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ORIGINAL RESEARCH

Predictors of In-Hospital Mortality in *Helicobacter pylori*–Negative, Non-Variceal Upper Gastrointestinal Bleeding: A Retrospective Cohort Study

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Purpose: With the global decline in *Helicobacter pylori* infection, upper gastrointestinal bleeding (UGIB) is increasingly driven by non-infectious, non-Nonsteroidal Anti-Inflammatory Drug (NSAID) mechanisms, particularly antithrombotic use and comorbidity-related mucosal injury. This study aimed to characterize the etiology, clinical profile, and in-hospital mortality predictors in patients with *H. pylori*-negative, non-variceal UGIB in a Colombian tertiary care setting.

Patients and Methods: We conducted a retrospective cohort study at a quaternary hospital in Barranquilla, Colombia, including all adults (≥18 years) hospitalized with endoscopically confirmed non-variceal UGIB and negative *H. pylori* testing (rapid urease test and/or histology). Clinical, endoscopic, and medication data were analyzed.

Results: Of 285 patients, the median age was 60 years (IQR: 39–73), and 54% were male. NSAID use was rare (2.8%), whereas antithrombotic exposure was prevalent (28.8%), including low-dose aspirin (18.2%) and dual antiplatelet therapy (4.9%). The most common endoscopic findings were erosive gastropathy (45%) and ulcers (12%). Overall in-hospital mortality was 5% (n=13). In multivariable analysis, age >60 years (aOR: 2.9; 95% CI: 1.7–10.2; p = 0.05), cardiovascular complications (aOR: 7.8; 95% CI: 1.9–32.0; p = 0.004), encephalopathy (aOR: 8.5; 95% CI: 2.2–33.0; p = 0.009), and antiplatelet plus anticoagulant therapy (aOR: 5.3; 95% CI: 1.6–17.5; p = 0.006) were independently associated with in-hospital mortality.

Conclusion: In this cohort, in-hospital mortality in non-variceal UGIB patients without *H. pylori* infection was associated with systemic factors such as advanced age, cardiovascular complications, encephalopathy, and antiplatelet–anticoagulant combination therapy rather than bleeding lesions. These findings support risk stratification based on comorbidities and medication use in this growing population.

Keywords: upper gastrointestinal bleeding, *Helicobacter pylori*, in-hospital mortality, anticoagulant therapy, melena, hematemesis

Introduction

Upper gastrointestinal bleeding (UGIB) is a common medical emergency with significant clinical and epidemiological implications. It remains a major cause of hospitalization, blood transfusion, and mortality worldwide.[1] Historically, peptic ulcer disease secondary to *Helicobacter pylori* infection has been the most prevalent etiology of UGIB, particularly in developing regions.[2] However, the prevalence of *H. pylori* has progressively declined in many populations due to eradication campaigns, improved sanitary conditions, and the widespread use of proton pump inhibitors, which has altered the etiological profile of UGIB.[3]

UGIB is broadly classified into variceal and non-variceal etiologies.[4] The most common causes of non-variceal UGIB include peptic ulcer disease, gastritis/duodenitis (erosive or hemorrhagic), vascular lesions (eg., angiodysplasia, Dieulafoy's lesion), malignancies, and bleeding related to antithrombotic or anti-inflammatory therapy.[5] Although *H. pylori* infection is not a direct cause of UGIB, it is a well-established etiological factor for bleeding peptic ulcers and chronic active gastritis, which may

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predispose to hemorrhage.[6] Importantly, *H. pylori*-associated gastritis is typically non-erosive and distinct from the erosive-hemorrhagic gastritis frequently observed in Nonsteroidal Anti-Inflammatory Drug (NSAID) users or critically ill patients.[6] Notably, persistent *H. pylori* infection in the context of NSAID use has been linked to a higher risk of recurrent bleeding, underscoring the complex interplay between infectious, pharmacological, and mucosal factors in UGIB pathogenesis.[4,6]

Accurate diagnosis of *H. pylori* infection during acute UGIB is challenging. The rapid urease test (RUT), commonly used at endoscopy, has reduced sensitivity due to blood, recent proton pump inhibitor (PPI) use, and mucosal disruption, often yielding false-negative results.[7,8] Test accuracy improves when biopsies are obtained ≥48 hours after hemostasis.[7,9] Accordingly, guidelines recommend deferring *H. pylori* testing or using alternative methods (histology, stool antigen, or urea breath test) after the acute phase.[6,9] In clinical practice, however, many patients are classified as *H. pylori*-negative based solely on a negative RUT during index endoscopy, potentially leading to misclassification.[6]

This has contributed to a rise in *H. pylori*-negative UGIB, increasingly driven by antithrombotic therapy, comorbidities (cardiovascular, metabolic, hepatic), and advanced age rather than NSAIDs alone.[10] Bleeding peptic ulcers still occur in this group, often idiopathically or due to antiplatelet/anticoagulant use.[4,6] Endoscopically, lesions range from ulcers (classified by Forrest criteria[7]) to non-ulcerative mucosal injury, including erosive gastropathy and vascular lesions linked to endothelial dysfunction.[7,11] This heterogeneity underscores the need for a focused characterization of *H. pylori*-negative UGIB to guide personalized management.[4]

