

# Evolution of the causes of upper gastrointestinal bleeding

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**Abstract.** Upper gastrointestinal bleeding is one of the most common emergencies in medical practice. The etiologic spectrum of gastrointestinal bleeding is very diverse and highly variable from one geographical area to another. Our study aimed to examine the main causes of upper gastrointestinal bleeding in patients who have presented to two reference hospitals in Transylvania (Hunedoara County and Cluj County) every seven years, as well as to assess their evolutionary trend. The study has also tracked the variations in the causes of disease based on patient age and gender.

**Key Words:** causes, variceal and non-variceal upper gastrointestinal bleeding.

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## Introduction

The causes of upper gastrointestinal bleeding (UGIB) are one of the main factors that determine the evolution and prognosis of patients with UGIB.

With the widespread introduction of proton pump inhibitor-based therapy and sustained treatment of *Helicobacter pylori* infection, there should be a reduction in the incidence of ulcers and gastritis, as shown in most studies (Sung *et al* 2009). In parallel, however, there is an increased consumption of NSAIDs, anticoagulants and antiplatelet drugs, which are important risk factors for gastrointestinal bleeding.

Studies report varying shares of the main causes in different countries, differences probably resulting from the specific socio-economic development (incidence of *Helicobacter pylori* infection, alcohol consumption, incidence of hepatitis virus infections, etc.) (van Leerdam *et al* 2008).

Prevalence of *Helicobacter pylori* infection varies between 20-40% in industrialized countries and 80% in developing countries (Ilie *et al* 2011). In 1994, *Helicobacter pylori* infection still had a high 60-62% prevalence in Romania (Andreica *et al* 1994). Another important aspect is the high prevalence of viral hepatitis infection and alcohol consumption in our country, which results in a large spread of liver cirrhosis.

These factors, accompanied by smoking habits and the use of NSAIDs (often without a prescription and without PPI protection), can influence the share of the various causes of upper gastrointestinal bleeding.

## Materials and methods

The study included all patients with upper gastrointestinal bleeding who presented to two reference hospitals in Cluj-Napoca and Hunedoara in 2003 and 2010.

These patients have been separated into two groups, based on the two study years.

Patients in both groups were divided by gender and age groups. Patient age groups were the following: 18-40 years, 40-60 years, 60-80 years, >80 years.

The etiologic diagnosis of UGIB was established based on patient history, biological samples and upper gastrointestinal endoscopy. The causes of upper gastrointestinal bleeding were monitored both globally and based on age groups and genders in order to demonstrate the time evolution of the various causes of upper gastrointestinal bleeding.

## Results

A number of 1,185 patients with upper gastrointestinal bleeding presented to the two reference hospitals in the two years considered for the study, 473 patients in 2003 and 712 in 2010. A number of 65 patients were excluded from the study (37 in 2003 and 28 in 2010) as, for various reasons, they did not undergo upper gastrointestinal endoscopy (refused examination, their critical general condition did not allow performing the examination, upper gastrointestinal endoscopy was not available or was not indicated by the physician).

In the group from 2003, of the 436 patients remaining in the study, 121 were women (27.7%) and 315 were men (72.2%).

In 2010, 684 patients remained in the study of whom 230 were female patients (33.6%) and 454 were male patients (66.3%). There is a statistically significant difference in gender distribution between the two groups ( $p=0.4$ ).

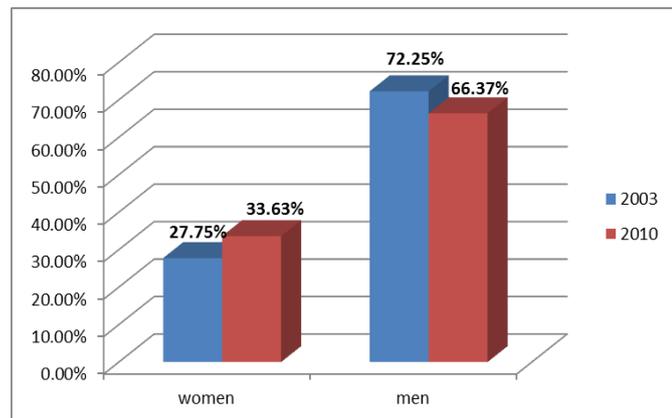


Fig. 1. Gender distribution of patients in the two groups

In the patient group from 2003, minimum age was 19 and maximum age was 90, with a mean age of 59 (47.2; 68) years. In the patient group from 2010, minimum age was 18 and maximum age was 96, with a mean age of 61 (52; 71) years.

