INTRODUCTION

Upper gastrointestinal bleeding is defined as bleeding in the gastrointestinal proximal to the ligament of Tretiz, and is categorized into variceal and non variceal bleeding ***(Barkun et al., 2003).***

Upper gastrointestinal bleeding is the commonest emergency medical admission for gastroenterology worldwide and has a significant inpatient mortality rate of 10% ***(Hearnshaw et al., 2011).***

Upper gastrointestinal bleeding worldwide occurs at a rate of approximately 40 – 150 cases per 100,000 per year ***(Gralnek et al., 2015)***, with more than 350,000 annual hospital admissions in Canada ***(Longstreth et al., 1995).***

In Egypt the variceal bleeding is the commonest cause of UGIB as documented by various studies, 60.1% by ***Abeid, (2006),*** 36% by ***Bayoumi, (2009)*** and 31% by ***Gado et al. (2012).***

Endoscopy plays a central role in the diagnosis and management of upper gastrointestinal bleeding; advances in endoscopic techniques have rendered endoscopy as the first line of diagnostic & therapeutic interventions for patients with upper gastrointestinal bleeding ***(Kwan and Norton, 2007).***

Patients who continue in hemodynamic instability need urgent endoscopy, preferably in the intensive care

unit. All others can undergo endoscopy as soon as possible, hopefully within 24–48 h. The chance of missing a second bleeding lesion under a pool of blood is low for patients with acute upper gastrointestinal bleeding, but is not obviously zero, and thus all such patients should undergo repeat endoscopy in 24–48 hours ***(Putchaet al., 1997).***

The mortality rate of acute upper gastrointestinal bleeding decreasedslightly following the introduction of endoscopic interventionmodalities in the 1980s and better care in high dependency bleedingunits ***(Putcha et al., 1973).*** Rebleedingis considered the most important risk factor for mortality andoccurs in 10-30% of those successfully treated ***(Saeed et al., 1995).***

Common causes of acute upper gastrointestinal bleeding are as follows: Peptic ulcer disease, Esophageal or gastric varices, arteriovenous malformations, Mallory-Weiss tears, Tumors, Esophagitis and Dieulafoy's lesions ***(Savides et al., 1996).***

Variceal bleeding treatments frequently include endoscopic banding or sclerotherapy of esophageal varices in parallel with splanchnic vasoconstrictors and intensive medical care ***(Harry et al., 2002).*** Alternative interventions include; decompressive surgical shunts and Transjugular Intrahepatic Portosystemic Shunts (TIPS) ***(Zoli et al., 2005).***

Peptic ulcer due to the Helicobacter pylori and Non-Steroidal Anti-inflammatory Drugs (NSAIDs) is responsible for the majority of bleeding ulcers ***(Bardou et al., 2003).*** In patient with bleeding peptic ulcer and high risk stigma, endoscopic treatment is the best used approach ***(Bardou et al., 2003).*** It improves outcome of these patients significantly decreasing both recurrent bleeding and mortality ***(Barkun et al., 2003).***

Endoscopy is of great importance in accurate diagnosis of the site of upper gastrointestinal bleeding whether variceal or from other gastrointestinal lesions ***(Pagliaro et al., 1995).***

Aim of the Work

To measure the prognostic factors of patients presented by haematemesis to the Emergency Department of Ain Shams University Hospital over the period of six months, from January to June 2015.

Literature Review

Definition

Upper Gastroentestinal Bleeding:

Upper gastrointestinal bleeding (UGIB) is defined as bleeding in the gastrointestinal proximal to the ligament of Tretiz, and is categorized into variceal and non variceal bleeding ***(Barkun et al., 2003).***

Epidemiology:

UGIB is the commonest emergency medical admission for gastroenterology worldwide and has a significant inpatient mortality rate of 10% ***(Hearnshaw et al., 2011).*** It occurs at a rate of approximately 40-150 cases per 100,000 per year, worldwide ***(Gralnek et al., 2015)***, with more than 350,000 annual hospital admissions in Canada ***(Longstreth et al.,1995).***