Clinically, advanced age and male sex have been linked to worse outcomes in UGIB, though gender differences may reflect comorbidity burden rather than biological factors.[12] Hypertension, type 2 diabetes, and chronic kidney disease are the most prevalent comorbidities, all associated with higher bleeding risk and impaired hemodynamic response.[13,14] In *H. pylori*-negative UGIB, these conditions contribute not only to mucosal injury but also to more complex clinical courses and greater care needs.[6] Presentation with hematemesis typically indicates acute, high-volume bleeding, whereas melena often reflects slower, distal bleeding, commonly seen in older patients with altered gastrointestinal transit.[15,16] Although initial symptoms may influence diagnostic and therapeutic timeliness, mortality in UGIB is now driven less by the bleeding source and more by systemic factors.[15,17]

Despite advances in endoscopic and multidisciplinary care, in-hospital mortality remains significant, particularly in patients with comorbidities or organ failure.[7,16] Age >60 years, cardiovascular events, and encephalopathy are well-established mortality predictors and are incorporated into validated scores such as Rockall,[18] Glasgow-Blatchford,[19] and AIMS65.[20] Timely recognition of these factors is critical for risk stratification and resource optimization. This study aims to characterize the etiology, clinical profile, and independent predictors of in-hospital mortality in patients with *H. pylori*-negative, non-variceal UGIB at a quaternary hospital in Colombia, with a focus on comorbidity burden, antithrombotic exposure, and systemic risk thereby addressing a key evidence gap in Latin American gastroenterology.

Materials and Methods

Study Population and Sample

A retrospective, observational, and analytical study was conducted at a fourth-level referral hospital located in Barranquilla, Atlántico (Colombia), between January 1, 2021, and December 31, 2023. Inclusion criteria were: (i) age ≥18 years; (ii) clinical suspicion of UGIB, defined by the presence of hematemesis, coffee-ground emesis or gastric aspirate, melena, or maroon stool (in cases suggestive of rapid or massive upper GI bleeding); and (iii) confirmation of UGIB by esophagogastroduodenoscopy performed during the index hospitalization, showing a visible source of bleeding (eg., ulcer, erosive gastritis, vascular lesion).

Cases were initially identified through the hospital's electronic medical records using ICD-10-CM diagnosis codes for UGIB: K92.0 (hematemesis), K92.1 (melena), and K92.2 (gastrointestinal hemorrhage, unspecified). This automated query retrieved all patients potentially diagnosed with UGIB during the study period. All retrieved records were then manually reviewed by two independent investigators to verify eligibility.

All included patients were in-patients in whom active *H. pylori* infection was ruled out during the index endoscopy using direct diagnostic methods on gastric biopsies: RUT in 248 patients (87.0%), histopathological examination (hematoxylin-eosin and/or Giemsa staining) in 212 patients (74.4%), or both in 175 patients (61.4%). A patient was

classified as *H. pylori*-negative if all performed tests were negative. Indirect tests (serum IgG, stool antigen, urea breath test) were not used during acute hospitalization, per current guidelines.[9]

Patients were excluded if they had variceal bleeding (esophageal or gastric, of portal or hepatocellular origin), a confirmed *H. pylori* infection during hospitalization or follow-up, incomplete records, significant missing data, or readmission for recurrent UGIB within the same episode. A census sampling strategy was used, identifying all eligible cases from electronic medical records and departmental databases (Gastroenterology and Internal Medicine).

Variables

The variables were defined and classified into sociodemographic, clinical, paraclinical, outcome, and diagnostic categorization domains. Sociodemographic variables included age (in years, analyzed as both a continuous and dichotomous variable: ≤60 and >60 years), with the cut-off selected based on its inclusion in validated UGIB prognostic scores (eg., Rockall and AIMS65) and its established association with increased mortality risk in UGIB;[18,20,21] sex (male or female), and health insurance affiliation scheme.

Clinical variables encompassed the initial presentation of UGIB, categorized as: (i) hematemesis (with or without melena) or (ii) melena without hematemesis (ie., isolated melena). Additional clinical variables included vital signs at admission (blood pressure, heart rate) and comorbidities including hypertension, type 2 diabetes mellitus, chronic kidney disease, liver cirrhosis, ischemic heart disease, decompensated heart failure, prior ischemic stroke, active malignancy, as well as NSAID or antithrombotic use, all identified through documented medical history and medication reconciliation at admission. Validated prognostic scores including the admission Rockall score[18] were calculated for all patients using available admission data.

Paraclinical variables included endoscopic and histopathological findings, categorized as gastric or duodenal ulcer, chronic gastritis, vascular lesions, or other diagnoses based on available biopsy reports. Medical complications during hospitalization were also recorded and defined as follows: (1) cardiovascular events: acute coronary syndrome, acute heart failure, or clinically significant arrhythmias confirmed by clinical assessment and supporting diagnostics (ECG, troponin, or echocardiography); (2) pneumonia: new pulmonary infiltrate on chest imaging plus at least one of: fever (>38°C), leukocytosis (>11,000/μL), or purulent respiratory secretions;[22] (3) Complicated urinary tract infection (UTI): positive urine culture with systemic signs such as fever, leukocytosis, or sepsis;[23] (4) Acute kidney injury (AKI): defined according to KDIGO criteria as an increase in serum creatinine by ≥0.3 mg/dL within 48 hours or a 1.5-fold rise from baseline known or presumed to have occurred within the prior 7 days;[24] and (5) encephalopathy: acute altered mental status not attributable to primary neurological disease, classified as hepatic (in cirrhotic patients with elevated ammonia), septic/metabolic (in the context of infection or organ failure), or unspecified.[23]

