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Original Article

Factors Affecting Outcome of Patients with Upper Gastrointestinal Haemorrhage Presenting to Emergency Department: A Prospective observational cohort study

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ABSTRACT

Background: Upper gastrointestinal bleeding (UGIB) is one of the most common presentations in an emergency department (ED). UGI endoscopy is the definitive diagnostic and therapeutic modality for UGIB. Aim of the study were look into the outcomes of UGIB and outcomes based on the timing of endoscopy (early endoscopy mean before 24 hours and late endoscopy mean after 24 hours).
Methods: 180 patients presented in ED with UGIB and undergo Upper gastrointestinal (UGI) endoscopy. Socio-demographic profiles, with presenting signs and symptoms, co-morbidities, vitals, lab parameters, endoscopic diagnosis with the treatment of the patient were collected. They were followed up to day 7 of presentation to determine all-cause mortality, re-bleed, development of hemorrhagic shock, admission rate and length of ED stay, early endoscopy and late endoscopy.
Result: The mortality difference in the early endoscopy (3.2%) and late endoscopy (16.1%) group was significant with a p-value of 0. 012. Late endoscopy (18.6%) was associated with a higher risk of development of hemorrhagic shock compared to the early group (4.8%) with a p-value of 0.011. The factors that had a significant association with mortality on univariate analysis were, late endoscopy, systolic blood pressure on presentation less than 90, variceal bleeding, blood transfusion requirement, AIMS 65 score greater than 0. Multivariate analysis showed that late endoscopy (OR 5.35(1.12-25.3)) and AIMS 65 score (OR 11.76(1.48-93.3)) were independent risk factors for mortality.
Conclusion: We concluded that early endoscopy was associated with decreased mortality, decreased length of ED stay and decreased risk of development of hemorrhagic shock.

Keywords: Endoscopy, haemorrhage, mortality, shock

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INTRODUCTION

Upper gastrointestinal bleeding (UGIB), defined as bleeding derived from a source proximal to the ligament of Treitz, is a common and potentially life-threatening GI emergency with a wide range of clinical severity, ranging from insignificant bleeds to catastrophic haemorrhage, and is associated with significant morbidity and mortality.[1] The prevalence of upper gastrointestinal haemorrhage is 20 to 60 per 100,000 populations and the mortality rate is 5 to 10%.[2]

Upper gastrointestinal (GI) bleeding is more common in men than women and its prevalence increases with age.[3] A Study have shown peptic ulcer disease (60-75 %) and variceal bleeding (6-14 %) as the most common causes of upper gastrointestinal haemorrhage.[4] A Study have shown causes of upper gastrointestinal haemorrhage by variceal bleeding (65%) as compared non-variceal bleeding (26%).[5]

Upper gastrointestinal (GI) bleeding have varied clinical presentation from hematemesis, "coffee -ground" emesis, melena, hemodynamic instability, altered mental status, symptoms of anaemia such as lethargy, fatigue, and syncope.[3] Important historical information includes medication history especially the use of clopidogrel, warfarin, NSAID s, aspirin, SSRIs, corticosteroids because these medications increase the risk of upper gastrointestinal bleeding. The physician should also elicit the previous history of upper gastrointestinal bleeding, surgery, alcohol use or illicit drug use. Other factors to consider in history include diabetes mellitus, previous abdominal surgery, coronary artery disease, chronic renal or liver disease or chronic

obstructive pulmonary disease. Vital parameters may be normal on presentation. If bleeding is severe, patients may become tachycardia and hypotensive.

