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IS UPPER GASTROINTESTINAL BLEEDING STILL A LIFE-THREATENING CONDITION?

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ABSTRACT

Background: Upper gastrointestinal bleeding is a common clinical problem and one of the main reasons for emergency hospitalization. It is associated with an overall mortality rate of 2% to 13%, despite advances in medical therapy. First-choice management is conservative treatment with endoscopic hemostasis.

Aim of the study: The aim of the study was to examine the epidemiological and clinical characteristics of patients with upper gastrointestinal bleeding with a focus on the course of hospitalization based on the etiology

Material and methods: A retrospective study was conducted in the Department of Surgery at the 4th Military Teaching Hospital in the years 2011–2016, comprising a total of 200 hospitalizations. 150 (75%) of the study group were men, and the mean age was 63.6±15.8 years.

Results: Patients most frequently presented with melena (n=105; 53.1%) and hematemesis (n=79; 40%) or coffee ground vomiting (n=57; 28.7%). . 138 (69%) of hemorrhages were managed with endoscopic hemostasis, and in 43 (21.5%) of cases conservative treatment was adequate. In 12 (6%) of cases, laparotomy was the first-choice therapy and in 7 (3.5%) cases, surgery was performed after an attempt at endoscopic treatment had failed. The sources of bleeding were: gastric ulcer – 58 (29%), duodenal ulcer – 48 (24%), esophageal varices – 31 (15.5%), gastric tumor – 15 (7.5%), Mallory-Weiss syndrome – 10 (5%), and Dieulafoy's lesion – 3 (1.5%). 16 (8%) of the hospitalizations were fatal.

Conclusions: Upper gastrointestinal bleeding still has a high mortality rate (8%). It more frequently affects men and the elderly. Gastric and duodenal ulcers are the most common etiologies of bleeding. Esophageal varices and neoplasms are also a significant source of bleeding. Despite the progress in the pharmacological treatment of peptic ulcers, the complications resulting from gastrointestinal bleeding continue to be a serious clinical problem.

KEYWORDS: gastrointestinal hemorrhage, endoscopy, peptic ulcer, esophageal and gastric varices

Background

Upper gastrointestinal bleeding (UGIB) is defined as a significant loss of blood the source of which is located proximally to the suspensory muscle of the duodenum, also known as the Treitz ligament. It is a common clinical problem and one of the main reasons for emergency admissions associated with abnormalities of the gastrointestinal tract. In the general population, its incidence is three times higher than that of lower gastrointestinal bleeding [1]. Despite the advent and development of endoscopic hemostasis techniques, the mortality rate remains high at an estimated at 2–13% [1–11]. The most frequently observed signs and symptoms of UGIB are hematemesis or coffee

ground vomiting (*melaenemesis*), and melaena, sometimes accompanied by local or generalized abdominal tenderness. If the hemorrhage is massive, hematochezia and signs of hypovolemic shock noticed an result. The most serious complications include incidents of re-bleeding and the exacerbation of comorbidities.. Peptic ulcers are the most common source of UGIB, accounting for 22% [3] up to 67% [11] of all recorded incidents, depending on the study. Varices of the esophagus and stomach are the cause of bleeding in approximately 5–30% of patients [3–6] and are also associated with a significantly higher mortality rate [9]. Many other conditions may lead to UGIB, including acute and erosive esophagitis, gastritis or duodenitis, portal hypertensive gastropathy, angiodysplasia, neoplasm, Mallory–Weiss syndrome and Dieulafoy's lesion [12,13]. In 15% of cases the etiology remains unknown. UGIB more often affects men and its incidence increases with age [14–16]. Widely known and confirmed risk factors for peptic ulcer bleeding are *Helicobacter pylori* infection, nicotine consumption (tobacco smoking), excessive production of gastric acid and chronic use of non-steroidal anti-inflammatory agents (NSAIDs) [17]. Varices of the esophagus or stomach are usually secondary to liver disease. UGIB in hemodynamically stable patients is typically diagnosed and treated with an esophagogastroduodenoscopy. Both guidelines published by the *European Society of Gastrointestinal Endoscopy* [18] and the *American College of Gastroenterology* [19] emphasize the role of early endoscopy (up to 24 hours after the onset of symptoms) in effective therapy. Early endoscopy minimizes the chance of complications, including reducing the risk of re-bleeding or death, and the necessity of surgical intervention. Conservative treatment is applied simultaneously with endoscopic hemostasis. First-choice intravenous drugs are proton-pump inhibitors (PPIs). H2 antagonist, somatostatin analogs and tranexamic acid are also used.