The primary outcome was in-hospital mortality (discharge status: survivor vs. deceased). Additional Outcome variables included length of hospital stay, categorized based on institutional clinical care pathways and literature-derived benchmarks for UGIB: expected stay (≤3 days) reflects uncomplicated cases eligible for early discharge; adjusted stay (4–7 days) represents standard recovery; and prolonged stay (>7 days) indicates complications, clinical instability, or need for extended monitoring.[17]

Ethical Considerations

The *Research Ethics Committee* of Clínica de la Costa, through Minute No. 527 of 2025, and the *Institutional Review Board* of the Faculty of Health Sciences at Universidad Simón Bolívar, through Minute No. 640–017-2025, approved the conduct of this study. In accordance with Resolution 8430 of 1993 issued by the Colombian Ministry of Health, the study was classified as risk-free, as it was a documentary, observational, and retrospective investigation based solely on the review of medical records. Therefore, both committees authorized access to and analysis of the data without requiring informed consent from patients, in compliance with the ethical regulations applicable to this type of research.

Statistical Analysis

The normality of continuous variables was assessed using the Kolmogorov–Smirnov test. As all continuous variables showed non-normal distributions, they are reported as median (range). Categorical variables are presented as absolute

and relative frequencies. To compare continuous variables (eg., age, length of stay) between two independent groups (eg., female vs. male; hematemesis vs. melena; survivors vs. non-survivors), the Wilcoxon rank-sum test was used. For comparisons across three or more groups (eg., hospital stay categories: expected, adjusted, prolonged), the Kruskal–Wallis test was applied. Associations between categorical variables were evaluated using Pearson's chi-squared test or Fisher's exact test when expected cell counts were <5. Given the exploratory nature of the study and the low number of events (n=13 deaths), a sample size calculation was not performed a priori; however, post hoc analysis indicated that our cohort provided sufficient power (≥80%) to detect large effect sizes (OR ≥3) for major predictors.

Multivariable logistic regression was used to identify factors independently associated with in-hospital mortality. Candidate variables for the initial model were selected based on clinical relevance and univariable analysis ($p < 0.20$). A backward stepwise elimination procedure was applied, removing the least significant variable at each step ($p > 0.05$) until only statistically significant predictors ($p < 0.05$) remained in the final model. This approach balances model parsimony and predictive accuracy in settings with limited events. All analyses were conducted using R (version 4.3.0),[25] and a two-sided p-value < 0.05 was considered statistically significant.

Results

Baseline Characteristics

Of 342 patients initially identified through ICD-10 codes, 285 met all inclusion criteria and were included in the final analysis. The main reasons for exclusion were variceal bleeding (n=18), confirmed *H. pylori* infection (n=12), incomplete medical records (n=15), misclassified lower gastrointestinal bleeding (n=7), and recurrent bleeding within the same hospitalization (n=5) (Figure 1).

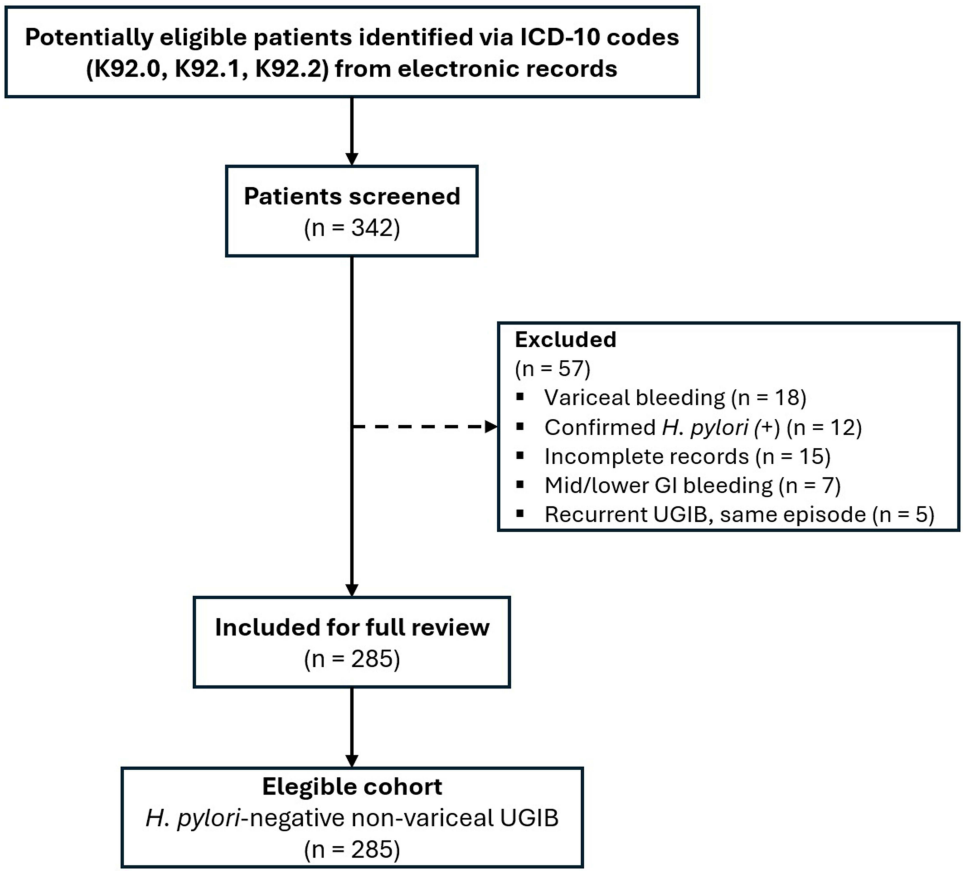

Figure 1 Study Flow Diagram of Patient Selection.