Physical examination should assess for guarding, rebound tenderness, sequelae of chronic liver disease. Initial laboratory tests include measurement of hemoglobin, hematocrit, creatinine, platelet count, coagulation profile, liver function tests, and arterial blood gas analysis. The rapid assessment followed by resuscitation should precede diagnostic evaluation in unstable patients with severe bleeding. Patients with active bleeding and coagulopathy should be considered for transfusion with fresh frozen plasma and those with active bleeding and thrombocytopenia should be considered for transfusion with platelets. Blood transfusion should be administered to patients whose hemoglobin levels of 7 g/dL or less. Some patients require airway protection and mechanical ventilation to decrease the risk of aspiration. A nasogastric lavage has a low sensitivity and poor negative likelihood ratio for upper gastrointestinal bleeding in patients with melena or hematochezia. A positive nasogastric tube lavage that yields blood or coffee-ground vomitus implies that upper gastrointestinal bleeding is more likely and predicts that bleeding is caused by a high-risk lesion. Patients with active bleeding and hemodynamic instability should be admitted to an intensive care unit for resuscitation and close observation.[3]

The gold standard for upper gastrointestinal haemorrhage is esophagogastroduodenoscopy because it can identify etiology and can also provide hemostasis.[6] Endoscopic therapy reduces transfusion requirements, shortens the length of hospital stay and reduces mortality.[3] Early endoscopy within 24 hrs is recommended because it can enable faster diagnosis early treatment and early disposition from emergency. [7-10]
Previous retrospective studies have evaluated outcomes of early vs delayed endoscopy and they found an increased rate of mortality in the delayed group and patients of the delayed group stay longer in the hospital. [11-13]

There is a paucity of data on clinical characteristics, presentation and outcomes of a patient with an upper gastrointestinal bleed in an overcrowded emergency department. There is also no data on outcomes based on the timing of endoscopy in patients presenting to the emergency department. Aim of the study was look into the outcomes of upper gastrointestinal haemorrhage and outcomes based on the timing of endoscopy (early endoscopy mean before 24 hours and late endoscopy mean after 24 hours) hospital mortality, development of haemorrhagic shock, rebleed, emergency department death, length of emergency department stays, weekend effect in a patient presenting to the emergency department with upper gastrointestinal haemorrhage.

METHODS

This prospective observational cohort study was conducted after approval from institutional ethics committee (IEC/PG-743). Inclusion criteria were patients of either sex, age 18 years or above with presenting to Emergency Department with upper gastrointestinal haemorrhage and undergoing upper GI endoscopy. Patients diagnosed to have bleeding from sites other than the upper gastrointestinal tract after admission, upper gastrointestinal bleeds due to trauma, foreign body ingestion, poisoning and patients on anticoagulation therapy were excluded from the study.

Sample size for the proposal has been computed as in a prospective cohort study by anticipating the percentage of mortality as 10% (p) and taking the confidence interval at 95% and relative precision as 5-10 % (d) and by using the formula $4XpX(100-p)/d^2$, calculated sample size is 180 patients.

Data collection included patients demographic profile, history of presentation, duration of bleed, comorbidities, addiction, whether received treatment from outside and vital parameters on presentation. After medical stabilization data on investigations like hemoglobin and platelets were recorded. Data on the number of units of blood components transfused for each patient were also obtained. Time taken for endoscopy from emergency department presentation was obtained from each patient. Patients were then divided into early and late endoscopy groups. Endoscopy findings of each patient were also collected.
The patients were followed up for 1 week to note the outcomes. For those who were admitted, data was taken from their admission file and for those who were transferred to other hospital outcome was enquired telephonically. Various outcomes were measured at day 7 including hospital mortality, development of haemorrhagic shock, rebleed, emergency department death, length of emergency department stay. These outcomes were compared among early endoscopy and late endoscopy groups and weekend and weekdays groups. Informed consent was taken from all patients enrolled in the study.

In statistical analysis, comparing outcomes in the early vs delayed group continuous variables were presented with mean and standard deviation and categorical variables were presented as percentage frequency of occurrence. The Mann Whitney U test was used to compare continuous variables and the Fisher exact was used to compare categorical variables as appropriate. A p value of <0.05 was considered statistically significant. The data was entered in MS EXCEL sheet and analysis was done using Statistical Package for Social Sciences version 21.0.

