

Thirty Days Mortality and Morbidity in Non Variceal Upper Gastrointestinal Bleeding (NVUGIB)

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ABSTRACT

AIM: To determine the mortality and morbidity among patients presented with acute NVUGIB, co-morbid illnesses, the intake of aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), endoscopic therapy and proton pump inhibitors (PPIs) on clinical outcomes.

METHODS: A prospective cohort study on all patients presented with acute NVUGIB to Specialized Arab Hospital (SAH), Nablus-Palestine, during the period April 2011-April 2013. The medical history for each patient was collected, all patients were given esomeprazole 80 mg IV push and then 8mg/hour IV pump. Timing of endoscopy with Forrest grading, hospital course, and the 30 day mortality after being discharged from hospital, all variables analyzed and Chi square test was used to test the significance of relationships. A *p* value of < 0.05 was considered statistically significant.

RESULTS: Total number, 86 patients, with a female to male ratio of 1:3, Patient's age: - 48/86(56%), 38/86(44%) were above and below the age of 60, respectively. Melena was the most common presentation, followed by hematemesis and general symptoms. Smokers 32/86(40%). Co-morbid illnesses 55/86 (64%), most common reported diseases were hypertension, diabetes, coronary artery diseases, and CHF. Ingestion of Aspirin or non-steroidal anti-inflammatory drugs (NSAID's) was reported in (64/86)74% of patients. Upper endoscopy was done after 24 hours of symptoms in 64/86 (74%). The most common endoscopic diagnosis was peptic ulcer disease 64/86 (74%), Forrest grade 3 clean base ulcers 37/64 (57%), Forrest grade II black spot, adherent clot or non

bleeding visible vessel (NBVV) 17/64 (26%), and Forrest grade I oozing or spurter 10/64 (16%). Number of blood units given was more in patients with active bleeders (Forrest I). High dose of IV esomeprazol (80 mg then 8 mg/hour) was given, before endoscopic intervention, in 38/86 (44%), 24/38 (65%) found to have Grade 3 (clean base) ulcer. All of NVUGIB patients were subsequently given esomeprazol, after endoscopy. Blood transfusion was needed in 65/86 (76%). Re-bleeding events have occurred in 5/86 (6%). The overall mortality was 4/86 (4.6%) all have co-morbid illnesses. Endoscopic intervention failed in 5/86 (5.8%) 4 referred for surgical intervention and one referred to interventional radiologist.

CONCLUSION: Peptic ulcer is the most common cause of NVUGIB, bleeding is highly associated with Aspirin and NSAID's intake. High dose IV esomeprazol, (80 mg then 8 mg/hour), before EGD decreases the proportion of patients with stigmata of recent hemorrhage. The mortality and morbidity of NVUGIB in this study is slightly lower than that found in most previous studies.

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Key words: Non variceal upper GI bleeding; Mortality and morbidity

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INTRODUCTION

Acute upper gastrointestinal bleeding (UGIB) is defined as bleeding from a source proximal to the ligament of Treitz, a potentially life-threatening condition, that remains a common challenging emergency for gastroenterologists and general physicians. The annual incidence of hospitalization Non variceal upper gastrointestinal bleeding (NVUGIB), is 102 per 100,000 of populations in the UK; it was twice as common in males as in females and increased with age^[1,2] The vast majority is secondary to peptic ulcer, particularly duodenal ulcer, is the most frequent cause followed by other etiologies^[2] the causes of NVUGB with their

incidence are shown in table¹^[3].

The incidence of NVUGIB varies worldwide and ranges from 50 to 150 per 100,000 of the population with highest incidence reported in Scotland^[2], and the overall mortality remains around 10% and may even reach 35% in hospitalized patients with serious co-morbidity^[3].

Rockall score, the Baylor bleeding score and the Blatchford score which have been developed to direct appropriate patient management and enabled cost effective treatment^[4]. Furthermore, we can do risk stratification using endoscopic parameters as established by Forrest classifications^[5].

Endoscopy plays a central role in the management of NVUGIB, being able to identify and treat the source of bleeding up to 70%-90% in patients.

From a theoretical point of view, a stable blood clot in a peptic ulcer is crucial to homeostasis, however, if the pH of gastric content is more than 6, the pepsin will become inactivated. Thus, the hypothesis that by suppressing the intragastric acid, using proton pumps inhibitors (PPIs), may benefit patients at risk for further hemorrhage; this hypothesis has been supported by evidence based on randomized controlled trials^[6].

Table 1 Common causes of NVUGIB.