The cohort consisted of 285 adults (median age 60 years, IQR 39–73; 54% male) hospitalized for *H. pylori*-negative, non-variceal UGIB (Table 1). Hematemesis (± melena) was the most common presentation (53%), followed by isolated melena (47%). The median length of stay was 6 days (IQR 3–15), and the admission Rockall score was 2 (IQR 1–3).

Table 1 Baseline Characteristics of Hospitalized Patients with *H. pylori*-Negative Non-Variceal UGIB

Characteristics	Overall N = 285[a]
Age, years	60 [39–73]
Sex	
Female	130 (46%)
Male	155 (54%)
Length of Hospital Stay, days	6 [3–15]
Admission	
Hematemesis (± melena)	150 (53%)
Isolate Melena	135 (47%)
Rockfall score	2 [1–3]
Comorbidities	
HTN	120 (42%)
T2DM	48 (17%)
CKD	24 (8.4%)
Liver Cirrhosis	12 (4.2%)
Treatment	
NSAID Use	8 (2.8%)
Low-dose aspirin (75–100 mg/day)	52 (18.2%)
DAPT	14 (4.9%)
Vitamin K antagonists	9 (3.2%)
DOACs	7 (2.5%)
Complications	
CV	23 (8.1%)
Pneumonia	9 (3.2%)
Complicated UTI	9 (3.2%)
AKI	16 (5.6%)
Encephalopathy	3 (1.1%)
Biopsy Report	
Acute Gastritis	45 (16%)
Chronic Gastritis	84 (29%)
Congestive Gastritis	30 (11%)
Follicular Gastritis	8 (2.8%)
GIU	35 (12%)
Forrest Classification*	
IA	2 (5.4%)
IB	5 (14%)
IIA	7 (19%)
IIB	1 (2.7%)
IIC	3 (8.1%)
III	19 (51%)

Notes: [a]Median [Q1–Q3]; n (%). *Forrest classification was applied only to patients with endoscopically confirmed peptic or gastrointestinal ulcers.

Abbreviations: HTN, Arterial Hypertension; T2DM, Type 2 Diabetes Mellitus; CKD, Chronic Kidney Disease; AKI, Acute Kidney Injury; CV, Cardiovascular (Heart failure, Ischemic heart disease); UTI, Urinary Tract Infection; GIU, Gastrointestinal Ulcer; DAPT, Dual antiplatelet therapy; DOAC, Direct oral anticoagulants.

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Comorbidities were prevalent: hypertension (42%), type 2 diabetes (17%), and chronic kidney disease (8.4%). Notably, NSAID use was rare (2.8%), whereas antithrombotic exposure was common (28.8%), including low-dose aspirin (18.2%), dual antiplatelet therapy (DAPT) (4.9%), vitamin K antagonists (3.2%), and direct oral anticoagulants (DOACs) (2.5%). Endoscopically, only 12% of cases showed overt ulcers; the majority presented with erosive or hemorrhagic gastropathy (45%), vascular lesions (6%), or non-specific mucosal irritation (35%).

Endoscopically, the most common findings were erosive or hemorrhagic gastropathy (45%) and non-specific mucosal irritation (35%), with gastrointestinal ulcers present in only 12% of cases and vascular lesions (eg., angiodysplasia, Dieulafoy's) in 6%. Among the 35 patients with ulcers, the Forrest classification revealed that the majority had low-risk stigmata (Forrest III, 51%).

Histopathological findings showed that gastrointestinal ulcers were significantly more common in patients with isolated melena than in those with hematemesis (± melena) (17% vs. 8%; p = 0.023), whereas chronic gastritis was the most frequent finding overall and did not differ significantly between groups (33% vs. 26%; p = 0.23) (Figure 2). Additionally, patients with isolated melena were more likely to have an adjusted-length hospital stay (58% vs. 42%), while those with hematemesis (±melena) more often experienced prolonged stays (54% vs. 46%) (p = 0.03 for both comparisons).

Factors Associated with In-Hospital Mortality

The overall in-hospital mortality rate was 5% (n=13). Deceased patients were significantly older (median 76 vs. 60 years; p=0.003) (Figure 3) and had a higher admission Rockall score (median 4 vs. 2; p<0.001) compared to survivors (Table 2). Antithrombotic use was markedly higher in non-survivors: low-dose aspirin (62% vs. 16%, p<0.001), DAPT (31% vs. 3.7%, p<0.001), and DOACs (38% vs. 4.0%, p<0.001). In contrast, NSAID use did not differ significantly (7% vs. 2.6%, p=0.34). Key complications associated with death included cardiovascular events (38% vs. 6.6%, p=0.002), acute kidney injury (23% vs. 4.8%, p=0.029), and encephalopathy (15% vs. 0.4%, p=0.006). Chronic kidney disease was also more