Aim of the study

The aim of the study was to examine the epidemiological and clinical characteristic of patients with upper gastrointestinal bleeding with a focus on the course of hospitalization based on the etiology.

Material and methods

A retrospective analysis was performed of the medical charts of patients treated in the Department of Surgery at the 4th Military Teaching Hospital between 2011 and 2016, compromising a total of 200 hospitalizations. The following data were collected: demographics, medical history (comorbidities, intake of medications, and presenting symptoms), physical examination and endoscopic findings, laboratory test results, history of blood transfusions, previously performed procedures and clinical outcomes. Patients included in the study were initially admitted to the emergency department and then transferred to the surgical ward with a diagnosis of upper GI bleeding. The intensity of ulcer hemorrhage was assessed endoscopically using the Forrest classification. Patients who were not admitted to the Department of Surgery were excluded from the analysis. Some patients were hospitalized more than once; 15 patients twice, 2 patients three times and one patient four times. The study reported on data from all hospitalizations (n=200). 150 (75%) of the patients were men. The mean age was 63.6 years (SD 15.8, range 21–98 years). The age distribution is presented in fig. 1.

The results were statistically evaluated, comparisons were carried out with the chi-squared test for contingency tables and the Kruskal-Wallis test. A significance level was established at α=5%. If a medical history was incomplete, those records were excluded from the analysis. Rates of nicotinism, may have been underestimated due to insufficient data concerning smoking. The study was approved by the local ethics committee of Wroclaw Medical University (No KB - 121/2011).

Results

In the course of bleeding, patients most frequently presented with melena - 105 (53.1%) and hematemesis - 79 (40%) or coffee ground vomiting – 57 (28.7%). Among comorbid illnesses hypertension - 74 (37.0%), alcohol abuse - 62 (30.8%) and nicotinism - 46 (22.8%) predominated. 35 (17.3%) patients had taken prophylactic aspirin before hospitalization, 21 (10.6%) and had regularly used NSAIDs. Patients' characteristics according to the etiology of bleeding are shown in tab. 1.

