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Research Article

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Description of A Court of Adult Patients with High Digestive Bleeding of Non-Variceal Origin: Clinical Study Developed at Colombia University Clinic from 2016 – 2019

Patricia Olarte

Department of radiology, IBN TOUFAIL hospital, CHU Mohammed VI Marrakech, Marrakech, Morocco.

Department of general surgery, IBN TOUFAIL hospital, CHU Mohammed VI Marrakech, Marrakech, Morocco.

***Corresponding author**

Patricia Olarte, Department of radiology, IBN TOUFAIL hospital, CHU Mohammed VI Marrakech, Marrakech, Morocco. Department of general surgery, IBN TOUFAIL hospital, CHU Mohammed VI Marrakech, Marrakech, Morocco.

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Abstract

Introduction and objectives: *Upper gastrointestinal bleeding is considered a common emergency in gastroenterology and a large percentage corresponds to bleeding of non-variceal origin. The main objective of the study is to describe the characteristics of the patients with non-variceal bleeding admitted to the gastroenterology department of a fourth-level clinic.*

Materials and Methods: *A cross-sectional study was developed, which included all adult patients admitted to the Gastroenterology Unit at Colombia University Clinic between June 1, 2016 and on June 1, 2019, for endoscopic procedures aimed at analyzing upper digestive bleeding.*

Results: *Samples from 2.902 patients were collected, the average age being 59,68 years and the majority of participant's women. Regarding endoscopic findings, the most prevalent were gastric ulcer (36,32%), erosive bulboduodenitis (16,51%) and duodenal ulcer (16,33%). 12,85% of the patients used NSAIDs, 10,47% used antiplatelet agents and 6,65% were on anticoagulant treatment. When comparing the different types of treatment with the endoscopic findings of this study, significant differences were found in the frequency of gastric ulcer, which was much higher in patients using NSAIDs compared to those who were not receiving NSAIDs.*

Conclusions: *The results of this study are similar to those reported in the literature regarding endoscopic findings and risk factors to present upper gastrointestinal bleeding of non-variceal origin.*

Keywords: Non-variceal Upper Digestive Hemorrhage, Etiology (Q000209), Risk Factors (D012307), Observational Study (D064888), Colombia (D003105)

Introduction and Objectives

Upper gastrointestinal bleeding (UGIB) is considered a common emergency in gastroenterology. A prevalence of 48 to 160 cases per 100.000 inhabitants per year has been reported according to data published by Villanueva et al. [1, 2]. When analyzing the causes of this condition, bleeding secondary to peptic ulcer is the most frequent cause. According to a publication carried out in Montreal Canada in which the costs derived from the care of patients with UGIB were analyzed, these ranged between $3.000 - $6.000 for cases of uncomplicated and complicated non-variceal hemorrhage respectively and from $6.000 - $23.000 dollars for the subgroup of hemorrhage of variceal origin; the critical variable for the increase in the days of stay was the presence of rebleeding which determined a stay time between 2 and 4 days [3, 4]. Among the risk factors described for presenting UGIB are the consumption of non-steroidal anti-inflammatory drugs (NSAIDs) and the use of aspirin, which have been reported in about 50% of patients [4, 5]. In a study published in 2003 it was also reported that the mortality attributed to UGIB is between 10% and 14% [4]. In Colombia, a retrospective cohort study was carried out in the city of Medellín in 2011 in which the risk factors for mortality in 464 patients with UGIB were described. The main cause of bleeding was peptic ulcer (41%) followed by erosive gastropathy (34,9%) and variceal bleeding (10,1%). The presence of bleeding in hospitalized patients and the number of comorbidities were associated with higher mortality [6]. Due to the scarce information around the

characterization of UGIB cases in Colombia this study was proposed, which aims to describe the characteristics of adult patients with non-variceal UGIB admitted to the Gastroenterology Service at Colombia University Clinic in a period of 3 years. Among the specific objectives of the study are characterizing the sociodemographic profile of patients, describing the risk factors of the population and the endoscopic findings, detailing the frequency of the endoscopic findings according to previous pharmacological treatment associated with the highest risk of upper digestive bleeding, and calculating the prevalence of non-variceal upper gastrointestinal bleeding in the population of patients admitted for endoscopic procedures between June 2016 and June 2019.

Materials and Methods

An observational, descriptive, cross-sectional study was developed, which included all adult patients admitted to the Gastroenterology Unit at Colombia University Clinic between June 1, 2016 and June 1, 2019, for endoscopy of the upper digestive tract aimed at analyzing UGIB.

