

Profile and Outcome of Patients with Upper Gastrointestinal Bleeding Presenting to Urban Emergency Departments of Tertiary Hospitals in Tanzania

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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 to EDs, especially within limited resource settings where emergency medicine is a new specialty. We aim to describe the patient profile, clinical severity and outcomes of the patients who present with UGIB to the ED of tertiary referral hospitals in Tanzania.

Methodology: This was a prospective cohort study of consecutive adult (≥ 18 years) patients presenting to the EDs of Muhimbili National Hospital (EMD-MNH) and MUHAS Academic Medical Centre (EMD-MAMC), in Tanzania with non-traumatic upper gastrointestinal bleeding (UGIB) from July 2018 to December 2018. We used the clinical Rockall score to assess disease severity. The primary outcome of 7-day mortality was summarized using descriptive statistics. Regression analysis was performed to identify predictors of mortality.

Results: During the study period, 123 patients presented to one of the two EDs with an UGIB. 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%). Within 7 days, 23 (18.7%) patients died and one-third 8 (34.8%) of these died within 24 hours. There were no ED deaths. About 65.1% of the patients had severe anemia but only 60 (48.8%) received blood transfusion in the ED. Amongst those with h/o esophageal varices 7 (41.2%) did not receive octreotide. Only 8 (17.4%) received endoscopy within 24 hours, all of who had a low or moderate clinical Rockall score i.e. <3 and 3-4. Age >40 years was a significant independent predictor of mortality (OR=7.00 (95% CI 1.9-26.4)). Receiving UGI endoscopy was independently associated with a lower risk of mortality (OR= 0.27; 95% CI 0.08-0.9.)

Conclusion & Recommendations: In this urban ED in Sub-Saharan Africa, UGIB carried a high mortality rate. Age < 40 years and endoscopic evaluation during the hospital stay were independent predictors of lower mortality. Future studies should focus on evaluating how to improve access to UGI endoscopy so as to improve outcomes

Background

Upper Gastrointestinal bleeding (UGIB) is a medico-surgical emergency. Although there has been a global decline in the mortality associated with UGIB, the incidence and mortality associated with GI bleeding remains high in limited income countries. In the United States, UGIB accounts for 300,000 admissions per year with approximately 5% mortality rate (1), whereas in several studies from sub-Saharan Africa, mortality is as high as 20%; 5.9% – 13.6% in Nigerian studies, 17% in Malawi and 8.74% in Egypt (2–5). In Tanzania, mortality appears to be much higher, ranging approximately from 10–30% (8–11). It is not clear if the higher mortality seen in LIMC's is due to patient demographics, severity on presentation, etiology or compliance with care standards. Esophageal varices has been implicated as a commonest cause of UGIB in several African studies, including studies carried out in Tanzania (2–11). Rather than being due to alcoholic liver disease as in HIC's, varices in sub-Saharan Africa result from Schistosoma-related portal hypertension (7,11,12). This is in contrast to HIC where erosive gastritis has been commonly implicated (1,13,14). Other potential contributors to the higher mortality may be the severity of disease presentation, as there is little primary care in our setting, and many patients seek care very late in their disease.

Another potential contributor is failure to follow appropriate management guidelines. Proton pump inhibitor (PPI) for those with suspected Non-variceal UGIB (NVUGIB), somatostatin analogues such as octreotide and antibiotics in suspected cases of variceal UGIB (VUGIB) and in those with clinical suspicion of liver disease, timely blood transfusion and early use of endoscopy may not occur in these settings due to lack of appropriate specialists, lack of resources or supply chain issues. (15)(16)(17). A knowledge gap on the current UGIB management guidelines and recommendations amongst the health care providers may also contribute to inadequate management of UGIB cases. Earlier Tanzanian studies demonstrate lack of appropriate care offered to patients with UGIB. Nearly half of the patients in one the studies did not receive endoscopic evaluation and treatment (11) whereas 47.1% of the patients who required blood transfusion, did not receive blood transfusion in another study (9).

There is little information on the presentation, etiology and management of patients presenting to EDs. The presence of full capacity Emergency departments at Muhimbili National Hospital (MNH) and MUHAS Academic Medical Centre (MAMC) - a branch of MNH, have provided the opportunity for early stabilization and management of patients presenting with UGIB. The aim of this study was to look at the patient profile, the clinical severity and outcomes of the patients who presented with UGIB to the ED.

Methods

Study design

This was a prospective cohort study of adult patients presenting to the EMD MNH with upper gastrointestinal bleeding from July 2018 to December 2018.

