Factors Associated with Outcome in Patients with Acute Upper Gastrointestinal Bleeding in a Tertiary Referral Center in Northern Iran

Fatemeh Baradaran[1] , Alireza Norouzi[1*], Samaneh Tavassoli[1], Abdolvahab Baradaran[2], Gholamreza Roshandel[1]

1. Golestan Research Center of Gastro-enterology and Hepatology, Golestan University of Medical Sciences, Gorgan, Iran
2. Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran

ABSTRACT

BACKGROUND

Upper gastrointestinal bleeding (UGIB) is a major healthcare problem and is the most frequent gastrointestinal reason for admission to hospital. We aimed to investigate the prognosis of patients with UGIB referred to a referral hospital in northern Iran in 2013.

METHODS

All patients with UGIB who admitted to Sayyad Shirazi Hospital, in Gorgan, northern Iran, in 2013 were enrolled. The patients' demographic data as well as data about admission, diseases, drug history, and patients' prognosis were collected by structured questionnaire using information in hospital files. The relationships between different factors with the proportion of mortality and recurrence were assessed using Chi-square test.

RESULTS

In total, 168 patients were enrolled of whom 109 (64.9%) were male. The mean (SD) age of the patients was 59.4 (18.2) years. Mortality and recurrence occurred in 23.2% and 34.5% of the subjects, respectively. We found significant relationships between older age and diagnosis of malignancy with mortality ($p =0.03$ and $p <0.01$) and recurrence ($p<0.01$ and $p <0.01$).

CONCLUSION

We found relatively high rates of mortality and recurrence among patients with UGIB. Our results suggested older age and diagnosis of malignancy as the most important indicators of mortality and recurrence in such patients. Considering these factors in clinical settings may result in better and more effective management of patients with UGIB.

KEYWORDS
Upper Gastrointestinal Bleeding; Mortality; Recurrence

* Corresponding Author:

Alireza Norouzi, MD
Golestan Research Center of Gastroenter-ology and Hepatology, 10th Azar alley, 5th Azar street, Gorgan, Iran
Tel: + 98 17 32340835
Fax: + 98 17 32369210
Email: norouzi54@gmail.com

INTRODUCTION

Upper gastrointestinal bleeding (UGIB) is a major healthcare problem and is the most frequent gastrointestinal reason for admission to hospital.[1,2] It is a common presentation to emergency departments. Approximately 45-172 of every 100,000 adult patients are admitted to emergency departments each

year because of symptoms related to UGIB.[1] Upper GI endoscopy is the tool of choice in diagnosing and treating UGIB.[3]

Despite advances in the treatment of UGIB, 4-14% of affected patients have a poor prognosis, such as rebleeding or death.[4] Risk factors for recurrent bleeding and death have been identified in large studies. Some of these studies included all cases of UGIB, while others focused on patients admitted to hospital because of bleeding or peptic ulcer bleeding only.[5] Risk factors for mortality include advanced age, low hemoglobin level, low systolic blood pressure, blood in a gastric aspirate, presence of severe co-morbidity (neoplasia, cirrhosis), worsening health status (American Society of Anesthesiology classification 3 or 4), rebleeding, hypoalbuminemia, elevated creatinine, elevated serum aminotransferase level, onset of bleeding during hospital admission, and active bleeding or other stigmata of recent hemorrhage at the time of endoscopy.[6]

Many scoring systems have been developed to recognize whether patients are at risk for subsequent adverse outcomes.[4] These systems have been designed to identify patients with high risks of adverse outcomes and to differentiate them from patients with lower risks. These measures have been developed from mathematical models of patients' risks of death or rebleeding.[7] There is growing evidence to suggest that low risk patients (Blatchford score 0) can be discharged from hospital within 24 hours without endoscopy and may be managed entirely on an outpatient basis.[1] In this study we aimed to investigate the prognosis of patients with UGIB referred to a tertiary center hospital in northern Iran (Sayad Shirazi Hospital) in 2013.