Selection criteria

- Inclusion criteria: Clinical records of patients over 18 years of age who underwent diagnostic or therapeutic endoscopy, presented digestive bleeding symptoms, were diagnosed non-variceal UGIB and accepted the use of data through the signing of an informed consent.
- Exclusion criteria: Records of patients with an incomplete medical history or that did not allow an adequate interpretation, as well as records of patients taken to endoscopy in which overlapping findings of coexisting variceal and non-variceal bleeding were documented.

Statistical Analysis

To guarantee the quality control of the registered information, data analyzed by 2 independent observers was recorded. After data collection, adequate registration of the data was verified according to the type of variable, its definition and its codification. With the data obtained in the characterization variables of the sample, the distribution by relative frequencies and percentages was determined for the qualitative variables, and measures of central tendency and dispersion such as mean, median, mode and standard deviation were obtained for the quantitative variables. For these variables, correspondence to a normal distribution was evaluated using the Shapiro Wilk test under a significance level of 5% ($p < 0,05$). For nominal variables, based upon the objective the presence or absence of association was analyzed using the Chi-Square test. Statistical software STATA 11 was used to analyze the data.

Ethical Considerations

The research complies with current regulations on bioethical research and the protocol obtained the authorization of the Research Ethics Committee of the Keralty Organization, to which Colombia University Clinic belongs.

Results

Initial Features: Samples were collected from 2.902 adult patients who underwent upper digestive tract endoscopy at Colombia University Clinic between June 1, 2016 and June 1, 2019, aimed at analyzing UGIB of non-variceal origin. During this period, 48.118 endoscopies of upper digestive tract were performed, with prevalence of UGIB being 6,03%. The average age was 59,68 years with a standard deviation of 19,25 years and 51,41% of the patients were women (Table 1). Regarding the age distribution, more than 50% of the patients were over 60 years old and the oldest patient was 102 years old (Figure 1). 35,42% of patients in the study were included in 2018, 27,95% in 2017 and about 18% in both 2016 and 2019 (Figure 2). Regarding the indication for endoscopy, the most frequent reason was upper gastrointestinal bleeding with 35,84%, followed by anemia with 27,39% and melena with 18,26% (Table 2).

Table 1: Initial characteristics of patients

Characteristics	n = 2902
Age in years, mean (DE)	59,68 (19,25)
Women, number (%)	1492 (51,41)
Year endoscopic procedure was performed	
Year 2016, number (%)	535 (18,44)
Year 2017, number (%)	811 (27,95)
Year 2018, number (%)	1028 (35,42)
Year 2019, number (%)	528 (18,19)

Table 2: Indication for performing upper digestive tract endoscopy

Indication	Total n = 2902
Upper digestive bleeding, number (%)	1040 (35,84)
Anemy with or without iron deficiency, number (%)	795 (27,39)
Manes, number (%)	530 (18,26)
Hematemesis, number (%)	287 (9,89)
Digestive bleeding study, number (%)	66 (2,27)
Lower digestive tract bleeding, number (%)	62 (2,14)
Hematochezia, number (%)	55 (1,90)
Ulcers, number (%)	38 (1,31)
Positive hidden blood, number (%)	10 (0,34)
Trombophilia, number (%)	5 (0,17)
Melanemesis, number (%)	4 (0,14)
Esophageal varices, number (%)	3 (0,10)
Suspected midgut bleeding, number (%)	2 (0,07)
Post-papillotomy bleeding, number (%)	2 (0,07)
Vasculitis, number (%)	1 (0,03)
Mallory-Weiss syndrome, number (%)	1 (0,03)
Gastrostomy site bleeding, number (%)	1 (0,03)

