Etiology and Outcome of Acute Gastrointestinal Bleeding in Iran: A Review Article

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ABSTRACT

Upper gastrointestinal bleeding (UGIB) is defined as bleeding that results from lesions located above the ligament of Treitz and is a common cause for emergency hospital admissions in patients with gastrointestinal disorders. UGIB also increases the risk of morbidity and mortality in patients already hospitalized for other reasons. According to epidemiological surveys of acute UGIB in Iran, peptic ulcer is the most common endoscopic diagnosis. Gastric and duodenal erosion accounts for 16.4%-25% of etiologies. Other relatively common causes of UGIB are variceal hemorrhage, Mallory-Weiss tears, and arterial and venous malformations. However, in 9%-13.3% of patients, the endoscopy is normal.

KEYWORDS
Upper gastrointestinal bleeding; Etiology; Outcome; Endoscopic

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INTRODUCTION

Acute upper gastrointestinal bleeding (UGIB) can be a life-threatening emergency and is a common cause for hospitalization. UGIB is defined as bleeding due to lesions located above the ligament of Treitz from the esophagus, stomach and duodenum. The annual incidence of hospitalization for acute UGIB is 1 per 1000 people in the United States. UGIB is more frequent in men than women and increases with age.[1,2] The etiology of acute UGIB can be divided into variceal and non-variceal causes. The main sources of non-variceal bleeding are peptic ulcers, esophagitis, drug-induced mucosal damage, vascular anomalies, traumatic and postoperative lesions, and tumors. Variceal UGIB is caused by the sequelae of portal hypertension such as varices of the esophagus, stomach, duodenum, and portal hypertensive gastropathy. The overall mortality of acute UGIB is around 6% to 10%, and occurs more in variceal than non-variceal etiologies. The introduction of endoscopic procedures has not decreased the mortality rate of UGIB over the past decades. Improvements in diagnosis and management of acute UGIB such as increased numbers of specialists, improvements in diagnostic and therapeutic endoscopies and interventional radiology, the use of newer drugs, and better surgical approaches may have led to better patient outcome over the last ten years.[1-8] Epidemiological data are

important for gaining an insight into the etiology, outcome, management and preventive healthcare measures for UGIB. However, only a few epidemiological surveys have been performed with regards to acute UGIB in Iran. In this review we intend to discuss important data about UGIB in Iran according to research over the past ten years.

Gender

According to Iranian studies, 57%-76% of UGIB cases were male,[9-13] which was comparable to other countries. In Boston (United States), the rates increased with age and were approximately twice as high in males compared to females.[14] In Libya, the ratio of UGIB male to female cases was 3:2; males comprised 60.3% of UGIB cases and were significantly younger than females.[15] In another study, the incidence of UGIB was twice as frequent in males and increased with age.[16,17]

Mortality and associated factors

Mortality from UGIB according to Iranian studies was 0.5%-12.5%.[9-13,18-20] Currently, the average mortality has been proposed to range from 5% to 10%.[16] According to a nationwide audit in the UK, 7% of patients died due to complications that arose from UGIB.[8] Mortality from UGIB has remained stable (5% to 10%) over the past decades despite improvements in the diagnosis and management of acute cases; the cause may be an aging population and comorbidities.[16,21-24] Additionally, the mortality rate for UGIB is more than the rate observed with bleeding from the lower gastrointestinal tract.[15] Factors such as increasing age, length of hospital stay, emotional (shock) state on admission, and underlying comorbidities impact overall mortality. In a study by Kaviani et al., age, orthostatic hypotension upon admission, and steroid use have been reported as factors that increase mortality rate. Increased mortality in patients over the age of 60 might possibly be related to increased use of alcohol, hookah, cigarettes, aspirin, warfarin, and steroids. Interestingly, overall mortality was omparable in variceal and non-variceal bleeding in this study, which may be due to increased availability of medical and endoscopic treatments such as rubber band ligation, sclerotherapy and vasoconstrictor drugs.[12]

