Gastroenterology and Hepatology From Bed to Bench

ORIGINAL ARTICLE

Non-*Helicobacter pylori*, non-NSAIDs peptic ulcers: a descriptive study on patients referred to Taleghani hospital with upper gastrointestinal bleeding

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ABSTRACT

Aim: The purpose of the present study was to evaluate the number and proportion of various causes of upper gastrointestinal bleeding and actual numbers of non-NSAID, non-*Helicobacter pylori* (*H.pylori*) peptic ulcers seen in endoscopy of these patients.

Background: The number and the proportion of patients with non- *H.pylori*, non-NSAIDs peptic ulcer disease leading to upper gastrointestinal bleeding is believed to be increasing after eradication therapy for *H.pylori*.

Patients and methods: Medical records of patients referred to the emergency room of Taleghani hospital from 2010 with a clinical diagnosis of upper gastrointestinal bleeding (hematemesis, coffee ground vomiting and melena) were included in this study. Patients with hematochezia with evidence of a source of bleeding from upper gastrointestinal tract in endoscopy were also included in this study.

Results: In this study, peptic ulcer disease (all kinds of ulcers) was seen in 61 patients which were about 44.85% of abnormalities seen on endoscopy of patients. Among these 61 ulcers, 44 were duodenal ulcer, 22 gastric ulcer (5 patients had the both duodenal and gastric ulcers). Multiple biopsies were taken and be sent to laboratory for Rapid Urease Test and pathological examination. About 65.53% of patients had ulcers associated with *H.pylori*, 9.83% had peptic ulcer disease associated with NSAIDs and 11.47% of patients had ulcers associated with both *H.pylori* and consumption of NSAIDs. 13.11% of patients had non-NSAIDs non- *H.pylori* peptic ulcer disease.

Conclusion: The results of this study supports the results of other studies that suggest the incidence of *H.pylori* infection related with duodenal ulcer is common, and that non-*H pylori* and non-NSAIDs duodenal ulcer is also common.

Keywords: Upper gastrointestinal bleeding, Peptic ulcer, Nonsteroidal antiflammatory drugs (NSAIDs), *H.pylori*.

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Introduction

Upper gastrointestinal bleeding is defined as bleeding proximal to the ligament of Treitz. Upper gastrointestinal bleeding is one of the most common emergencies managed by gastroenterologists that results in high patient morbidity and medical care costs (1). The mortality of this condition was between 5% and 11 % (2).

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The main sources of upper gastrointestinal bleeding are peptic ulcers, esophagitis, drug-induced mucosal damage, sequelae of portal hypertension (esophageal varices, varices of the gastric fundus, portal hypertensive gastropathy), vascular anomalies, traumatic and postoperative lesions, and tumors (3).

More recent data suggest that the proportion of cases caused by peptic ulcer disease has declined (4,5,7). Peptic ulcers were responsible for only 21 percent of episodes of upper gastrointestinal bleeding among 7822 patients included in a national, United States database between 1999 and 2001. Gastric ulcers were more common than duodenal ulcers (55 versus 37 percent). Patients with variceal bleeding were excluded from the analysis (6).

In the present study all kinds of duodenal and gastric ulcers were treated as a single entity - peptic ulcers. Every patient with peptic ulcer should already be tested for *H.pylori* at the initial endoscopy with Rapid Urease Test and pathologic exam (Giemsa staining for *Helicobacter pylori*).

Peptic ulcer as one of the most important reasons leading to upper gastrointestinal bleeding are mainly resulting from *H.pylori* infection or inappropriate and progressive use of nonsteroidal antiinflammatory drugs (NSAIDs), stress in hospitalized patients and gastric acid and pepsin (9,10). Although *Helicobacter pylori* infection is prevalent in developing countries, recent reports from different parts of Asia have shown a declining trend for *H. pylori*-associated ulcers (11,12). Since *H. pylori*-negative ulcers have been shown to have a higher incidence of mortality and recurrent bleeding, documenting the proportion of such cases is important (13). Therefore more new studies are required to show recent changes in the incidence of various causes resulting in upper gastrointestinal bleeding. The number and the proportion of patients with Non- *H.pylori*, non-NSAIDs peptic ulcer disease is important, given the increase in use of eradication therapy for *H. pylori* and widespread use of acid suppressor agents accompanied by NSAIDs (26).