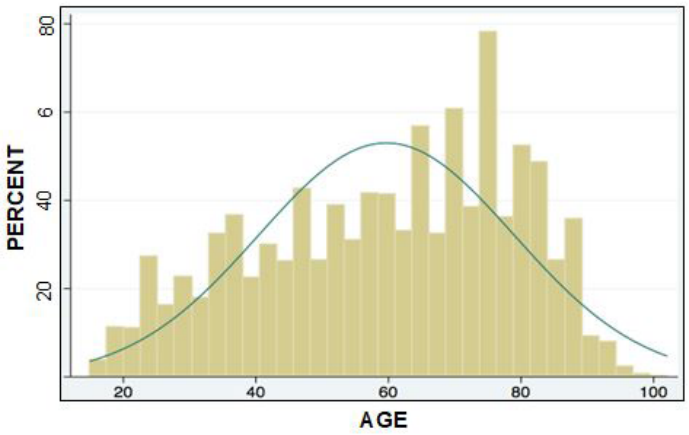

Figure 1: Patients' age distribution

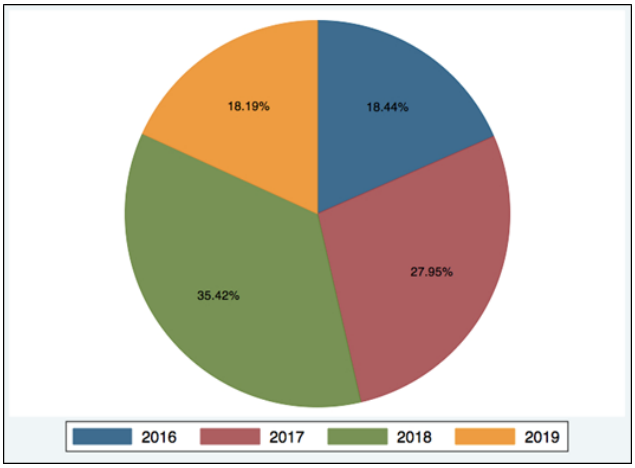

Figure 2: Year procedure was performed

Endoscopic Findings: When analyzing the endoscopic findings of the 2902 patients, presence of gastric ulcer was documented in 36,32% of patients, erosive bulboduodenitis in 479 patients, and duodenal ulcer in 16,33% of patients. The least frequent causes were Cameron ulcers (1,72%), Dieulafoy lesions (0,93%) and stomach in watermelon (0,69%). Neoplasms were reported as a cause of upper gastrointestinal bleeding in 5,82% of patients (Table 3).

Table 3: Findings from endoscopy of upper digestive tract

Endoscopic findings	Women n = 1492	Men n = 1410	Total n = 2902
Gastric ulcer, number (%)	591 (39,61)	463 (32,84)	1054 (36,32)
Erosive bulboduodenitis, number (%)	222 (14,88)	257 (18,23)	479 (16,51)
Duodenal ulcer, number (%)	243 (16,29)	231 (16,38)	474 (16,33)
Grade D esophagitis, number (%)	184 (12,33)	216 (15,32)	400 (13,78)
Neoplasms, number (%)	83 (5,56)	86 (6,10)	169 (5,82)
Bleeding from the anastomosis, number (%)	50 (3,35)	34 (2,41)	84 (2,89)
Mallory-Weiss syndrome, number (%)	28 (1,88)	44 (3,12)	72 (2,48)
Angiodysplasias, number (%)	40 (2,68)	31 (2,20)	71 (2,45)
Cameron's ulcers, number (%)	26 (1,74)	24 (1,70)	50 (1,72)
Dieulafoy's injuries, number (%)	11 (0,74)	16 (1,13)	27 (0,93)
Stomach in watermelon, number (%)	12 (0,80)	8 (0,57)	20 (0,69)
Other, number (%)	2 (0,13)	0 (0)	2 (0,07)

Risk Factors: When analyzing the drugs and the underlying diseases of patients, it was documented that 12,85% used non-steroidal anti-inflammatories, 10,47% antiplatelet agents - the most frequent being aspirin - and 6,65% were on anticoagulant treatment - the most frequent one involving the use of enoxaparin. It is striking that about 40% of the patients were on a proton pump inhibitor treatment (Table 4). Figure 3 shows the percentage of patients with each of the basic treatments that have been said to increase the risk of digestive bleeding, sorted by sex. The percentage of men and women receiving each of the treatments is very similar. Among other risk factors for the presence of upper digestive bleeding are comorbidities. 38,38% of patients had been diagnosed hypertension and 10,47% of them had a history of coronary heart disease. Few cases of patients with other cardiovascular diseases were reported (Table 5).

Table 4: Basic treatment of patients

Basic pharmacological treatment	n = 2902
Proton pump inhibitor, number (%)	1133 (39,04)
Non-steroidal anti-inflammatory drugs, number (%)	373 (12,85)
Antiplatelets, number (%)	304 (10,47)
Anticoagulants, number (%)	193 (6,65)
Type of anticoagulant	n = 193
Enoxaparin, number (%)	175 (90,67)
Heparin, number (%)	9 (4,66)
Warfarin, number (%)	9 (4,66)
Type of antiplatelet	n = 304
Aspirin, number (%)	270 (88,81)
Clopidogrel, number (%)	34 (11,18)

Table 5. Additional risk factors for digestive bleeding

Risk factor	n = 2902
Arterial hypertension	1114 (38,38)
Coronary heart disease	304 (10,47)
Acute myocardial infarction, number (%)	5 (0,17)
Atrial fibrillation, number (%)	4 (0,14)
Valve replacement, number (%)	4 (0,14)
Deep vein thrombosis, number (%)	2 (0,07)

