatchford **(Appendices IV & V)**. The ED management provided, including provision of urgent or emergent endoscopy were documented. All diagnostics, treatment and disposition were followed up, recorded and were based on the sole discretion of the treating physician.

c) Case follow-up

The research assistant(s) traced all patients enrolled (through their clinical files), throughout the duration of the study and observed and recorded the duration of ED and in- hospital stay, whether endoscopy was provided any time during the hospital stay, the outcome of the patient (discharged or died) and length of stay.

Quality and accuracy of data

The data were transferred from a handwritten standardized data collection checklist into an electronic data storage platform i.e. Research Electronic Data Capture (REDCap) (Version 6.0.1, Vanderbilt University, Tennessee, USA) on a daily basis and were overseen by the principle researcher to maintain the quality and accuracy of the data entered.

2.11 Data Analysis

Data were coded and imported into Research Electronic Data Capture (REDCap). Statistical Package for Social Science (IBM SPSS version 25, IBM, LTD, Carolina, USA) was used for analysis. Descriptive statistics were computed with continuous variables presented as mean +/- SD or median (IQR) depending on distribution. Categorical variables are expressed as number and percentage. Univariate associations between categorical variables and outcomes were computed using the Pearson Chi-square test. Multivariate regression analysis was completed on variables with p value ≤ 0.20 in the univariate analysis to identify predictors of 7-day mortality due to UGIB. Statistical significance was set at p-value < 0.05.

Outcomes of Interest

The following were the outcomes of interest of this study: Mortality (ED, 24-hour and in-hospital), active bleeding episode in ED, median length of stay (ED and in-hospital), patients' receiving endoscopy and risk factors and predictors of mortality.

2.12 Ethical Considerations

Permission to conduct the study was sought from relevant ethical committees at MNH and MUHAS. All patients were entered into the study after an informed consent was signed either by the patients themselves or their guardians in the case where patients were not able to do so. The investigator received the waiver of consent from the MUHAS Institutional Review Board incase patients weren't able to consent such as unconscious patients with absence of relatives to provide consent. All patients received treatment as per standard hospital policies. The data obtained during the study was kept anonymous.

The data were coded to hide patient's identity and stored in computer with password known by researcher and his assistant(s) only. The written forms were kept in a safe locker accessible by the researcher and his assistant(s) only.

There were no direct benefits to the patient from the study, though information gained form this study shall aid in improvement of patient care and management of UGIB, with more emphasis on ED management. There were no identifiable risks to the participants from this study.

CHAPTER THREE

3.0 RESULTS

During the period of study, there were 31,987 patient visits (30,800 from EMD-MNH and 1,187 from EMD-MAMC). From these we identified 123 (0.4%) patients with upper GI bleeding; all of whom were eligible and consented to be in the study. Of the patients who had UGIB, 113 (91.8%) were admitted (111 (90.2%) in the wards and 2(1.6%) in the ICU). 10 (8.20%) were discharged/absconded. The in-hospital 7 day mortality was 23(18.7%). While no death occurred amongst those discharged, the corresponding in-hospital mortality for those who were admitted to ICU and those who were admitted to the wards was 2 (100%) and 21 (18.9%) respectively. Figure 1.