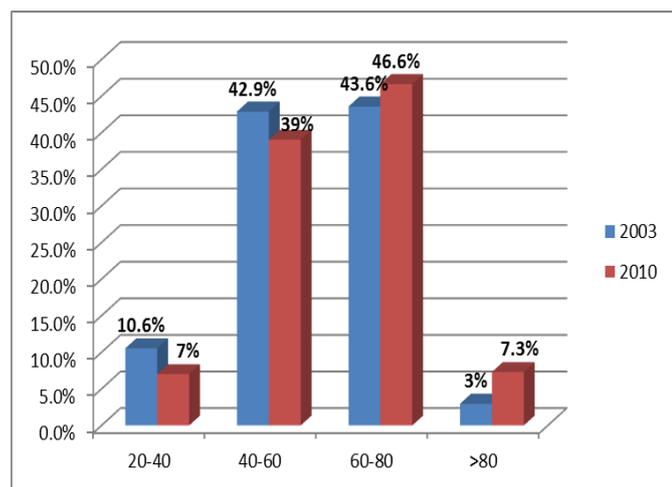


Fig. 2. Age group distribution of patients in the two groups

Age of patients in the group from 2003 was significantly lower (59 (47.2; 68)) than that of patients in the group from 2010 (61 (52; 71) ( $p= 0.001$ )).

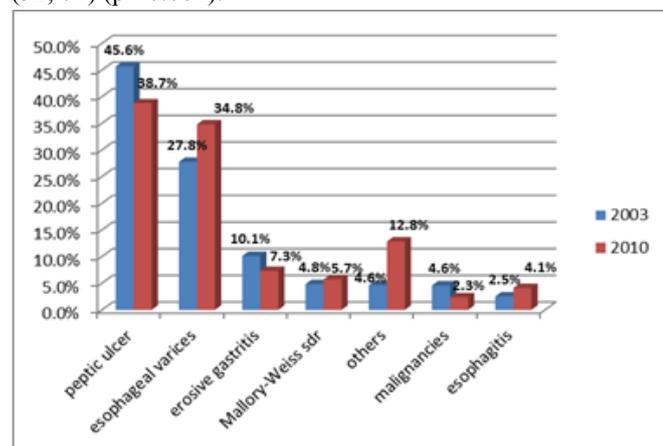


Fig. 3. The main causes of upper gastrointestinal bleeding

Patients in both groups studied had ulcerative disease as the predominant causes of UGIB. Patients with gastric ulcers, including hiatal hernia ulcers and duodenal ulcers, were included in this category.

There is a downward trend in the share of UGIB caused by ulcers.

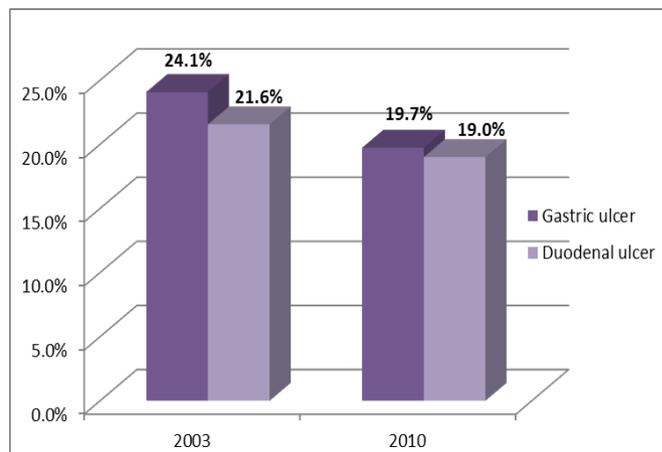


Fig. 4. The share of gastric and duodenal ulcers

UGIB was observed in 27.8% of patients in 2003 and 34.8% of patients in 2010, caused by hypertension in the portal vein system. Most of them had esophageal varices as a source of UGIB, and a significantly smaller number (2 patients in 2003 and 2 in 2010) had gastric varices as source, or presented diffuse haemorrhage resulting from portal hypertensive gastropathy (1 patient in 2003 and 6 patients in 2010).

Distribution of esophageal varices was not significantly different between genders ( $p=0.03$ ).

Erosive gastritis caused about 10% of gastrointestinal bleeding cases in 2003 and 7.3% of the cases in 2010.

Mallory-Weiss syndrome was detected in 4.8% of patients in 2003 and 5.7% of patients in 2010.

Esophagitis and esophageal ulcers have increased from 2.5% in 2003 to 4.1% in 2010.

Neoplastic disease caused bleeding in 4.6% of patients in 2003 and 2.3% of patients in 2010. These malignancies included esophageal cancer, gastric cancer (including gastric lymphoma), duodenal tumors (primary, duodenal ampullary cancers or neoplastic invasions of neighboring organs).

There is a statistically significant difference in cancer distribution between the age groups ( $p<0.001$ ).

In the group from 2003, 3.2% of the cases had the following conditions as causes of UGIB: 2.1% had erosive duodenitis, 1 patient (0.2%) had angiodysplasia, 1 patient had Dieulafoy ulcer, and 2 patients had gastric polyps. In 1.4% of cases, the cause of bleeding was not detected.

In the group from 2010, 2.9% of cases did not reveal the source of bleeding. Angiodysplasia was present in 0.9% of the patients, erosive ulcer in 1.2% of patients, Dieulafoy ulcers in 0.7% of patients, polyps in 0.7% of patients, and other injuries in 0.3% of patients (1 patient had postoperative bleeding from the suture line, 1 had gastric antral vascular ectasia - GAVE, and 1 had gastrointestinal stromal tumor - GIST).