Primary objectives of the study were calculating all cause in hospital mortality rate in patients with upper gastrointestinal haemorrhage presenting to the emergency department at day 7. Secondary objectives of the study were calculating all cause in-hospital mortality in early (endoscopy before 24 hours from presenting to the emergency department) vs delayed endoscopy (endoscopy after 24 hours from presenting to the emergency department) group, development of haemorrhagic shock, need for blood transfusion, length of emergency department stay, admission rate, re -bleed < 7 days.
AIMS65 is a simple, accurate, non-endoscopic risk score that can be applied early (within 12 h of hospital admission) in patients with acute upper gastrointestinal bleeding`AIMS65 scores >2 predict high in-hospital mortality. One point is given if parameters are as follows: albumin<3, INR>1.5, Altered mental status, systolic blood pressure <90 mm Hg and age > 65.

RESULT

A total of 180 cases were recruited out of which 79% were males. As many as 52% of patients were from the age group 39-58 years with a mean age of 44.5 years. Common co-morbidities among patients were chronic liver disease and previous upper gastrointestinal bleeding. Over 55.5% of patients were addicted to alcohol whereas 39.4% had no addictions. The majority of the patients (76%) presented to the emergency department > 12 h after symptom onset. Hematemesis and melena were the most common presentation. The mean time for endoscopy was 34.3 hours (Table 1).

Table 1. Sociodemographic details, symptoms and co-morbidities

Variable	n= 180 (%)
Gender	
Male	142(79%)
Female	38(21%)
Age(years)	
Mean ± SD	44.5 ± 13.06
Addictions	
Alcoholic	100(55.5%)
Current smoker	16(8.8%)
Alcohol use in last 7 days	16(8.8%)
No addiction	71(39.4%)
Duration of bleeding before reaching	
ED	4(2%)
<1 h	5(3%)
1-2 h	13(7%)
2-6 h	22(12%)
6-12 h	136(76%)
>12 h	
Comorbidities	
Chronic Liver disease	99 (55%)
Previous Upper GI bleeding	76 (42.2%)
No comorbidities	25 (13.8%)
Clinical Presentation	
Hematemesis	126(70%)
Malena	123(68.3%)
Altered mental status	16(8.8%)
Hematochezia	13(7.2%)

Early endoscopy was done in 34% of cases and delayed endoscopy in 66% of cases. In 44.9% of cases, endoscopy was delayed because the patient was vitally stable and there was no active bleeding. The most common endoscopy findings were oesophageal varices in 57.3% of cases followed by gastric varices (8.8%), GAVE (7.6%), duodenal ulcer (6.6%) (Table 2).

Table 2. Summary of endoscopy related data

Endoscopy related data	Number of patients 180 (%)
Early endoscopy (<24h)	62(34%)
Delayed endoscopy	118(66%)
Reason for delayed endoscopy	
Vitally stable and no active bleeding	53(44.9%)
Weekend/holiday presentation	31(26.2%)
Shock	22(18.6%)
Severe anaemia	33(29.4%)
Altered mental status	12(10.1%)
Endoscopy Findings	
Oesophageal varices	103(57.2%)
Gastric varices	16(8.8%)
Duodenal ulcer	12(6.66%)
Gastric ulcer	10 (5.5%)
Oesophageal ulcer	7 (3.8%)
Portal hypertensive gastropathy	10 (5.5%)
GAVE	14(7.6%)
Malignancy	6 (3.33%)
Hemostatic intervention	
Yes	114(63.3%)
No	66(36.7%)
Second endoscopy	
Yes	13(7.2%)
No	167(92.8%)