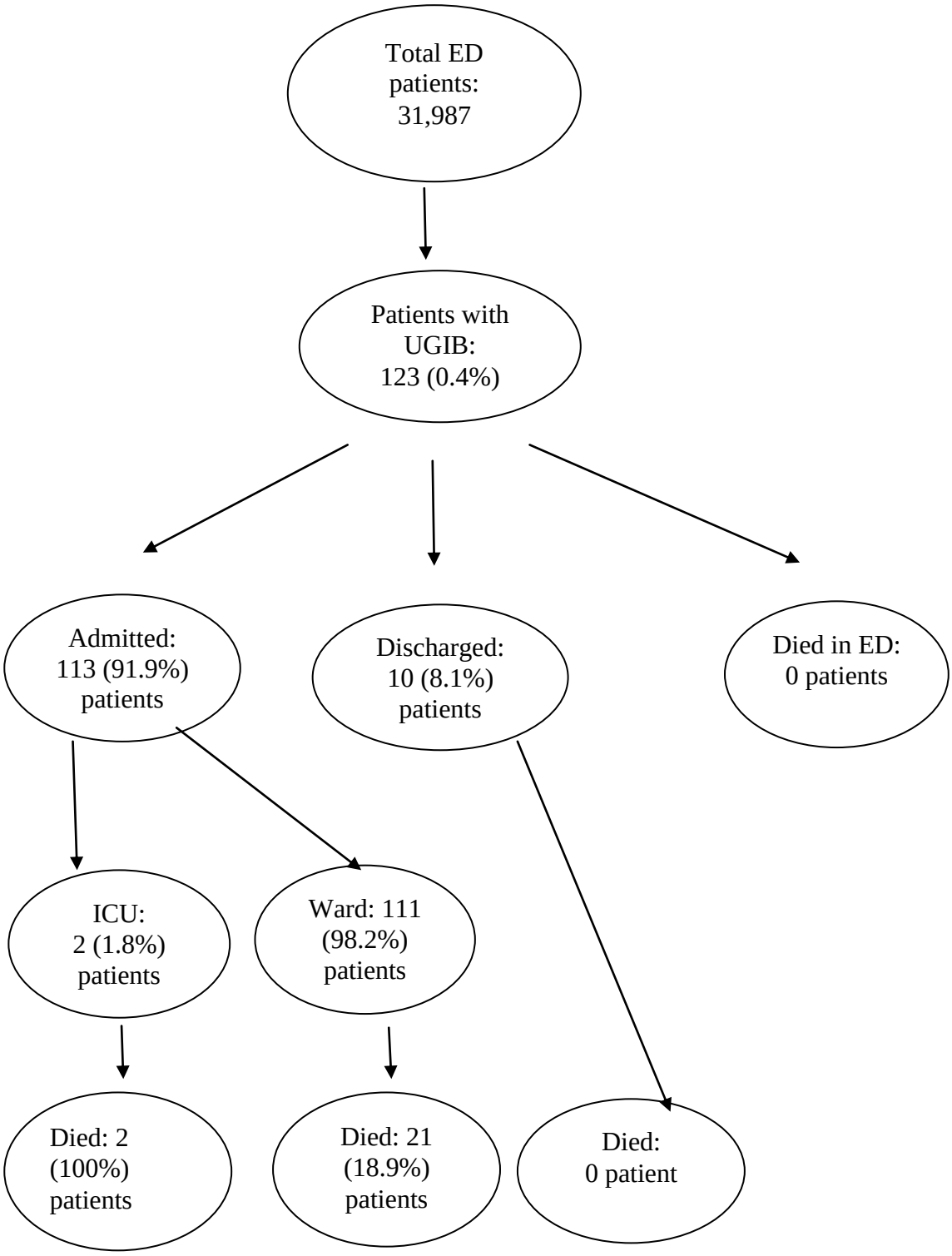


Figure 1: Flow of Patients with UGIB at the ED

3.1 Baseline Demographic of Study Population

Among the 123 patients with UGIB, 87 (70.7%) were male, and the overall median age was 42 years (with interquartile range of 32-64 years). Majority of patients 77 (62.6%) were referred from low health facilities, 87 (70.7%) were married 44 (35.8%) were self-employed and 99 (80.5%) were public patients. (Table 1)

Table 1: Demographic Characteristics of Patients Presenting With UGIB

Variable	Frequency (%)
Age (yrs.)	
Median age	42 years (IQR 32-64)
>40 years	64 (52.0%)
Sex	
Male	87 (70.7%)
Marital Status	
Married	87 (70.7%)
Single	29 (23.6%)
Widow/Widower	7 (5.7%)
Occupation	
Self-employed	44 (35.8%)
Unemployed	39 (31.7%)
Employed	20 (16.3%)
Retired	20 (16.3%)
Referral Status	
Hospital referred	77 (62.6%)
Insurance Status	
Cost sharing/public	99 (80.5%)

3.2 Baseline Clinical Characteristics of Patients Presenting With UGIB

The most frequently encountered presenting complaints was hematemesis and melena 39 (31.7%). Tachycardia was the most frequently reported abnormal vital sign 56 (45.5%). (Table 2)

Table 2: Clinical Characteristics of Patients Presenting With UGIB

Variable	Frequency (%)
Presenting Complaint	
Hematemesis	34 (27.6%)
Melena	33 (26.8%)
Hematochezia	11 (8.9%)
Hematemesis and Melena	39 (31.7%)
Hematemesis and Hematochezia	6 (4.9%)
Active Bleeding episode in ED*	8 (6.5%)
Vital Signs	
Tachycardia (HR>100 /min)	56 (45.5%)
Hypotension (SBP <100mmHg)	23 (18.7%)
Hypertension SBP≥140mmHg**	17 (13.8%)
Hyperglycemia (RBG >11.1mmol/l)**	11 (8.94 %)
Sp02<90%	6 (4.89%)
Bradycardia (HR<60 /min)	2 (1.62%)
Medical history	
PUD	39 (40.2%)
UGIB	25 (25.8%)
Esophageal Varices	17 (17.5%)
Liver disease	12 (10.3%)
Schistosoma infection	2 (2.1%)
Others	49 (50.5%)
UGI endoscopy	20 (16.3%)
Band ligation	4 (3.3%)

*New episode of either vomiting blood/coffee ground colored liquid and/or passing fresh blood per rectum whilst in the ED.

**Hypertension and Hyperglycemia classified according to National Institute for Health and Care excellence (NICE) guidelines(34,35)

3.3 Severity Scores for UGIB

All 123 patients with UGIB were scored for the clinical Rockall score. 82 patients were scored for the Glasgow-Blatchford score (GBS). This was due to missing of one or more of the POC/Lab results required in the scoring system. The majority of the patients 63(51.2%) had a moderate risk clinical Rockall score. Majority 71 (86.6%) patients had GBS score of ≥3, thus characterizing these patients as high risk for adverse events. (Table 3)

Table 3: **Severity Scores for UGIB**

Severity Scores	**Frequency (%)**
Clinical Rockall Score (n= 123)	
<3	52 (42.3%)
3-4	63 (51.2%)
>4	8 (6.5%)
Glasgow-Blatchford Score (n=82)*	
≥3	71 (86.6%)
<3	11 (13.4%)

***Cut-off value for GBS severity determined as per the study by *Ramfrez et al.* (22)**

3.4 Management strategies at the Emergency Department.

The majority of the patients (71.5%) received intravenous fluid whilst at the ED (Mean volume: 1394.3 mls). PPI was given in 71.5% of patients, of which 38.6% had prior PUD history. A small proportion of patients (18.7% and 20.3%) received Octreotide and Tranexamic acid respectively. 10(58.8%) with h/o esophageal varices and 7(58.3%) with h/o liver disease received octreotide. There was no clear indication for its use in 6(26.1%) patients. 8(47.1%) patients with prior h/o esophageal varices and 8(66.7%) patients with h/o liver disease received antibiotics in the ED. 27(62.8%) of the patients had no clear indication for antibiotic administration. Nearly half (48.8%) of patients received blood transfusion, with 80% of them receiving 1 unit of blood. None of the patients received emergent endoscopy service. (Table 4)