Causes of Nvugib	Incidence
Peptic ulcer disease	25 - 50 %
Mallory Weiss syndrome	15 - 20 %
Erosive gastritis/ duodenitis	10 - 15 %
Erosive esophagitis/ esophageal ulcer	5 - 10 %
Angiodysplasia/ malformations	5 %
Malignancy	1-2 %
Others	5 %

METHODS

The study was approved by Institutional Review Board, School of Medicine at AnNajah University, between April 2011 and April 2013, all patients presented with non variceal upper GI bleeding (NVUGIB), were included in the final analysis. Patients may be excluded if they did not agree to participate in the study.

A prospective cohort study, endoscopy and endoscopic intervention, was done in Specialized Arab Hospital (SAH), Nablus, Palestine. History on admission from all the patients who presented or were referred to SAH as cases of acute NVUGIB during the assigned duration of the study and data were collected: (patients age, gender, chief complain, past medical and drug history, hemoglobin on admission, time of endoscopy after complaining. All patients were given esomeprazol IV 80 mg push and then 8 mg/hour for 72 hours). The endoscopic findings and the intervention were recorded, and then the patients were followed for one month. *H pylori* status was not examined, (we are looking for causes of bleeding and not cause of ulcers).

Thirty days mortality was obtained by direct contact of patients or their families. Morbidity was defined as the need for surgical intervention after failure of second trial of endoscopic therapy or any complication related to the bleeding (hypotension, stroke or death) or endoscopic intervention. Drugs of concern are those with antiplatelet effect (Aspirin, Clopidogrel), NSAIDs, or anticoagulant (Warfarin or low molecular weight heparin). Also, the usage and the mode of PPI were documented and if esomeprazol was given before endoscopy.

Statistical analysis

Collected data was analyzed by SPSS program version 17. Mortality rate was calculated using patients' numbers with NVUGIB who died within 30 days after endoscopy (if NVUGIB was the direct cause or

not). The morbidity was expressed using the numbers of patients who were referred to surgical intervention after rebleeding.

Chi square test was used to test the significance of relationships and a *p* value of < 0.05 was considered statistically significant

RESULTS

Total number of patients (86), mean age was 61+-28.6 years. Male to female ratio was 3:1

Complaint: Melena was found to be the most frequent presentation among patients presented with acute NVUGIB as it was reported in 65/86 (75.6%) of cases either as a primary complaint or combined with other symptoms. The second most common complaint was hematemesis 31/86 (36%) Other general symptoms such as dizziness and fatigue reported in 19/86 (22.1%) (Figure 1).

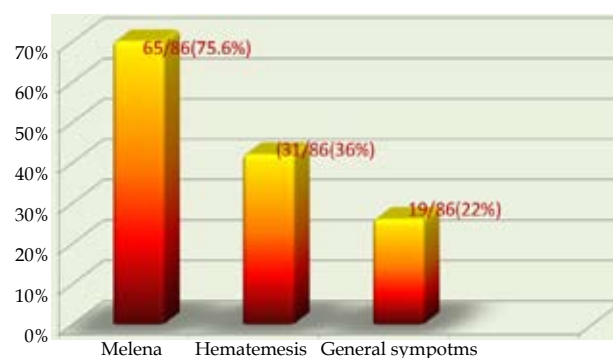


Figure 1 How the patients presented with NVUGI bleeding.

Demographic data: From April 2011 to April 2013, there were 86 cases of acute NVUGIB admitted or referred to SAH for upper endoscopy. Their ages were variable as illustrated in table 2. Male gender represented 64/86 (74%) of the total patients' population. Fifty five patients (64%) has co-morbid conditions (diabetes mellitus, hypertension, coronary artery disease, congestive heart failure, malignancy and vasculitis) (Figure 2, 3), and 32/86 (38%) are smokers.

Table 2 Age distribution among patient.

Age	Number (%)
< 60 years	38 (44.2%)
60-79 years	35 (40.7%)
≥ 80 years	13 (15.1%)

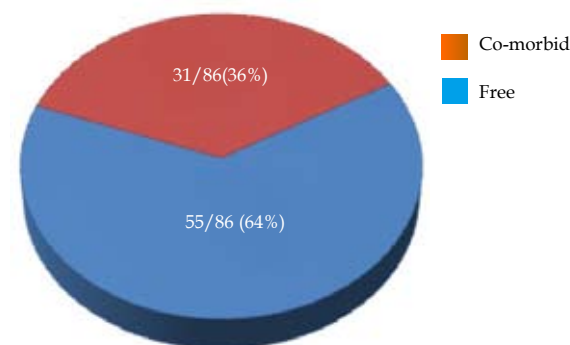


Figure 2 How the patients presented with NVUGI bleeding.

