

## Assessment of Mortality and Causes after Re-bleed In Patients Having Endoscopy for Upper Gastrointestinal Bleeding

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### Abstract

**Introduction:** Acute Upper gastrointestinal bleeding (AUGIB), with prevalence of 36 to 172/100,000 natives per year, is a common medical emergency. Mortality rate after UGIB ranges from 4–14% while re-bleeding is evident in 10–30% of these patients. Despite advances in treatment modalities of UGIB, the in-hospital mortality rate remains high and it is commonly due to re-bleeding. However, the causes and frequency of mortality among patients with re-bleeding are not well known in Pakistan.

**Objective:** To determine the frequency and causes of in-hospital mortality after re-bleeding among patients undergoing endoscopy for upper gastrointestinal bleeding.

**Methodology:** A descriptive cross-sectional study was done in Military hospital Rawalpindi from December 2014 to June 2015. A total 150 patients aged between 18 to 65 years who presented with upper gastrointestinal bleeding (UGIB) and underwent upper GI endoscopy and re-bleed were included through purposive sampling. Structured questionnaire used to record data. The patients were observed for mortality and causes after re-bleeding in the hospital for about 5 days. Patients who died, the cause of the death was assessed by 2 senior consultant physicians. SPSS version 21 was used for data entry and analysis. Variables like mortality were presented as percentage and frequencies. Effect modifiers like age and gender were controlled by stratification.

**Results:** The mean age of patients (n=150) was 43.97±12.28 years. Among total cases, 97 (64.7%) were males and 53 (35.7%) were females. The in-hospital mortality rate was 20% (n=30), re-bleed was cause in 12 (40%) while in 18 (60%) cause was other than re-bleed (cardiac, multi-organ failure, neurological, pulmonary, and advanced malignancy). Mortality in male patients was higher (n=18, 60.0%) as compared to female patients (n=12, 40.0%). The highest mortality (n=22, 73.3%) was observed in age group >43 years. The association of in-hospital mortality was statistically significant (p value = 0.02) by age but not by gender.

**Conclusion:** In-hospital mortality after UGIB is 20 %, frequent cause is other than the re-bleed. Male above aged 43 are more vulnerable. Management of UGIB should also focus on optimization of non-re-bleeding causes and other co-morbid related deaths instead of merely maintaining homeostasis and blood transfusions.

**Keywords:** Re-bleeding, Mortality, Acute Upper Gastrointestinal Bleeding, Upper GI Endoscopy.

### Introduction:

Upper gastrointestinal bleeding (UGIB) is a major affliction that has been known from ancient times and remained a frequent medical problem worldwide<sup>1</sup>. It is associated with significant mortality, morbidity, and health care resource utilization<sup>2</sup>. It is defined as bleeding originating in the distal esophagus, stomach or duodenum proximal to the ligament of Treitz. Acute Upper gastrointestinal bleeding (AUGIB) is a common medical emergency and potentially life-threatening condition that needs timely assessment and aggressive medical management<sup>3</sup>.

Upper gastrointestinal bleeding is a frequent cause of hospitalization, incidence range from 36 to 172/100,000 natives per year. Mortality rate of UGIB range from 4–14% while re-bleeding is evident in 10–30% of these patients<sup>4</sup>.

The most important prognostic factors include the history of malignancy, liver cirrhosis, presentation with massive UGIB and signs of hypovolemia (tachycardia, hypotension, shock and a hemoglobin < 8 g/dL)<sup>5</sup>. Patients with significant comorbidities usually require admission regardless of the severity of UGIB.

UGIB is usually classified as variceal or non-variceal bleeding depending on the source of bleeding. Variceal bleeding (VB) has been extensively studied in cirrhotic patients and it is shown that in 30–40% of cirrhotic patients who bleed have non-variceal upper gastrointestinal

bleeding (NVUGIB), which is commonly due to gastric and duodenal ulcers<sup>6</sup>.