Table 4: ED Management Strategies

VARIABLES	FREQUENCY (%)
ED Management	
Intravenous fluid	88 (71.5%)
Proton pump Inhibitor	88 (71.5%)
Blood Transfusion (BT)	60 (48.8%)
Antibiotics	43 (35.0%)
Tranexamic acid	25 (20.3%)
Octreotide	23 (18.7%)
Inotropy/Vasopressor support	3 (2.4%)
NGT Placement	3 (2.4%)
Emergent endoscopy	0 (0.0%)
POC results	**n(n/N)**
Hemoglobin <8 g/dl (n=106)*	69 (65.09%)
Urea >7.1 mmol/l (n= 85)**	51 (60.0%)
Lactate >2 meq/l (n= 20)	11 (55.0%)

*****Cut-off value based on WHO Anemia severity classification

******Cut-off based on the high normal limit as stated in Glasgow-Blatchford score.

3.5 Upper GI Endoscopy

Upper GI endoscopy was performed in 46 (37.4%) of patients. Of these, none received emergent endoscopy i.e. straight from the ED. 17.4% received urgent Upper GI endoscopy within 24 hours. The majority of patients received UGI endoscopy from 72 hours up to 7 days post admission 15 (32.6%). (Table 5)

Table 5: Timing of Upper GI Endoscopy

VARIABLE	N=123
Time To Endoscopy	**n (%)**
>72 hr	15 (32.6%)
24-48 hr	13 (28.3%)
48-72 hr	10 (21.7%)
Within 24 hr	8 (17.4%)

3.6 Disposition Status of Patients Presenting with UGIB

Most of the patients were admitted to the general ward (90.2%), whereas only 1.6% were admitted to the ICU. None of the patients Died in the ED. The overall 7-day mortality was 18.7%, of whom 34.8% died within 24 hours. The median ED LOS was 5Hrs (IQR 3-7Hrs) with half of the patients 73(59.3%) staying for >4 Hrs. The median hospital LOS was 5 days (IQR 3-9 days). (Table 6).

Table 6: Disposition Status of Patients presenting with UGIB

Disposition and outcome	Number	Percentage
Wards	111	90.2%
Discharge home	8	6.50%
ICU	2	1.60%
Absconded	2	1.60%
ICU mortality	2	100%
Ward mortality	21	18.9%
Overall Inpatient mortality*	23	18.7%
7-days mortality**	23	18.7%
24-hour mortality**	8	6.50%

*This excludes EMD mortality, **Includes EMD, Inpatient and discharged

3.7 Factors Associated With 7-Day Mortality

Overall 23 (18.7%) patients died during the 7-day follow up period. Factors associated with mortality in the univariate analysis are listed in table 6, showing that age group >40, prior H/o liver disease, active bleeding episode in the ED, provision of antibiotics and clinical Rockall score ≥4 were all significantly associated with mortality. (Table 7)

Table 7: Univariate Analysis of Factors Associated With of 7-Day Mortality

	DIED n = 23	**SURVIVED n = 100**	**p- value**
Age Groups*			**0.005**
≤ 40	5 (8.5%)	54 (91.5%)	
> 40	18 (28.1%)	46 (71.9%)	
Male Sex	14 (16.1%)	73 (83.9%)	0.249
Medical History			
UGIB	5 (20.0%)	20 (80.0%)	0.852
PUD	7 (17.9%)	32 (82.1%)	0.884
Liver Disease	6 (50.0%)	6 (50.0%)	**0.003**
Esophageal Varices	3 (17.6%)	14 (82.6%)	0.905
UGI Endoscopy	3 (15.0%)	17 (85.0%)	0.643
Prior Hospitalization	18 (20.5%)	70 (79.5%)	0.429
Active Bleeding Episode In ED	5 (62.5%)	3 (37.5%)	**0.001**
ED Management			
Intravenous fluid	19 (21.6%)	69 (78.4%)	0.192
Octreotide	6 (26.1%)	17 (73.9%)	0.314
Tranexamic acid	6 (24.0%)	19 (76.0%)	0.446
PPI	15 (17.0%)	73 (83.0%)	0.456
Antibiotics	13 (30.2%)	30 (69.8%)	**0.016**
Blood Transfusion	13 (22.0%)	46 (78.0%)	0.410
Receiving Endoscopy	4 (8.7%)	42 (91.3%)	**0.028**
Clinical Rockall Score			0.081
< 4	18 (15.7%)	97 (84.3%)	
≥4	5 (62.5%)	3 (37.5%)	

*Age group cut-off based on study by *Moledina et al* (13).

3.8 Predictors of 7-Day Mortality

Multivariate regression analysis completed on variables with p value ≤0.20 in the univariate analysis found that age more than 40 years was independently associated with increased mortality, whereas receiving endoscopy reduced the risk of mortality. (Table 8)

Table 8: Multivariate Regression of Predictors of Mortality

	OR (95% CI)	**p-value**
Age >40 years	7.0(1.9-26.4)	**0.004**
H/o Liver Disease	2.5(0.5-11.1)	0.245
Active Bleeding Episode in ED	4.6(0.8-27.6)	0.096
Intravenous Fluid	1.9(0.5-7.5)	0.381
Antibiotics In ED	2.8(0.8-9.8)	0.101
Endoscopy	0.3(0.08-0.9)	**0.047**
Clinical Rockall Score ≥4*	1.3(0.4-4.8)	0.655

* cut-off value for clinical Rockall score as per study by *Wang et al.*(19)

CHAPTER FOUR

4.0 DISCUSSION

This study was aimed at identifying the clinical characteristics, ED management strategies and outcome of patients presenting with UGIB at ED-MNH and MAMC.