Table 3. Bivariate analysis of factors associated with 7-day mortality

	Died n=21(%)	Survived n=159 (%)	P-value
Age groups			
>45 years	11 (52.38%)	73 (45.91%)	
≤ 45 years	10 (47.61%)	86 (54.08%)	0.114
Gender			
Female	4 (19.04%)	34 (21.38%)	1.000
Male	17 (80.95%)	125 (78.61%)	
Ed presentation			
Morning	4 (19.04%)	36 (22.64%)	
Evening	8 (38.09%)	57 (35.84%)	
Night	9 (42.85%)	66 (41.50%)	0.930
Weekend			
Yes	4 (19.04%)	59 (37.10%)	
No	17(18.95%)	100 (62.89%)	0.143
Endoscopy			
Early	2 (9.52%)	60 (38.99%)	0.012
Late	19 (90.47%)	99 (62.26%)	
Shock Index			
>1	6 (28.57%)	46 (28.93%)	1.000
<=1	15(71.42%)	113 (71.06%)	
SBP on presentation			
< 90	6 (28.57%)	13 (8.17%)	0.012
>=90	15(71.42%)	146 (91.82%)	
Heart rate			
>100	10 (47.61%)	69 (43.39%)	0.810
<= 100	11 (52.38%)	90 (56.60%)	
Previous UGI bleed			
Yes	12 (57.14%)	64 (40.25%)	0.160
No	9 (42.85%)	95 (59.74%)	
Addiction			
Yes	13 (61.90%)	88 (55.34%)	0.640
No	8 (38.09%)	71 (44.65%)	
Alcohol use in last 7 days			
Yes	2 (9.52%)	13 (8.17%)	0.680
No	19 (90.47)	146 (91.82%)	
Variceal bleeding			
Yes	18 (85.71%)	93 (58.49%)	0.016
No	3 (14.28%)	66 (41.50%)	
Ulcer bleeding			
Yes	3 (14.28%)	26 (16.35%)	1.000
No	18(85.71%)	133(83.64%)	
Received blood transfusion			
Yes	18 (18.71%)	97 (61.00%)	0.029
No	3 (14.28%)	62 (38.99%)	
AIMS 65 Score > 0			
Yes	20 (95.23%)	85 (53.45%)	0.0001
No	1 (4.76%)	74 (46.54%)	

Table 4. Multivariate regression analysis for significant predictors of mortality

Variables	Odds ratio	P-value
Late endoscopy	5.35(1.12-25.3)	0.034
Systolic blood pressure< 90 mm hg	2.64(0.75-9.25)	0.127
Variceal bleeding	3.26(0.86-12.34)	0.081
Blood transfusion	3.79(0.99-14.45)	0.005
Aims 65> 0	11.76(1.48-93.3)	0.019

As much as 31% of patients presented with shock index>1. Forty-four per cent of patients had tachycardia on presentation and 9%patients had hypotension. The mean hemoglobin (g /dL) in our sample of patients was 7.53 with 56% of patients having hemoglobin less than 7. INR was greater than 1.5 in 54% cases and albumin was less than 3 in 20% cases. As many as 63.8% of the patients required at least 1 unit of the blood component. The mean AIMS 65 score of our patients was 1.02. AIMS 65 scores improved after endoscopy in 14% of cases. A higher AIMS 65 score was associated with a higher rate of mortality in our study. Out of 180 patients, 53.3%patients were discharged, 21.6% were transferred out, 17.7% were admitted and 7.2% had died.

All-cause in-hospital mortality at day 7 was 11.6%. Mortality was 7.2% in the emergency department. Mortality was 4.4% among admitted patients. The mortality difference in the early endoscopy (3.2%) and late endoscopy (16.1%) group was significant with a p-value of 0. 012. Late endoscopy (18.6%) was associated with a higher risk of development of hemorrhagic shock compared to the early group (4.8%) with a p-value of 0.011. Patients who underwent late endoscopy stayed longer (3.6 days) compared to early endoscopy patients (2.97 days) (p= 0.01). 23.3 % of total patients developed rebleed at day 7. Patients who presented on weekdays had a higher admission rate (23.9%) compared to those presented on weekends (6.3%) (p =0.0037). Patients presented on weekdays had a higher risk of development of rebleed (28.2%) and haemorrhagic shock (19.6%) at day 7 compared to those presented on weekends (3.1% and 14.2%). The p values were 0.0015 and 0.0042 respectively. Patients who presented on weekends (29h) had a lower median time to endoscopy compared to the late endoscopy (36 h) group (p=0.04).