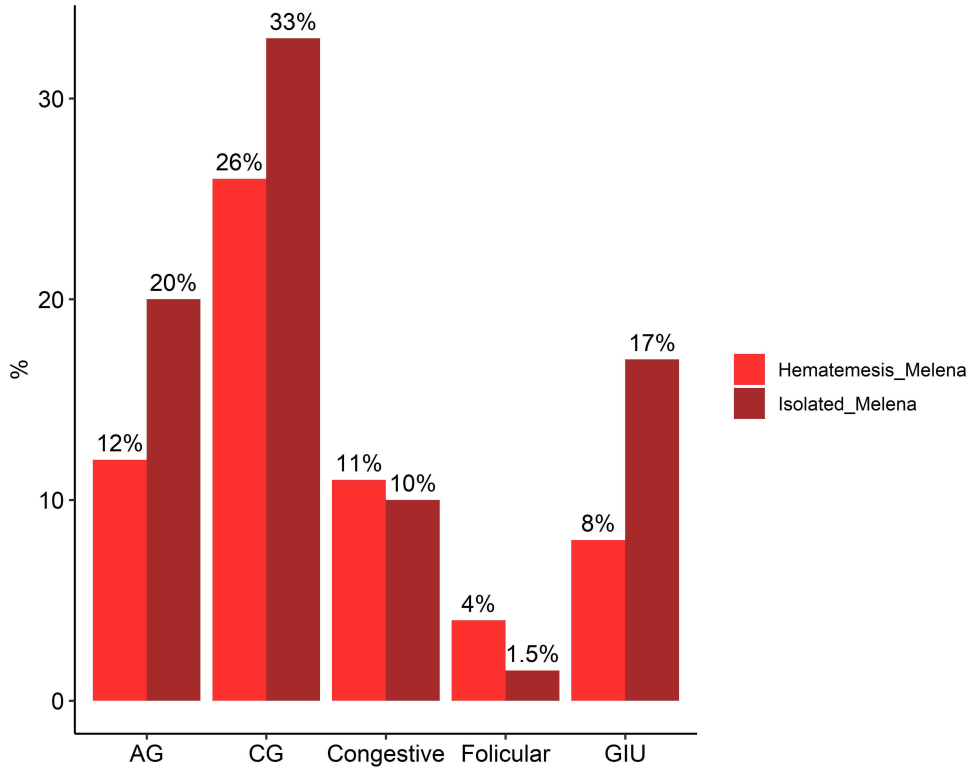

Figure 2 Distribution of histopathological findings in non-variceal UGIB without *Helicobacter pylori* infection, by admission diagnosis (isolated melena vs. hematemesis ± melena).

Abbreviations: UGIB, Upper Gastrointestinal Bleeding; AG, Acute Gastritis; CG, Chronic Gastritis; GIU, Gastrointestinal Ulcer.

Figure 3 Comparison of age (left) and hospital stay duration (right) between deceased and surviving patients with non-variceal UGIB without *H. pylori* infection.
Abbreviation: UGIB, Upper Gastrointestinal Bleeding.

frequent among deceased patients (31% vs. 7.4%, p=0.017). There were no significant differences in sex, admission diagnosis (hematemesis vs. isolated melena), hospital stay duration, or histopathological findings.

Independent Predictors of Mortality

In multivariable analysis, four factors were independently associated with in-hospital mortality: age >60 years (adjusted OR: 2.9; 95% CI: 1.7–10.2; p = 0.05), cardiovascular complications (adjusted OR: 7.8; 95% CI: 1.9–32.0; p = 0.004),

Table 2 Clinical Factors Associated with In-Hospital Mortality in *H. pylori*-Negative Non-Variceal UGIB

Characteristics	Deceased N = 13[a]	Survivor N = 272[a]	p-value
Age	76 [61–81]	60 60 [38–73]	0.003[b]
Sex			0.21[c]
Female	8 (62%)	122 (45%)	
Male	5 (38%)	150 (55%)	
Length of Hospital Stay (days)	4 (0, 71)	6 (0, 280)	0.21[b]
Admission			0.23[c]
Hematemesis (± melena)	9 (69%)	141 (52%)	
Isolate Melena	4 (31%)	131 (48%)	
Rockfall score	4 [3–5]	2 [1–3]	<0.001[b]
Comorbidities			
HTN	6 (46%)	114 (42%)	0.81[c]
T2DM	1 (7.7%)	47 (17%)	0.73[d]
CKD	4 (31%)	20 (7.4%)	0.017[d]
Liver Cirrhosis	0 (0%)	12 (4.4%)	0.91[d]

(*Continued*)

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Table 2 (Continued).

Characteristics	Deceased N = 13[a]	Survivor N = 272[a]	p-value
Treatment			
NSAID Use	1 (7%)	7 (2%)	0.72[d]
Low-dose aspirin (75–100 mg/day)	8 (62%)	44 (16%)	<0.001[d]
DAPT	4 (31%)	10 (3.7%)	<0.001[d]
Vitamin K antagonists	3 (23%)	6 (2.2%)	<0.001[d]
DOACs	2 (15%)	5 (1.8%)	0.004[d]
Complications			
CV	5 (38%)	18 (6.6%)	0.002[d]
Pneumonia	1 (7.7%)	8 (2.9%)	0.3[d]
Complicated UTI	1 (7.7%)	8 (2.9%)	0.3[d]
AKI	3 (23%)	13 (4.8%)	0.029[d]
Encephalopathy	2 (15%)	1 (0.4%)	0.006[d]
Biopsy Report			
Acute Gastritis	1 (7.7%)	44 (16%)	0.7[d]
Chronic Gastritis	3 (23%)	81 (30%)	0.8[d]
Congestive Gastritis	2 (15%)	28 (10%)	0.6[d]
Follicular Gastritis	1 (7.7%)	7 (2.6%)	0.3[d]
GIU	1 (7.7%)	34 (13%)	>0.9[d]

Notes: [a]Median [Q1–Q3]; n (%). [b]Wilcoxon rank sum test. [c]Pearson's Chi-squared test. [d]Fisher's exact test.