The study included 123 participants who presented to the ED with UGIB. The median age of the study participants was 42 years. A higher age at presentation was noted in many non-African studies (2,3,4,5,9,28) which is in contrast to this and other African studies which have shown a lower age at presentation (11–13,30,31).

Males accounted for just over twice the number of patients as female participants. Most African (11–13,30) and Non-African (2,4,28) studies of UGIB have found a high ratio of males to females which is similar to our study group.

4.1 ED presentation and clinical severity

Hematemesis with melena was the most frequently observed complaint in this study. A previous MNH study of *Kimu N* (32) reported similar presentation. Conversely, other studies have reported hematemesis as being the most commonly encountered presentation (2,9,12).

The participants in our study had a median pre-endoscopic Rockall score of 3. The majority of our patients (57.7%) were categorized as moderate to high risk for adverse events. Comparing this to a study conducted at MNH by *Moledina et al* with the majority (68.8%) having a low risk (≤3) score (13). Similar to our study, in the study by *Jaka et al,* majority (64.3%) were categorized as moderate to high risk in the endoscopic Rockall score (12). In the Malawian study by *Mulima et al*, a lower mean pre-endoscopic Rockall score of 1.87 but a higher post-endoscopic score of 3.23 was noted (30). Comparing this to couple of studies done in the developed countries; 66.6% in the Chinese study by *Wang et al* and 86% in the Iceland study by *Hreinsson et al* both concluded that their patients were categorized as moderate to high risk group (19,29). Majority of our patients had a Glasgow-Blatchford score of ≥3, thus

categorizing them as high risk for adverse events or in need for urgent intervention(s). In a Spanish study by *Ramfrez et al*, a similar high risk category of patients accounted for most (76.7%) of the study participants (22).

Almost three-quarter of our patient population had a hemoglobin level of <8g/dl, which the World Health Organization (WHO) classifies this as severe anemia (36). In comparison, less than a half of the patients in studies conducted in developed countries had a Hb of <8g/dl (2,29). Possible reasoning to the high number of patients with severe anemia in our study include: Prolonged episode of GI bleeding for which medical attention might not have been sought ((as noted PUD was the commonest comorbidity in 40% of our patients), poor dietary intake and possible concomitant hookworm infestation. Only a small proportion of patients had an active bleeding episode in the ED. A study conducted by *Thiebaud et al* revealed 51% of their study population had active and exteriorizing bleeding. The difference noted between these two studies is vast, however not much can be concluded due to scarcity of studies performed in the ED (2).

4.2 ED management strategies and disposition status

Fluid resuscitation was provided to a large number of participants. Only one-third of the patients with a prior history of PUD received PPI. This appears to be a deviation from international recommendations by the European Society of Gastrointestinal Endoscopy (ESGE), which recommend PPI use in patients with suspected or prior PUD history (25). Financial constraints and possible administration of PPI by referring hospital (note that MNH is a national referral hospital and patients usually pass through multiple health facilities before arriving at our ED) maybe the plausible reasoning to low utility of PPI in those with prior h/o PUD. Literature suggests that as opposed to H2 blockers, PPIs significantly reduce re-bleeding episodes of UGIB (37)(18). No patients in this study received the former thus showing compliance with current guidelines.

A small proportion of patients received Octreotide, of whom half (58.6%) had indication for its use based on historical features (such esophageal varices and liver diseases). Octreotide or Terlipressin (not available in our setting) is known to be an effective treatment strategy in acute variceal bleeding and is recommended by the National Institute for Health and Care Excellence (NICE) for use in patients with suspicion of VUGIB (7). Though not routinely recommended, it may be utilized in settings of acute non-variceal bleed especially in situations where endoscopic therapy isn't available (37). The utilization of Octreotide in our study was low. This may be a subject for further investigation.

Small number of patients received Tranexamic Acid. Similar results were also observed in one study by *Chertoff et al*(38). A Cochrane review found tranexamic acid to have beneficial effect in reduction of mortality, but no significant effect in the reduction for need of surgery, provision of blood transfusion or increasing adverse thromboembolic phenomena (39)(37). Further studies are required to prove its beneficial effect in UGIB. To date, the European Society of Gastrointestinal Endoscopy (ESGE) does not recommend use of tranexamic acid in NVUGIB (25).

Antibiotic administration especially in patients with prior history of liver disease and esophageal varices was low i.e. 16(37.2%). This is in contrary to the current literature suggestion by the National Institute of Health and Care Excellence (NICE), which emphasizes prophylactic antibiotic use in patients with suspected or confirmed variceal bleed or a history suggestive of liver disease including cirrhosis (7). Antibiotic use is associated with reduced morbidity and mortality in such cases. Furthermore, hospitalized patients have a reduced risk of recurrent bleeding episodes. Although this study did not aim to look into the type of antibiotic used, ceftriaxone was found to be the most commonly utilized and readily available antibiotic in our setting. Ceftriaxone is found to be superior to quinolones such as norfloxacin in hospitalized patients (37) (40). Basing on our study results, a need for further improvement in this aspect of ED antibiotic administration is needed. Provision of antibiotics was associated with increased incidence of mortality however the difference observed was statistically insignificant following a regression analysis. (p= 0.096)

Nearly half of the participants received blood transfusion, with majority receiving only one unit. The number of units is less compared to what was observed in the study by *Kimu N,* and *Jaka et al* (32)(12). It was noted in our study, similar to the one conducted by *Jaka et al* in Mwanza (12) that those who received BT had a higher mortality rate than those who didn't. The difference nonetheless was not found to be statistically significant. (p=0.488).

