Upper Gastrointestinal Bleeding in Khorramabad City in 2011
A Single Referral Center Experience

Koroušh Ghanadi¹, Khatereh Anbari², Zia Obeidavi³

ABSTRACT

BACKGROUND

Acute upper gastrointestinal bleeding (UGIB) is a common medical emergency and is known as one of the main causes of mortality and morbidity. This research was conducted to study the causes and risk factors for UGIB, in a referral center.

METHODS

In this cross sectional study, carried out in a one year period, all patients with acute UGIB living in Khorramabad city and surrounding area, entered the study. A control group with age and sex matched was selected from outpatient visits and their relatives who had referred to hospital clinics. Data collecting tool was a self-made questionnaire, demographic, clinical manifestations and endoscopic findings. The data was analyzed using chi-square test, Fisher exact test and Odds ratio estimation.

RESULTS

Sixty-two patients with acute UGIB were studied, 67.7% of them were males. The mean age of patients was 54.5±12.1. The most common causes of acute UGIB were peptic (42.7%), erosive gastritis (19.8%) and esophageal varices (19.8%). 29%, and 9.7% of patients, and control group had a history of regular consumption of Non Steroidal Anti-Inflammatory Drugs (Odd’s ratio 3.8, CI: 1.3-4.8). 35.5% of episodes of acute UGIB were in age more than 60 years.

CONCLUSION

Peptic ulcer disease is the most common cause of acute UGIB in our region. Episodes of acute UGIB were correlated with regular NSAIDs use, but not with alcohol consumption, smoking, and gender. Identifying people who are at risk and providing preventive strategies can reduce the rate of this disease and its complications.

KEYWORDS

Upper Gastrointestinal Bleeding; NSAIDs; Endoscopy; Peptic Ulcer

INTRODUCTION

Acute upper gastrointestinal bleeding is a common life threatening condition, that it causes significant economic and health burden. Despite new diagnostic modalities and endoscopic therapeutic interven-
tions, it’s mortality rate has remained unchanged around 10%.

It’s incidence reported between 50-150 patients per 100000 people, which is around 1% of total emergency department admissions. In the United States 46-160 cases per 100000 adult population suffer from acute UGIB with 10-14 deaths per 100000 people annually. The leading cause of death is inability to compensate hemodynamic status due to concurrent disease. The vast majority of bleeding episodes (45-60%) are due to peptic ulcers. In a study by Gholi Pouri et al. in Tabriz, UGIB consisted 12% of admissions and 13% of mortality of internal medicine ward. Acute UGIB was the cause of mortality in 16.2% of the surgical ICU. Duodenal and gastric ulcer were reported as the most common causes of acute upper gastrointestinal bleeding in a study from southern Iran.

Increased use of low dose aspirin for primary and secondary prevention from cardiac and cerebral vascular disease has increased life expectancy, and so increasing the degenerative joint diseases and osteoarthropathies. Consequently more use of Non Steroidal Anti-Inflammatory Drugs (NSAIDs) in elderly patients have changed the pattern, age distribution, and site of bleeding in patients with acute non variceal UGIB over the last decade. On the other hand, it seems that with much improvement in lifestyle, vaccination against hepatitis B virus, preventive use of propranol and liver transplantation have changed the incidence of variceal bleeding in patients with hepatic disorders. In the recent years the number of studies exclusively examining epidemiologic patterns of UGIB has been quite limited. However, most epidemiologic studies have shown a decrease in the incidence of all causes of upper gastrointestinal bleeding. Although the incidence of peptic ulcers have remained unchanged. Age more than sixty years old, concurrent diseases, hemodynamic status disorder, active bleeding, hypertension, coagulation problems, NSAIDs, and helicobacter pylori infection are the main risk factors for upper gastrointestinal bleeding. Therefore having information about etiology is helpful for physicians in order to choose the best treatment techniques and set the ground to control and manage this disease and its consequences. The aims of this study are to identify the most common causes of acute UGIB, and risk factors to introduce preventive strategies, and to reduce the consequences and mortality rate of this disease, in our area.