MATERIALS AND METHODS

Study Design and Population: This study was performed at the Department of Internal Medicine, Golestan University of Medical Sciences from January 1st to December 30th, 2013. We performed a prospective study of all patients who were admitted with upper gastrointestinal hemorrhage to our hospital during this period.

Upper gastrointestinal hemorrhage was defined as history of hematemesis (vomiting of blood or blood clots), coffee ground vomit, or the passage of melena (passage of dark, tarry stools, or fresh blood as witnessed by nursing or medical staff or discovered on rectal examination) or other firm clinical or laboratory evidence of blood loss from the upper gastrointestinal tract.[7]

The study protocol was approved by the institutional review board of the University before commencement. After taking informed consent, a structured questionnaire was filled in for each subject containing data on sociodemographic status, clinical and laboratory data, medical history, and drug history. The questionnaire was generally completed by medical students, and the audit coordinator was then responsible for checking and returning a complete questionnaire for each patient who was correctly identified. 168 patients were included in the study consecutively.

The collected data included date of admission and discharge/death (any death occurring during hospital stay), date of bleeding, first symptom(s) of hemorrhage, and length of hospital stay (the difference between day of discharge and day of admission). The patients' characteristics recorded at the time of admission were demographic factors (age, sex), known risk factors including smoking status, previous or current drugs (corticosteroids, non-steroidal anti-inflammatory drugs, (NSAIDs), history of previous gastrointestinal bleeding, history of malignancy, and vital signs (pulse rate, systolic and diastolic blood pressure). After hospital discharge, all cases were followed up as outpatients by telephone for recurrence and death within 3 months of discharge.

Recurrence and continued bleeding were defined as signs of bleeding, as outlined below: bleeding recurring within 10 days of admission with signs of high pulse rate and low blood pressure without other obvious cause, hematemesis, passage of fresh melena, and serum hemoglobin drop more than the level that could be explained by hemodilution or shock.[7]

Inclusion criteria: Patients were included in the study if they were aged16 years or older, had clinical evidence of UGIB on admission, or had clinical evidence of UGIB in an established inpatient for any other reason occurring between 1 January and 30 December 2013.

Exclusion criteria: Those with a lower gastrointestinal source of bleeding and those for whom UGIB was not approved in endoscopic examination were excluded.

Variable		Frequency	
		Number	Percent
Sex	Male	109	64.9
	Female	59	35.1
Age group	Middle age	85	50.59
	Old age	83	49.40
Cigarette smoking	Yes	25	14.9
NSAIDs* use	Yes	73	43.5
Final diagnosis	Malignant lesion	18	10.71
	Non-Malignant lesion	150	89.2

*NSAIDS: Non-steroidal anti-inflammatory drugs

Statistical Analysis: We divided the patients into two groups using the median age to older (over 62 years) and middle age (62 years or lower) groups. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) software version v16. Chi-square test was used to assess the relationship between different variables and mortality and recurrence. P value less than 0.05 was considered as statistically significant.

RESULTS

In total, 168 patients were enrolled of whom 109 (64.9%) were male. The patients' age ranged from 17 to 92 years. The mean (SD) age of the patients was 59.4 (18.2) years. At the time of admission, 14.9% had history of cigarette smoking and 43.5% were taking NSAIDs. The final diagnosis in 10.7% (18 subjects) was malignancy. For the 150 patients with non-malignant lesion, the most common diagnosis were duodenal ulcer (38.7%), gastric ulcer (21.3%), varices (10.7%), and others (e.g. Mallory-Weiss tear) (29.3%). Table 1 shows the characteristics of the study subjects.

Mortality: We found two cases of hospital mortality in the first admission and the cause of death was massive GIB in both cases. 39 patients (23.2%) died during 3 months of follow-up. Causes of death included malignant diseases (33.3%), cardiovascular diseases (28.2%), massive GIB (20.5%), renal failure (10.3%), and chronic liver diseases (7.7%). We found significant higher mortality rates in older patients and those with final diagnosis of malignancy (table 2). There was no significant relationship between mortality rate and sex, cigarette smoking, and NSAID use. There was significant rela-

tionship between mortality rate and final diagnosis of malignant lesion or older age.

