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Research Article

Effects of Aspirin and Anticoagulants on Morbidity and Mortality in Patients with Non-Variceal Upper Gastrointestinal Bleeding - @

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ABSTRACT

Background: Non-variceal Upper Gastrointestinal Bleeding (UGIB) is a critical clinical condition that requires an urgent management. Although there was a significant reduction in the incidence of bleeding peptic ulcers with the introduction of Proton Pump Inhibitor (PPI) and eradication of *Helicobacter pylori*, UGIB still remains a clinically important issue due to the increase in the proportion of elderly population, use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and in-hospital UGIB.

Objectives: We determined the impact of antiplatelets and anticoagulants on the clinical outcomes of patients who were admitted to hospital and hospitalized due to gastrointestinal bleeding, and to investigate the etiology of death in patients who had a fatal outcome.

Patients and methods: The study included 75 patients with complaint of melena or haematemesis and were diagnosed by esophagogastroduodenoscopy. The patients are divided into 5 groups based on their drug:

Group A: Those who had not taken anticoagulants and antiplatelets

Group B: Those taking heparin, warfarin and LMWH only

Group C: Those taking aspirin only

Group D: Those taking clopidogrel, ticlopidine with or without aspirin and

Group E: Those taking combined anticoagulants and antiplatelets. Patients were known to have non-PUD-related UGIB or small intestinal or LGIB identified by colonoscopy, ileoscopy and push enteroscopy were excluded from the study.

All patients were subjected to full history taking, full examination, full laboratory investigations (including complete blood count, liver function tests, renal function tests, prothrombin time and partial thromboplastin time) and upper endoscopy.

Results and conclusion: There were non-significant differences between the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding regarding sex, hematemesis only and mortality. There were statistically significant differences between the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding regarding age, type of Analgesic used, melena only, both hematemesis and melena, HB, WBCs, PTT, history of hematemesis, melena, need for blood transfusion and rebleeding. There were non-significant differences between the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding regarding endoscopic findings, except for duodenal ulcer which exhibited a significant difference.

Keywords: Non-variceal upper gastrointestinal bleeding; Anticoagulant; Antiplatelet

INTRODUCTION

Upper Gastrointestinal Bleeding (UGIB) is a common, potentially life-threatening condition responsible for more than 300,000 hospital admissions and about 30,000 deaths per annum in America. Acute upper gastrointestinal bleeding remains a common medical emergency and is a major source of morbidity and mortality; and despite the progress in endoscopic and intensive care therapies, the mortality remains unchanged; it results from increasing number of high-risk patients mainly the older ones with significant comorbidity [1].

The incidence of UGIB is 2-fold greater in males than in females, in all age groups; however, the death rate is similar in both sexes. The population with UGIB has become progressively older, with a concurrent increase in significant comorbidities that increase mortality. Mortality increases with older age (> 60 years) in males and females [1].

Non-variceal Upper Gastrointestinal Bleeding (UGIB) is a critical clinical condition that requires an urgent management. It remains a clinically important issue due to the increase in the proportion of the elderly population, use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and in-hospital UGIB [2].

Anticoagulant therapy has historically consisted of heparins for the treatment of acute thrombosis and Vitamin K Antagonists (VKA) for long-term or chronic treatment. Though effective if appropriately dosed and monitored, these traditional agents have shortcomings that stem mainly from their nonspecific mechanisms of action and variable pharmacodynamics. This has left a persisting need for novel anticoagulants that have more specific and targeted action and are

easier to administer and manage [3].

The platelet is integral to the initiation of thrombosis. The indications for the use of antiplatelet drugs in the management of thrombotic diseases include stroke, Acute Myocardial Infarction (AMI), Acute Coronary Syndrome (ACS), angina, Percutaneous Coronary Intervention (PCI), cardiac surgery, primary and secondary cardiovascular disease prevention, peripheral vascular disease, and thrombotic disorders such as atrial fibrillation. There are several antiplatelet drugs available for use in clinical practice and several under investigation [4].

Management of patients who are receiving antiplatelet drugs during the perioperative period requires an understanding of the underlying pathology and rationale for their administration, pharmacology and pharmacokinetics, and drug interactions [5].