**MATERIALS AND METHODS**

In the present cross sectional study, all patients with acute upper gastrointestinal bleeding in Khorramabad city and its suburbs who have been referred for subspecialty care in 2011 were included. During this study, 18 out of 35 patients with acute UGI bleeding were referred to other hospitals of Khorramabad city, but then were transferred to Ashayer Shohada Hospital for subspecialty treatment. All patients had consented orally to participate in this study. Sampling method was census. Sampling method for control group was convenience sampling. The subjects were collected from patients and outpatients relatives referred to different clinics of hospital. The qualified subjects in control group didn’t have any history of heart problems, gastrointestinal, rheumatologic diseases and discopathy. Through group matching control group was matched with patient group based on age and sex. The purpose of experimental group in this study is to compare risk factors such as smoking, and routinely taking NSAIDs. Two groups were compared for the estimation of odds ratio. Information was collected through researcher by a questionnaire including demographic characteristics, the history of smoking (smoking more than 10 cigarette per day for at least one year), alcohol consumption (with DSM-IV-TR criteria, and alcoholic products with daily consumption including beer, vodka, whisky, wine, fortified wine and hard liquor), NSAIDs usage and the type of consumed drugs (low dose daily aspirin, or other drugs including naproxen, indomethacin, ibuprofen, diclofenac Na, piroxicam, and mefenamic acid except celecoxib), use of multiple NSAIDs, length of time taking NSAIDs, vital signs and hemoglobin level ( on their arrival, patient’s hemoglobin test was carried out using chromatography by BT devices), clinical manifestation in patients within early hours of admission, clinical
features of disease and finally endoscopic findings in patients. The questionnaire was completed by clinical interview. Endoscopic reports of each patient were collected from endoscopy department of hospital. Two consultant gastroenterologists have done the endoscopies. The validity of study was confirmed by expert panel. After collecting and completing information about patients, the data was analyzed through descriptive statistical techniques (standard mean scores, ratios, frequency percent and Fishers exact test). To investigate the relationship between regular smoking, NSAIDs consumption, and gastrointestinal bleeding in subjects under study chi-square test was used. To show the significance of the given relationship odds ratio (OR) with 95% confidence interval was used.

RESULTS

Sixty two patients with upper gastrointestinal bleeding and 62 subjects as control group were studied in a one-year period. The average age of patients was 54.5±12.1, with range of 16 to 88 years. There was no significant difference regarding age (55.2±11.7, p=0.890 and sex with control group. Patients with acute UGIB included 42 male (67.7%) and 20 female (32.3%). 35.5% of patients were in age 60-79 years, while 4.8% were below 20 years, 22.6%, 25.8%, and 11.3% of patients were in 20-39, 40-59, and more than 80 years old respectively. With respect to smoking history of all patients’ only 15 subjects (24.2%) had history of smoking, and only 2 patients (3.2%) mentioned alcohol consumption history, while in control group 9 patients (14.5%) had smoking history and none consumed alcohol (p=0.173) (Table 1). 18 patients (29%) reported that they had routinely taken NSAIDs compared to control group with 6 patients (9.7%). Based on chi-square test, there was significant difference between these two groups (p=0.006, OR with 95% CI; 3.8 with range 1.3-4.8) (Table 1). Of NSAIDs, aspirin with or without other drugs (61.9%) has the highest consumption in under study patients, followed by indomethacin (14.3%). In addition the average Hb level of patients within early hours of admission was 11.3±3.2, and systolic hypertension average was estimated 119±28.3 mmHg. Diastolic hypertension average was 71±15.8 mmHg. The leading underlying disorder was cirrhosis of liver (61.5%), regular consumption of NSAIDs (23.1%), chronic obstructive lung disease in 7.7% and Budd Chiari syndrome in 7.7%.

The clinical presentations of 39 patients (62.9%) were with just hematemesis, 10 (16.2%) with hematemesis and melena, 11 (17.7%) with only melena, and 2 (3.2%) with hematemesis, melena and hematochezia.

The most common cause of acute UGIB was peptic ulcer disease in 42.7% (duodenal ulcer disease in 27.8%, and gastric ulcer in 13.3%). 64.7% of duodenal ulcers were clean based appearance and 35.5% were associated with visible vessels. All ulcers with visible vessel were located in lesser curvature of stomach. Esophageal varices were present in 19.8%, and erosive gastritis (gastropathy) in 19.8% of patients.

The leading cause of upper gastrointestinal bleeding in men (26.8%) and women (30%) was duodenal ulcer, followed by erosive gastritis (22%) in men and esophageal varices (25%) in women. According to Fisher exact test, there were no significant differences regarding the causes of bleeding with respect to sex (p=0.77) (Table 2).

The most common cause of bleeding in patients under 40, and over 60 years old was duodenal ulcer in 35%, and respectively. In patients with 40-60 years old of age esophageal varices (43.8%) was the most common cause of acute UGI bleeding (p=0.033 based on Fisher exact test) (Table 3).