Though this study was not aimed to look at this aspect, scarcity of blood at the blank bank, unavailability of un-cross matched blood and a general delay in obtaining blood from the blood bank are likely contributing factors to the low level of blood transfusions observed. In a study conducted by *Shari et al.* published in 2017 at MNH, only a quarter of the patients with criteria for BT received blood and amongst those who didn't receive blood, the need for transfusion was either not identified by the treating physician, blood was not available at the blood bank or there was a significant delay in obtaining blood (median time=7 hours) (41). The reason for increased mortality maybe attributed to the facts that those who received the most BT had a higher pre-endoscopic Rockall score.

Majority of the patients with a clinical severity of either moderate or high risk (i.e. Rockall score of 3-4 or >4 respectively) were admitted to the general ward. This is due to fewer available slots in the ICU/High-Dependency Unit (HDU). This means that the sicker patient would not get the close attention and care that they need in the general wards, thus increasing their likelihood to have adverse outcomes.

4.3 Endoscopy throughout Hospital Stay and Predictors of receiving it

Approximately one-third of the patients received endoscopy at any point during their hospital stay. This number is significantly lower than what was observed by *Moledina et al,* where almost half of the patient population received endoscopy (13). Of these patients, none received emergent endoscopy. Only a handful of participants received urgent endoscopy i.e. within 24 hour of the ED presentation. Majority received endoscopy >72 hours following ED presentation. Overall those who received endoscopy at any point throughout their hospital stay had significantly less mortality (p=0.047). While literature suggests endoscopy should be done

within 24 hours, we found that endoscopy was associated with lower mortality, even though it was late. This suggests that the endoscopy was really more of a marker of patients who were going to survive. This findings tally with that noted by *Moledina et al*, whereby they noticed a 4 folds increase in mortality in those who didn't receive endoscopy (13). Similar trend of reduced mortality in patients receiving endoscopy can be appreciated in the study conducted by *Chofle et al* (11). Contrasting high income countries, a French study by *Thiebaud et al* observed that majority of their patients had endoscopy done during the hospital stay, of whom $1/4^{th}$ had emergent endoscopy i.e. straight from the ED (2). Similarly in a study conducted in London by *Sarin et al*, 66% of the patients had endoscopy performed throughout the hospital stay (42). On the other hand, literature and guidelines advocate that early endoscopy, preferably within 24 hours of presentation is associated with reduced mortality; on the other hand it has been also noted that emergent endoscopy performed within 12 hours of presentation is associated with increased risk of mortality, presumably due to inadequate resuscitation (7,24,37,43).

4.4 Mortality

An overall 7-day mortality of 18.7% was noted in our study. None of these patients died in the ED, however one-third (34.8%) of those who died, died within 24 hours of ED presentation. In comparison to two previous studies done at MNH, *Moledina et al* found a lower 24 hour mortality rate (24.6%) but a considerably higher 60 day mortality of 33.6% (13) whereas *Kimu N.* found a mortality of 15.6% (32). The higher mortality observed in *Moledina et al.*'s study can be explained a higher pre-endoscopic Rockall score (score >3) of their patients i.e. 31.2% vs. 6.5% in our study; thus signifying severe disease in their cohort, but also they followed up patients for 60 days and mortality due to any cause was included in their analysis (13). The mortality observed in *Kimu N.*'s study was slightly lower than ours; though no inference on the possible reason for the difference observed can be made. Furthermore, the majority of patients with a high Rockall score in our study were admitted into the general ward, where they were unlikely to receive the necessary aggressive care for their severity of illness; thus contributing to a high mortality rate observed. Although the Rockall score was not an

independent predictor of mortality, the study was not powered for this comparison. High Rockall scores have been implicated as a risk factor for increased adverse events, prolonged hospital length of stay and requirement for blood transfusion in the Tanzanian study by *Jaka et al* (12)..

Age >40years was associated with 7X increased risk of mortality (p=0.004) whereas provision of UGI endoscopy was associated with reduced risk of mortality ($p=0.047$). In Non-African countries and in the previous study done at MNH, mortality has been implicated with increasing age above 40 years (2,3,29)(13). In the study performed in Mwanza by *Jaka et al.* advanced age >60 years was associated with increased mortality (12).

4.5 Strengths

This was a Two-Centered, prospective study whereby consecutive recruitment of participants was done, thus reducing the chance of missing a potential participant(s). Furthermore all patients were followed up in this study.

4.6 Limitations

Some laboratory variables were not obtained for all the patient participants, thus this may have underestimated or overestimated the significance of these variables to the outcomes understudy, including the scores such as Glasgow-Blatchford score.

Comorbidities were assessed using information provided by either patients/relatives or any prior hospital documentation brought by them. This may have either over or under stated some of the comorbidity, this in turn could have affected the pre-endoscopic Rockall score and its association with the primary outcome.

The sample size for the study was estimated for our overall outcome of mortality, but not necessarily for risk factors analysis, and thus some factors not found to be significant may show statistical significance in a larger study.