Many patients receive chronic antithrombotic therapy for various cardiac diseases. Antiplatelet drugs are widely used in patients with coronary artery disease. Dual antiplatelet therapy, with a combination of aspirin plus a P2Y₁₂ receptor inhibitor (such as clopidogrel, prasugrel or ticagrelor), is often necessary for a period of 12 months after an acute coronary event or after the implantation of a coronary stent [6].

Vitamin-K antagonists (VKA) are indicated in patients with atrial fibrillation, thromboembolic venous disease or a mechanical heart valve, while recently the Novel Oral Anticoagulants (NOAC), such as dabigatran, rivaroxaban, and apixaban, have been used increasingly in nonvalvular atrial fibrillation and venous thromboembolism [7].

In this study, we aim to determine the impact of aspirin and anticoagulants on the clinical outcomes of patients who were

admitted to hospital due to PUD-related UGIB, and to investigate the etiology of death in patients who had a fatal outcome.

PATIENTS AND METHODS

The study included 75 patients with a complaint of hematemesis or melena and diagnosed by esophagogastroduodenoscopy.

Patients

A written consent was taken from all participants and oral explanation of the whole procedure and their participation in the study. The patients are divided into 5 groups based on their drug:

Group A: Those who had not taken anticoagulants and antiplatelet.

Group B: Those taking heparin, warfarin, and LMWH only

Group C: Those taking aspirin only.

Group D: Those taking clopidogrel, ticlopidine with or without aspirin.

Group E: Those taking combined anticoagulants and antiplatelet.

Exclusion criteria

1. Non-PUD-related UGIB identified by upper endoscopy.
2. Small intestinal or LGIB identified by colonoscopy, ileoscopy and push enteroscopy.

METHODS

All patients were subjected to the following:

1. Full history taking including age-associated medical conditions as D.M, Cardiac, HTN. Gender, history of drug intake (NSAID) and antithrombotic drugs.
2. Full examination.
3. Full labs including complete blood count, liver function tests (including ALT, AST, serum albumin, total and direct bilirubin), renal function tests including serum creatinine and blood urea and prothrombin time and partial thromboplastin time).
4. Upper endoscopy was done by endoscopist by using Fibre-optic endoscopy after good sterilization. Initial assessment and resuscitation according to the amount of bleeding (mild-moderate-massive) urgently or within 24-48 hrs.

STATISTICAL ANALYSIS

The collected data were organized, tabulated and statistically analyzed using SPSS software (Statistical Package for the Social Sciences, version 16, SPSS Inc. Chicago, IL, USA).

For quantitative data, the range, mean and standard deviation were calculated. For qualitative data, the comparison between two groups and more was done using Chi-square test [2].

For comparison between more than two means of parametric data, F value of ANOVA test was calculated for parametric data, where the Scheffé's test was performed to compare between every two means if F value was significant. For comparison between more than two means of non-parametric data, Kruskal-Wallis (X² value) was calculated.

Significance was adopted at $p < 0.05$ for interpretation of results of tests of significance.

RESULTS

HB varying from (7.73-10.75 g / dl) WBCs from (7.164-10.650 cmm), Bl. Urea from (25.50-33.00 mg/dl), S. Creat from (0.8-1.1 mg/dl) and PTT from (29.52-35.78 sec). There were Endoscopic findings as shown in table 1, variation of lesions as Erosion, Gastritis, and Ulcer. 42 from 75 patients given blood transfusion. With follow up for 6 months for rebleeding attacks 2 patients rebleed again while no mortality between the studied patients.

Table 2 showed that there were significant differences between the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding regarding age and nonsignificant regarding sex ($p > 0.05$).

Table 3 showed that there were statistically significant differences between the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding regarding their medical history (DM, HTN, and Cardiac diseases).

Table 4 showed that there was statistically of significant difference between the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding regarding the type of Analgesics used and a non-significant difference regarding the type of NSAID.

Table 5 showed that there was statistically a significant difference between the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding regarding the history of hematemesis and melena.

Table 6 showed that there was the statistically significant difference between the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding regarding HB, WBCs and PTT among the studied patients. Non-statistically significant difference regarding other laboratory investigation between the studied patients.