DISCUSSION

The present study examined 62 patients with acute UGI bleeding who referred to the Shohada hospital in a one-year period. Shohada hospital is the only referral center for gastrointestinal specialty treatment services in Lorestan (a province in western of I. R. Iran), so this study would provide a valuable information about epidemiologic patterns, and risk factors and it’s underlying diseases responsible for this serious presentation in our area.

Acute UGI bleeding was higher among men
(about 2 times higher than that of women) (32/3%). Our finding is in agreement with the Hearnsaw’s study from England, which the incidence was 2 times higher among men.12 In this study, the highest numbers of patients were in the 60-79 age range. The high incidence rate in this group can be explained by excessive use of NSAIDs due to an increase in musculoskeletal pains and cardiovas-

| Table1: Comparison of regular smoking and NSAIDs consumption in patients and control group |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Risk factors                      | Patients N(%)   | Control N(%)    | *p-Value*       | OR              | CI              |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Regular NSAIDs consumption        | YES             | 18(29)          | 6(9.7)          | 0.006           | 3.8             | 1.3- 4.8        |
|                                   | NO              | 44(71)          | 56(90.3)        |                 |                 |                 |
| Regular smoking                   | YES             | 15(24.2)        | 9(14.5)         | 0.173           | 1.8             | 0.75- 4.6       |
|                                   | NO              | 47(74.8)        | 53(85.5)        |                 |                 |                 |

*Significant level was<0.05
**Statistical test: Chi-square

| Table2: Frequency distribution of main causes of upper Gastrointestinal bleeding in patients under study |
|-------------------------------------------------------------------------------------------------------|
| Causes of bleeding                                                                                   |
| N (%)                                                                                                 |
| Duodenal ulcer                                                                                       | 17(27.8) |
| Gastric ulcer                                                                                       | 8(13.3)  |
| Esophageal varices                                                                                   | 12(19.8) |
| Erosive gastropathy                                                                                  | 12(19.8) |
| Disseminated erosive esophagitis                                                                     | 3(4.9)   |
| Mallory-weiss syndrome                                                                              | 2(3.2)   |
| Stomach tumor                                                                                        | 2(3.2)   |
| Dieulafoy’s lesion                                                                                   | 2(3.2)   |
| Erosive duodenitis                                                                                   | 2(3.2)   |
| Esophageal ulcer                                                                                     | 1(1.6)   |
| Total                                                                                                | 61(100)  |

| Table3: Cross table of upper gastrointestinal bleeding in patients under study based on sex and age |
|------------------------------------------------------------------------------------------------------|
| Causes of bleeding                                                                                   |
| Sex                                                                                                   |
| Age                                                                                                   |
| Male                                                                                                  |
| Female                                                                                                |
| <40                                                                                                   |
| 40-60                                                                                                 |
| >60                                                                                                   |
| Esophageal ulcer N (%)                                                                               | 0(0)     | 0(0)         | 0(0)           | 0(0)           |
| Gastric ulcer N (%)                                                                                  | 6(14.6)  | 2(10)        | 1(5)           | 2(12.5)        | 5(20)          |
| Duodenal ulcer N (%)                                                                                 | 11(26.8) | 6(30)        | 7(35)          | 1(6.3)         | 9(36)          |
| Erosive esophagitis N (%)                                                                            | 3(7.3)   | 0(0)         | 0(0)           | 0(0)           | 3(12)          |
| Erosive gastritis N (%)                                                                              | 9(22)    | 3(15)        | 6(30)          | 1(6.3)         | 5(20)          |
| Erosive duodenitis N (%)                                                                             | 2(4.9)   | 0(0)         | 1(5)           | 1(6.3)         | 0(0)           |
| Esophageal varices N (%)                                                                             | 7(17.1)  | 5(25)        | 3(15)          | 7(43.8)        | 2(8)           |
| Mallory-weiss syndrome N (%)                                                                         | 1(2.4)   | 1(5)         | 1(5)           | 1(6.3)         | 0(0)           |
| Gastric tumor N (%)                                                                                  | 1(2.4)   | 1(5)         | 0(0)           | 2(12.5)        | 0(0)           |
| Dieulafoy’s lesion N (%)                                                                             | 1(2.4)   | 1(5)         | 1(5)           | 1(6.3)         | 0(0)           |
| *p-Value                                                                                              | 0.77     | 0.033        |                 | 0.37           |