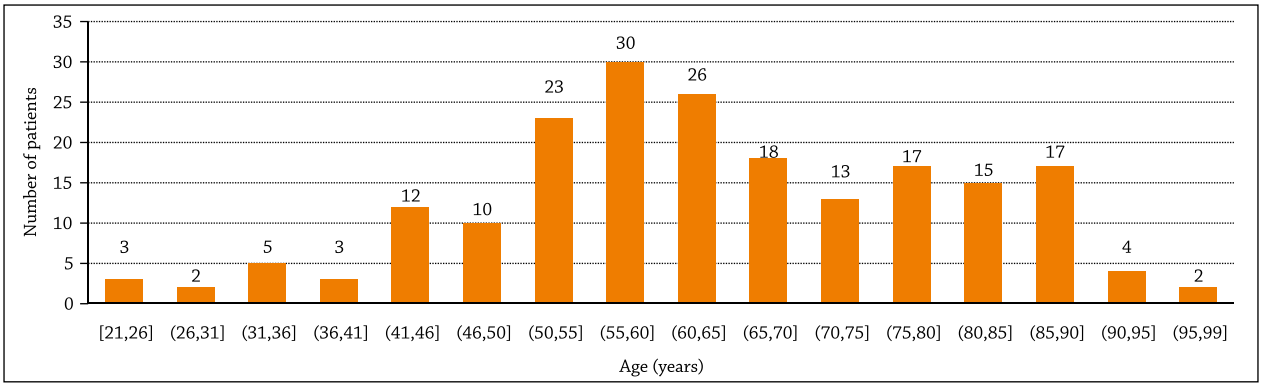

Figure 1. Patient' distribution by age

Table 1. Characteristics of patients

Variable	Etiology							p	total
	GU	DU	Ut**	EV	NPL	MWS	other		
Hospitalizations (n; %)	58 (29%)	48 (24%)	108 (54%)	31 (15.5%)	20 (10%)	10 (5%)	31 (15.5%)		200 (100%)
Mean age (years)	62.5	63.3	63	57.7	74.9	60.5		0.001	63.6
Males (n; %)	45 (77.6%)	36 (75%)	82 (75.9%)	22 (71%)	17 (85%)	7 (70%)		0.14	150 (75%)
Females (n; %)	13 (22.4%)	12 (25%)	26 (24.1%)	9 (29%)	3 (15%)	3 (30%)			50 (25%)
Symptoms present on the admission									
Hematemesis	47.6%	22.2%	35%	55.6%	36.8%	70%		0,02	40%
Coffee-ground vomiting	23.8%	22.2%	22.5%	33.3%	21.1%	50%		0.45	28.8%
Melena	54.8%	63.9%	58.8%	33.3%	47.4%	50%		0.19	53.1%
Hypovolemic shock	4.8%	16.7%	10%	14.8%	5.3%	0%		0.37	10%
Comorbid illnesses									
Alcohol use disorder	28.6%	10.8%	19.8%	70%	5.3%	40%		<0.001	30.9%
Smoking (ever)	31%	16.2%	24.7%	23.3%	21.1%	30%		0.75	22.8%
Cirrhosis	2.4%	5.4%	3.7%	100%	5.3%	20%		<0.001	22.9%
Hypertension	35.7%	27%	32.1%	30%	57.9%	50%		0.19	37%
Diabetes	19.%	8.1%	13.6%	30%	36.8%	10%		0.04	19.1%
Drug intake									
ASA	15%	18.8%	17.6%	11.5%	21.1%	10%		0.96	17.3%
NSAIDs	20%	25%	20.3%	0%	0%	10%		0.03	10.7%
β-blockers	17.5%	21.9%	20.3%	34.6%	57.9%	30%		0.01	28.7%
Anticoagulants	17.5%	18.8%	18.9%	11.5%	31.6%	10%		0.61	17.3%
IPP	15%	9.4%	12.2%	15.4%	52.6%	0%		<0.001	18%
Initial laboratory data									**mean**
Hb (g/dl)	9.83	8.26	9.13	8.36	7.44	11.77		<0.001	8.92
HCT (%)	29.4	25.55	27.71	25.28	22.88	34.74		<0.001	27.03
PLT (10^3/μl)	236	270	247	152	266	187		<0.001	227
RBC (10^6/μl)	3.29	2.75	3.05	2.78	2.62	3.83		0.0002	3
WBC (10^3/μl)	11.71	11.47	11.54	11.5	10.73	9.43		0.57	11.23
Creatinine (mg/dl)	1.17	1.21	1.18	1.09	1.27	1.12		0.89	1.25
INR	1.5	1.4	1.45	1.69	1.64	1.3		<0.001	1.54
APTT (s)	26.64	27.05	26.79	29.28	28.99	27.5		0.04	27.9
Average number of transfused units									
PRBCs	3.4	4.3	3.8	4.3	4.7	4		0.058	3.99
FFP	2.8	3.1	2.9	3	2.7	4		0.61	2.91
Mean hospitalization length (days)	4.4	4	4.2	4	5.6	3		0.28	4.15
Mortality	2 (3.5%)	6 (12.5%)	8 (7.4%)	5 (16.1%)	1 (5%)	0	2	0.23	8%

* The differences between the analyzed groups were considered significant with $p<0.05$

** The two patients in whom simultaneously hemorrhage from gastric and duodenal ulcers were observed, were included only in the Ut (Ulcers total) group, hence n=108.

