Turk J Gastroenterol *2014; 25 (Suppl.-1): 110-5*

Clinical outcomes of nonvariceal upper gastrointestinal bleeding in Kosova

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Original Article

ABSTRACT

Background/Aims: The aim was to determine the sociodemographic and etiologic factors, endoscopic accuracy, treatment efficiency and clinical outcome of patients with nonvariceal upper gastrointestinal system bleeding in Kosova.

Materials and Methods: We retrospectively evaluated patients who had applied to our Gastroenterology Department between January 2006 and December 2010.

Results: There were 460 eligible cases with mean age 56.85+16.18 years, while male /female ratio was 2.71/1. The greatest occurrence was at age group of 60-69 years (27.1 %). The most common clinical symptom was melena (62.6%). Comorbid diseases were present in 57, 6% of the patients. The percentage of patients using acetylsalicylic acid and /or other non-steroidal anti-inflammatory drugs was 43.7%. Five point two percent were using anticoagulants. Peptic ulcer was the main cause of bleeding (82.2%) and most of them were Forrest III (41.6%). Endoscopic treatment was performed in 90 patients, primary hemostasis was achieved in 96.7% while rebleeding developed in 10% of these patients. The average length of hospital stay was 9.29+5.58 (1-35) days. Rebleeding was reported in 4.1% of all patients while the overall mortality rate was 5.7%.

Conclusion: Age over 60 years, previous history of gastrointestinal bleeding, treatment with anticoagulants, low hemoglobin values at presentation(< 7g/dL), hematemesis, Forrest class, localization of lesion of bleeding, comorbidities, tachycardia, transfusion requirement > 2 unit, type of treatment and time of endoscopy were predictors of poor outcome in study present.

Keywords: Nonvariceal upper gastrointestinal bleeding, Kosova, predictors of outcome

INTRODUCTION

Upper gastrointestinal hemorrhage (UGIH) is a common medical emergency with nonvariceal bleeding responsible for 50-70% of cases (1). Peptic ulcer remains the most common cause (50-70%); other causes of upper gastrointestinal bleeding include erosions, esophagitis, Mallory-Weiss tear, and Dieulafoy's lesion (1,2).

Upper gastrointestinal bleeding represents a substantial clinical and economic burden, with reported incidence ranging from 48 to 160 cases per 100 000 adults per year, and mortality generally from 10% to 14 % (3-5). Mortality is linked to age. In those under 60 years mortality was 8%, whereas in those over 60 years is around 13%. This phenomenon is explained by the fact that today's patients are older and have more comorbidities than those in the past (6).

Approximately 20% of patients with bleeding ulcers present with melena, 30% with hematemesis, 50% with both, and 5% with hematochezia. Approximately 70% of acute non-variceal bleeding stops spontaneously, 10% bleeds continuously, and up to 20% rebleeds in the first 24-72 hours (7).

Endoscopic therapy has been shown to be successful in controlling the bleeding, reduce repeated bleeding,

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Received: October 06, 2012 **Accepted:** October 27, 2012
 • Available online at www.turkjgastroenterol.org • DOI: 10.5152/tjg.2014.4351

mortality, emergency surgery, transfusion requirements and hospital expenses (8-10).

The data about upper gastrointestinal bleeding in Albania and Kosova are poorly described (11). Prevalence of *H. pylori* infection in Albanian population is very high (12,13).

To our knowledge this is first paper on nonvariceal upper gastrointestinal bleeding in Kosova.

The aim of the study was to determine the sociodemographic and etiologic factors, management and outcome of non-variceal upper gastrointestinal system bleeding in Clinical University Centre of Kosova in Prishtina.

MATERIALS AND METHODS

This study was designed as a transversal, cross-sectional study. Between January 2006 and December 2010, 460 of patients with upper gastrointestinal bleeding were admitted at the Department of Gastroenterology of the Clinical University Centre of Kosova in Prishtina. We included in our study the patients with nonvariceal upper gastrointestinal bleeding older than 17 years.