In Egypt the variceal bleeding is the commonest cause of UGIB as documented by various studies, 60.1% by ***Abeid, (2006),*** 36% by ***Bayoumi (2009)*** and 31% by ***Gado et al. (2012).***

Endoscopy plays a central role in the diagnosis and management of UGIB; advances in endoscopic techniques have rendered endoscopy as the first line of diagnostic & therapeutic interventions for patients with UGIB***(Kwan et al., 2007).***

Upper endoscopy is required for most patients with UGIB and should be performed within 24 h of hospital admission after adequate prior fluid resuscitation ***(Szura at al., 2015).***

Rebleeding in upper gastrointestinal bleeding occurs in 7%–16%, despite endoscopic therapy. Rebleeding is especially high in variceal bleeding and peptic ulcer bleeding ***(Kumar and Sibia, 2015).***In cases of rebleeding, a second attempt at endoscopic therapy is recommended to reduce the need for surgery ***(Szura at al., 2015).***

The mortality rate of acute UGIB decreasedslightly following the introduction of endoscopic intervention modalities in the 1980s and better care in high dependency bleedingunits ***(Stollman et al., 1973).***

Causes & Pathophysiology

Upper gastrointestinal bleeding (UGIB) is a common medical condition that results in increased patient's morbidity and medical care costs. Vomiting of blood or coffee-ground like material (hematemesis) and/or melena (black, tarry stools) is the common presentation of this condition ***(Jutabha and Jensen, 1996).***

Common causes of acute upper gastrointestinal bleeding are as follows:Peptic ulcer disease, Esophageal or gastric varices, arteriovenous malformations, Mallory-Weiss tears, Tumors, Esophagitis and Dieulafoy's lesions ***(Loperfido et al, 2009; Gralnek et al, 2015).***Acute UGIB can be categorized into several broad categories as followed (Table1)***(Jutabha and Jensen, 1996):***

"A prospective series of 1000 cases of severe upper gastrointestinal bleeding at the UCLA and West Los Angeles Veterans Administration Medical Centers published in 1996 found the following distribution of causes" ***(Jutabha and Jensen, 1996):***

- Peptic ulcer disease — 55%
- Esophagogastric varices — 14%
- Arteriovenous malformations — 6%
- Mallory-Weiss tears — 5%
- Tumors and erosions — 4%
- Dieulafoy's lesion — 1%
- Other — 11%

Table (1): Etiology of acute UGIB.

Etiology of Acute Upper Gastrointestinal Bleeding

Ulcerative or erosive
Peptic ulcer disease
  Idiopathic
  Drug induced
    Aspirin
    Nonsteroidal antiinflammatory drugs
  Infectious
    Helicobacter pylori
    Cytomegalovirus
    Herpes simplex virus
  Stress-induced ulcer
  Zollinger Ellison Syndrome
Esophagitis
  Peptic
  Infectious
    Candida albicans
    Herpes simplex virus
    Cytomegalovirus
    Miscellaneous
  Pill-induced
    Alendronate
    Tetracycline
    Quinidine
    Potassium chloride
    Aspirin
    Nonsteroidal antiinflammatory drugs

Portal hypertension
Esophageal varices
Gastric varices
Duodenal varices
Portal hypertensive gastropathy

Arterial, venous, or other vascular malformations
Idiopathic angiomas
Osler-Weber-Rendu syndrome
Dieulafoy's lesion
Watermelon stomach (gastric antral vascular ectasia)
Radiation-induced telangiectasia
Blue rubber bleb nevus syndrome

Traumatic or post-surgical
Mallory-Weiss tear
Foreign body ingestion
Post-surgical anastamosis
Aortoenteric fistula
Post gastric/duodenal polypectomy

Tumors
Benign
  Leiomyoma
  Lipoma
  Polyp (hyperplastic, adenomatous, hamartomatous)
Malignant
  Adenocarcinoma
  Gastrointestinal stromal tumor
  Lymphoma
  Kaposi's sarcoma
  Carcinoid
  Melanoma
  Metastatic tumor
Miscellaneous
  Hemobilia
  Hemosuccus pancreaticus