Abbreviations: HTN, Arterial Hypertension; T2DM, Type 2 Diabetes Mellitus; CKD, Chronic Kidney Disease; AKI, Acute Kidney Injury; CV, Cardiovascular (Heart failure, Ischemic heart disease); UTI, Urinary Tract Infection; GIU, Gastrointestinal Ulcer; DAPT, Dual antiplatelet therapy; DOAC, Direct oral anticoagulants.

encephalopathy (adjusted OR: 8.5; 95% CI: 2.2–33.0; p = 0.009), and concomitant antiplatelet plus anticoagulant therapy (adjusted OR: 5.3; 95% CI: 1.6–17.5; p = 0.006). All other variables including comorbidities, endoscopic findings, and hospital stay duration were not statistically significant in the final adjusted model (Table 3).

Table 3 In-Hospital Mortality Predictors in Non-Variceal UGIB Without *H. pylori* Infection. Multivariable Logistic Regression

Characteristic	Multivariable			Adjusted		
	OR[a]	95% CI[a]	p-value	OR[a]	95% CI[a]	p-value
Age > 60 years	5.27	1.79, 22.0	0.03	2.9	1.72, 10.2	0.04
Male	0.43	0.15, 1.52	0.22	0.49	0.18, 1.89	0.07
Melena	1.97	0.12, 3.90	0.32			
Expected hospital stay	8.35	0.46, 18.2	0.31			
Prolonged hospital stay	0.84	0.18, 9.87	0.92			
HTN	1.42	0.11, 4.66	0.22	1.43	0.12, 6.57	0.25
T2DM	0.12	0.11, 1.87	0.06	0.17	0.12, 1.90	0.18
CKD	4.95	0.92, 28.2	0.10	3.49	0.76, 16.1	0.11
Liver Cirrhosis	0.25	0.12, 9.35	0.41	0.16	0.01, 4.06	0.3
AKI	1.47	0.25, 8.84	0.7			
Antiplatelet + Anticoagulant[‡]	6.8	2.1, 22.0	0.001	5.3	1.6, 17.5	0.006
CV complications	9.2	2.72, 48.7	0.001	7.8	1.99, 32.0	0.004

(*Continued*)

Table 3 (Continued).

Characteristic	Multivariable			Adjusted		
	OR[a]	95% CI[a]	p-value	OR[a]	95% CI[a]	p-value
Pneumonia	0.83	0.10, 7.12	0.9			
Complicated UTI	3.75	0.36, 39.3	0.3			
Encephalopathy	8.2	1.81, 26	0.041	8.5	2.2, 33.0	0.009
Acute Gastritis	0.45	0.18, 5.92	0.72			
Chronic Gastritis	0.91	0.89, 5.23	0.91			
Congestive Gastritis	2.90	0.34, 19.1	0.52			
Follicular Gastritis	3.54	1.17, 29.1	0.62			
GIU	0.24	0.90, 6.51	0.81			

Notes: [a]OR, Odds Ratio; CI, Confidence Interval. [‡]Use of any antiplatelet (low-dose aspirin or DAPT) plus any anticoagulant (VKA or DOAC) at admission.

Abbreviations: HTN, Arterial Hypertension; T2DM, Type 2 Diabetes Mellitus; CKD, Chronic Kidney Disease; AKI, Acute Kidney Injury; CV, Cardiovascular (Heart Failure, Ischemic Heart Disease); UTI, Urinary Tract Infection; GIU, Gastrointestinal Ulcer; UGIB, Upper Gastrointestinal Bleeding.

Discussion

In this cohort of 285 patients hospitalized for *H. pylori*-negative UGIB, the in-hospital mortality rate was 5% consistent with contemporary reports from high-income settings.[17] The median age of 60 years reflects the epidemiological shift toward older, multimorbid patients in the context of declining global *H. pylori* prevalence.[21] Critically, mortality was not driven by the bleeding source or clinical presentation, but by baseline physiological reserve and systemic comorbidities, reinforcing a patient-centered model of risk stratification.

Notably, traditional NSAID use was rare (2.8%), whereas exposure to antiplatelet or anticoagulant therapy was substantially more common. Based on admission medication records, low-dose aspirin, dual antiplatelet therapy, and oral anticoagulants were documented in nearly 29% and were associated to in-hospital mortality aligning with regional trends in aging populations with high cardiovascular risk.[26,27] This suggests that in our Latin American cohort, UGIB arises less from classic ulcerogenic drugs and more from antithrombotic-related mucosal injury, stress gastropathy, or vascular fragility.[15,28] Endoscopically, only 12% of cases showed overt ulcers; the majority presented with erosive or hemorrhagic gastropathy (45%) or non-specific mucosal irritation (35%), further supporting a non-ulcerative, comorbidity-driven pathogenesis.[4]

Advanced age (>60 years) emerged as the strongest demographic predictor of death (adjusted OR: 3.14, p=0.04), corroborating decades of evidence that aging impairs hemostatic response, delays healing, and increases vulnerability to hemodynamic stress.[17,20] This finding validates the inclusion of age as a cornerstone of prognostic scores such as Rockall and AIMS65,[18,20] which performed well in our population despite its unique etiological profile.

Cardiovascular complications during hospitalization such as acute heart failure or ischemic events were the most potent clinical predictor of mortality (adjusted OR: 7.8, p<0.001). Gastrointestinal bleeding can precipitate myocardial ischemia through hypovolemia-induced hypotension or exacerbate preexisting cardiac dysfunction, creating a vicious cycle of multiorgan decompensation.[29,30] This underscores the importance of cardiovascular monitoring and early intervention in high-risk UGIB patients, particularly those with known heart disease.[4]

Encephalopathy was also associated with a markedly elevated risk of death (adjusted OR: 8.5, p=0.008); however, this finding must be interpreted with caution, as it was observed in only three patients. While encephalopathy is a recognized marker of poor prognosis in cirrhotic patients,[31,32] its presence in non-cirrhotic or critically ill individuals likely reflects global organ dysfunction, sepsis, or metabolic derangement rather than a direct causal factor.[32] Thus, we consider this association hypothesis-generating rather than definitive.