In response to recent changes in the incidence of various causes of upper gastrointestinal bleeding and peptic ulcer diseases, the present study aimed to determine the proportion and actual numbers of patients with various causes of upper gastrointestinal bleeding, referred to the emergency room of Taleghani hospital from January 2010 till December 2010 with a diagnosis of upper gastrointestinal bleeding and also the proportion and actual numbers of non-NSAID, non-*Helicobacter pylori* peptic ulcers seen in endoscopy of these patients.

Patients and Methods

This was a descriptive study conducted retrospectively on 157 medical records of patients admitted with a diagnosis of upper gastrointestinal bleeding referred to Taleghani hospital. Medical records of patients referred to the emergency room of Taleghani hospital from January the first 2010 till December the 29th 2010 with a diagnosis of upper gastrointestinal bleeding in the form of hematemesis (regurgitation or vomiting of blood), coffee ground material in nasogastric tube or melena (black tarry stool with positive occult blood test) were included in this study. Patients with hematochezia (passage of bright red blood per rectum) with evidence of a source of bleeding from upper gastrointestinal tract in endoscopy were also included in this study.

Occasionally, the only finding pointing to a gastrointestinal hemorrhage is a laboratory result, such as iron-deficiency anemia or a positive test for occult blood in the stool with or without subjective signs such as fatigue, pallor, dyspepsia and etc. These patients were not enrolled in our study because our study focused on patients referred to emergency room.

21 patients were excluded from study; 15 patients were referred with melena but with evidence of proximal lower gastrointestinal bleeding and no evidence of upper gastrointestinal bleeding in endoscopy, 4 patients did not consent to follow up with endoscopy and 2 patients had a diagnosis of

hemoptysis and blood swallowing due to epistaxis respectively. Therefore, care was taken not to enter patients with bleeding from upper respiratory tract or paranasal sinuses and lower gastrointestinal tract in this study. The mean age of patients was 55.9 years old with range of 15-89 years. Gender distribution of patients was 51 females and 85 males. Ethnicity distribution of patients was 133 Iranians, 2 Afghans, 1 Armenian. 40 patients were hemodynamically unstable on the day of admission.

After enrolment in the study, a questionnaire including demographic data, important points in the history, history of acid peptic disease, NSAID use, regular ingestion of aspirin, anticoagulants and other drugs can cause gastrointestinal bleeding eg, bisphosphonates, previous history of upper gastrointestinal bleeding and the cause of it, co-morbidities, physical exam such as ongoing vital signs, pallor, organomegaly, ascites, jaundice, laboratory tests such as ongoing bleeding, admission hemoglobin (Hgb), activated prothrombin time (PT), platelet count (Plt), partial thromboplastin time (PTT), and the results of endoscopy and etc was filled. Also, mortality rate and re-bleeding in hospital and within 3 days after admission, blood transfusion need and surgery were registered.

The ethical committee of university approved the study. Differences at $P<0.05$ were considered significant. Statistical package for social sciences (*SPSS, version* 17.0) was used for data analysis.

Results

A hundred and thirty six patients entered the study, of which 51 (37.5%) were female and 85 (62.5%) were male. The mean (±SD) age of our patients was 55.9±17.8 years.

The most common signs on presentation among our patients were hematemesis and coffee ground vomiting (35%) and melena (69%).

40 patients were hemodynamically unstable on arrival. Hemotochezia was seen among unstable patients. They had shock (blood pressure <90/60 mmHg in supine position) or orthostatic hypotension (>20 mmHg decrease in systolic blood pressure or >10mmHg in diastolic blood pressure from supine to standing position). The incidence of patients with coagulopathy (prolonged prothrombin or thromboplastin time compared with standard rates or low platelet levels <150000) was 25%.

The incidence of patients referred with comorbidities such as cirrhosis, diabetes, kidney stones, chronic renal failure, pancreatitis, chronic obstructive pulmonary disease, coronary artery disease, malignancies of the upper gastrointestinal tract was 39.7%. The frequency and incidence of patients referred with different comorbidities are shown in table 1.

Table 1. Comorbidities seen in study population (n=136)

Chronic diseases	Frequency(%)	Mean age	P-value
Cirrhosis	30(22.1)	53.43±12.17	NS*
Kidney stone	3(2.2)	48.67±26.1	NS
Chronic renal failure	7(5.1)	57.57±19	NS
Chronic obstructive Pulmonary disease	7(5.1)	53.25±14.2	NS
Coronary artery disease	9(6.6)	69.89±14.63	0.014
Pancreatitis	1(0.7)		
Diabetes	32(23.5)	54.84±19.53	NS
Malignancy not related to UGI tract	8(5.9)	64.5±20.8	NS

* Not significant

Note that it was probable to see more than one comorbidity in one patient. Sixty percent of patients gave a history of acid-peptic disease before presentation with upper gastrointestinal bleeding.