Study setting

This study was conducted at the EMD- MNH and EMD-MAMC, Dar es Salaam Tanzania. MNH is a public, tertiary referral hospital and the site of the first full capacity public ED in Tanzania which opened in 2010. MNH is the primary training site for the only Emergency Medicine (EM) residency program in the country. MAMC is a recently inaugurated full capacity university health facility with a state of the art emergency medicine department, located approximately 30km from MNH. MNH and MAMC both have a fully equipped endoscopy unit.

Study Participants

All consenting adults (age greater than or equal to 18years) presenting with UGIB unrelated to a recent trauma were eligible for the study. We excluded patients who had previously been enrolled in the study who presented with recurrent episodes of UGIB during the period of the study.

Study protocol

Research assistants were scheduled to collect data 24 hours a day, seven days a week and during that time patients were consecutively approached and asked for consent to be followed for the study. Demographics, clinical presentation, initial management, and ED outcomes were collected by the research assistant using information given by the patient or caregiver, the treating physician, and data found in the electronic medical record (Wellsoft). A structured case report form was used to record all participants' information. All patients were followed up in a hospital ward (if admitted) or through mobile phone calls to determine their outcome from the ED-MNH and MAMC, at 24-hours and 7-days.

Outcomes

The primary outcome was 7 -day mortality and secondary outcomes were ED and hospital length of stay and 24 hour mortality.

Data analysis

Data from the CRF was entered into REDCap (version 7.2.2, Vanderbilt, Nashville, TN, USA) and transferred into the Statistical Package for Social Science (SPSS) (version 25.0, IBM, LTD, North Carolina, USA). 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.

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. Median age was 42 [IQR 32–64] years and 87 (70.7%) were male; 87 (70.7%) were married 44 (35.8%) were self-employed. The majority of patients 77 (62.6%) had been previously seen at a lower capacity health facility and transferred to one of the two study sites. Most patients (99, 80.5%) were uninsured.

Of those enrolled, 113 (91.8%) were admitted and 10 were discharged or absconded prior to discharge. Among admissions, 111 (90.2%) were admitted to the wards and 2 (1.6%) to the ICU. The overall 7-day mortality was 18.7%. (*Figure 1*)

Clinical presentation

The most frequently encountered presenting complaint 39 (31.7%) was a combination of hematemesis and melena. Nearly half 56 (45.5%) were tachycardic on arrival. All 123 patients with UGIB were scored for the clinical Rockall score. 63(51.2%) of the patients had a moderate risk clinical Rockall score of 3–4. A Glasgow-Blatchford score (GBS) could be obtained for 82 patients; this was due to missing of one or more of the POC/Lab results required for this scoring system. Of those scored, the majority (71, 86.6%) had GBS score of ≥ 3 , thus characterizing these patients as high risk for adverse events. (*Table 1*)

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. Less than half (10, 43.5%) of those receiving Octreotide had prior h/o esophageal varices. Amongst those with h/o esophageal varices (7, 41.2%) did not receive octreotide. A minority (8, 18.6%) of those with a known history of liver disease received antibiotics in the ED. Nearly half (48.8%) of patients received blood transfusion, with 80% of them receiving 1 unit of blood. No patient received emergent endoscopy.

Upper GI endoscopy was performed in 46 (37.4%) of patients. Of these, (8, 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%). None of the patients with h/o esophageal varices received urgent endoscopy. (*Table 2*)

All patients were followed up, including those discharged. Overall mortality rate was 18.7%. Both patients admitted to the ICU died within 7 days. Among those admitted to the ward, 21 (18.9%) patients died within 7 days and no patients who were discharged died. 24-hour mortality was 8 (34.8%).

Predictors of 7-Day Mortality

Factors significantly associated with mortality were age group >40 , prior H/o liver disease, active bleeding episode in the ED, provision of antibiotics in the ED and clinical Rockall score ≥ 4 . (*Table 3*)

In multivariate regression, age and endoscopy were independently associated with 7 day outcome: age more than 40 years was independently associated with increased mortality, whereas receiving endoscopy reduced the risk of mortality. (*Table 4*)

Discussion

This study showed that UGIB was associated with a high mortality rate (18.7%). The 24-hour mortality was significantly high (34.8%); which may be an indirect reflection of the emergency care provided or maybe explained by a high disease severity amongst these patients. Endoscopic evaluation at any point during the hospital stay was found to be protective factor against mortality. Despite this fact, only 37.4% of the patients received UGI endoscopy of which only a handful received urgent endoscopy i.e. within 24 hour of ED presentation.

In contrast to HIC, patients in our study were of younger age, with the median age being 42 years (1,13,14,18). We observed that age above 40 years was an independent predictor of mortality. This has also been noted in prior studies both in HIC and LMIC (1,11,13,14). The mortality observed in our study is much higher compared to developed countries (1,13,14). Factors contributing to the high observed mortality rate include; higher disease severity, disposition status and gaps in management of these patients.