Table 7 showed that there were non-significant differences between the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding regarding endoscopic findings, except for duodenal ulcer which exhibited a significant difference.

Table 8 showed that there was statistically a significant difference between the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding regarding the need for blood transfusion.

Table 9 showed that there was statistically a significant difference between the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding regarding rebleeding and a non-significant difference regarding mortality.

DISCUSSION

Upper Gastrointestinal Bleeding (UGIB) is associated with high morbidity and mortality. In the USA the annually estimated hospitalization nationwide due to Peptic Ulcer Disease (PUD) ranged from 156 108 to 222 601, with a decreasing trend from 1993 to 2006 [8]. Up to two-thirds of UGIB admissions are due to PUD [9].

Despite the development of treatment modalities, the 30-day mortality in patients suffering from UGIB was reported to be 8.9% in the UK [10], 6.2% in Hong Kong SAR, China and 8.5% in the USA [11].

Antiplatelet agents and anticoagulants are increasingly applied in the clinic setting for the treatment and prophylaxis of cardiovascular diseases, especially in elderly populations [12].



Table 1: Laboratory investigations.

Variables	The studied patients with non-variceal upper GIT bleeding(n=75)					F-value	P value	
	Group A (n = 25)	Group B (n = 18)	Group C (n = 20)	Group D (n = 8)	Group E (n = 4)			
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD			
HB (g/dl)	10.75 ± 1.21	7.73 ± 0.45	8.96 ± 1.52	7.77 ± 0.54	10.05 ± 1.11	23.475	0.0001*	A vs B, C, & D, p = 0.0001* B vs C & E, p = 0.032* & 0.012* D vs E, p = 0.036*
WBCs (x 1000) cmm	7.164 ± 1.803	7.203 ± 2.265	7.365 ± 1.525	9.300 ± 1.641	10.650 ± 0.238	5.276	0.001*	A vs E, p = 0.018* B vs E, p = 0.025* C vs E, p = 0.035*
Platelets (x 1000) cmm	193.68 ± 72.29	184.33 ± 65.2	187.82 ± 94.5	206.87 ± 17.53	240.25 ± 154.64	0.503	0.734	
AST (U/L)	22.00 ± 7.84	23.00 ± 8.76	22.00 ± 9.69	24.00 ± 7.89	27.00 ± 10.36	0.735	0.571	
ALT (U/L)	32.00 ± 6.78	34.00 ± 6.42	35.00 ± 8.39	30.00 ± 6.99	35.00 ± 5.00	0.762	0.554	
Total bilirubin (mg/dl)	0.90 ± 0.12	1.32 ± 1.67	0.91 ± 0.14	0.15 ± 0.06	1.07 ± 0.15	3.983	0.408	
Direct bilirubin (mg/dl)	0.14 ± 0.05	0.59 ± 1.87	0.15 ± 0.06	0.16 ± 0.05	0.87 ± 1.42	3.605	0.462	
Serum albumin (g/dl)	4.02 ± 0.37	3.92 ± 0.39	3.85 ± 0.35	4.20 ± 0.27	4.17 ± 0.60	1.790	0.141	
Blood urea (mg/dl)	27.32 ± 8.14	33.00 ± 5.92	31.65 ± 18.52	25.50 ± 5.34	32.00 ± 5.89	3.507	0.512	
Serum creatinine (mg/dl)	0.90 ± 0.16	1.10 ± 0.05	0.89 ± 0.13	0.89 ± 0.10	1.00 ± 0.14	1.832	0.109	
PT (seconds)	11.70 ± 0.48	12.03 ± 0.44	11.99 ± 0.41	12.30 ± 0.75	12.15 ± 0.13	2.150	0.084	
PTT (seconds)	29.52 ± 2.47	35.78 ± 2.98	31.45 ± 4.26	35.12 ± 4.85	35.50 ± 2.52	11.193	0.0001*	A vs B, D & E, p = 0.0001*, 0.005* & 0.043* B vs C, p = 0.008*
INR	1.12 ± 0.21	1.19 ± 0.15	1.16 ± 0.15	1.24 ± 0.17	1.22 ± 0.09	1.012	0.407	

Table 2: Age and sex of the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding (n = 75).