NSAIDs

According to studies from Iran, 26%-75% of patients with UGIB have histories of NSAID use.[9,12,25-28] NSAIDs, including low-dose aspirin, are a common cause of gastrointestinal ulceration, with a four- to six-fold increase in acute UGIB and perforation in people who take NSAIDs compared to those who do not.[14,29-31] One study has reported NSAID use in 9.7% of cases.[15] However data have suggested that although the incidence of bleeding peptic ulcer decreased between 1993 and 2002, the proportion of ulcers caused by NSAIDs increased. Other data between 1990 and 2000, however, found no change in overall peptic ulcer bleeding rates, rather there was an increase in the rate of bleeding among older patients who took NSAIDs.[32] In one large multicenter study of patients with severe peptic ulcer bleeding, 57% of those with bleeding from a gastric ulcer took aspirin or other NSAID, and 45% were infected with *H. pylori*, whereas 53% of those with a bleeding duodenal ulcer took aspirin or other NSAID, or both, and 50% were infected with *H. pylori*.[33,34]

Peptic ulcers

Peptic ulcer disease is the most common etiology for acute UGIB. In the majority of Iranian studies on patients with UGIB duodenal ulcers (19.5%-41%) have been reported to be more common than gastric ulcers (10.8%-29.5%).[9,10,13,18,19,35] In contrast, other studies report that gastric ulcers occur more frequently.[11,12] Of note, in Iran *H. pylori* infection is present in nearly 90% of the adult population. *H. pylori* is known to be the main cause of gastritis and peptic ulcer disease and its resulting complications.[36-41] In some studies bleeding peptic ulcers are the most common cause of UGIB, responsible for approximately 31%-67% of all cases. Of these, duodenal ulcers are the most common.[21,30,34,42-44] In a 1996 prospective series of 1000 cases of severe UGIB at the UCLA and West Los Angeles Veterans Administration Medical Centers, peptic ulcer

disease accounted for 55% of all UGIB.[45] Between 2000 and 2004 a large database study conducted in a practice setting noted the most common endoscopic findings in patients with UGIB were ulcers (33%) followed by erosion (19%). Gastric ulcers (55%) were more common than duodenal ulcers (37%). Patients with variceal bleeding were excluded from the analysis.[46] More recent data showed a decline in the proportion of cases caused by peptic ulcer disease.[47,48] In a report from the national United States database from 1999 to 2001, peptic ulcers comprised approximately 20% of UGIB episodes. The rate of peptic ulcer disease declined in the above report.[47,48] In recent years important changes have taken place that might have influenced the incidence, etiology, and outcome for patients with acute UGIB. The most common cause was nonspecific mucosal abnormalities (42%). 6,8A study from Semnan Province, Iran, evaluated all cases (n=873 for all, males: 70.7%) with UGIB admitted to hospitals from 1991 to 2004.During this period, the incidence rate of UGIB decreased from 98.4 to 40.1 per 100,000 persons per year.($p<0.001$). The incidence rates of bleeding due to peptic and non-peptic ulcers have decreased. However, in the second analysis the rate of acid peptic disease decreased, but the rate of non- acid peptic disease remained unchanged during the study period. The data suggested that the proportion of cases caused by peptic ulcer disease increased from 44% to 62%. The rates of therapeutic endoscopy, surgical interventions, and death did not undergo any dramatic changes.[18]

Gastric and duodenal erosive diseases

In Iranian studies of UGIB a total of 16.4%-25% of adults and 28% of children had erosive gastritis.[9,10,12,13,19] Hemorrhagic and erosive gastropathy, often incorrectly labeled as "gastritis," refers to subepithelial hemorrhages and erosions. These lesions are restricted to the mucosa where no large blood vessels are present. The most common causes for this condition are NSAID use, alcohol intake, and stress. The overall incidence of gastric and duodenal erosive disease in other areas of the world is 4%-19%.[15,30,34,49-51]