The following data were recorded on every patient: age, sex, presenting symptom, history of previous bleeding, comorbid conditions, using drugs (non-steroid anti-inflammatory drugs, aspirin use, anticoagulants), drinking of alcohol, smoking, blood pressure, pulse, tests of hemostasis, hemogram, urea, creatinine, location of the lesion, bleeding stigmata (visible vessel, oozing hemorrhage, spurting or clot), treatment, volume of injected adrenaline, blood transfusion, hospital stay, need for surgery, rebleeding and mortality.

In statistical analysis were used the following tests:

- Chi-square and Fisher's exact test were used to compare treatment with anti-inflammatory drugs according to age-group; treatment history with anti-inflammatory drugs and presence of hemorrhage.
- Binary logistic regression was used to assess the relationship between demographic factors, lifestyle factors, the progress of the disease, treatment of disease with the recurrence of bleeding (dependent variable, presented as a dichotomous variable / binary level).
- The analysis of variance (ANOVA) was used to compare the mean values between more than two groups.
- T test (student test) was used for independent variables.
- Analysis of survival by Kaplan-Meier method was used to compare rebleeding by gender, the used drugs and the history of previous hemorrhage.

The values of $p<0.05$ were considered to be statistically significant. The whole statistical analysis of the data was conducted in Statistical Package for Social Sciences (SPSS) (SPSS, version 17.0, Chicago, IL).

RESULTS

Clinical characteristics of the patients

Between January 2006 and December 2010, a total of 460 patients with diagnoses of upper nonvariceal gastrointestinal bleeding were admitted to Department of Gastroenterology of Clinical University Centre of Kosova in Prishtina. 336 (73%) of them were male, while male/female ratio was 2.71/1.

The mean age was 56.85±16.18 years (range 17-94 years), Forty five percent of patients were ≥60 years, and 32 (6.95%) of them were under 30 years. The greatest occurrence was at age group of 60-69 years (27.1 %) (Figure 1).

The most common clinical symptom on presentation was melena (62.6%). A history of previous gastrointestinal bleeding was present in 47% of the patients. Comorbid diseases were present in 57.6% of the patients; the most common were cardiovascular diseases (34%), connective tissue and kidney diseases.

The percentage of patients using acetylsalicylic acid and /or other NSAIDs was 43.7%. Twenty four of them (5.2%) were using anticoagulants.

Smoking was reported by 122 patients (26.5%) while alcohol use was reported by only 24 patients (5.2%).

Endoscopic Data

Endoscopy was performed within 24 hours of the bleeding episode in 86,1% of patients. Anatomically, the lesions were localized in the esophagus in 2.4%, gastric in 23%, duodenum in 64.8%, and in the region of anastomosis in 1.5%.

Peptic ulcer was the main cause of bleeding (82.2%) and most of ulcers were Forrest III (41.6%) (Table 1).

Treatment and Outcome

Bleeding was stopped with medical therapy in 79.8%. Seven patients (1.1%) had surgery for further bleeding. Endoscopic

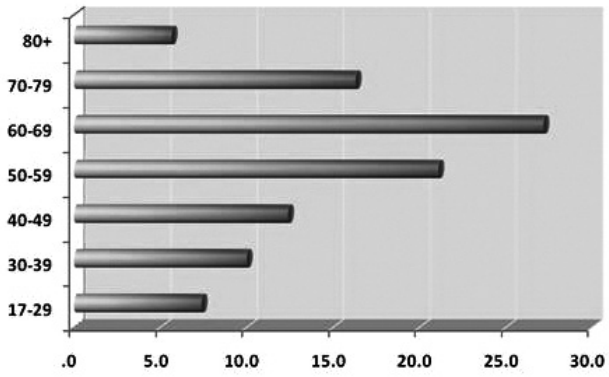

Figure 1. The distribution of patients according to age groups

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Table 1. Characteristics of the patients with nonvariceal upper gastrointestinal bleeding