Thirty six percent of patients required emergent endoscopic intervention such as band ligation or sclerotherapy and 6.6% of patients required urgent surgery.

During 3-day follow up of patients, 14 patients, (10.29%) died. Mean age of patients who died was

62.08±20.04 years. Statistical analysis suggested no significant relationship between age and death in our study.

There was a significant relationship between death and existence of comorbidities (p=0.02) and unstable hemodynamic on arrival (p=0.01). Frequency and incidence of abnormalities seen in endoscopy of these patients referred to Taleghani hospital with the impression of upper gastrointestinal bleeding are shown in table 2. These results indicated the abnormalities related or unrelated to recent upper gastrointestinal bleeding.

Table 2. Frequency and incidence of abnormalities seen in endoscopy of study population (n=136)

Endoscopic findings	Frequency(%)	Age*	P-value
Duodenal ulcer	44(32.4)	17.26±59.04	NS†
Gastric ulcer	22(16.2)	18.78±54.5	NS
Esophageal ulcer	6(4.4)	20.82±65.33	NS
Esophageal varices	30(22.1)	13.2±52.5	NS
Gastric varices	5(3.7)	4.92±61.4	NS
Hypertensive Gastropathy	2(1.5)	2.82±60	NS
Esophagitis	27(19.85)	16.60±60.52	NS
Erosive duodenitis	22(16.2)	17.03±52.22	NS
Erosive gastritis	14(10.3)	19.44±57.92	NS
Petechia	2(1.5)	5.65±56	NS
Angioectasia	2(1.5)	1.41±18	0.02
Mallory weiss tearing	3(2.2)	28.35±54	NS
Anthral erythema	27(19.9)	17.45±62.22	0.027
Malignancy in upper gastrointestinal tract	9(6.6)	17.09±62.88	NS
Gastrocolic fistula	1(0.7)		

* Mean±SD; † Not significant

Abnormalities responsible for recent upper gastrointestinal bleeding in patients referred to Taleghani hospital with upper GI bleeding are shown in table 3.

Normal endoscopies could be due to subtle abnormalities, such as Dieulafoy's lesions, that can be missed easily during endoscopy. Further studies are required to find out the real reason of upper gastrointestinal bleeding in these patients because normal results may be due to a careless endoscopy. In this study, peptic ulcer disease (all kinds of ulcers such as ulcers with simple clot, with oozing from ulcer bed, with adherent clot, with visible vessels, and with spurting artery in stomach and duodenum were calculated as duodenal and gastric ulcers) was seen in 61 patients (5 patients had the both duodenal and gastric ulcers).

Table 3. Abnormalities responsible for recent upper gastrointestinal bleeding in study population (n=136)

Endoscopic findings responsible for bleeding	Frequency(%)
Duodenal ulcer	35(25.73)
Gastric ulcer	12(8.82)
Esophageal ulcer	4(2.94)
Esophageal varices	30(22.05)
Esophagitis	27(19.85)
Erosive duodenitis	3(2.2)
Erosive gastritis	13(9.55)
Angioectasia	2(1.47)
Mallory weiss tearing	2(1.47)
Malignancy in upper GI tract	3(2.2)
Gastrocolic fistula	1(0.73)
Normal	4(2.94)

Incidence of different drugs used in patients referred to the emergency room of Taleghani hospital with upper gastrointestinal bleeding is shown in table 4.

Table 4. Incidence of different drugs used by study population

Drugs	Frequency	Percent
NSAIDs	28	20.6
Warfarin	8	5.9
Steroids	4	2.9
Chemotherapy drugs	14	10.3
Alcohol	6	4.4
Opium	17	12.5
Cigarette	47	34.60

Only 47 of these ulcers were source of recent bleeding in these patients. Multiple biopsies were taken and be sent to laboratory for rapid urease test and pathologic exam (Giemsa staining for *H.pylori*). About 65.53% of patients had ulcers associated with *H.pylori* alone. 9.83% of patients had peptic ulcer disease associated with NSAIDs alone. 11.47% of patients had ulcers associated with both reasons

(*H.pylori* and consumption of NSAIDs). 13.11% of patients had non-NSAIDs, non-*H. Pylori* peptic ulcer disease. The frequency and incidence of peptic ulcers related and not related to *H.pylori* and NSAIDs are shown in table 5.