In Egypt, it was also showed that the most common causes of acute UGIB were oesophago-gastric varices (53.3%), erosions (41.7%) and ulcers (24.9%) ***(Esmat et al., 2002).***

Gastroesophageal varices:

"The major blood supply to *esophageal varices* is the left gastric vein. The posterior branch drains into the azygos system, whereas the anterior branch communicates with varices just below the esophageal junction and forms a bundle of thin parallel veins that run in the junction area and continue in large tortuous veins in the lower esophagus"**.** *Gastric varices* get their blood supply from the short gastric veins and drain into the deep esophageal intrinsic veins ***(Kitano et al., 1986).***

In portal hypertension there is a hepatofugal (reversal) flow, leading to diversion of venous blood *uphill* in the cephalic direction, through the left gastric vein to the esophageal venous plexus. The resulting varices are highly eminent in the lower-to-mid thirds of the esophagus***(Cihangiroglu et al., 2001).****Downhill varices* are due to Superior Vena Cava (SVC) obstruction***(Cihangiroglu et al., 2001).***

"Gastroesophageal variceal hemorrhage, a major complication ofportal hypertension resulting from cirrhosis, occurs in 25-35% of patientswith cirrhosis and accounts for 80-90% of bleedingepisodes in these patients"***(Groszmann et al., 1990).***

Variceal bleeding is associatedwith more substantial morbidity and mortality than others & with higher hospitalcosts ***(Gralnek et al., 1999).***

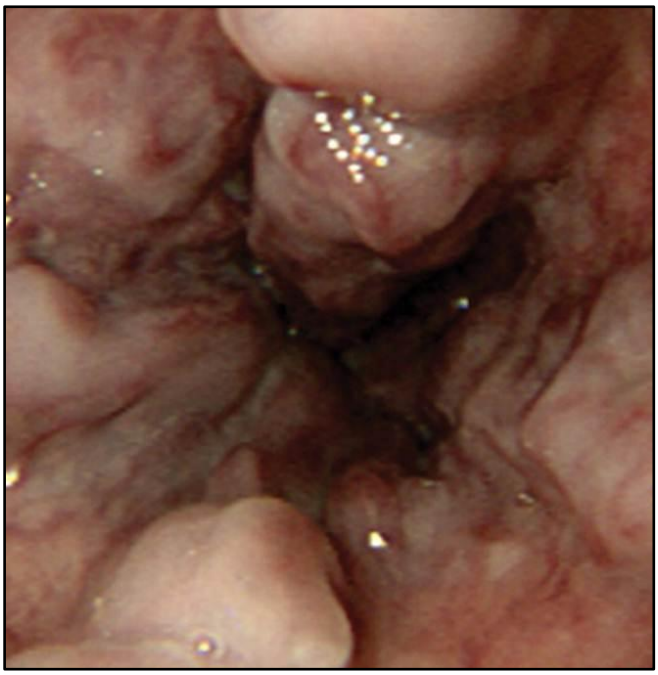

Fig. (1A): Oesophageal varices ***(Makhlouf, MA)***

"Up to 30% of initial bleeding episodes arefatal and as many as 70% of survivors haverecurrentbleeding after a first variceal hemorrhage"***(Northern Italian Endoscopic Club, 1988).*** Moreover, theone-year survival rate of patients after variceal bleeding can be poor(32-80%) ***(Graham and Smith, 1981).***

The most commoncause of portal hypertension is liver cirrhosis (as a result of chronic liver disease)***(Rockey and Chung, 1998).*** Most patients with liver cirrhosis develop portal hypertensiondue to increased intrahepaticresistance (presinusoidal, sinusoidal, and postsinusoidallocations) as well as increased flow through a hyperdynamicsplanchnic system ***(Rockey and Chung, 1998)***.