(GU - gastric ulcer; DU - duodenal ulcer; Ut - ulcers (total); EV - esophageal varices; NPL - neoplasm; MWS - Mallory-Weiss syndrome).

138 (69%) hemorrhages were managed with endoscopic hemostasis, while in 43 (21.5%) - conservative treatment was adequate. In 12 (6%) hospitalizations, laparotomy was the first-choice therapy and in 7 (3.5%) - surgery was performed after an attempt at endoscopic treatment had failed. The most frequent sources of bleeding were gastric ulcer – 58 (29%), duodenal ulcer – 48 (24%), esophageal varices – 31 (15.5%), gastric tumor – 15 (7.5%), Mallory-Weiss syndrome – 10 (5%), and Dieulafoy's lesion – 3 (1.5%). Less prevalent (≤1%) were esophageal ulcer, gastric submucosal tumor (SMT), gastrointestinal stromal tumors , esophageal tumor, bleeding from an endoscopic retrograde cholangiopancreatography (ERCP) cicatrix, neoplastic infiltration of the duodenal bulb, erosive esophagitis, hemorrhagic gastropathy and polyps. In 9% of hospitalizations, the source of bleeding was not determined. In patients who suffered from alcohol use disorder, esophageal varices represented the largest percentage (37%) of findings.

The intensity of ulcer bleeding, assessed using the Forrest classification, is presented in tab. 2.

Table 2. Distribution of the bleeding intensity assessed with the Forrest classification

Forrest category	Gastric ulcers (n=60)	Duodenal ulcers (n=50)	Ulcers total (n=110)
Ia (spurting hemorrhage)	6 (10%)	6 (12%)	12 (10.9%)
Ib (oozing hemorrhage)	34 (56.7%)	26 (52%)	60 (54.5%)
IIa (non-bleeding visible vessel)	6 (10%)	4 (8%)	10 (9.2%)
IIb (adherent clot)	7 (11.7%)	5 (10%)	12 (10.9%)
IIc (hematin on ulcer base)	5 (8.3%)	7 (14%)	12 (10.9%)
III (clean ulcer base)	2 (3.3%)	2 (4%)	4 (3.6%)

A total of 19 laparotomies were performed, for the following reasons: unsuccessful endoscopic management (7), gastric ulcer perforation (6), gastric tumor without perforation (2),gastric tumor with perforation (1), gastric SMT (1), duodenal perforation (1), acute abdomen (diagnostic laparoscopy, with source of bleeding defined) (1).

16 (8%) hospitalizations were fatal. The mean length of hospitalization was 4.1 days (SD 3.6). During one stay, on average 4 units of PRBCs and 3 units of FFP were transfused.