Characteristic of patients		
Number of patients	460	
Gender (male/female)	336 (73%) /124(27%)	
Male: female ratio	2.71	
Mean age	56.85 + 16.18 years (range 17-94)	
Age >60 years	45%	
Presentation	melena	287 (62.4%)
Previous bleeding	0.47	
Comorbiditiies	57.6%	
NSAIDs/ASA	43.7%	
Anticoagulants	5.2%	
Alcohol	5.2%	
Smoking	26.5%	
Hemoglobin<7g/dL	347 (75%)	
Location of bleeding	duodenum	(64.8%)
Endoscopy within 24 hours	86.1%	
Endoscopic diagnosis	peptic ulcer	(82.2%)
Forrest class	Forrest III	(41.6%)
Medical treatment	79.8%	
Surgery	7 (1.1%)	
Endoscopic therapy	90 patients	
Transfusions	in 73.9%	
Blood units	3.79±2.88 (1-22)	
Hospital stay	9.29+5.58 (1-35)	
Rebleeding	4.1%	
Mortality	5.7%	

NSAIDs: non-steroidal anti-inflammatory drugs; ASA: acetylsalicylic acid

treatment with epinephrine injection was performed in 90 patients; primary hemostasis was achieved in 96.7 % while rebleeding developed in 10% of these patients. Primary failure to achieve hemostasis occurred in 3 patients. Blood transfusions were required in 73.9% of the patients. The average number of blood unit was 3.79±2.88 (1-22) per patient. The average length of hospital stay was 9.29±5.58 (1-35) days. Rebleeding was reported in 4.1% of all patients while the overall mortality rate was 5.7% (Table 1).

Analyzing possible predictive factors of rebleeding, we found that age over 60 years, previous history of gastrointestinal bleeding, treatment with anticoagulants, low hemoglobin values at presentation (<7 g/dL), hematemesis, Forrest class, localization of lesion of bleeding, tachycardia, transfusion requirement >2 unit, type of treatment and time of endoscopy were predictors of rebleeding.

While rebleeding ($p<0.05$), age over 60 years, previous history of gastrointestinal bleeding, treatment with anticoagulants, low hemoglobin values at presentation (<7 g/dL), Forrest class, time of endoscopy, comorbidities, localization of lesion of bleeding, tachycardia and transfusion requirement >2 unit were predictors of mortality (Table 2).

DISCUSSION

In this study the mean age was 58.65±16.18 years (range, 17-94) with 45% of patents being over 60 years. The greatest occurrence was at age group of 60-69 years (27.1 %), while 7.4% were under 30 years. These results are compatible with those reported in other studies related to age, gender and age distribution (14,15). In Western studies the mean age was over 60 years and those above 60 years made 50-70% of the total. Our patients were younger than those of Italian PNED study (16), the Canadian RUGBE study (17) as well as the ENERGIB observational, retrospective study (18). This finding may be explained by the age distribution of our population. Sixty six percent of our population is located between 15 and 64 years of life (19).

In the developed countries the percentage of older patients suffering from upper nonvariceal gastrointestinal bleeding has been increasing rapidly over the last years. The main reasons are the increase in the life expectancy and increased consumption of many drugs (20).

The male: female ratio was 2.71 which is similar to the ratio of some European countries and the United States (19,21). Worldwide male patients have higher prevalence.

A bleeding site was detected in 97.6% of the patients in the present study. When considered by site of bleeding, the duodenum was the most common site (64.8%), followed by stomach (23%). Similarly to other surveys the most common bleeding lesions identified at upper gastrointestinal endoscopy was peptic ulcer disease, duodenal ulcer (65%) being more common than gastric ulcer (17.2%) (22-24). Other forms like Mallory-Weiss tear and Dieulafoy's lesion were less frequent.

In the present study, duodenal ulcer was the leading cause of nonvariceal upper gastrointestinal bleeding. This finding could probably be due to the high prevalence of *H. pylori* infection in Albanian population (12,13).