*Significant level was<0.05
**Statistical test: Fisher exact test
cular disease with age. Most studies, consider age as a risk factor for upper gastrointestinal bleeding. Mortality rates due to gastrointestinal bleeding are higher among patients over 75 years old. In addition, these studies show that in elderly patients, due to their susceptibility to underlying diseases, the risk for upper gastrointestinal disease is higher.\(^{13,14}\) In similar studies, alcohol has been reported as an important risk factor for upper gastrointestinal bleeding.\(^{15,16}\) In our study only 3.2% of patients reported a history of alcohol consumption. In the Iranian society, relatively lower rates of alcoholism can be accounted for by cultural, religious, and legal prohibitions. However some patients may denied alcohol consumption. The results of this study show that 24.2% of patients reported a history of smoking. However, in the present study, no significant relationship between smoking and gastrointestinal bleeding was found. In other studies, smoking has been found to be a risk factor for peptic ulcer and, consequently, gastrointestinal bleeding due to ulcers.\(^{17}\) It seems that smoking slows down ulcer healing and response to the treatment. Although different theories have been proposed regarding the mechanism responsible for the increased risk for ulcer among smokers, there is no globally agreed mechanism.

The most common clinical presentation among patients was hematemesis (62.9%). In addition to hematemesis, bleeding proximal to ligament of Treitz can cause melena also.\(^{18}\)

It has been reported that upper gastrointestinal bleeding rate is 3 times higher in patients taking NSAIDs.\(^{17,18}\) Among different types of NSAIDs, aspirin with 76.5% use accounts for the highest amount of medication use among the patients under study. This high amount of consumption can be explained by the increased incidence of cardiovascular disease with age. Among patients under study, 61.9% reported the consumption of only (Acetylsalicylic Acid) ASA, while 14.4% of the patients have taken ASA simultaneously with other drugs such as indomethacin, mefenamic acid and warfarin. In addition to concomitant use of other NSAIDs the bleeding rate due to ASA is dependent on the dosage of the medication.\(^{19}\)

The most common underlying disease was chronic liver disease. In a study by Pike et al, liver problem has been reported as the most common disease responsible for upper gastrointestinal bleeding.\(^{20}\) According to Reference’s book, the most common cause of acute upper gastrointestinal bleeding is gastrointestinal ulcers followed by esophageal varices. Vascular ecstasies are among the least common causes of bleeding and the present study confirms this. The only difference between this study and other studies is the rate of patients with gastro-duodenal erosions.

In a study by Pike carried out in Korea, peptic ulcer (50.9%) followed by esophageal varices (28.3%) and Mallory-Weiss Syndrome (10.3%) were found to be the leading causes of upper gastrointestinal bleeding.\(^{21}\) This study demonstrated that a high percentage of patients (23%) suffered from erosion. Since the use of NSAIDs is considered an important risk factor, this finding is indicative of high consumption of NSAIDs medications in the population under study. In another study by Kaviani et al. in southern Iran, gastric ulcer (30%) followed by duodenal ulcer were reported as the most common causes of acute upper gastrointestinal bleeding.\(^{6}\) Finally, it should be mentioned that duodenal and stomach ulcers are the most common causes of acute gastrointestinal bleeding. These patients have either taken drugs without prescription or have taken empirical ranitidine or omeprazole without thorough examination and diagnosis. These drugs have temporary effects and don’t conclusively treat the condition, because the main cause of ulcers is *Helicobacter pylori* infections and the use of NSAIDs. Promoting public awareness of gastrointestinal symptoms, and prohibition of NSAIDs empirical or over the counter us of these drugs is important for prevention of this serious presentation.

In the present study most patients consumed ASA because of cardiovascular problems, therefore it is recommended that cardiologists be more cautious in prescribing ASA for patients with cardiovascular problems, and when feasible order prophylactic treatment for the gastrointestinal system such
as proton pump inhibitors should be considered. In addition, careful examination of patients over 40 years old with abdominal pain is recommended, since a large number of patients with ulcers have experienced some periods of abdominal pain. Given the fact that cirrhosis is a factor that makes patients susceptible to gastrointestinal bleeding, examination of cirrhotic patients is necessary. Unfortunately, many patients do not refer to physicians for conclusive treatment of esophageal varices due to cultural and economic problems and high costs of band ligation. Therefore, given the multiplicity of causes and risk factors involved in upper gastrointestinal bleeding, the identification of patient risk factors and utilization of preventive strategies and prompt treatment play an important role in the prevention of this disease and control and management of its complications.

In addition to low number of patients, lack of hospital or short term outcomes are the major limitations of present study. This is due to the lack of cooperation and death of patients because of disease side effects and incomplete endoscopic reports prepared by other colleagues who were unaware of the purpose of this study. Finally, it is suggested to carry out studies with higher number of patients and in different hospitals in order to examine the consequences of disease.