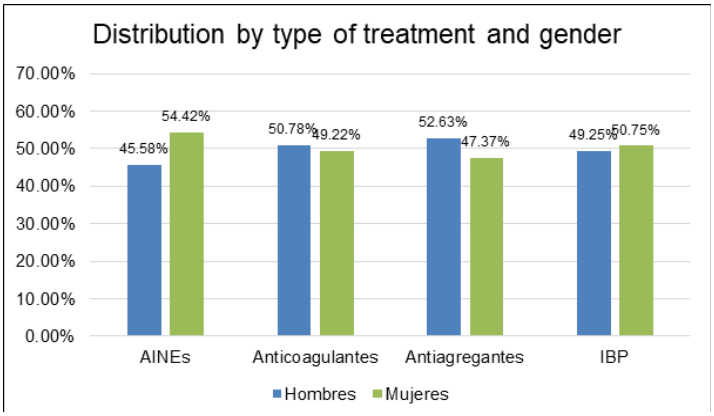

Figure 3: Distribution by type of treatment and gender

Previous Treatment Versus Endoscopic Findings

An analysis of the base pharmacological treatment of patients and of the presence or not of association with the endoscopic findings was performed applying the Chi-Square test. When comparing the endoscopic findings and the previous use or not of anticoagulants, it was found that the presence of erosive bulboduodenitis was reported in 17,65% of patients who did not use anticoagulants versus 4,15% of the patients who did use them, this difference being statistically significant. Also, the frequency of neoplasms in patients who used anticoagulants was higher (21,24%) versus those who did not use anticoagulants (4,72%), this difference being statistically significant as well. The remaining endoscopic findings did not have a statistically significant difference with respect to the base anticoagulant treatment (Table 6).

Table 6. Use of anticoagulants vs Endoscopic findings

Most frequent endoscopic findings	Use of anticoagulants YES (n = 193)	Use of anticoagulants NO (n = 2709)
Gastric ulcer, number (%)	64 (33,16)	990 (36,54)
Erosive bulboduodenitis, number (%)	8 (4,15)	471 (17,39)
Duodenal ulcer, number (%)	33 (17,10)	441 (16,28)
Grade D esophagitis, number (%)	27 (13,99)	373 (13,77)
Neoplasms, number (%)	41 (21.24)	128 (4,72)

304 study patients were on antiplatelet therapy, with aspirin being the most common. The presence of gastric ulcer was documented in 42,11% of patients who received antiplatelet therapy compared to 35,64% of patients without antiplatelet therapy, this difference meeting statistical significance with a p value of 0,027. A significant difference was also found regarding the frequency of erosive bulboduodenitis, it being higher in patients who did not use antiplatelet agents (Table 7). NSAIDs are drugs that increase the risk of upper digestive bleeding. 12.85% of patients in the study were being treated with this type of medication. Gastric ulcer was documented in 53,89% of patients using NSAIDs versus 33,73% of patients who did not use them, this difference being statistically significant. Presence of erosive bulboduodenitis was more frequent in patients who had not been using NSAIDs (17,67%) compared to the group of patients who had been using them previously (8,58%) (Table 8). Finally, the frequency of use of a proton pump inhibitor (PPI) was compared with the most frequent endoscopic findings. Frequency of patients with erosive bulboduodenitis and grade D esophagitis was higher in the group of patients who were not undergoing treatment with PPI, these differences being statistically significant. Regarding the report of malignancies, 7,03% of the patients undergoing PPI presented findings suggestive of neoplasia versus 5,03% of the patients without prior use of PPI, this difference being statistically significant (Table 9).

Table 7: Use of antiplatelets vs Endoscopic findings

Most frequent endoscopic findings	Use of antiplatelets YES (n = 304)	Use of antiplatelets NO (n = 2598)
Gastric ulcer, number (%)	128 (42,11)	926 (35,64)
Erosive bulboduodenitis, number (%)	33 (10,86)	446 (17,17)
Duodenal ulcer, number (%)	44 (14,47)	430 (16,55)
Grade D esophagitis, number (%)	42 (13,82)	358 (13,78)
Neoplasms, number (%)	18 (5,92)	151 (5,81)

Table 8: Use of non-steroidal anti-inflammatories vs Endoscopic findings

Most frequent endoscopic findings	Use of AINEs YES (n = 373)	Use of AINEs NO (n = 2529)
Gastric ulcer, number (%)	201 (53,89)	853 (33,73)
Erosive bulboduodenitis, number (%)	32 (8,58)	447 (17,67)
Duodenal ulcer, number (%)	55 (14,75)	419 (16,57)
Grade D esophagitis, number (%)	40 (10,72)	360 (14,23)
Neoplasms, number (%)	16 (4,29)	153 (6,05)