Our patients appeared to have a higher disease severity in comparison to those in HIC. A large proportion of our patients had a moderate to severe clinical Rockall score (i.e. score of 3–4 and >4) as compared to a Chinese study carried out in the ED, where most (50.6%) had a low Rockall score of 0–2 (19). Several studies suggest an association between high Rockall score and increased mortality (19,20). Similarly, the Glasgow-Blatchford observed in our study was much higher compared to a British study carried out

between the years 2008–2009, whereby majority of their patients had a GBS score ≤ 2 (21). Severe anemia (Hb $< 8\text{g/dl}$) was observed in over a half of our patients. Comparing studies conducted in HIC, less than one-third of the patients had a Hb count suggestive of severe anemia (13,14,22). Regardless of the high proportion of patients with severe anemia, less than half of the patients received BT. Previous study carried out at MNH, revealed that a general unavailability of blood and scarcity of un-cross matched blood at the blood bank along with delays in obtaining blood were amongst the major cause of low levels of blood transfusion (23).

Small proportion of patients were admitted to ICU. In view of the higher disease severity in our study, a larger number of patients were expected to be admitted into the ICU. Admission to the general ward implies that these patients were unlikely to receive the necessary aggressive care for their severity of illness; thus contributing to a high mortality rate observed. In a systematic review by *Chiu et al* it was noted that majority of patients with a higher severity score were admitted to the ICU (24). ICU admission for such high-risk patients has further been recommended in couple of international guidelines (15,16). Although the reasoning to low levels of ICU admission was not a focus of this study, it is presumed to be due to bed unavailability in the unit. MNH and MAMC being national referral hospital, receives patients of all sorts with varied disease severity from all over the country. Thus patient congestion and scarcity of ICU bed is expected.

UGI Endoscopic evaluation and treatment is a major cornerstone in the management of UGIB. A handful number of patients (37.4%) in our study received UGI endoscopy throughout the hospital stay, moreover only 17.5% received urgent endoscopy. Comparing to studies in HIC, a larger proportion of their patients receive UGI endoscopy services with most of them receiving urgent endoscopies (13,14). Studies have suggested urgent UGI endoscopy to be associated with reduced mortality and hospital length of stay (25,26). 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.

As part of the ED management, majority of the patients received intravenous fluids and proton-pump inhibitor (PPI). A small proportion of the patients received octreotide, of whom half of them had indication for its use based on historical features (such esophageal varices and liver diseases). The utilization was probably limited by the availability and the cost of the drug in our setting. Antibiotic administration especially in patients with prior history of liver disease and esophageal varices was low. 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 (15). The need for further improvement in this aspect of ED antibiotic administration is needed. Provision of antibiotics was associated with increased incidence of mortality, probably due to it being confounded by liver disease which had a poor outcome.

LIMITATIONS

This study was conducted at two high capacity, referral EDs and so the patient population and outcomes could be different at smaller, or lower capacity facilities. However, because these EDs receive referrals from all over the country, the patients sampled likely provide a wide representation of the Tanzanian population.

Investigations were ordered at the discretion of the physician, and thus not all patients received all tests. 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 under study, including the scores such as Glasgow-Blatchford score.

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.

Conclusions

The mortality rate for UGIB in our setting remains substantially higher than in non-African countries. This appears to be due to the higher severity of disease in our patients, lack of ICU care for the ones with higher severity score, and lower use of endoscopy.

Endoscopic evaluation and treatment at any point during the hospital stay still remains an independent predictor of mortality. Efforts are needed to increase the number of patients receiving endoscopic evaluation and treatment in a timely fashion. Under-utilization of some medications such as octreotide and antibiotics may have an implication on patient outcome.

Clearly there was an attempt to meet the suggested guidelines for management of UGIB, and some of these efforts may have been met with lack of resources. However further studies are needed to assess the knowledge of providers on managing patients with UGIB and

familiarity with the international recommendations.

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.

Declarations

Competing interests

The author declare no conflicts of interest

Ethics approval and consent to participate

The study was conducted after obtaining permission from the MUHAS Institutional Review Board and MNH. 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. Only participants who on their free will consent were included in the study. Confidentiality was observed on the questionnaires filled with participants information. All patients received treatment as per standard hospital policies. The data obtained during the study was kept anonymous.