UGIB must be managed quickly and appropriately to prevent adverse outcome. It is one of the most common medical emergencies managed by the physicians and gastroenterologists. Older age and male gender have the relatively higher incidence of UGIB as compare to young age and female gender<sup>7</sup>. Therapeutic endoscopic procedures used for UGIB includes, rubber band ligation, injection sclerotherapy hemoclip and endoscopic coagulation technique such as a heater probe, monopolar and bipolar coagulation and plasma argon coagulation. These procedures are used both in emergency and electively to treat different causes of UGIB<sup>8</sup>. Endoscopic treatment modalities are very effective for UGIB, as it reduces incidence of re-bleeding and its risk, requirement of blood transfusion and the need for ulcer related surgery to secure definitive hemostasis. In addition, timely and appropriate use of various endoscopic therapeutic modalities significantly reduces the outdoor visits, length of stay in hospital and health care related costs<sup>9</sup>.

Despite newer advances in treatment modalities of UGIB, the in-hospital mortality rate remains high (13%) and it is commonly due to re-bleeding (15%)<sup>10</sup>. The high case fatality rate of 7% to 10% remained unchanged even today probably due to the fact that these patients are older and have more comorbidities than those in the past<sup>11</sup>.

The frequency of mortality varies greatly after endoscopy for UGIB among different studies. It is observed that re-bleeding is considered to contribute a major bulk of mortality among patients with UGIB. However, the causes and frequency of mortality among patients with re-bleeding are not well known in Pakistan. It is commonly perceived that mortality after re-bleeding is due to bleeding causes rather than non-re-bleeding causes. Consequently, physicians focus upon blood replacement etc. However, Sunget *al*, showed that mortality after UGIB in majority of the patients is related to non-re-bleeding causes rather than bleeding causes<sup>6</sup>.

The purpose of this study is therefore to determine the frequency of in-hospital mortality, in patients undergoing endoscopy for upper gastrointestinal bleeding, and to assess the cause of death whether it is due to re-bleeding or no re-bleeding.

#### Methodology:

A descriptive cross-sectional study was conducted from December 2014 through June 2015 at the Medical Department of Military Hospital Rawalpindi. Sample size of 150 patients was calculated with 5% margin of error, 95 % confidence level taking expected percentage of mortality among patients with UGIB as 6.2%.<sup>1</sup> Non-probability purposive sampling was used to recruit patients. The inclusion criteria included all the patients of upper gastrointestinal bleeding whom the diagnosis has been established by endoscopy. We excluded patients having history of upper GI bleed after trauma, surgery on stomach or esophagus, failed initial homeostasis during endoscopy, failed initial resuscitation and patients who have refused for endoscopy.

This study aimed to determine the frequency and causes of in-hospital mortality after re-bleeding in patients having endoscopy for upper gastrointestinal bleeding who are admitted through emergency or OPD. The written permission of hospital ethical review committee was taken before start of the data collection procedure. 150 patients who had re-bleeding after an upper GI endoscopy for UGIB meeting inclusion criteria were selected in study. Written and informed consent of every patient was taken prior to include them in current study. The data was collected in pre-structured, predesigned questionnaire which include details about sociodemographic data, clinical diagnosis, mortality and its cause by researchers themselves. Following operational definitions were used: Upper GI Bleeding was defined as “when the patient presents with blood in the vomitus or stools, confirmed by the presence of bleeding point in the esophagus, stomach or duodenum through endoscopy”. Re-Bleeding was defined as “when patient had a repeat episode of blood in vomitus or stools, or both associated with a drop in systolic blood pressure below 90 mm of Hg and diastolic blood pressure below 60 mm of Hg within 5 days after endoscopy”. Patient’s medical history was recorded, and clinical examination was performed, and findings of prior endoscopy were noted. The

patients were admitted for about 5 days and observed for mortality and its causes (re-bleeding VS. non- re-bleeding). The patients who hemodynamically stable had no repeat episode(s) of UGIB were discharged from the hospital. Among the patients who died, the cause of the death was ascertained by two consultant physicians having 5 years post fellowship experience in medicine.