The factors that had a significant association with 7-day mortality on bivariate analysis were, late endoscopy, systolic blood pressure on presentation less than 90, variceal bleeding, blood transfusion requirement, AIMS 65 score greater than 0. (Table 3). Multivariate analysis showed that late endoscopy (OR 5.35(1.12-25.3)) and AIMS 65 score (OR 11.76(1.48-93.3)) were independent risk factors for mortality at day 7(Table 4).

DISCUSSION

Our study investigated age, gender, the onset of bleeding, emergency department visit timings, and co-morbidities of these patients. Out of 180 patients, a greater number of patients were middle-aged in both gender groups. The mean age of patients was 44.5 years. Male (79%) patients were more in our study compared to female (21%) patients. This profile was similar to studies by Parvez et al and Gupta et al. [4-5]

Out of 180 patients, 99(55%) patients were known cases of chronic liver disease and 76 (42.2%) had a previous history of upper GI bleeding. 25 (13.8%) patients had no prior comorbidities. This finding is consistent with study by Parvez et al. [1] Hematemesis was the most common presenting symptom which was present in 126(70%) patients closely followed by melena in 123(68.3%). Other symptoms were altered mental status in 16 (8.8%) and hematochezia in 13(7.2%). This finding is consistent with study by Parvez et al and Rajan et al. [4.14]

Upper gastrointestinal bleeding is a cause of hemorrhagic shock which manifests as hypotension and tachycardia. Tachycardia was present in 79(44%) patients,17(9%) patients were hypotensive on presentation which is slightly lower compared to another study which showed 13.1 %.[4] Out of 180 patients, 107(56%) had severe anaemia on presentation. The hemoglobin (g/dL) ranged from 2.1 to 17 with mean of 7.53 and standard deviation of 2.7. In our study mean hemoglobin was similar to the findings in a study by Lau et al.[15] The most common diagnosis arrived at endoscopy was bleeding due to oesophageal varices 103(57.2%) followed by gastric varices in 16 (8.8%), duodenal ulcer in 12(6.6%), gastric ulcer in 10(5.5%). This data is consistent with the study by Gupta et al. [1]

Out of 180 patients enrolled, 21 (11.6%) patients had in-hospital mortality at day 7. 13(7.2 %) patients had mortality in emergency department and 8(4.4%) had mortality after admission which is consistent with study by Lau et al. [15] A total of 42 (23.3%) had an episode of rebleeding on day 7. This data is consistent with the study conducted by Lau et al. [15]

We determined all-cause in-hospital mortality in the early and delayed endoscopy group which was 3.2% and 16.1% respectively. The p-value was calculated as 0.012 which showed that the difference is significant. This finding is consistent with the study by Nam Kyung et al [8] which found out that mortality was high in patients undergoing delayed endoscopy (>24 hrs) (6.4%) compared to those among the early group (2.8%) among 1101 patients. This may be because of early identification of the cause of bleeding leading to early hemostatic intervention before clinical deterioration. A study by Shih et al was done to determine the potential impact of the weekend effect on various outcomes of patients with upper gastrointestinal hemorrhage. They concluded that weekend admissions are associated with an increased risk of death, especially among variceal upper gastrointestinal hemorrhage patients. [16] Result was similar to our study.

The factors that had a significant association with 7-day mortality on univariate analysis were, late endoscopy, systolic blood pressure on presentation less than 90, variceal bleeding, blood transfusion requirement, AIMS 65 score greater than 0. Multivariate analysis showed that late endoscopy (OR 5.35 (1.12-25.3)) and AIMS 65 score >0 (OR 11.76 (1.48-93.3)) were independent risk factors for mortality at day 7. This is consistent with the finding by Cho et al. [17] Limitations of our study was a single centre study. We could work with a smaller sample size. The study was carried out in a tertiary care hospital, so hospital bias cannot be ruled out.

CONCLUSION

We concluded that early endoscopy was associated with decreased mortality, decreased length of ED stay and decreased risk of development of hemorrhagic shock. A late endoscopy and AIMS 65 score greater than 0 were independent predictors of mortality.

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CONFLICT OF INTEREST

The author declares there is no conflict of interest.

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