## Discussion

Similar to the general evolutionary trend observed in recent years in the epidemiology of upper gastrointestinal bleeding,

the patients included in the study also showed an increase in the mean age of patients with UGIB (Blatchford *et al* 1997; Vreeburg *et al* 1997; Pastasis *et al* 2000; Thomopoulos *et al* 2000).

In our study, there was an increase in the percentage of women among patients with UGIB from 2003 to 2010. In 2010, there was a 2:1 female/male ratio, similar to that observed in most studies (Longstreth *et al* 1995).

As shown by data in the literature, ulcers were also the most common causes of upper gastrointestinal bleeding in our study, followed by varicose veins.

Gastric ulcer has significantly prevailed in the elderly. This fact can be attributed to several factors that act synergistically in this population group: lower production of mucus, bicarbonate and prostaglandins, higher consumption of NSAIDs correlated with higher frequency of arthropathies at this age, frequent use of aspirin, clopidogrel and anticoagulants in this geriatric population, drugs needed to treat cardiovascular diseases. Not last, *Helicobacter pylori* infection is more common in elderly patients than in younger patients. The increase in the share of gastric ulcers in the elderly has been found by other authors as well (Blatchford *et al* 1997; Vreeburg *et al* 1997; Pastasis *et al* 2000; Czernichow *et al* 2000).

Regarding gender distribution, there was a significantly higher percentage of bleeding duodenal ulcers in men, similar to other results in the literature (Vreeburg *et al* 1997; Pastasis *et al* 2000; Thomopoulos *et al* 2000). Gastric ulcer was more common in women, most likely in combination with higher consumption of NSAIDs for various rheumatic diseases.

The share of duodenal ulcer was lower than that of gastric ulcer in both groups studied, probably due to increasing patient age and extensive use in primary care practices of both PPI therapy and screening for *H. pylori* infection and eradication of this infection in patients with dyspepsia. Predominance of gastric ulcer versus duodenal ulcer was also found by other authors.

The patients in the study group had variceal hemorrhage as the second cause of UGIB in terms of frequency in both groups. There was an increase in the share of variceal bleeding from 27.8% in 2003 to 34.8% in 2010. This percentage is higher than that described in the literature (4-20%) (Longstreth *et al* 1995; Blatchford *et al* 1997; Holster *et al* 2012) and it is due to the increased number of patients with liver cirrhosis caused by both viral infections and alcohol consumption in our geographic area. In a report published by WHO in 2004, mortality rate due to liver cirrhosis was 33.7 cases per 100,000 population in Romania, one of the highest in the world, but an EASL review from 2010 stated that the prevalence of hepatitis B in Romania is the highest in Europe (5.6%). The same situation is observed for hepatitis C, Romania and Italy being the first most affected countries in Europe (Blachier *et al* 2013). There are few other studies in the literature reporting such a high frequency in variceal bleeding (Dursun *et al* 2005; Kimm *et al* 2013). Similar results regarding the share of variceal bleeding were found in a study conducted in Turkey, also correlated with the higher rates of viral cirrhosis observed for the region (Dursun *et al* 2005). Age of patients with variceal bleeding was of lower than that of patients with non-variceal bleeding. Liver cirrhosis is a severe condition with high mortality as a consequence of its many complications, the life expectancy of patients with cirrhosis being lower than that of the general population.

Erosive gastritis predominated in women aged between 20 and 60 years, probably correlated with the consumption of alcohol and/or NSAIDs.

Gastroesophageal reflux disease affects all ages but is more common after 40 years. The frequency of esophagitis and esophageal ulcers was significantly higher in age groups over 40 years in the patients in our study group. In the age group of patients over 80 years, the diagnosis of esophagitis and esophageal ulcer was significantly more frequent than other diagnoses. Many elderly patients are treated with multiple drugs, which unless swallowed with a sufficient amount of liquid can result in esophageal ulcers and erosions. This is associated with increased consumption of NSAIDs and with the fact that the pathology of reflux disease is emphasized in some of these patients by the effects of extended supine position.

The percentage of cancers complicated with UGIB was similar to that described in several other studies (Longstreth *et al* 1995; Blatchford *et al* 1997). There were significantly more neoplasms among patients over 60 years of age and in male subjects, in consistency with the data in the literature on the epidemiology of gastric cancers. There was a highly significant decrease in the number of cases of upper gastrointestinal neoplasms found in our study from 2003 to 2010, this decrease being interpreted in the context of the general decline in the incidence of gastric cancer worldwide (Valean 2011).

In our study, the cause of bleeding was not identified in 1.4% of cases in 2003 and 2.9% of cases in 2010, a much lower percentage than that described in the literature (7-25%) (van Leerdam *et al* 2008).

## Conclusions

Upper gastrointestinal bleeding also tends to occur at an older age in our geographic region.

Gastric and duodenal ulcers are still the most common causes of upper gastrointestinal bleeding.

Unlike most data in the literature, the percentage of variceal bleeding was higher in our study, consistent with the large number of liver cirrhosis in our country compared to other countries. The percentage of upper gastrointestinal bleeding cancers has halved in the studied groups in the period between 2003 and 2010.

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