Statistical package for social sciences (SPSS<sup>®</sup>21) was used to analyze data. Continuous variables were measured as mean and standard deviation (SD) while categorical variables were described as frequency and percentage. Stratification of age and gender were done, and post stratification chi square was applied to see the effects of these upon outcome variables, p-value less than 0.05 was considered as statistically significant.

**Results:** A total of 150 patients meeting inclusion criteria were investigated to determine the frequency and causes of in-hospital mortality after re-bleed among those patients who had endoscopy done for UGIB. Out of 150 patients 97(64.3%) were male and 53(35.7%) were females with male to female ratio 1.8:1 see table I.

Table: I. Frequency distribution of patients according to gender

	Frequency (n=150)	Percentage (%)
Male	97	64.7%
Female	53	35.3%
Total	150	100%

The mean age of patients was 43.97±12.28 years, with range of 18–64 years. The patients were stratified in two groups with respect to age, those less than or equal to 43 years of age (n=68, 45.3%) and those more than 43 years of age (n=82, 54.7%). The in-hospital mortality among study subjects was observed in 30(20.0%) patients, as shown in table II.

Table II Frequency distribution of in hospital mortality

In-Hospital Mortality	Frequency (n=150)	Percentage (%)
Yes	30	20.0%
No	120	80.0%
Total	150	

Among patients who expired, the mean age was 48.47±12.18 years with range 20–64 years. Among those patients who survived, the mean age was 42.84±12.10 years with range 18–64 years. Out of 30 patients who died 12(40%) were due to re-bleed and 18(60%) were due to non- re-bleed causes as shown in table III. The non-re-bleeding causes and their frequencies are as shown in table VI.

Table– III Frequency distribution of causes of in-Hospital mortality

	Frequency (n=30)	Percentage (%)
Re-bleeding	12	40.0%
Non-re-bleeding causes	18	60.0%
Total	30	100%

Table– IV. Frequency distribution of non-re-bleeding causes of in-hospital mortality.

	Frequency (n=18)	Percentage (%)
Cardiac Cause	2	11.1%
Pulmonary Causes	4	22.2%
Multi-Organ Failure	4	22.2%
Neurological Causes	2	11.1%
Advanced Malignancy	6	33.3%
TOTAL	18	100%

Among 30 patients who died, 18 (60.0%) were males and 12 (40.0%) were females, 22 (73.3%) patients were of age group more than 43 years as compared to 8 (26.7%) patients of age less than 43 years. The in-hospital mortality was significantly associated with age ( $p=0.022$ ) but not with gender ( $p=0.550$ ) (table V)

Table –V Frequency and association of in-Hospital mortality according to age (years) (n=150)

	In-Hospital Mortality		Total	p-value
	Yes (n=30)	No (n=120)		
≤ 43 years (n=68)	8	60	68	0.022 *
> 43 years (n=82)	22	60	82	
TOTAL	30	120	150	

**Discussion:** The frequency of in-hospital mortality after re-bleeding among patients having endoscopy for upper gastrointestinal bleeding in our study was 20% and is more commonly due to non-re-bleed causes (60%) as compared to re-bleed cause (40%). Non-re-bleeding causes are related to cardiac, pulmonary, multiorgan failure, neurological and malignancy. A large relevant study by Sung et al, in Prince of Wales Hospital Australia showed that non-re-bleeding related causes are more common cause of death as compared to re-bleeding in patients of UGIB.<sup>1</sup> Findings of our study thus endorse that non-re-bleeding related mortality is commonly responsible for death in patient who re-bleeds, after endoscopy for upper GI bleed. Upper gastrointestinal bleeding (UGIB) is common life threatening medical emergency and one of the leading cause for referral to gastroenterologists that requires esophago-gastro-duodenoscopy for the diagnosis and to secure hemostasis.<sup>1</sup> UGIB consistently continues to be a significant cause of mortality and morbidity worldwide, which impose a significant stress and heavy burden on healthcare facilities.<sup>2</sup> The diagnosis and management of UGIB have remarkably evolved, particularly with recent rapid advances in diagnostic and therapeutic endoscopic procedures and available new medications.<sup>12</sup> In a large Canadian study by Conard SA showed that endoscopic treatment and anti-ulcer therapy with proton pump inhibitors has significantly decreased re-bleeding, mortality and morbidity in high risk patients.<sup>13</sup> Presence of massive bleed, life-threatening co-morbid conditions and older age are commonly associated with higher mortality. The

incidence for AUGIB in a large population-based study was 87/100000 people per year and it is more prevalent in old age and male gender<sup>14</sup>.