Table 9: Use of proton pump inhibitor vs Endoscopic findings

Most frequent endoscopic findings	Use of IBPs YES (n = 1133)	Use of IBPs NO (n = 1769)
Gastric ulcer, number (%)	429 (37,86)	625 (35,33)
Erosive bulboduodenitis, number (%)	147 (12,97)	332 (18,77)
Duodenal ulcer, number (%)	186 (16,42)	288 (16,28)
Grade D esophagitis, number (%)	136 (12)	264 (14,92)
Neoplasms, number (%)	80 (7,06)	89 (5,03)

Discussion and Conclusions

Upper gastrointestinal bleeding is considered a common emergency in gastroenterology and 80% of cases correspond to bleeding of non-variceal origin [1-7]. In the present study, the prevalence of the different endoscopic findings and risk factors for the presence of UGIB of non-variceal origin was calculated in 2.902 adult patients with upper gastrointestinal bleeding, who were evaluated through endoscopy of the upper digestive tract at the Gastroenterology Unit of Colombia University Clinic in Bogotá, in the last 3 years.

The average age of patients was 59 years, a condition similar to that reported in a Colombian study published in 2011 that included 464 patients with UGIB in Medellín, Colombia. In our study, the most frequent cause of UGIB of non-variceal origin was gastric ulcer followed by erosive bulboduodenitis and duodenal ulcer, which is consistent with previous publications where these endoscopic findings are the most frequent followed by vascular lesions and ectasias [8-10].

Regarding the risk factors associated with these causes of UGIB, NSAIDs and aspirin induce damage to the gastroduodenal mucosa, which increases in cases where patients present H. pylori infection (5,10). In our study, 12,85% of patients were using NSAIDs and 10,47% antiplatelets, the most frequent type being aspirin. According to a publication by van Leerdam, NSAIDs use among patients with high gastrointestinal bleeding ranged from 29% to 60% in Europe [11].

More recently, in a 2014 publication analyzing the behavior of consumption of NSAIDs and aspirin as a risk factor for peptic ulcer in 1007 patients in Germany, it was reported that the prevalence of consumption of these drugs increased from 37,5% to 47% between 2001 and 2010, this difference being statistically significant [12, 13].

In 2019, Lenti et al. published a study that described the mortality rate and risk factors for gastrointestinal bleeding in 3.872 patients older than 65 years, where an association was found between the consumption of non-aspirin antiplatelets, the diagnosis of liver cirrhosis and a high comorbidity score, with an increased risk of digestive bleeding [14]. In our study, the frequency of use of anticoagulants was 6,65% and the frequency of use of antiplatelet agents was 10,47%. Additionally, more than a third of the patients had high blood pressure and about 10% had coronary heart disease, comorbidities that increased the risk of bleeding.

Burr and collaborators published a meta-analysis on the risk of digestive bleeding with direct-acting anticoagulants, in which they found no difference between the risk with the use of warfarin versus low molecular weight heparin such as enoxaparin [15]. In this study, 90,67% of the anticoagulated patients were receiving enoxaparin, a low molecular weight heparin. When analyzing the group of patients with atrial fibrillation, Xu et al. reported that the use of warfarin significantly increased the risk of bleeding compared to other oral anticoagulants such as dabigatran [16].

When comparing the different types of treatment with the endoscopic findings of this study, significant differences were found in the frequency of gastric ulcer, which was much more frequent in patients using NSAIDs compared to that of those not receiving NSAIDs. This matches reports from literature stating that the risk of upper gastrointestinal bleeding increases by up to 10% in patients with this type of medication [17, 18].

Finally, in this study the presence of erosive bulboduodenitis was higher in patients who were not undergoing treatment with anticoagulants, antiplatelet agents or NSAIDs. According to the literature, peptic duodenitis is the result of an excess of gastric acid in the proximal duodenum, which in about 44% of patients is secondary to H. pilory infection [19, 20]. It is likely that for this reason the finding of this type of injury was not so frequent in patients participating in this study.

In conclusion, the characteristics of patients in this study are similar to those reported in the literature. Peptic ulcer, erosive bulboduodenitis, and duodenal ulcer were the most frequent findings in our study, which is consistent with previous publications. Prevalence of the use of NSAIDs, antiplatelet agents and anticoagulants as risk factors for the presence of gastric ulcer was significant.

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