Consent to publish:

Not applicable

Availability of data and material

The dataset supporting the conclusion of this article is available from the authors on request

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This was a non-funded project; the principal investigators used their own funds to support the data collection and logistics

Authors' contributions

SSR was involved in the study design conceptualization, data collection, analysis and interpretation, drafted the manuscript, and made all necessary changes to the manuscript. HRS involved in the study design conceptualization, review of the data analysis and interpretation, and critical review of the manuscript. AJI was involved in the study design conceptualization, data analysis and interpretation and revision of the manuscript. DAK was involved in the study design, data analysis and interpretation and revision of the manuscript. JAM was involved in the study design, data analysis and interpretation, and revision of the manuscript. EJW was involved in the study design conceptualization, review of the data analysis and interpretation together with revision of the manuscript. NAO was involved in the study design, data analysis and interpretation and revision of the manuscript. All authors have read and approved the final manuscript.

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Tables

Table 1: Demographic and Clinical Characteristics of adult 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%)
Referral Status	
Hospital referred	77 (62.6%)
Insurance Status	
Uninsured	99 (80.5%)
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%)
SpO ₂ <90%	6 (4.89%)
Medical history	
PUD	39 (40.2%)
UGIB	25 (25.8%)
Esophageal Varices	17 (17.5%)
Liver disease	12 (10.3%)
Others	51 (52.6%)
UGI endoscopy	20 (16.3%)
Band ligation	4 (3.3%)
Clinical Rockall Score (n= 123)	
3-4	63 (51.2%)
<3	52 (42.3%)
>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 *Ramirez et al.* (27)

Table 2: Management Strategies at Emergency Department

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%)
UGI Endoscopy	46 (37.4%)
Time to Endoscopy	
>72 hr	15 (32.6%)
24-48 hr	13 (28.3%)
48-72 hr	10 (21.7%)
Within 24 hr	8 (17.4%)

*Cut-off value based on WHO Anemia severity classification **Cut-off based on the high normal limit as stated in Glasgow-Blatchford score.

Table 3: 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%)	
Sex	14 (16.1%)	73 (83.9%)	0.249
Clinical 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
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
Active 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%)	

Table 4: 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.*(20)

Figures

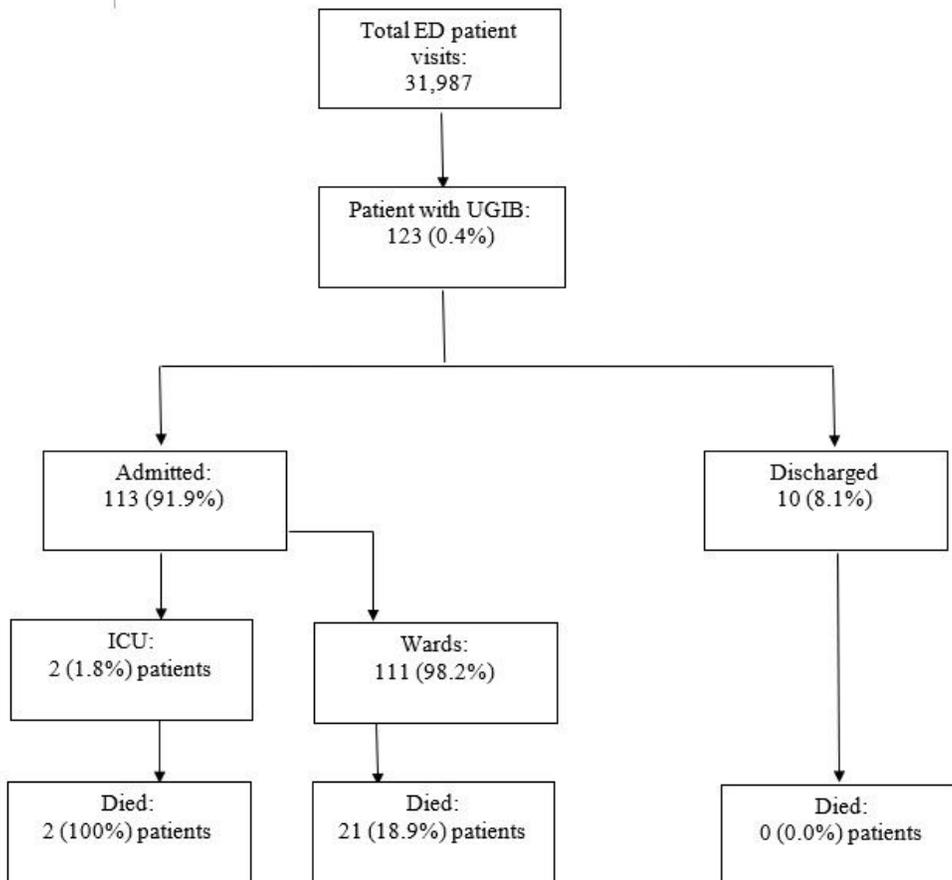


Figure 1

STROBE Flow Diagram