The mean age at presentation in current study was 43.9±12.2 years which is comparable to other studies by Gurung et al<sup>15</sup>, and Hussein et al<sup>16</sup>, that showed the mean age of 45.32±18.47 years and 44.6 years respectively. Predominance of male gender was reported by Gurung et al, 64.4%. 71% and Bhattarai et al<sup>15,17</sup>, which is also comparable (63.7%) to current study as shown in table 1. Data revealed that hemorrhage from the GI tract continues to carry a mortality rate as high as 20% to 30% and the re-bleeding occurs in 18% of the patients of which 9% died.<sup>18</sup> Our study also showed comparable mortality rate of 20%.

Re-bleeding is associated with high morbidity and mortality, therefore timely identification of re-bleeding and aggressive management in patients at high risk for massive, continued or re-bleeding should be the main focus of UGIB management<sup>19</sup>. González et al, in a study of 1067 patients with UGIB showed that the most common causes of bleeding are duodenal and gastric ulcers. Re-bleeding observed in 36 patients (3.4%) of which 50% has expired, which is higher than current study (20%). In-hospital mortality was 10.2%, of which 3.1% was associated due to bleeding. When comparing the causes of death among patients with and without co-morbid conditions, only hypovolemic shock was found significant. Rockall scale score, number of co-morbidities, plasma albumin less than 2.6 g/dL on admission, re-bleeding and prolonged hospital stay are independent risk factors of in-hospital mortality in patients of UGIB<sup>20</sup>.

In our research malignancy, multi organ failure, pulmonary, cardiac and neurology related causes were prevalent as causes of non-re-bleeding mortality which are, almost identical to non-re-bleeding causes as shown by Sung et al in large study of 18,508 cases of UGIB showed that there were significantly more patients died of non-ulcer bleeding causes (79.7%) than bleeding causes (18.4%). The mean age in bleeding-related deaths was higher than non-bleeding related causes of deaths, a finding which is identical to current study. Most of bleeding-related deaths occurred when the immediate control of bleeding has not achieved or when the patients died early within 48 hours after endoscopic treatment. Among those patients who died of non-bleeding causes, pulmonary conditions (23.5%), multi organ failure (23.9%) and advanced malignancy (33.7%) were most common<sup>6</sup>.

There are few limitations in our study. It was conducted in a single hospital, and therefore possibility of missing patients of UGIB cannot be ruled out. Our study lacked some information on etiology and diagnoses of some bleeds, although this can also be quite commonly observed in clinical audits and case series. Finally, it is conducted with small sample size and at urban environment, so the findings might not be generalized.

**Conclusion:** Management of UGIB should also focused upon optimization of non-re-bleeding causes and associated co-morbid related deaths instead of merely focusing on successful hemostasis and blood transfusions.