CHAPTER FOUR

5.0 CONCLUSION AND RECOMMENDATION

5.1 Conclusion

The mortality rate for UGIB in our setting remains substantially higher than in non-African countries. Endoscopic evaluation and treatment at any point during the hospital stay still remains an independent predictor of mortality. Future studies should focus on assessing knowledge of providers on managing patients with UGIB and familiarity with the international recommendations.

5.2 Recommendation

1. A high 24-hour mortality may in part be a reflection of ED care and management. Aggressive patient management including adequate blood resuscitation, provision of drugs such as octreotide and antibiotics in those patients with indications and potentially tranexamic acid can improve the care. Admitting patients to appropriate sites based on their severity score may prove crucial in reduction of mortality.

2. Current application of UGI endoscopies in this setting is suboptimal and more lives can be saved if done earlier. Efforts should be made to increase number of urgent endoscopies performed.

3. A larger study can be conducted to look at some of the potential predictors or causative factors that were statistically insignificant in this study for the interest of public health.

4. Develop standardize guidelines in collaboration with the gastroenterology unit basing on the current international recommendations for the management of UGIB. This guideline should not only be applicable to MNH and MAMC ED but also to low referring facility whereby a standardized basic management (within the resources of the facility) can be provided to UGIB patients.

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APPENDICES

Appendix 1: Questionnaire/Case Report Form

This is a Data collection checklist which will be used for each participant with UGIB, meeting the inclusion criteria for the study. Please fill all the details mentioned in the checklist.

Code no: _____

Patient's contact: _____

MR no: _____

1st of Kin contact: _____

Date of EMD visit: _____

2nd of Kin contact: _____

Date of Discharge: _____

Time of EMD visit: _____hr

IRB No: _____

A. DEMOGRAPHICS

1. **Age: _____**
2. **Sex:**

☐Male

☐Female

3. **Marital status:**

☐Married

☐Single

☐Divorced

☐Widow/Widower

4. **Occupation:**

☐Employed

☐Self-employed

☐Unemployed

☐Retired

5. Referral status:

☐Self-presented

☐Hospital referred

6. Insurance status:

☐Insured

☐Cash paying/public

B. CLINICAL PROFILE

1. Presenting complaint(s):

☐Hematemesis

☐Melena

☐Hematochezia

☐Hematemesis & Melena

☐Hematemesis & Hematochezia

☐Other: _____

2. Comorbidities:

☐H/o UGIB

☐H/o PUD

☐H/o Esophageal varices

☐H/o Liver disease

☐H/o Schistosoma infection

☐H/o Diabetes

☐H/o Hypertension

☐H/o Cardiac failure

☐H/o Renal failure

☐HIV

☐H/o Malignancy

Charlson's comorbidity index: _____

3. H/o Band ligation:

☐Yes Number of times: _____

☐No

4. H/o UGI endoscopy

☐Yes

☐No

5. Prior Hospitalization- UGIB:

☐None

☐1-2

☐3-4

☐>4

6. Drug ingestion within 24 hrs:

☐Alcohol

☐NSAID

☐Anti-platelet/Anticoagulant

☐Beta-blocker

☐Proton-Pump inhibitors

1. Initial Vital signs:

BP: _____ HR: _____ RR: _____ SPO2: _____ RBG: _____

SBP (mmHg):

☐>100

☐<100

HR (BPM)

☐>100

☐<100

2. Initial POC/Lab results:

Lactate: _____

Hb: _____

BUN: _____

3. Clinical Severity:

Clinical (pre-endoscopic rockall) score: _____ Glasgow Blatchford score: _

☐<3

☐3-4

☐>4

C. <u>ED MANAGEMENT</u>

1. Fluid Resuscitation:

☐Yes

☐No

2. Type of fluid:

☐NS

☐RL

☐Other: _____

3. Volume of Fluid given:____/4hrs

☐<1000mls

☐1000-2000mls

☐3000-4000mls

☐>4000mls

4. NGT placement:

☐Yes

☐No

5. NGT Aspirate findings:

☐Clear/Bilious

☐Coffee-ground

☐Red-blood

5. IV Octreotide/TXA:

☐Yes

☐No

6. IV Proton Pump Inhibitor:

☐Yes

☐No

7. Antibiotics:

☐Yes

☐No

8. Inotropy/Vasopressor support:

☐Yes

☐No

9. Gastroenterology consult:

☐Yes

☐No

4. DRE done?

☐Yes

☐No

11. DRE findings:

☐Normal

☐Fresh blood

☐Melena

12. Blood Transfusion:

☐Yes

☐No

13. Number of Units transfused: _____units

☐1-2

☐3-4

☐>4

14. Disposition:

☐Admitted to ward Specify which ward: _____

☐Admitted to ICU

☐Urgent OGD

☐Surgery

☐Discharged

☐DAMA

15. OGD: Did the patient receive OGD?

☐Yes

☐No

16. Time to OGD? _____ hrs

☐Within 24 hrs

☐24-48 hrs

☐48-72 hrs

☐>72 hrs

17. ED length of stay: _____ hrs

☐<1 hr ☐1-2 hrs ☐3-4 hrs ☐> 4 hrs

D. <u>MORTALITY AND ACTIVE BLEEDING IN ED</u>

1. Mortality:

☐Yes

☐No

2. If yes, did the patient pass away in the ED?

☐Yes

☐No

3. Time to mortality from arrival to ED: _____ hrs

☐Within 24 hrs ☐24-72 hrs ☐7 days

4. Active bleeding: Did the patient have active bleeding in ED?

☐Yes

☐No

Appendix II: Informed Consent Form (English Version)

Greetings, my name is Dr. Shaffin Rajan, a postgraduate student in Emergency Medicine, conducting a research on Upper Gastrointestinal Bleeding. You may be eligible to take part in this research project. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study. Please take time to review this information carefully. If you have any queries, please do not hesitate to consult me. Once you understand the information in this form, please sign below if you agree to take part in the study.

