INTRODUCTION

Upper gastrointestinal hemorrhage is defined as bleeding in the gastrointestinal tract proximal to the ligament of tretiz and it's categorized into variceal and non variceal ***(Barkun et al., 2003)***.

Upper gastrointestinal bleeding from esophageal or gastric fundus varices is a common complication of portal hypertension in liver cirrhosis and carries a high mortality rate of 20-35% ***(Tacke et al., 2007)***.

In Egypt the variceal bleeding is the commonest cause of upper gastrointestinal bleeding as documented by various studies 75% by ***Madwar and Abdelghfar, (1979)***, 35% by ***El-Zayadi et al. (1988)*** and 57.6% by ***Zakaria et al. (1988)***.

Endoscopy plays a central role in the diagnosis and management of upper gastrointestinal bleeding; advances in endoscopic techniques have rendered endoscopy as the 1st line of diagnostic and therapeutic interventions for patients with upper gastrointestinal bleeding ***(Kwan et al., 2007)***.

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 such as decompressive surgical shunts, transjugular intrahepatic systemic shunts and liver transplantation are needed in patients refractory to endoscopic intervention ***(Zoli et al., 2005)***.

Peptic ulcer remains the commonest and most significant cause of non varcieal upper gastro-intestinal bleeding, the incidence of peptic ulcer bleeding is rising particularly for duodenal ulcer which accounts for two third of all peptic ulcers and affects nearly 10% of population ***(Curch et al., 2003)***.

Peptic ulcer due to the Hpylori and NASIDs is responsible for the majority of bleeding ulcers ***(Bradou et al., 2003)***. In patient with bleeding peptic ulcer and high risk stigmata, 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 weather variceal or from other gastrointestinal lesions ***(Pagliaro et al., 1995)***.

AIM OF THE WORK

To study the causes of upper gastrointestinal tract bleeding among the patients presenting by hematemesis and/or melena to Emergency Endoscopy Unit of Ain Shams University Hospital and outcome of these patients.

UPPER GASTRO INTESTINAL BLEEDING

Upper gastrointestinal bleeding commonly presents with hematemsis (vomiting of blood or coffee-ground like material) and/or melena (black, tarry stole). A nasogastric lavage which yields blood or coffee-ground like material confirms this clinical diagnosis ***(Vangeli et al., 2002)***.

Upper gastrointestinal bleeding can be classified into several broad categories based upon anatomic and pathophysiologic factors. A prospective series of 1000 cases of severe UGI bleeding at the West Los Angeles Veterans Administration Medical centers published in 1996 found the following distribution of causes ***(D'Amico et al., 1990)***.

Peptic ulcer disease	→ 55 percent
Esophagogastric varices	→ 14 percent
Arteriovenous malformations	→ 6 percent
Mallory-Weiss tears	→ 5 percent
Tumors and erosions	→ 4 percent each
Dieulafoy's lesion	→ 1 percent
Others	→ 11 percent

Thirty percent of patients with compensated cirrhosis and 60% of patients with decompensated cirrhosis have

gastrointestinal vairces at the time of presentation ***(Lebrec et al., 1980; Garcia-Tsao et al., 1985)***. Among cirrhotic patients who have no esophageal varices on diagnosis, the incidence of new varices ranges between 5% and 23% after 1 year of follow-up ***(Christensen et al., 1981; D'Amico et al., 1990)***. In a prospective study, D'Amico et al. reported that the incidence of varices in newly diagnosed compensated cirrhosis is around 4.5% per year and mortality from bleeding 0.5% per year ***(D'Amico et al., 1990)***.

Bleeding from ruptured esophagogastric varices is the most severe complication of cirrhosis and is the cause of death in about one third of cirrhotic patients ***(Wu and Sung, 2002)*:**

Ruptured esophageal varices cause 60%to70%of all episodes of upper gastrointestinal bleeding in patients with portal hypertension ***(D'Amico, 2000)***.

Portal Hypertension

Portal hypertension is defined as an increase in portal venous pressure more than 5mmHg greater than inferior vena caval pressure or portal venous pressure greater than 30cm H_2O ***(Luketic and Sanyal, 2000)***.

Portal pressure is about **(**7 to 14cm H_2O**)** ***(Luketic and Sanyal, 2000)***, 7mmHg ***(Sherlock and Dooley, 2002)***.

Development of portal hypertension (pH) regardless of its etiology is due to increased vascular resistance or increased portal venous flow or both ***(Ferraz et al., 2001)***.