Esophagitis and Mallory-Weiss tears

Esophagitis and Mallory-Weiss tears account for 2.5%-8% of all UGIB.[9,12,13,18,19] Forceful vomiting or sudden tension on the cardia region that occurs with repeated retching can be the etiology for mucosal tearing or laceration and UGIB. In reports from different geographic areas, Mallory-Weiss tears account for 4%-8% of all cases of UGIB, according to upper GI endoscopy. In several series, erosive esophagitis has accounted for only 1%-13% of all cases of acute UGIB, which was less common than peptic ulcer disease. Patients with severe erosive esophagitis can present with either hematemesis or melena.[15,30,34,45]

Varices

Portal hypertension arising from various causes is one of the major etiologies of UGIB. Most bleeding varices are in the esophageal lumen, however may they be located in the fundus and cardia of the stomach, distal stomach, duodenum and small bowel, or colonic segments. The majority of cases of portal hypertension are related to cirrhosis of the liver.Often, variceal hemorrhage is massive with hematemesis and/or melena. In patients with end stage liver disease, variceal bleeding may present with increasing ascites or hepatic encephalopathy, which causes liver decompensation in a previously compensated liver. Around 6%-39% of patients undergoing endoscopy for UGIB have variceal bleeding, of which the large majority are bleeding esophageal varices.[15,30,34,45] In Iranian studies, 2%-11.7% of the causes for UGIB have been attributed to varices. In one study from Shiraz, 27% of UGIB were from varices; in children the amount was 16%.[9,11-13,18,19,25,52]

Cancer

In Iran, 1.2%-3.7% of those with UGIB had malignant and benign tumoral lesion.[9,12,13,18,25,52].Less than 2%-8% of severe UGIB have been reported to result from malignant and benign tumors of the upper gastrointestinal tract. These tumors can be ulcerated or eroded on the surface with growth and ulceration that can cover a large artery, resulting in severe bleeding particularly during the late stages.[15,30,34,45,53]

Vascular anomalies

Dieulafoy's lesion or a small mucosal erosion located over a large dilated artery can cause massive gastrointestinal bleeding. Dieulafoy's lesion can be difficult to identify at endoscopy because of the intermittent nature of the bleeding; when the lesion is not bleeding the overlying mucosa may appear normal. Dieulafoy's lesion accounts for 1%-2% of UGIB and arteriovenous malformations account for 3%-6% of such bleeding.[15,30,34,45] Arterial, venous, and other vascular malformations comprise 0%-1.4% of UGIB as reported in Iranian studies.[9,11-13,18,19,25]

Normal endoscopy

Normal endoscopies occurred in 9%-13.3% of UGIB cases in Iranian studies.[10,13,18,19] UGIB has been shown to arise from a variety of sources, many of which are apparent on endoscopic studies. However in 5%-14% of cases of gastrointestinal hemorrhage, no source is identified by standard endoscopy.[15,30,34,45,54,55]

CONCLUSION

Until recently, only limited data was available on the epidemiology of UGIB in Iran. Most studies in Iran have investigated UGIB over short time periods in small populations. There are no true population-based registries in Iran that systematically collect information on UGIB; hospital-based studies have been used to analyze clinical characteristics. 56 It is well known that hospital-based studies may include only select patients and data may be less reliable, making standardization and comparison of data impossible. Despite these limitations, it is possible to obtain some valuable information from such studies. In this study we have aimed to obtain information on the epidemiology, in particular the etiology, of UGIB in Iran (Table 1).

CONFLICT OF INTEREST

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

Table 1: Major causes of upper gastrointestinal hemorrhage in Iran.

Diagnosis	Proportion of cases (%)
Peptic ulcer disease	
Duodenal ulcers	19.5-41
Gastric ulcers	10.8-29.5
Gastric and duodenal erosion	16.4-25
Esophagitis and Mallory-Weiss tears	2.5-8
Gastroesophagealvarices	2-11.7
Neoplasms	1.2-3.7
Arterial, venous malformations	0-1.4
Normal endoscopy	9-13.3

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