**Conflict of Interests** All the authors declare no conflict of interests.

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#### **References:**

1. Alatise OI, Aderibigbe AS, Adisa AO, Adekanle O, Agbakwuru AE, Arigbabu AO. Management of overt upper gastrointestinal bleeding in a low resource setting: a real-world report from Nigeria. *Bio Med Central Gastroenterol.* 2014; 14:210.
2. Esraïlian E, Ian M, Gralnek IM. Nonvariceal upper gastrointestinal bleeding: epidemiology and diagnosis. *Gastroenterol Clin N Am.* 2005; 34:589–605.
3. Dewan KR, Patowary BS, Bhattarai S. A Study of Clinical and Endoscopic Profile of Acute Upper Gastrointestinal Bleeding. *Kathmandu Univ Med J* 2014;45(1):21-5.
4. Coskun F, Topeli A, Sivri B. Patients admitted to the emergency room with upper gastrointestinal bleeding: factors influencing recurrence or death. *Adv Ther.* 2005;22(5):453-61.
5. Taylor AA, Redfern OC. The management of acute upper gastrointestinal bleeding: a comparison of current clinical guidelines and best practice. *Eur Med J Gastroenterol.* 2014; 3:73-82.
6. Sung JJ, Tsoi KK, Ma TK, Yung MY, Lau JY, Chiu PW. Causes of mortality in patients with peptic ulcer bleeding: a prospective cohort study of 10,428 cases. *Am J Gastroenterol.* 2010;105(1):84–9.
7. Gado A, Ebeid B, Axon A. Prevalence and outcome of peptic ulcer bleeding in patients with liver cirrhosis. *Alex J Med.* 2014;50(2):143-8.
8. Bowman MA, Neale AV, Seehusen DA. Data Supporting Key Components of Family Medicine—Scope, Continuity, Interprofessional Care, and More. *J Am Board Fam Med.* 2015;28(2):163-5.
9. Sharif N, Irfan M, Hussain J, Khan J. Factors associated within 28 days in-hospital mortality of patients with acute respiratory distress syndrome. *Bio Med Res Int.* 2013;564-7.
10. Hippisley-Cox J, Coupland C. Predicting risk of upper gastrointestinal bleed and intracranial bleed with anticoagulants: cohort study to derive and validate the Qbleed scores. *Br Med J.* 2014; 349:4606.
11. Wilkins T, Khan N, Nabh A, Schade RR. Diagnosis and management of upper gastrointestinal bleeding. *Am Fam Phys.* 2012;85(5):470-6.
12. Laine L, Jensen DM. Management of patients with ulcer bleeding. *Am J Gastroenterol.* 2012; 107:345.
13. Conrad SA. Acute upper gastrointestinal bleeding in critically ill patients: causes and treatment modalities. *Crit Care Med.* 2002; 30:365-8.
14. Barkun A, Sabbah S, Enns R. The Canadian registry on nonvariceal upper gastrointestinal bleeding and endoscopy (RUGBE): endoscopic hemostasis and proton pump inhibition are associated with improved outcomes in a real-life setting. *Am J Gastroenterol.* 2004; 24:1238-46.
15. Gurung RB, Joshi G, Gautam N, Pant P, Pokhrel B, Koju R, et al. Upper gastro-intestinal bleeding: Aetiology and demographic profile based on endoscopic examination at Dhulikhel Hospital, Kathmandu University Hospital. *Kathmandu Uni Med J.* 2010; 8:208-11.
16. Hreinsson JP, Kalaitzakis E, Gudmundsson S, Björnsson ES. Upper gastrointestinal bleeding: incidence, etiology and outcomes in a population-based setting. *Scand J Gastroenterol.* 2013;48(4):439-47.
17. Bhattarai J, Acharya P, Barun B, Pokharel S, Uprety N, Shrestha NK. Comparison of endoscopic findings in patients from different ethnic groups undergoing endoscopy for upper gastrointestinal bleed in eastern Nepal. *Nepal Med Coll J.* 2007;9(3):173-5
18. Salih H, Ibnouf MAM, Siddig A, Masaad A. Rockall score of the acute upper gastrointestinal bleeding patients the experience in Sudan. *Sudan JMS.* 2009; 4:232-5.
19. Vlavianos P, Westaby D. Management of acute variceal haemorrhage. *Eur J Gastroenterol Hepatol.* 2001;13(4):335–42.
20. González-González JA, Vázquez-Elizondo G, García-Compeán D, Gaytán-Torres JO, Flores-Rendón AR, Jáquez-Quintana JO, et al. Predictors of in-hospital mortality in patients with non-variceal upper gastrointestinal bleeding *Rev Esp Enferm Dig.* 2011; 103:196-203.