Recurrence: Recurrence was occurred in 58 (34.5%) patients. We found significantly higher recurrence rates in older patients and those with final diagnosis of malignancy (table3). There was no significant relationship between recurrence rate and sex, cigarette smoking or NSAID use. There was a significant relationship between recurrence rate and final diagnosis of malignant lesions and older age (table 3).

DISCUSSION

Acute UGIB is one of the common medical emergencies. [4] The mortality rate varies from 4% to 14%.[12]

This study provided information about mortality and rebleeding according to age, malignant lesion, sex, smoking, and taking NSAIDs. According to our results, mortality and rebleeding were related to older age and the diagnosis of malignancy.

Many researchers found the same results. For example, Ahmed and colleagues revealed that UGIB is common in the elderly, with a high mortality. Age was an independent risk factor for mortality in UGIB.[8]

In our study, overall mortality was 23.2%, but mortality in patients with diagnosis of malignant lesions was 72.2%. Large series of data on UGIB reported mortality rates between 5% and 15%. However, mortality is dependent on the study population, and inclusion and exclusion criteria. In studies on inpatients, mortality ranged from 28% to 63%.[3] Similar results were found by other researchers. For example, Stephen E. and co-workers reported an overall mortality rate of 36.7%, based on 5215 fatalities. It was highest for diagnosis of malignant lesions. Mortality was increased 27 times during the first month after admission. The most important independent prognostic predictors of mortality at three years were older age (mortality increased 53 fold for people aged 85 years and more compared with those under 40 years), and esophageal and gastric/duodenal malignancies (48 and 32 respectively). This study showed early mortality for UGIB due to malignancies and varices.[9]

In another study by Rockall and others on the emergency admissions, 65% of deaths in those aged under 80 years were associated with malignancy or organ failure at

Table 2: Distributions of mortality by age, sex, cigarette smoking, taking NSAIDs, and final diagnosis in patients with upper gastrointestinal bleeding

Variable		Mortality		P value
		Number	Percent	
Sex	Male	24	22.0	0.62
	Female	15	25.4	
Age group	Middle age	14	16.5	0.03
	Old age	25	30.1	
Cigarette smoking	Yes	7	28.0	0.63
	No	32	23.0	
NSAIDs* use	Yes	26	28.9	0.10
	No	13	17.8	
Final diagnosis	Malignant lesion	13	72.2	<0.01
	Non-Malignant lesion	26	17.3	

*NSAIDS: Non-steroidal anti-inflammatory drugs.

Table 3: Distributions of recurrence by age, sex, cigarette smoking, taking NSAIDs, and final diagnosis in patients with upper gastrointestinal bleeding

Variable		Recurrence		P value
		Number	Percent	
Sex	Male	35	32.1	0.37
	Female	23	39.0	
Age group	Middle age	21	24.7	<0.01
	Old age	37	44.6	
Cigarette smoking	Yes	11	44.0	0.30
	No	45	33.1	
NSAIDs* use	Yes	20	27.4	0.10
	No	36	40.0	
Final diagnosis	Malignant lesion	16	88.9	<0.01
	Non-Malignant lesion	42	28.0	

*NSAIDS: Non-steroidal anti-inflammatory drugs.

presentation.[7] Bae and colleagues reported that the age-specific incidence rate of mortality increased with advanced age. Incidence rate of mortality was three times more in men than women. The adjusted 30-day mortality rate ratio for patients older than 80 years was 8.13 compared with those younger than 60 years.[10]

In our study in 34.5% of the patients, an episode of bleeding occurred in next 3 months. A cross sectional hospital-based study that was performed on 1000 patients presenting with acute UGIB over a 7-year period showed complications in 70 patients (7%). The overall mortality was 15%. Mortality was 24% in older patients, and 37% among inpatients. Mortality after acute UGIB was particularly high among elderly patients.[11]

In a large Canadian study, endoscopic treatment and treatment with proton pump inhibitors decreased rebleeding and mortality in high-risk patients such as old patients with severe comorbidities and history of NSAIDS or anticoagulants use. Several factors, such as co-morbidities, type of treatment, or clinical and endoscopic findings, were related to rebleeding or death in patients admitted to the emergency room with UGIB necessitating intensive care.[4]