Etiology: The most common endoscopic diagnosis was peptic ulcer 64/86 (74%), of which DU 85% and GU 15% (Figure 4). Etiology of bleeding showed significant difference between males and females, as 40/64 (62%) of males were diagnosed to have duodenal ulcer while 11/22 (50%) of females were diagnosed to have causes other

than peptic ulcer. (*P* value 0.036).

Drugs: Most of our patients' 64/86 (75%) were taking NSAIDs and/or low dose aspirin before complaining and 14% of them were on anticoagulant therapy. None of our patient was on prophylactic PPI. (Figure 5).

All of them were given esomeprazol after endoscopic intervention, 61/86 (71%) through IV route initially for three days followed by oral treatment and 25/86 (29%) of them through oral route alone. Patients referred from other hospitals were given PPI IV before transfer.

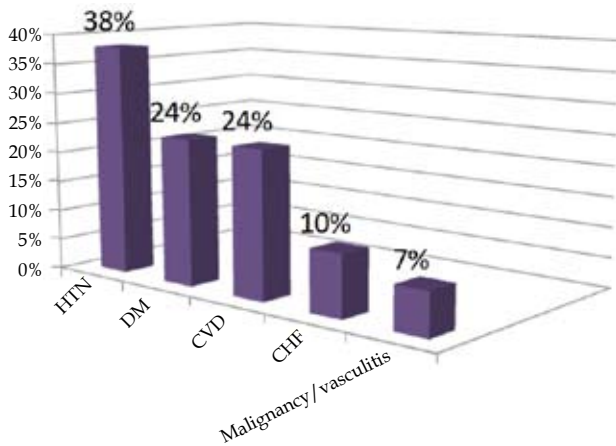


Figure 3 The most common causes of co-morbid illnesses.

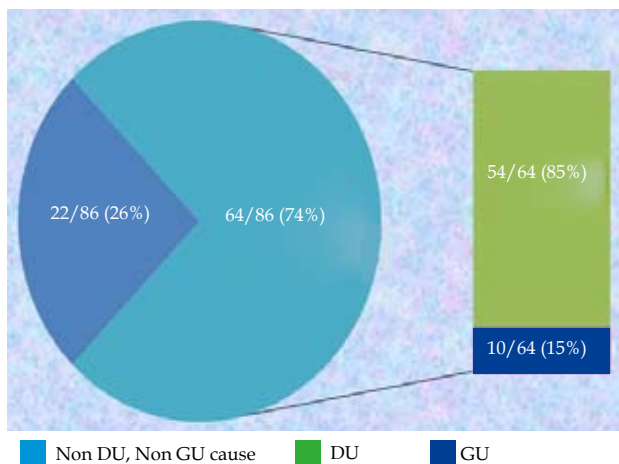


Figure 4 Peptic ulcer, particularly DU, is the most frequent cause.

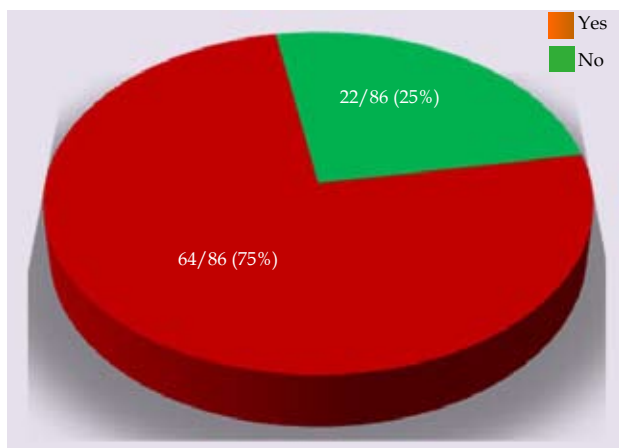


Figure 5 75% of bleeding peptic ulcer patients had a history of NSAIDs or/and Aspirin intake, 14% were on anticoagulant.