The pathogenic role of *Hp* in the development of peptic ulcer is a well established

phenomenon. The prevalence of *Hp* infection is reported to be higher in developing countries and it may influence the etiology of upper gastrointestinal system bleeding (25,26).

However, we could not determine the prevalence of the infection in this study, because tests for *H. pylori* status were not

Table 1. Predictors of rebleeding and mortality in nonvariceal upper gastrointestinal bleeding

	Rebleeding (n=19)		Mortality (n=26)	
	OR (95% CI)	p value	OR (95% CI)	p value
Age(>60 vs.<60 years)	0.684 (0.454-0.914)	0.040	0.431 (0.384-0.478)	0.000
Gender	0.632 (0.393-0.870)	0.330	0.737 (0.696-0.791)	0.074
History of bleeding	0.579 (0.334-0.823)	0.000	2.147 (2.092-2.203)	0.000
Comorbidities	0.684 (0.454-0.914)	0.163	0.528 (0.480- 0.575)	0,000
Alcohol	0.000 (0.000-0.000)	0.614	0.555 (0.034-0.077)	0.218
Smoking	0.316 (0.086-0.546)	0.590	0.258 (0.217-0.299)	0.322
NSAIDs	0.526 (0.279-0.774)	0.410	0.424 (0.377-0.471)	0.056
Anticoagulants	0.158 (0.023-0.338	0.034	0.044 (0.024-0.063)	0,001
Hemoglobin(<7g/dLvs.>7g/dL)	0.368 (0.130-0.607)	0.000	0.776 (0.737-0.816)	0,000
Melena	0.474 (0.226-0.721)	0.167	0.631 (0.586-0.677)	0.79
Hematemesis	0.316 (0.086-0.546)	0.005	0.111 (0.081-0.140)	0,205
Melena and hematemesis	0.211 (0.009-0.412)	0.610	0.258 (0.217-0.299)	0,576
Forrest class	2.500 (1.622-3.378)	0.031	4.470 (4.307-4.632)	0.031
Localization of lesion	2.222 (1.710-2.735)	0.048	2.271 (2.670-2.772)	0.000
Systolic blood pressure	1.947 (1.837-2.058)	0.203	1.836 (1.801-1.871)	0.088
Pulse (>100/min vs.<100/min)	1.316 (1.086-1.546)	0.000	1.816 (1.779-1.852)	0.000
Transfusions >2U	1.105 (0.953-1.257)	0.000	1.846 (1.1768-1.923)	0.000
Time of endoscopy	0.737 (0.383-1.090)	0.000	1.530 (1.469-1.591)	0.000

NSAIDs: non-steroidal anti-inflammatory drugs

routinely made in patients with acute upper gastrointestinal bleeding during the period studied in our institution.

NSAIDs are among the most frequently prescribed medications worldwide. Kosova is characterized by high rate of prescription and over the count availability of NSAIDs.

In present study, the percentage of patients using acetylsalicylic acid and /or other NSAIDs was 43.7%. Five point two percent of them were using anticoagulants.

The main factor limiting use of NSAIDs is the concern about their gastrointestinal side effects, and the use of NSAIDs is a well established risk factor for upper gastrointestinal bleeding (27-29). However, the majority of patients are not aware of the risks of these medications. The elderly are especially susceptible to NSAIDs-induced gastrointestinal system bleeding. Although the bleeding risk increases with increasing NSAIDs dose, it is a well-known fact that any amount can cause bleeding. It is important to be cautious in prescribing NSAIDs with risk factors particularly in the elderly and patients having comorbid diseases.

The presence of comorbidity is a well-known cause of increased incidence for upper gastrointestinal system bleeding (30,31) and accordingly, 57.6% of our patients had comorbid diseases. The most common were cardiovascular diseases (34%), connective tissue and kidney diseases.