Study Title: Profile and outcome of adult patients presenting with upper gastrointestinal bleeding at the Emergency medicine department of Muhimbili National Hospital

Researcher: Dr. Shaffin Rajan, MD, Department of Emergency Medicine Muhimbili University of Health and Allied Sciences.

Purpose of this study: Upper gastrointestinal bleeding is a condition that affects many individuals in our population. It can lead to various health problems including mortality. Proper management of this problem will lead to better outcomes for the patients. This study is aimed at looking at what possible factors can help us predict the outcome and appropriate care of patients with upper gastrointestinal bleeding. With this information, we may be able to manage you and any other patient that may present with this disease to our department.

Who can take part in this study? This study is for all adults above the age of 18 years who are seen at the emergency department with upper gastrointestinal bleeding. Participation in this study is entirely voluntary. You may also leave this study at any time without any harm on you. You will not lose any benefits, nor will you be given improper treatment if you decide not to take part in this study.

What will happen in this study? When you agree to be part of this study, you will be asked a few questions about your demographic characteristics. We will also look at your blood investigation results and the management provided to you. All this will be done to identify which factors can affect the outcome in patients with upper gastrointestinal bleeding. You will be given all information regarding your results during this study. You will also receive the standard of care that is appropriate for you, as per the hospital policies.

Are there any risks of taking part in this study? There are no risks for you for participating in this study. The laboratory/Point-of-care investigations that will be done are the same routine ones that are done for all patients with upper gastrointestinal bleeding. You will not be given any experimental medication, nor will any additional test be done on you as part of the research.

Are there any benefits of taking part in this study? You may not receive any personal benefits from being in this study. However, any new information that will be learned in this study will be used to manage your condition better.

Are there any costs or fees for entering this study? There will be no additional costs to you or your family for being in this study. You will only pay for all the things that you would have paid for if you were not in the study.

Is there confidentiality in this research project? The information gained in this study about you will only be known to you and the researcher. No other person will be given open access to the information. If your information is needed in the future by another doctor for your treatment, it will be made available to him. The results of this study could be published in an article for other researchers to read but would not include any information that would let others know who you are.

Your signature below means you have read the above information, understood it well and are voluntarily ready to participate in this study.

Signature of Participant **Date**

_____ _____

Thank you for agreeing to participate in the study. Please do not hesitate to contact me for any clarification should need arise.

Contact Information:

Dr. Shaffin Rajan,
Principal Investigator.
Mobile No: 0788 417 138

Dr. Bruno Sunguya
Director of Research and Publications,
Research and Publication Committee,
Muhimbili University of Health and Allied Sciences,
P.O. Box 65001, Dar es Salaam.
Telephone Number: 2150302-6

Appendix III: Consent Form (Swahili Version)

Jina langu naitwa Dkt. Shaffin Rajan, mwanafunzi wa udaktari bingwa wa ugonjwa wa dharura. Nina fanya utafiti kuhusu kutokewa na damu tumboni. Unaweza kuwa na haki ya kushiriki katika mradi huu utafiti. Hati hii inakupa habari muhimu kuhusu utafiti. Inaelezea madhumuni ya utafiti, hatari na faida ya kushiriki katika utafiti. Tafadhali chukua muda wa kupitia taarifa hii kwa makini. Kama una maswali yoyote, tafadhali usisite kuwasiliana na mimi. Baada ya kuelewa habari katika fomu hii, tafadhali saini hapa chini kama utakubali kushiriki katika utafiti.

Mada: Wasifu na matokeo ya wagonjwa waliolazwa kwasababu ya kutokwa na damu utumboni katika idara ya dharura ya hospitali ya Taifa Muhimbili.

Mtafiti: Dk. Shaffin Rajan, MD, Idara ya Tiba ya dharura, Chuo Kikuu cha Afya na Sayansi Muhimbili.

Lengo la utafiti huu: Kutokwa na damu utumboni ni hali ambayo huathiri watu wengi katika jamii yetu. Ugonjwa huu unaweza kusababisha matatizo mbalimbali pamoja na vifo. Matibabu sahihi ya tatizo hili itasababisha matokeo bora kwa wagonjwa. Lengo la utafiti huu ni kuangalia sababu ipi inaweza kutusaidia kutabiri matokeo na matibabu sahihi ya wagonjwa wanaolazwa na ugonjwa huu. Kwa utafiti huu, tunaweza kuwa na uwezo wa kutibu wewe na wagonjwa wengine ambao wana ugonjwa huu.

Nani anaweza kushiriki katika utafiti huu? Utafiti huu ni kwa ajili ya watu wazima wote juu ya umri wa miaka 18 ambao wamelazwa katika wodi ya Dharura na ugonjwaa wa kutoka damu utumboni. Kushiriki katika utafiti huu ni hiari kabisa. Unaweza pia kuacha utafiti huu wakati wowote bila ya madhara yoyote kwako. Huwezi kupoteza faida yoyote, wala hautapewa matibabu yasiyofaa kama wewe huamua kutoshiriki au kuacha utafiti huu.