Forrest Classification & Endoscopic Intervention: All patients had EGD, most of them 74/86 (75%) within 24 hours, of beginning of symptoms, while they were on IV esomeprazol. They were classified according to Forrest classification. Clean base (grade 3) was the most common finding 37/64 (57%) of patients with peptic ulcer, followed by grade 2 17/64 (27%) and grade 1 10/64 (16%). Patients with clean base did not need any endoscopic or surgical intervention, in comparison 17% of patients with grade 2 and 55% of those with grade 1 needed endoscopic intervention (*P* value <<0.001). The total number of patients who needed endoscopic or surgical intervention was 14/86 (16.3%). According to the relation between Forrest grade and PPI administration before EGD, 19/29 (65.5%) of patients who were on PPI before EGD was found to be grade 3 on Forrest classification, while 3/29 (10.3%) of them were found to be Grade 1. (*P* value 0.406). In relation to the need for blood transfusion after endoscopic management, 30/41 (74%) of patients with grade 3 took ≤ 3 units of blood, while 6/10 (60%) with grade 1 took four units of blood or more (*P* value 0.02).

Mortality and morbidity: The mortality rate was found to be 4/86 (4.6%) all were due to co-morbid illnesses, disseminated intravascular coagulation-DIC, hepato-cellular carcinoma and previous history of abdominal aortic aneurism-AAA repair surgery). The re-bleeding rate after second session of endoscopic intervention was 3/86 (3.4%) of patient with the need for surgical procedure.

DISCUSSION

In this study, which was conducted on 86 patients, the mean age was 61±28.6 years. Male to female ratio was 3:1, which was comparable to universal values, as shown by Yavorski RT *et al* and Paspatis GA *et al*^[7,8]. The main complaint on hospital admission was melena in about three quarters of the patients. Many studies conducted worldwide had the same finding such as the study done in Turkey in 2010 by Akbas T *et al*^[9] Peptic ulcer was reported in 74% of cases, which was higher than the universal value (50%)^[3,10,11]. DU formed 85% peptic ulcer causes, and this is consistent with the universal studies^[2], In relation to gender, etiology of the bleeding shows a significant difference, and this may be due to the fact that DU is 5 folds more common in males than in females.

Fifty seven percent of patients with peptic ulcer were found to be grade 3 on Forrest classification, in comparison to forty two percent in a study which was done in USA by Bruno J in 2005^[5]. There is a significant relationship between Forrest grades and the need for endoscopic or surgical intervention, as we illustrated above, which confirms the high sensitivity of Forrest classification for predicting patients with acute NVUGIB at high risk for severe bleeding^[5].

NSAIDs or Aspirin intake was reported in 75% of the total sample, with 69% of bleeding peptic ulcer patients having a history of NSAIDs or Aspirin intake, in comparison to 30%-60% only given this history internationally^[10]. 19/29 (65.5%) of the patients who were on PPI before EGD were found to have clean base (grade 3 on Forrest classification). There is no study to establish the effect of PPIs on Forrest grade, but many studies had confirmed that high-dose intravenous PPIs before EGD reduces the need for endoscopic intervention^[12], and the proportion of patients with stigmata of recent hemorrhage^[13] and so increases Forrest grade.

Our patients were given PPIs after endoscopic management as many studies confirmed that PPIs were the most cost-effective and the best proven strategy to reduce re-bleeding rate and surgical intervention after EGD management^[12,14,15], although their effectiveness for treatment of acute peptic ulcer bleeding had been controversial in some studies^[11]. Also, we found that

IV PPIs was needed in 91% of patients with grade 1 on Forrest classification, which is significantly higher than the patients with Forrest classification grade 3 (46%), this correlation, in addition to the relation between Forrest grade and the units' number of blood transfused, as mentioned in the result, is consistent with the ability of Forrest classification to detect patients with severe risky bleeding.

Surgical intervention was needed in three patients to stop bleeding after endoscopic management. Doudenoplasty was needed after EGD in another patient who was found to have deformed duodenal bulb with stenosis. The overall 30-day mortality rate is (4.6%) as it had occurred in four patients and was due to associated morbid condition (disseminated intravascular coagulation-DIC, hepatocellular carcinoma and previous history of abdominal aortic aneurism-AAA repair surgery). It is less than that observed in other population-based studies conducted worldwide as it was 9% in United Kingdom (UK), 6.9% in Italy during period (2000-2005) and 7.3% in China^[16,17,18,19,20,21].

CONCLUSION

Compared with the international references, our findings show that the mortality rate among patients presented with acute NVUGIB is the same, if not lower, than the expected. Surgical intervention was needed in a proportion consistent with the universal values. Bleeding peptic ulcer is highly associated with intake of low dose aspirin, and NSAIDs. Forrest classification is highly sensitive for predicting patients at high risk for severe bleeding and the need for blood transfusion.

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