Table 5. Different kinds peptic ulcer disease in study population (n=61)

Ulcers related to	Frequency (%)	Mean age	P-value
Helicobacter pylori alone	40(65.57)	16.05±56.4	NS
NSAIDs alone	6(9.83)	15.28±66.67	NS
Both NSAIDs and *Helicobacter pylori*	7(11.47)	21.283±53.57	NS
No NSAID no Helicobacter pylori	8(13.11)	19.58±55	NS

The relationship between different causes of peptic ulcer disease (*Helicobacter pylori* related, NSAID use related, both *Helicobacter pylori* and NSAID use related, no-NSAID no-*Helicobacter pylori* related) and existence of comorbidities is shown in table 6.

There was no significant relationship between existence of comorbidities and peptic ulcers related to *H.pylori*, NSAID use, both *H.pylori* and NSAID use. (p=0.734, p=0.598, and p=0.536 respectively) but there was a significant relationship between existence of comorbidities and no-NSAID no-*Helicobacter pylori* peptic ulcers. (p=0.035).

Table 6. The relationship between different causes of peptic ulcer disease and existence of comorbidities

	With comorbidity (%)	Without comorbidity (%)
H. pylori (n=40)	15(37.5)	25(62.5)
NSAIDs (n=6)	3(50)	3(50)
Both NSAIDs and *H. pylori* (n=7)	2(28.6)	5(71.4)
No NSAID, no *H. pylori* (n=8)	6(75)	2(25)

Discussion

In this study, peptic ulcer disease was seen in 61 patients, 45% of abnormalities seen at the endoscopy of patients referred to Taleghani hospital with a diagnosis of acute upper gastrointestinal bleeding. Only 47 of these ulcers were source of recent bleeding in these patients. About 65.53% of patients had ulcers associated with *Helicobacter pylori* alone. 9.83% of patients had peptic ulcer disease associated with NSAIDs alone. 11.47% of patients had ulcers associated with both reasons (*H.pylori* and consumption of NSAIDs). 13.11% of patients had non-NSAIDs non- *H.pylori* peptic ulcer disease. There was no significant relationship between existence of comorbidities and peptic ulcers related to *H.pylori*, NSAIDs use, both Helicobacter pylori and NSAIDs use. (p=0.734, p=0.598, and p=0.536 respectively) but there was a significant relationship between existence of comorbidities and non-NSAIDs non- *H.pylori* peptic ulcers (p=0.035). There was no significant relationship between age and different kinds of ulcers.

According to the study of Chow DK et al, Non-NSAID non-*H.pylori* ulcer disease, that was believed to account for a minority of bleeding gastroduodenal ulcers, has been increasingly recognized for the past decade. Their study suggests that both relative proportion and actual numbers of patients with non-NSAIDs and non-*H.pylori* ulcers have increased, whereas the prevalence of *H.pylori* -positive ulcers have declined. They made evidence to support non-NSAID non- *H.pylori* ulcers are associated with a higher risk of recurrent ulcer bleeding and a higher overall mortality as compared to *H. pylori*-positive ulcer disease. Patients with non-NSAIDs non-*H.pylori* ulcers are often older, sicker and more frequently experience bleeding episodes while in hospital (29). The results are in agreement with Chow DK et al. the proportion of non-NSAIDs non-*H. pylori* has been increased recently because of a decline in the proportion of ulcers related to *Helicobacter pylori* and NSAIDsThe pathogenesis of non-NSAIDs non- *H.pylori* ulcer is largely unknown. More studies are necessary to discuss

about causes resulting in non-NSAIDs non-*Helicobacter pylori* ulcers to justify the increase in the actual number of these ulcers in recent studies.

The results of this study supports the results of study done by Yakoob J et al. that suggests the incidence of *H.pylori* infection related with duodenal ulcer is common, and in the presence of co-morbidities, non-*H.pylori* and non-NSAIDs duodenal ulcers are likely to be present (24). In our study there was a significant relationship between comorbidities and non-NSAIDs, non- *H.pylori* peptic ulcers (p=0.035), but there was no significant relationship between non-NSAIDs, non- *H.pylori* ulcers and the age of patients.

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