Expirmental studies have shown that the initial factor in the pathophysiology of portal hypertension is the increase in vascular resistance to portal blood flow .in cirrhosis this increase in resistance occurs at the hepatic microcirculation (sinusoidal portal hyper-tension). It is important to emphasize that, contrary to what was traditionally thought, increased hepatic vascular resistance in cirrhosis is not only a mechanical consequence of the hepatic archetectural disorders caused by the liver disease, but there is also a dynamic component, due to the active contraction of portal/septal ***(Wiest and Groszmann, 2002)***. This increase in the intrahepatic vascular tone is modulated by the increased

activity of endogenous vasoconstrictors such as endothelin, alpha-adrenergic stimulus, leukotrines, thromboxane A2, angiotensin II and others, and lessend by nitric oxide (NO), prostacyclin and many vasodilating drugs (organic nitrates, adrenoletic agents, and calcium channel blokers ***(Graupera et al., 2002)***.

It is believed that in cirrhosis, the hepatic vascular resistance is increased because of imbalance between vasodilator and vasoconstrictor stimuli, the former being insufficient to counteract the influence of the latter. Indeed, in cirrhosis there is an increased activity of the above mentioned vasoconstrictors, while intrahepatic (NO) production is clearly decreased .the deficient intrahepatic NO production is the result of endothelial dysfunction in the liver microvasculature ***(Wiest and Groszmann, 2002)***.

Causes of portal hypertension

Classification of diseases that cause portal hypertension is based on the wedged hepatic venous pressure (WHVP) which represents sinusoidal pressure. When (WHVP) is normal or is less than portal pressure it is a presinusoidal cause and when it is increased or equals the portal pressure it is an intrahepatic or sinusoidal cause ***(Boyer and Henderson, 2000)***.

The most common classification is based on the relation to liver i.e., the location of the causative lesion. It is the classic classification of portal hypertension:

a- **Pre-hepatic** (splanchnic arterio-venous fistula, splenic vein and portal vein thrombosis, and splenomegaly not due to liver disease).

b- **Post-hepatic** (inferior vena cava obstruction and cardiac causes).

c- **Hepatic**: according to anatomic zone of obstruction to portal blood flow, it is further divided into:

- *Presinusoidal*: as portal tract lesions (schisto-somiasis, sarcoidosis,mastocytosis, myeloproli-ferative disorders, congenital hepatic fibrosis and early primary biliary cirrhosis).

- *Sinusoidal*: cirrhosis, non-cirrhotic liver diseases

such as chronic active hepatitis, primary biliary cirrhosis and Wilson disease, acute fulminant viral hepatitis, alcoholic liver diseases, toxic hepatitis, idiopathic portal hypertension, nodular regenerative hyper-plasia (NRH) and malignancy.

- *Postsinusoidal*: peliosis hepatis, venocclusive disease and Budd-Chiari syndrome.

However, many of hepatic causes overlap in different zones particularly in advanced cases ***(Groszmann and DeFranchis, 1999)***.

PATHOGENESIS OF ESOPHAGEAL VARICES

With portal hypertension, various collateral venous pathways develop with formation of multiple porto-systemic anastomosis. The most common collateral pathway is the coronary gastro-esophageal route which is present in 80-90% of patients ***(Nune et al., 1978)***.

Deviation of blood into these channels leads to varicosities in the submucosa of the lower end of the esophagus and the fundus of the stomach ***(Sherlock and Dooley, 2002)***.

In around 20% of these patients concomitant varices occur in the region of stomach, those are largely supplied by the short gastric veins and drain into the deep intrinsic veins of the esophagus. They are partic-ularly prominent in the patients with extra hepatic portal obstruction ***(Sherlock and Dooley, 2002)***.