The overall comorbidity profile hypertension (42%), type 2 diabetes (17%), and chronic kidney disease (8.4%) further supports a vascular-endothelial pathogenesis rather than classic ulcerogenic mechanisms.[21] These conditions promote microangiopathy, impair mucosal perfusion, and reduce healing capacity, creating a "fragile gut" susceptible to bleeding even in the absence of overt ulcers or erosions.[16,33] This pathophysiological shift may explain why traditional ulcer-focused

interventions show limited efficacy in this subgroup.[33] Our findings affirm that validated prognostic scores remain applicable even in *H. pylori*-negative UGIB, as age, cardiovascular disease, and markers of systemic instability (eg., encephalopathy) are integral to tools like Rockall, AIMS65 and Glasgow-Blatchford score.[18–20] This supports their routine use in risk stratification, regardless of *H. pylori* status.

This study has limitations. It is retrospective and single center, limiting generalizability. The small number of encephalopathy cases precludes robust inference. By design, we did not include a *H. pylori*–positive comparator group, as our aim was to characterize this specific subgroup rather than contrast etiologies. Likewise, the study was not intended to assess predisposing factors for the development of UGIB, but rather to identify in-hospital mortality predictors among patients already diagnosed with non-variceal, *H. pylori*–negative bleeding. Nevertheless, this work strengthens the evidence base for *H. pylori*–negative UGIB in Latin America, a region underrepresented in global literature. It demonstrates that in this population, mortality is less about the bleeding lesion and more about the patient's systemic resilience.

In conclusion, among hospitalized patients with *H. pylori*-negative non-variceal UGIB, in-hospital death is primarily predicted by advanced age, cardiovascular complications and antithrombotic use. The unexpectedly low NSAID exposure and high antithrombotic use suggest alternative pathophysiological pathways emphasizing the need for region-specific, comorbidity-focused management strategies in an aging, multimorbid era of gastrointestinal bleeding.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

This study was approved by the Institutional Ethics Committee of the clinic where the research was conducted (Approval No. 526). All procedures were performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. This was a retrospective, observational study based exclusively on the review of anonymized institutional medical records. No personally identifiable information was collected, recorded, or stored at any stage of the research. The manuscript contains no images, clinical details, or data that could compromise participant confidentiality. Given the retrospective and fully anonymized nature of the study, the Institutional Ethics Committee waived the requirement for informed consent and granted permission for the publication of the findings.

Disclosure

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References

1. Barkun AN, Bardou M, Kuipers EJ, et al; International Consensus Upper Gastrointestinal Bleeding Conference Group. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. *Ann Internal Med*. 2010;152:101–113. doi:10.7326/0003-4819-152-2-201001190-00009
2. Goh K-L, Chan W-K, Shiota S, Yamaoka Y. Epidemiology of *Helicobacter pylori* infection and public health implications. *Helicobacter*. 2011;16 (Suppl 1):1–9. doi:10.1111/j.1523-5378.2011.00874.x
3. Lau JY, Sung JJ, Lee KK, et al. Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. *New Engl J Med*. 2000;343:310–316. doi:10.1056/NEJM200008033430501
4. Barkun AN, Almadi M, Kuipers EJ, et al. Management of nonvariceal upper gastrointestinal bleeding: guideline recommendations from the International Consensus Group. *Ann Internal Med*. 2019;171:805–822. doi:10.7326/M19-1795
5. Lanas A, Dumonceau J-M, Hunt RH, et al. Non-Variceal Upper Gastrointestinal Bleeding. *Nature Reviews Disease Primers*. 2018;4:18020. doi:10.1038/nrdp.2018.20
6. Malfertheiner P, Megraud F, O'Morain CA, et al. Management of *Helicobacter pylori* infection-the Maastricht V/florence consensus report. *Gut*. 2017;66:6–30. doi:10.1136/gutjnl-2016-312288
7. Kamboj AK, Hoversten P, Leggett CL. Upper gastrointestinal bleeding: etiologies and management. *Mayo Clin Proc*. 2019;94:697–703. doi:10.1016/j.mayocp.2019.01.022
8. Azadbakht S, Azadbakht S, Azadbakht M. Upper gastrointestinal bleeding: diagnosis of *Helicobacter pylori* infection—descriptive study. *Health Sci Rep*. 2024;7. doi:10.1002/hsr2.1955