Variables	The studied patients with non-variceal upper GIT bleeding (n = 75)										χ ² P	Total n (75)	
	Group A (n = 25)		Group B (n = 18)		Group C (n = 20)		Group D (n = 8)		Group E (n = 4)			n	%
	N	%	N	%	N	%	n	%	n	%			
Sex:													
Males	11	44.0	7	38.9	9	45.0	6	75.0	3	75.0	4.336	36	48.0
Females	14	56.0	11	61.1	11	55.0	2	25.0	1	25.0	0.362	39	52.0
Age (years):													
Range	25-60		36-59		47-69		43-59		46-62			25-69	
Mean ± SD	43.96 ± 8.60		46.50 ± 5.57		55.30 ± 5.48		54.12 ± 4.97		57.25 ± 7.63			49.39 ± 8.41	
F-value	10.933												
P	0.0001*												
Scheffe test	A vs C, D & E p = 0.0001*, 0.013* & 0.015* BvsC & D p = 0.006*												

*Significant (p < 0.05)

Table 3: Medical history of the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding (n=75).

Medical history of disease	The studied patients with non-variceal upper GIT bleeding (n = 75)										χ ² P
	Group A (n = 25)		Group B (n = 18)		Group C (n = 20)		Group D (n = 8)		Group E (n = 4)		
	N	%	N	%	n	%	n	%	n	%	
Diabetes Mellitus	2	8.0	11	61.1	7	35.0	2	25.0	2	50.0	14.486 0.006*
Hypertension	6	24.0	13	72.2	13	65.0	7	87.5	4	100	22.328 0.004*
Cardiac disease	3	12.0	3	16.7	7	35.0	8	100	4	100	31.395 0.0001*

*Significant (p < 0.05)



Table 4: Analgesic drugs history of the studied patients with non-variceal upper gastrointestinal (GIT) bleeding (n = 75).

Variables	The studied patients with non-variceal upper GIT bleeding (n = 75)										X ² P
	Group A (n = 25)		Group B (n = 18)		Group C (n = 20)		Group D (n = 8)		Group E (n = 4)		
	N	%	N	%	n	%	n	%	n	%	
Type of Analgesics used:											
Steroidal AID	11	44.0	18	100	20	100	5	62.5	3	75.0	26.837
Non steroidal AID	14	56.0	0	0	0	0	3	37.5	1	25.0	0.0001*
Type of NSAID:											
Non_Selective	12	85.7	0	0	0	0	1	33.3	1	100	4.220
Selective	2	14.3	0	0	0	0	2	66.7	0	0	0.121

*Significant (P<0.05)

Table 5: History of hematemesis and melena among the studied patients with Non-Variceal Upper gastrointestinal (GIT) bleeding (n = 75).

History of hematemesis and melena	The studied patients with non-variceal upper GIT bleeding (n = 75)										X ² P
	Group A (n = 25)		Group B (n = 18)		Group C (n = 20)		Group D (n = 8)		Group E (n = 4)		
	N	%	N	%	n	%	n	%	n	%	
Hematemesis	17	68.0	5	27.8	10	50.0	0	0	1	25.0	40.173 0.0001*
Melena	8	32.0	5	27.8	10	50.0	2	25.0	0	0	
Both hematemesis and melena	0	0	8	44.4	0	0	6	75.0	3	75.0	

*Significant (p < 0.05)

Table 6: Mean values of laboratory investigation findings of the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding (n = 75).