Smoking has been implicated in the pathogenesis of peptic ulcer disease for decades, but its importance as a risk factor has declined after the discovery of *H. pylori*. A large body of literature suggests that smoking may predispose to peptic ulcer disease, but *H. pylori* infection remains a confounder that was not addressed in earlier studies. It is noteworthy that cigarette smoking does not increase the risk of recurrent ulceration once *H. pylori* has been eradicated, suggesting that smoking may only play a role in infected subjects (32).

The role of alcohol remains uncertain. Alcoholic beverages stimulate gastric acid production. Moreover, direct application of high concentrations of alcohol to the gastric mucosa causes demonstrable mucosal injury.

In present study smoking was reported by 26.5%, while alcohol consumption by 5.2% of patients. We did not find any correlation between smoking and alcohol abuse and specific bleeding lesions, rebleeding or a higher mortality rate.

The optimal timing for endoscopy remains under debate. Emergency endoscopy allows for early hemostasis, but can potentially result in aspiration of blood and oxygen desaturation

in insufficiently stabilized patients. International consensus guidelines recommend early endoscopy within 24 h of presentation, because it significantly reduces the length of hospital stay and improves outcome(33). However, emergency endoscopy should be considered in patients with severe bleeding.

In the present study, 94.1% of patients had endoscopy and 86,1% were performed within 24 hours of presentation to hospital. Due to severe general conditions 27 patients were unfit for gastroscopy.

A variety of endoscopic and pharmacological modalities are effective in achieving and maintaining homeostasis. Endoscopic therapy is a well-established procedure in the management of gastrointestinal bleeding and can be used as an effective tool for selected patients(9,34). Endoscopic treatment controls bleeding in up to 90% and reduces significantly the rates of further bleeding, the need for blood transfusions, hospital costs and emergency surgery. In our study group, endoscopic treatments were done in 90 patients, primary hemostasis was achieved in 96.7% while rebleeding developed in 8,9% of these patients.

Rebleeding was reported in 4.1% of all patients while the overall mortality rate was 5.7%. Due to lack of polidocanol, heater probe and argon plasma coagulator in our department we used only diluted adrenaline.

The rebleeding rate observed in our patients (4.1%) was similar to that observed in the Italian PNED study (3.2%) (21), but it was significantly lower than that reported in the Canadian RUGBE study (14.1%) (22). In addition, rebleeding was found to be an predictor of death in our study as equal as it has been described in other studies.

Age over 60 years, previous history of gastrointestinal bleeding, treatment with anticoagulants, low hemoglobin values at presentation(< 7g/dL), hematemesis, Forrest class, localisation of lesion of bleeding, tachycardia, transfusion requirement >2 unit, type of treatment and time of endoscopy were predictors of rebleeding. While rebleeding (p=0.000), age over 60 years, previous history of gastrointestinal bleeding, treatment with anticoagulants, low hemoglobin values at presentation (<7 g/dL), Forrest class, time of endoscopy, comorbidities, localization of lesion of bleeding, tachycardia and transfusion requirement >2 unit were predictors of mortality (Table 2).

This study is the first, to our knowledge, to characterize patients with upper nonvariceal gastrointestinal bleeding at the Clinical University Centre of Kosova and it has limitations that should be mentioned. The retrospective nature of the study and lack of a consistent, electronic system to store data resulted in non-intentional loss of some informations. We could not determine the prevalence of the infection in this study, because tests for *H. pylori* status were not routinely made in patients with acute upper gastrointestinal bleeding during the period studied in our institution.

In conclusion, the most common cause of nonvariceal upper GI bleeding was peptic ulcer in our series. Our study shows that age over 60 years, previous history of gastrointestinal bleeding, treatment with anticoagulants, low hemoglobin values at presentation (<7 g/dL), hematemesis, Forrest class, localization of lesion of bleeding, comorbidities, tachycardia (pulse above 100/minute), transfusion requirement >2 unit, type of treatment and time of endoscopy were predictors of poor outcome.

Conflict of Interest: No conflict of interest was declared by the authors.

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