9. Chey WD, Howden CW, Moss SF, et al. ACG clinical guideline: treatment of *Helicobacter pylori* infection. *Am J Gastroenterol*. 2024;119:1730–1753. doi:10.14309/ajg.0000000000002968
10. Lanas A, Chan FKL. Peptic ulcer disease. *Lancet*. 2017;390:613–624. doi:10.1016/S0140-6736(16)32404-7
11. Sostres C, Gargallo CJ, Lanas A. Nonsteroidal anti-inflammatory drugs and upper and lower gastrointestinal mucosal damage. *Arthritis Res Ther*. 2013;15(Suppl 3):S3. doi:10.1186/ar4175
12. González-González JA, García-Compean D, Vázquez-Elizondo G, Garza-Galindo A, Jáquez-Quintana JO, Maldonado-Garza H. Nonvariceal upper gastrointestinal bleeding in patients with liver cirrhosis. Clinical features, outcomes and predictors of in-hospital mortality. a prospective study. *Ann Hepatol*. 2011;10:287–295. doi:10.1016/S1665-2681(19)31540-6
13. Elfert K, Love J, Elromisy E, et al. Clinical outcomes of nonvariceal upper gastrointestinal bleeding in nonagenarians and octogenarians: a comparative nationwide analysis. *Clin Endoscopy*. 2024;57:342–349. doi:10.5946/ce.2023.130
14. Tielleman T, Bujanda D, Cryer B. Epidemiology and risk factors for upper gastrointestinal bleeding. *Gastrointest Endoscopy Clin North America*. 2015;25:415–428. doi:10.1016/j.giec.2015.02.010
15. Awadalla MS, Desimone M, Wassef W. Updates on management of nonvariceal upper gastrointestinal bleeding. *Curr Opin Gastroenterol*. 2019;35:517–523. doi:10.1097/MOG.0000000000000582
16. Gries JJ, Virk HUH, Birnbaum Y, et al. Understanding gastrointestinal bleeding in patients with cardiac disease: an interdisciplinary approach. *Expert Rev Cardiovasc Ther*. 2025;23:197–207. doi:10.1080/14779072.2025.2520831
17. Abougergi MS, Travis AC, Saltzman JR. The in-hospital mortality rate for upper GI hemorrhage has decreased over 2 decades in the United States: a nationwide analysis. *Gastrointest Endoscopy*. 2015;81:882–8.e1. doi:10.1016/j.gie.2014.09.027
18. Rockall TA, Logan RF, Devlin HB, Northfield TC. Risk Assessment after Acute Upper Gastrointestinal Haemorrhage. *Gut*. 1996;38:316–321. doi:10.1136/gut.38.3.316
19. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. *Lancet*. 2000;356:1318–1321. doi:10.1016/S0140-6736(00)02816-6
20. Saltzman JR, Tabak YP, Hyett BH, Sun X, Travis AC, Johannes RS. A simple risk score accurately predicts in-hospital mortality, length of stay, and cost in acute upper GI bleeding. *Gastrointest Endoscopy*. 2011;74:1215–1224. doi:10.1016/j.gie.2011.06.024
21. Vara-Luiz F, Mendes I, Palma C, et al. Upper gastrointestinal bleeding differences between older and younger adults: should bleeding in non-cirrhotic patients be considered a geriatric syndrome? *Ther Adv Gastroenterol*. 2025;18:17562848251343416. doi:10.1177/17562848251343416
22. Triana AJ, Molinares JL, Del Rio-Pertuz G, et al. Clinical practice guidelines for the management of community-acquired pneumonia: a critical appraisal using the AGREE II instrument. *Int J Clin Pract*. 2020;74. doi:10.1111/ijcp.13478
23. Rowe TA, Juthani-Mehta M. Diagnosis and management of urinary tract infection in older adults. *Infectious Dis Clinics North America*. 2014;28:75–89. doi:10.1016/j.idc.2013.10.004
24. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract*. 2012;120:c179–c184. doi:10.1159/000339789
25. Posit Team. *RStudio: Integrated Development Environment for R*. Boston, MA: Posit Software, PBC; 2025. http://www.Posit.Co/.
26. Schjerning Olsen A-M, Gislason GH, McGettigan P, et al. Association of NSAID use with risk of bleeding and cardiovascular events in patients receiving antithrombotic therapy after myocardial infarction. *JAMA*. 2015;313:805–814. doi:10.1001/jama.2015.0809
27. Bouck Z, Mecredy GC, Ivers NM, et al. Frequency and associations of prescription nonsteroidal anti-inflammatory drug use among patients with a musculoskeletal disorder and hypertension, heart failure, or chronic kidney disease. *JAMA Intern Med*. 2018;178:1516–1525. doi:10.1001/jamainternmed.2018.4273
28. Kocic M, Rasic P, Marusic V, et al. Age-specific causes of upper gastrointestinal bleeding in children. *World J Gastroenterol*. 2023;29:6095–6110. doi:10.3748/wjg.v29.i47.6095
29. Chen -C-C, Chong C-F, Kuo C-D, Wang T-L. Silent myocardial ischemia in coronary artery disease patients under aspirin therapy presenting with upper gastrointestinal hemorrhage. *J Gastroenterol Hepatol*. 2007;22:13–17. doi:10.1111/j.1440-1746.2006.04277.x
30. Rubinfeld GD, Berger JS, Smilowitz NR. Acute myocardial infarction following hospitalization for gastrointestinal bleeding: incidence, predictors, management, and outcomes. *Am J Med*. 2022;135:e263–e278. doi:10.1016/j.amjmed.2022.03.030
31. Wang J, Deng MJ, Shi PM, et al. Covert hepatic encephalopathy is associated with aggressive disease progression and poor survival in patients with cirrhosis. *J Digestive Dis*. 2023;24:681–690. doi:10.1111/1751-2980.13246
32. Bustamante J, Rimola A, Ventura PJ, et al. Prognostic significance of hepatic encephalopathy in patients with cirrhosis. *J Hepatol*. 1999;30:890–895. doi:10.1016/s0168-8278(99)80144-5
33. Tarnawski AS, Ahluwalia A. Increased susceptibility of aging gastric mucosa to injury and delayed healing: clinical implications. *World J Gastroenterol*. 2018;24:4721–4727. doi:10.3748/wjg.v24.i42.4721