Lewis did not observe a positive correlation between NSAIDs sales and mortality from GI bleeding. The absence of correlation between mortality from GI complications and NSAIDs sales could also be due to the effect of a reduction in the duration of therapy. The same result was observed in our study that the difference between taking NSAIDs and mortality was not statistically significant.[12]

In conclusion, we found relatively high rates of mortality and recurrence among patients with UGIB. Our results suggested older age and diagnosis of malignancy as the most important indicators of mortality and recurrence in such patients. Considering these factors in clinical settings may result in better and more effective management of patients with UGIB.

ACKNOWLEDGEMENTS

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

REFERENCES

1. Lahiff C, Shields W, Cretu I, Mahmud N, McKiernan S, Norris S, et al. Upper gastrointestinal bleeding: predictors of risk in a mixed patient group including variceal and nonvariceal haemorrhage. *Eur J Gastroenterol Hepatol* 2012;**24**:149-54. doi: 10.1097/MEG.0b013e32834e37d6.

2. Masoodi M, Saberifiroozi M. Etiology and outcome of acute gastrointestinal bleeding in iran:a review article. *Middle East J Dig Dis* 2012;**4**:193-8.

3. Klebl F, Bregenzer N, Schöfer L, Tamme W, Langgartner J, Schölmerich J, et al. Risk factors for mortality in severe upper gastrointestinal bleeding. *Int J Colorectal Dis* 2005;**20**:49-56. doi: 10.1007/s00384-004-0624-2

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**:453-61. doi: 10.1007/BF02849865

5. Rockall TA, Logan RF, Devlin HB, Northfield TC. Selection of patients for early discharge or outpatient care after acute upper gastrointestinal haemorrhage. National Audit of Acute Upper Gastrointestinal Haemorrhage. *Lancet* 1996;**347**:1138-40.

6. Saltzman JR, Tabak YP, Hyett BH, Sun X, Travis AC, Johannes RS. A simple risk score accurately predicts in-hospital mortality, length of stay, and cost in acute upper GI bleeding. *Gastrointest Endosc* 2011;**74**:1215-24. doi: 10.1016/j.gie.2011.06.024.

7. Rockall TA, Logan RF, Devlin HB, Northfield TC. Incidence of and mortality from acute upper gastrointestinal haemorrhage in the United Kingdom. Steering Committee and members of the National Audit of Acute Upper Gastrointestinal Haemorrhage. *BMJ* 1995;**311**:222-6. doi.org/10.1136/bmj.311.6999.222

8. Ahmed A, Stanley AJ. Acute upper gastrointestinal bleeding in the elderly: aetiology, diagnosis and treatment. *Drugs Aging* 2012;**29**:933-40. doi: 10.1007/s40266-012-0020-5.

9. Roberts SE, Button LA, Williams JG. Prognosis following upper gastrointestinal bleeding. *PloS One* 2012;**7**: e49507. doi: 10.1371/journal.pone.0049507.

10. Bae S, Kim N, Kang JM, Kim DS, Kim KM, Cho YK, et al. Incidence and 30-day mortality of peptic ulcer bleeding in Korea. *Eur J Gastroenterol Hepatol* 2012;**24**: 675-82. doi: 10.1097/MEG.0b013e3283525a56.

11. Gado AS, Ebeid BA, Abdelmohsen AM, Axon AT. Clinical outcome of acute upper gastrointestinal hemorrhage among patients admitted to a government hospital in Egypt. *Saudi J Gastroenterol* 2012;**18**:34-9. doi: 10.4103/1319-3767.91737.

12. Lewis JD, Bilker WB, Brensinger C, Farrar JT, Strom BL. Hospitalization and mortality rates from peptic ulcer disease and GI bleeding in the 1990s: relationship to sales of nonsteroidal anti-inflammatory drugs and acid suppression medications. *Am J Gastroenterol* 2002;**97**:2540-9. doi:10.1111/j.1572-0241.2002.06037.x