Varices can be defined as portosystemic collaterals formed after dilatation of preexistingvascular channels by the effect of portal hypertension***(Graham and Smith, 1981).*** The most commonsite of esophageal varices is the lower third of the esophagus (distal 3-5 cm) ***(Graham and Smith, 1981).***

Gastroesophagealvarices are present in 40%-60% of patients with cirrhosis;their presence and size are related to the underlying cause,duration, and severity of cirrhosis ***(Gupta et al., 1998).***

The risk of developing varices parallels with the severity of liver disease as reflected by Child's grading. It is further suggested that platelet count also predicts the development of varices ***(D'Amico et al., 2001).*** However**,** the rate of development and progression of OV in patients with cirrhosis has not been extensively evaluated ***(Merli et al., 2003).***

Despite the high prevalence of varices in patients with cirrhosis,bleeding only occurs in about one third of patients ***(Groszmann et al., 1990)***.

Endoscopicpredictors of bleeding include large varices and endoscopicred signs (e.g., red wale markings) on the variceal wall **(*Northern Italian EndoscopicClub, 1988).***

A combination of clinical and endoscopic findings includingan advanced Child–Pugh class of cirrhosis (Table 2), largevarices, and the presence of red wale markings

correlate highlywith the risk of a first bleeding episode in patients with cirrhosis **(*Northern Italian EndoscopicClub, 1988).***

The risk of bleeding from varices is correlated to the Child-Pugh's score, not just because of more severe portal hypertension, but also because it is related to other factors such as nutritional deficiency, coagulopathy, and increased fibrinolysis in advanced liver disease ***(Cales et al., 1990).***

Furhtermore, an association between bacterial infection and failure to control bleeding has been observed ***(Cales et al., 1990).*** And a diurnal periodicity of variceal bleeding has also been observed. Bleeding episodes occur more frequently in the early mornings and late evenings, probably as a result of hyperdynamic blood flow in the portal system after meals ***(McCormick et al., 1995).***

Table (2): Scoring systems for quantifying the severity of cirrhosisSeverity of liver disease can be described usingthe Child–Pughscore or MELD score.The Child–Pugh score is the sum of severity scores for Child class,variceal size and red wale markings the variables shown below.

Category	**1**	**2**	**3**
Encephalopathy	**0**	I/II	III/IV
Ascites	**Absent**	**Mild-moderate**	**Severe**
Bilirubin (µmol/L)	<34	34–51	>51
Albumin (g/L)	>35	28–35	<28
INR	<1.3	1.3–1.5	>1.5

Child–Pugh class A represents a score of ≤6, class B a score of 7–9, and class C, ≥10.

The MELD score is a formula that includes three laboratory-based variables reflectingthe severity of liver disease. It was originally used to predict the short-term mortalityafter placement of a transjugular intrahepatic portosystemic stent-shunt for varicealbleeding. Subsequently, it has been used in selecting candidates for livertransplantation. INR, international normalised ratio ***(Tripathi et al., 2015).***

Several prognostic indices have been developed to predict which patients with esophageal varices are likely to bleed **(*Northern Italian EndoscopicClub, 1988).*** The most widely used index is still the North Italian Endoscopic Club index (NIEC index). This index is based on (1) severity of liver disease (Child–Pugh class), (2) size of varices, and (3) presence of red markings on the varices **(*Northern Italian EndoscopicClub, 1988).***

Base on this index, cirrhotic patients have been classified into six risk classes, each with a prediction rate of bleeding (Table 3) **(*Northern Italian EndoscopicClub, 1988).***

The NIEC index has been prospectively validated on independent series. Yet, with the best prognostic index, one could only predict less than 40% of variceal bleeding. Obviously, some factors predisposing to variceal bleeding remain to be discovered ***(Northern Italian Endoscopic Club, 1988).***

Table (3): NICE index.