Nini kitatokea katika utafiti huu? Utaulizwa maswali kadhaa kuhusu tabia yako binafsi. Pia tutakuwa tunaangalia matokeo yako ya damu na matibabu utakayopewa. Wewe utapewa taarifa zote kuhusu matokeo yako wakati wa utafiti huu. Wewe pia utapata huduma sahihi kulingana na hali yako, kwa mujibu wa sera hospitali.

Je, kuna hatari yoyote kwa ajili ya kushiriki katika utafiti huu? Hakuna hatari kwako kwa kushiriki katika utafiti huu. Vipimo vya maabara ambavyo vitafanyika ni sawa na vipimo kwa wagonjwa wote wa kutokwa damu utumboni. Hautapewa dawa yoyote ya majaribio, wala vipimo vyovyote vya ziada havitafanyika kwasababu ya kushiriki katika utafiti.

Je, kuna faida yoyote ya washiriki katika utafiti huu? Hutapata faida yoyote ya kibinafsi kutoka kuwa katika utafiti huu. Hata hivyo, taarifa yoyote mpya ambayo kitatokea katika utafiti huu kitatumika kutibu hali yako bora.

Je, kuna gharama yoyote au ada kwa ajili ya kushiriki katika utafiti huu? Hakutakuwa na gharama za ziada kwa wewe au familia yako kwa kuwa katika utafiti huu. Wewe utalipa kwa ajili ya huduma zote ambazo ungepewa usingekuwa katika utafiti.

Je, kuna usiri katika utafiti huu? Taarifa zitakazopatikana katika utafiti huu kuhusu wewe zitabaki na wewe na mtafiti. Hakuna mtu mwingine atapewa uwezo wa kujua taarifa hizo. Kama taarifa yako zitahitajika katika siku zijazo na daktari mwingine kwa ajili ya matibabu yako, zitatolewa kwake. Matokeo ya utafiti huu inaweza kuchapishwa katika makala kwa ajili ya watafiti wengine kusoma lakini taarifa itakuwa bila ya taarifa yoyote ambayo ingeweza kuruhusu wengine kujua wewe ni nani.

Saini yako chini ina maana umesoma habari hapo juu, huelewa vizuri na unashiriki katika utafiti huu kwa hiari.

Saini ya mshiriki **Tarehe**

_____ _____

Asante kwa kukubali kushiriki katika utafiti. Tafadhali usisite kuwasiliana na mimi kwa maswali yoyote.

Mawasiliano:

Dkt. Shaffin Rajan,
Mtafiti Mkuu.
Namba ya Simu: 0788 417 138.

Dr. Bruno Sunguya
Mkurungenzi wa Utafiti na Machapisho,
Kamati ya Utafiti na Machapsiho,
Chuo Kikuu Cha Sayansi na Tiba Cha Muhimbili,
S.L.P. 65001, Dar es Salaam.
Namba ya Simu: 2150302-6

Appendix IV: Clinical (Pre-Endoscopic) Rockall Score

COMPONENT	**0**	**1**	**2**	**3**
AGE (yrs)	<60	60-79	>80	
HEMODYNAMICS	HR<100 SBP>100	HR>100 SBP>100	 SBP<100	
COMORBIDITIES	NONE	-	IHD, CHF, ANY MAJOR COMORBIDITIES	RENAL FAILURE, LIVER FAILURE, METASTASIS

Source: Wang2013

Total score is calculated by addition of individual scores. Scores<3 signifies low risk, scores 3-4 signifies moderate risk and score >4 signifies high risk for re-bleeding, mortality or surgery.

Appendix V: Glasgow-Blatchford Score

ADMISSION RISK MARKER	SCORE COMPONENT
BLOOD UREA(mmol/L)	
6.5-8	2
8.0-10.0	3
10.0-25.0	4
>25	6
HEMOGLOBIN FOR MEN(g/dl)	
12.0-12.9	1
10.0-11.9	3
<10	6
HEMOGLOBIN FOR WOMEN(g/dl)	
10.0-11.9	1
<10	6
SYSTOLIC BLOOD PRESSURE(mmHg)	
100-109	1
90-99	2
<90	3
OTHER MARKERS	
PULSE RATE >100bpm	1
PRESENATION WITH MELENA	1
PRESENTATION WITH SYNCOPE	2
HEPATIC DISEASE	2
CARDIAC FAILURE	1
TOTAL	

Source: Cheng2012

A score of <3 is considered Low-risk, whereas a score greater than ≥3 is high risk for needing intervention, transfusion, endoscopy or surgery. Cut-off value for GBS severity determined as per the study by *Ramfrez et al.* (22)

Appendix VI: Approval for ethical clearance

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

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Ref. No. DA.287/298/01A/

25th June, 2018

Dr. Shaffin S. Rajan
MMed. Emergency Medicine
MUHAS.

RE: APPROVAL OF ETHICAL CLEARANCE FOR A STUDY TITLED: "PROFILE AND OUTCOME OF ADULT PATIENTS PRESENTING TO THE EMERGENCY DEPARTMENT WITH UPPER GASTROINTESTINAL BLEEDING"

Reference is made to the above heading.

I am pleased to inform you that, the Chairman has, on behalf of the Senate, approved ethical clearance for the above-mentioned study. Hence you may proceed with the planned study.

The ethical clearance is valid for one year only, from 21st June, 2018 to 20th June, 2019. In case you do not complete data analysis and dissertation report writing by 20th June, 2019, you will have to apply for renewal of ethical clearance prior to the expiry date.

Dr. Emmanuel Balandya
ACTING: DIRECTOR OF POSTGRADUATE STUDIES

cc: Director of Research and Publications
cc: Dean, School of Medicine