Discussion

Recently conducted epidemiologic studies reported a decrease in the incidence of UGIB, which, depending on the center, ranges from 36 to 134 cases per 100,000 inhabitants [3,4,7,8,10,11]. This decrease may be associated with the popularization of *Helicobacter pylori* eradication protocols, the preventive intake of gastric acid secretion inhibitors in patients undergoing chronic NSAID therapy and the lower percentage of smokers in the population. The pattern of etiologies is also changing. A significant decline in the frequency of peptic ulcers as a source of bleeding has been observed, although peptic ulcers remain one of the main reasons for hospitalization due to UGIB. This trend applies particularly to duodenal ulcers, while the proportion of gastric ulcers has been reported to be slightly less [7–10] by some authors or, according to other authors, even increasing [5,11]. Several recent studies have reported that esophagitis [5,9] and neoplastic lesions [5,9,11] have also become a major cause of UGIB. As a consequence, the profile of a patient who presents to a hospital emergency department with signs of bleeding is also changing. Unfortunately, the literature lacks data specific to the Polish population. The aim of the study was to determine the epidemiological profile of patients admitted to the surgical ward with a suspicion of UGIB, with a focus on the etiology. The demographic profile of the group in this study is consistent with that of other centers in terms of both mean age and sex distribution [3,6,15,20]. The incidence of gastric and duodenal ulcers as a bleeding etiology (54.5%) is higher than reported by other authors [1,3,5,7,10,14,15,20], although not in all studies [4,6,9,11]. The reason for this disproportion may be the excessive use of nonsteroidal anti-inflammatory drugs and the high percentage of cigarette smokers in Poland, comparing to the Western Europe and North America [21–23]. Bleeding from esophageal varices accounted for 15.5% of all hospitalizations. The literature reveals a large discrepancy in the incidence of varices, with proportions ranging from 3% in a study conducted in the United Kingdom [3] to 33% in the United States [5]. These differences are primarily due to the socioeconomic status of the different populations, affecting the risk factors for liver disease leading to cirrhosis and the development of esophageal varices. In 10% of cases in our study, bleeding was caused by neoplastic lesions, which is a higher than that observed in other studies.

Our analysis also includes a comparison of the patient profile, the symptoms present on admission and the course of hospitalization based on the etiology. The greatest mean age was observed in the neoplasm group, and the youngest patients were those with bleeding esophageal varices. Variceal bleeding and Mallory-Weiss syndrome were associated with a higher likelihood of hematemesis as a manifestation of UGIB. Among the comorbidities, the incidence of variceal bleeding was significantly higher in patients with alcohol use disorder, cirrhosis and diabetes. The incidence of variceal bleeding was also higher in cancer patients. More than 20% of the patients with peptic ulcers as the cause of bleeding had a history of NSAID intake. Significant differences were also found in laboratory parameters at admission, primarily hemoglobin, hematocrit and platelet count, which were lowest in patients with variceal bleeding. These data are consist-

ent with other studies. A history of liver disease and alcoholism, being younger, having hematemesis and a low hemoglobin and platelet count have been reported as predictors of esophageal varices as a cause of UGIB in other studies [24,25]. An early assessment of the potential source of bleeding from the upper gastrointestinal tract allows appropriate therapeutic procedures to be implemented even before an endoscopic examination, the timing of which is also relevant.

The mortality rate of 8% which was observed is high compared to similar studies [1,4,5,7]. The reason for this difference may be the fact that the group of patients in this study were admitted to the surgical ward because they presented more severe symptoms. Less serious cases such as those with esophageal, gastric and duodenal erosions, which were primarily transferred to the gastroenterology unit at the department of internal medicine, were excluded from our study. In more than half of the patients with gastric or duodenal ulcers, the endoscopic examination showed active bleeding (Forrest IA and IB), while categories II and III predominated in other centers, and these were associated with a better prognosis. In our study, only in-hospital deaths were taken into account. There were no data on the 30-day survival rate.

Conclusions

1. Upper gastrointestinal bleeding is a serious condition and still has a high mortality rate (8%). It affects men and the elderly more often.
2. Gastric and duodenal ulcers are the most common causes of bleeding. Esophageal varices and neoplasms are also a significant source of UGIB.
3. Despite the progress in the pharmacological treatment of peptic ulcers, the complications resulting from the bleeding continue to be a serious clinical problem.

List of abbreviations

- UGIB - upper gastrointestinal bleeding
- NSAIDs - nonsteroidal anti-inflammatory drugs
- PPIs - proton-pump inhibitors
- GI - gastrointestinal
- ERCP - endoscopic retrograde cholangiopancreatography
- ASA - acetylsalicylic acid
- PRBCs - packed red blood cells
- FFP – fresh frozen plasma
- SMT - submucosal tumor
- GIST – gastrointestinal stromal tumor

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