ACKNOWLEDGMENT
I should like to express my great appreciation to all the hard-working personnel of the endoscopic department of the Shohada Hospital.

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

REFERENCES
1. 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.
2. van Leerdm ME. Epidemiology of acute upper gastrointestinal bleeding. Best Pract Res Clin Gastroenterol 2008;22:209-24.
3. Iamber M. International consensus group issues recommendations for management of upper GI bleeding. Am Fam Physician 2010;81:1495-7.
4. Theocharis GJ, Thomopoulos KC, Sakellaropoulos G, Katkoulis E, Nikolopoulos V. Changing trends in the epidemiology and clinical outcome of acute upper gastrointestinal GI bleeding in a defined geographical area in Greece. J Clin Gastroenterol 2008;42:128-33.
5. Gholi Pouri Ch. Evaluation of potentially preventable mortalities in patients with upper gastrointestinal tract bleeding at two hospitals of Tabriz University of Medical Sciences. Medical Journal of Tabriz University of Medical Sciences & Health Services 2005;27:63-6.
6. Kaviani MJ, Pirastehfar M, Azari A, Saberifroozi M. Etiology and outcome of patients with upper gastrointestinal bleeding: a study from south of Iran. Saudi J Gastroenterol 2010;16:253-9.
7. Boonpongmanee S, Fleischer DE, Pezzullo JC, Collier K, Mayoral W, Al-Kawas F, et al. The frequency of peptic ulcer as a cause of upper GI bleeding exaggerated. Gastrointest Endosc 2004;59:788-94.
8. Elmunzer BJ, Inadomi JM, Elta GH. Risk stratification in upper gastrointestinal bleeding. J Clin Gastroenterol 2007;41:559-63.
9. Zullo A, Hassan C, Campo SM, Morini S. Bleeding peptic ulcer in elderly: risk factors and prevention strategies. Drug Aging 2007;24:815-28.
10. Zippi M, Febbraro I, De felici I, Mateci E, Traversa G, Occhigrossi G. Diagnosis and treatment of bleeding peptic ulcer: our experience. Clin Ter 2008;159:249-55.
11. Lanas A, Perez-Aisa MA, Feu F, Ponce J, Saperas E, Santolaria S, et al. Nationwide study of mortality associated with hospital admission due to severe gastrointestinal event and those associated with non-steroidal anti-inflammatory drug use. Am J Gastroenterol 2005;100:1685-93.
12. Hearnshaw SA, Logan RF, Lowe D, Travis SP, Murphy MF, Palmar KR. Acute upper gastrointestinal bleeding in the UK: patient, characteristics and outcome in the 2007 UK audit. Gut 2011;60:1327-35.
13. Cheung J, Rajala J, Moroz D, Zhu Q, Stamm M, Sandha GS. Acetylsalicylic acid use in patients with acute myocardial infarct and peptic ulcer bleeding. Can J Gastroenterol 2009;23:619-25.
14. Straube S, Tramer MR, Moore RA, Derry S, McQuay HJ. Mortality with upper gastrointestinal bleeding and perforation: effects of time and NSAID use. BMC Gastroenterol 2009;9:41.
15. Haung ES, Strate LL, Ho WW, Lee SS, Chan AT. Long term use of aspirin and the risk of gastrointestinal bleeding. Am J Med 2011;124:426-33.
16. Aparisi L, Sabater L, Del-Olmo J, Derry S, McQuay HJ. Dose and association between chronic pancreatitis and liver cirrhosis in alcoholic subjects?. World J Gastroenterol 2008;14:6171-9.
17. Elghuel A. The characteristics of adults with upper gastrointestinal bleeding admitted to Tripoli medical center: a retrospective case-series analysis. Libyan J Med 2011 Mar 7;6.

18. Jairath V, Kahan BC, Logan RF, Hearnshaw SA, Doré CJ, Travis SP, et al. Outcomes following acute nonvariceal upper gastrointestinal bleeding in relation to time to endoscopy: results from a nationwide study. Endoscopy 2012;44:723-30.

19. Sibilia J, Ravaud P, Marck G. Digestive and hemorrhage complications of low-dose Aspirin. Presse Med 2003;32:17-28.

20. Ben-Menachem T, Dominitz JA. Acute upper gastrointestinal hemorrhage in an elderly woman taking aspirin and clopidogrel. Clin Gastroenterol Hepatol 2011;9:525-649.

21. Paik CN, Lee IS, Oh JH, Park JM, Cho YK, Kim SW, et al. Clinical characteristics of acute upper gastrointestinal bleeding in a tertiary referral center. Korean J Gastroenterol 2007;50:26-35.