Variables	The studied patients with non-variceal upper GIT bleeding (n=75)					F- value	P value	
	Group A (n=25)	Group B (n=18)	Group C (n=20)	Group D (n=8)	Group E (n=4)			
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD			
HB (g/dl)	10.75 ± 1.21	7.73 ± 0.45	8.96 ± 1.52	7.77 ± 0.54	10.05 ± 1.11	23.475	0.0001*	A vs B, C, & D, p = 0.0001* B vs C & E, p = 0.032* & 0.012* D vs E, p = 0.036*
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Platelets (x 1000) cmm	193.68 ± 72.29	184.33 ± 65.2	187.82 ± 94.5	206.87 ± 17.53	240.25 ± 154.64	0.503	0.734	
AST (U/L)	22.00 ± 7.84	23.00 ± 8.76	22.00 ± 9.69	24.00 ± 7.89	27.00 ± 10.36	0.735	0.571	
ALT (U/L)	32.00 ± 6.78	34.00 ± 6.42	35.00 ± 8.39	30.00 ± 6.99	35.00 ± 5.00	0.762	0.554	
Total bilirubin (mg/dl)	0.90 ± 0.12	1.32 ± 1.67	0.91 ± 0.14	0.15 ± 0.06	1.07 ± 0.15	3.983	0.408	
Direct bilirubin (mg/dl)	0.14 ± 0.05	0.59 ± 1.87	0.15 ± 0.06	0.16 ± 0.05	0.87 ± 1.42	3.605	0.462	
Serum albumin (g/dl)	4.02 ± 0.37	3.92 ± 0.39	3.85 ± 0.35	4.20 ± 0.27	4.17 ± 0.60	1.790	0.141	
Blood urea (mg/dl)	27.32 ± 8.14	33.00 ± 5.92	31.65 ± 18.52	25.50 ± 5.34	32.00 ± 5.89	3.507	0.512	
Serum creatinine (mg/dl)	0.90 ± 0.16	1.10 ± 0.05	0.89 ± 0.13	0.89 ± 0.10	1.00 ± 0.14	1.832	0.109	
PT (seconds)	11.70 ± 0.48	12.03 ± 0.44	11.99 ± 0.41	12.30 ± 0.75	12.15 ± 0.13	2.150	0.084	
PTT (seconds)	29.52 ± 2.47	35.78 ± 2.98	31.45 ± 4.26	35.12 ± 4.85	35.50 ± 2.52	11.193	0.0001*	A vs B, D & E, p = 0.0001*, 0.005* & 0.043* B vs C, p = 0.008*
INR	1.12 ± 0.21	1.19 ± 0.15	1.16 ± 0.15	1.24 ± 0.17	1.22 ± 0.09	1.012	0.407	



Table 7: Endoscopic findings among the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding (n = 75).

Variables	The studied patients with non-variceal upper GIT bleeding (n = 75)										χ ² P
	Group A (n = 25)		Group B (n = 18)		Group C (n = 20)		Group D (n = 8)		Group E (n = 4)		
	N	%	n	%	n	%	n	%	n	%	
Gastric ulcer	0	0	3	16.7	3	15.0	1	12.5	0	0	4.983 0.289
Duodenal ulcer	7	28.0	14	77.8	10	50.0	6	75.0	1	25.0	13.385 0.010*
Erosion	22	88.0	15	85.0	17	85.0	6	75.0	4	100	1.571 0.814
Gastritis	20	100	10	55.6	15	75.0	8	100	4	100	8.144 0.086

*Significant (p < 0.05)

Table 8: Need for blood transfusion among the studied patients with non-variceal upper gastrointestinal (GIT) bleeding (n = 75).

Variable	The studied patients with non-variceal upper GIT bleeding (n = 75)										χ ² P
	Group A (n = 25)		Group B (n = 18)		Group C (n = 20)		Group D (n = 8)		Group E (n = 4)		
	N	%	n	%	n	%	n	%	n	%	
Blood transfusion:											
No	23	92.0	2	11.1	5	25.0	3	37.5	0	0	37.489
Yes	2	8.0	16	88.9	15	75.0	5	62.5	4	100	0.0001*

*Significant (p < 0.05)

Table 9: Rebleeding and mortality after 6 months of follow up among the studied patients with non-variceal upper gastrointestinal (GIT) bleeding (n = 75).