Risk class	NIEC Index	Rate of bleeding (%)		
		6 months	1 year	2 years
1	< 20.0	0.0	1.6	6.8
2	20.0–25.0	5.4	11.0	16.0
3	25.1–30.0	8.0	14.8	25.5
4	30.1–35.0	13.1	23.3	27.8
5	35.1–40.0	21.8	37.8	58.8
6	> 40.0	58.5	68.9	68.9

Variceal pressure may be measured accurately and relatively noninvasively with a pressure-sensitive endoscopic gauge ***(Boschet al., 1986).***It may be an important predictor for variceal hemorrhage ***(Nevens et al., 1998).***

A commonly employed system of classification of OV includes the following ***(Beppu et al., 1981)*:**

- F1: Small straight varices
- F2: Enlarged tortuous varices that occupy less than one-third of the lumen
- F3: Large coil-shaped varices that occupy more than one-third of the lumen

It is important to insufflate the esophagus while estimating variceal size; failure to do so leads to overestimation ***(Beppu et al., 1981)***.

Varices in the gastric fundus also bleed frequently. Gastric varices are often classified according to their location, which correlates with their risk of hemorrhage ***(Sarin et al., 1992):***

- Varices in direct continuity with the esophagus along the lesser and greater curves of the stomach are called gastroesophageal varices (GOV) types 1 and 2 respectively.
- Isolated gastric varices in the fundus (IGV1) occur less frequently than GOVs (10% versus 90%).

Most variceal bleeding temporarily stops by the time the patient arrives at the hospital. Without proper treatment, however, recurrent bleeding occurs in 30–40% within the next 2–3 days, and up to 60% within 1 week ***(Burroughset al., 1989)***.

Two cohort studies have showed that after the index bleeding, mortality is highest in the first 5 days and returns to baseline levels by 3–4 months. This is the critical time window for optimal treatment to improve survival of variceal bleeders ***(Burroughset al., 1989).***

The risk of early rebleeding is greatest in the first 48 hours after admission and declines subsequently ***(Graham and Smith, 1981).***

Peptic ulcer disease:

The most common non-variceal bleeding etiologies include gastroduodenal peptic ulcer (20%-50%) ***(Szura et al., 2015).***

Four major risk factors for bleeding peptic ulcers ***(Hallaset al., 1995):***

- Helicobacter pylori infection

- Nonsteroidal antiinflammatory drugs (NSAIDs)
- Stress
- Gastric acid

Reduction or elimination of these risk factors reduces ulcer recurrence and rebleeding rates ***(Bayerdorfferet al., 1995).***

H. pylori are spiral bacteria that infect the superficial gastric mucosa and appear to be transmitted by the fecal-oral route (Figure 1B)***(Nakamuraet al., 1997).***

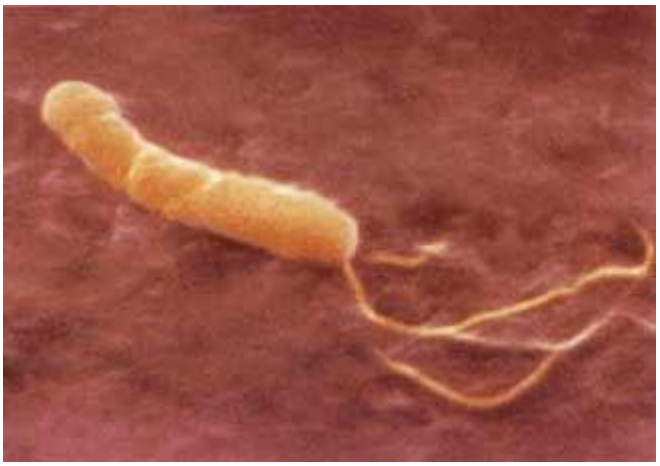

Figure (1B): Gastroenterological Society of Australia, GESA 2006

The bacterium generally does not invade gastroduodenal tissue. Instead, it renders the underlying mucosa more vulnerable to acid peptic damage by disrupting the mucous layer, liberating enzymes and toxins, and adhering to the gastric epithelium ***(Nakamuraet al., 1997).***

In addition, the host immune response to H. pylori incites an inflammatory reaction which further perpetuates tissue injury ***(Nakamuraet al., 1997).***The chronic