Pathogenesis of variceal bleeding

Erosion of varices secondary to acid reflux and spontaneous variceal rupture are the two most popular theories for why varices bleed ***(Thomas and Michael, 2003)***.

a- Erosion theory: According to this theory ulceration and acid reflux are considered important, however,

it is not yet supported by histological observation ***(Echradt and Grace, 1979)***. Also it was found that short episodes of reflux occurred with similar frequency in both patients with recent variceal bleeding and controls and this is with the concept that there is no significant relationship between reflux and the occurrence of variceal hemorrhage in cirrhotic patients ***(Sherlock and Dooley, 2002)***.

b- ***Explosion theory***: i.e. spontaneous variceal rupture. The concept of erosion has been abandoned and replaced by explosion theory. An oesophageal varix can be considered as an elastic structure, and the tension on the vessel wall is thought to be an important factor in determining when rupture occurs ***(Groszmann, 1984)***. Wall tension (T) varies as a function of both transmural pressure (TP), vessel a- radius (r) and wall thickness (W) as follow:

T = TPX r/w [Laplace low]

The wall tension (T) resists the expanding force and when the later exceeds the former at a critical level, rupture and bleeding occurs. When the varix distension has increased, the radius has increased and the wall thickness decreased ***(Paquet, 2000)***. So, oesophageal varices rupture most commonly at or near the cardio-esophageal junction. In this area of the esophagus the veins are most superficial and hence least surrounded by other tissues. Ascites and plasma volume

also have been thought to be important factors in the genesis of bleeding ***(Boyer and Henderson, 2000)***.

Ascites was thought to increase blood flow and pressure in EV, as it affects intra-abdominal pressure which influences several hemodynamic variables in portal hypertension. However, it is found that although paracentesis lower intra-abdominal pressure, portal pressure and hepatic blood flow were unchanged. So there is no convincing evidence that tense ascites per se, as apposed to decompensated liver disease, increases the risk of variceal bleeding ***(Burroughs, 1993)***.

An expanded plasma volume is observed in all forms of portal hypertension which is due to renal sodium retention that has been shown to precede the increase in the cardiac output and can be prevented or reversed by spironolactone. The expanded blood volume represents another mechanism that contributes to further increase in portal blood pressure ***(Bosch et al., 1992)***.

Factors predictive of variceal hemorrhage:

Numerous clinical and physiologic factors are useful in predicting the risk of variceal hemorrhage in patients with cirrhosis. These include:

a- Location of varices.

b- Size of varices.

c- Appearance of varices.

d- Clinical features of the patient.

e- Variceal pressure.

a) <u>Location of varices</u>:

The most common sites for development of varices are the distal esophagus, stomach, and rectum, although theoretically varices may develop at any level of the gastrointestinal (GI) tract below the esophagus. Varices develop deep within the submucosa in the mid-esophagus, but become progressively more superficial (nearer the mucosa) in the distal esophagus. Thus, esophageal varices at the gastroesophageal junction have the thinnest coat of supporting tissue and are most likely to rupture and bleed ***(Kim et al., 2007)***.

Varices in the gastric fundus also bleed frequently. Gastric varices are often classified according to their location, which correlates with their risk of hemorrhage. 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 (IGVI) occur less frequently than GOVs (10 versus 90 percent) ***(D'Amico et al., 1995)***.

b) <u>Size of varices</u>:

The risk of variceal bleeding correlates indepen-dently with the diameter (size) of the varix. While this generalization has been well established for eso-phageal varices ***(North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices, 1998)***, it has been shown to apply to gastric varices in the fundus of the stomach ***(Boyer, 1995)***. The explanation for the relationship between variceal size and bleeding risk is derived from Laplace's law; small increments in the vessel radius result in a large increase in wall tension (which is the force tending to cause variceal rupture).

There are several ways in which esophageal variceal size is quantified; non are exact and all involve subjective evaluation. A commonly employed system of classification includes the following ***(Paquet, 1982; North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices, 1998)***.

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.

c) <u>Appearance of varices</u>:

In addition to size, several morphologic features of varices observed at endoscopy have been correlated with an increased risk of hemorrhage ***(Boyer, 1995; D'Amico et al., 1995; D'Amico et al., 2001)***. Among these features include a number relating to a red appearance, or "red signs":

- Red wale marks are longitudinal red streaks on varices that resemble red corduroy walls.
- Cherry red spots are discrete red cherry-colored spots that are flat and overlie varices.

- Hematocystic spots are raised discrete red spots overlying varices that resemble "blood blisters".
- Diffuse erythema denotes a diffuse red color of the varix.

d) <u>Clinical features of the patients</u>:

Several clinical features of the patients are related to the risk of variceal hemorrhage ***(Goulis et al., 1998)***.

The degree of liver dysfunction is an important predictor of variceal hemorrhage. The child classi-fication is an index of liver dysfunction based upon serum albumin concentration, bilirubin level, prothrombin time, and the presence of ascites and encephalopathy. A higher score in this classification scheme is associated with a higher likelihood of variceal