Variables	The studied patients with non-variceal upper GIT bleeding (n = 75)										χ ² P
	Group A (n = 25)		Group B (n = 18)		Group C (n = 20)		Group D (n = 8)		Group E (n = 4)		
	N	%	n	%	n	%	n	%	n	%	
Rebleeding:											
No	25	100	18	100	20	100	7	87.5	3	75.0	12.393
Yes	0	0	0	0	0	0	1	12.5	1	25.0	0.015*
Mortality:											
No	25	100	18	100	20	100	8	100	4	100	0.000
Yes	0	0	0	0	0	0	0	0	0	0	1.0000

*Significant (p < 0.05)

Monotherapy with antiplatelet agents or anticoagulants is associated with an increasing risk of UGIB [13] and aspirin has been verified to play an important role in the pathogenesis of PUD. There-fore, it is common practice to discontinue these medications in patients with UGIB for days, even weeks, during and after bleeding episode [14].

Although the continuation of low-dose aspirin will increase the risk of rebleeding, it has been reported to be able to reduce the all-cause mortality rate (1.3% vs 12.9% compared with placebo) in a small sample of patients [11].

Current evidence on the effects of aspirin or anticoagulants on the clinical outcomes of patients with UGIB is controversial, as Sung, et al. [15] have reported that aspirin decreases the mortality of patients while Ortiz, et al. [16] have suggested these drugs have no effects. Similarly, conflicting results on the effects of anticoagulants such as warfarin have been reported [17].

These drugs have been reported to increase the patients' mortality significantly or having no influence on the disease course of UGIB, except that they are associated with the patients' pro-longed hospital stay [16].

In this study, we aimed to determine the impact of aspirin and anticoagulants on the clinical outcomes of patients who were admitted to hospital due to PUD-related UGIB, and to investigate the etiology of death in patients who had a fatal outcome.

This study was performed on 75 patients classified according to sex to 36 male and 39 female. Age of them varying from (25-69 yrs.) with Mean 49.39.

After taken full medical history it was found that 24 pt. Diabetic, 25pt Cardiac and 43 pt. Hypertensive. From the history of Analgesic, drug intake found that 18 pt. used NSAIDS and 14 of them used Nonselective NSAIDS and 2 pt. used Selective NSAIDS.

HB varying from (7.73-10.75g / dl) WBCs from (7.164-10.650 cmm), Bl. Urea from (25.50-33.00 mg/dl), S. Creat from (0.8-1.1 mg/dl) and PTT from (29.52-35.78 sec).

There were significant differences between the studied patients with Non-Variceal Upper Gastrointestinal (GIT) bleeding regarding age, medical history, type of analgesics used, history of hematemesis, melena, HB, WBCs, PTT, need for blood transfusion and rebleeding, these results are in conformity with Hearnshaw, et al. [10].



Aging and comorbidities are known predictors of mortality and adverse clinical outcomes. Furthermore, the protective effect of aspirin may not be fully attributable to its known cardiovascular benefits, because most deaths are due to non-cardiovascular issues. It is customary to discontinue aspirin in patients presenting with UGIB [13].

Similar protective effects of aspirin against UGIB-related deaths have been reported in a study that included both peptic and non-peptic ulcer patients [17]. However, Ahsberg, et al. [18] have reported no significant association between aspirin use and mortality although those taking non-steroidal anti-inflammatory drugs were included. Taha, et al. [19] associated a low-dose aspirin intake with longer length of hospital stay and increased requirement of blood transfusion.

Lanas, et al. [17] observed that anticoagulants increase requirements for blood transfusion and are associated with a longer length of hospital stay. Marmo, et al. [20] showed that heparin, but not warfarin, increases mortality risk. Patients on heparin are usually hospitalized and develop in-hospital UGIB, which is a known risk factor for worse outcomes.

In-hospital mortality is within the reported range; in fact, it decreased from 3.9% to 2.7% from 1993 to 2006. Non-bleeding-related causes accounted for most deaths, which is in accordance with a previous report [21].

The number of patients who died of acute renal failure in our study was much higher than that reported elsewhere, as it was considered to be an independent risk factor of death [21], while we regarded it as part of multi-organ failure or the consequence of another major cause of death.

Malignancies accounted for 30.8% of the non-bleeding-related deaths, which is in accordance with the previous results, while cardiovascular causes are higher than that reported [9].

Marmo, et al. [22] used rigorous criteria for the severe bleeding that occurred in 40.7% of the patients, which has been reported to be a risk factor for mortality.

Rebleeding is a predictor of mortality, the rate of which is similar to previously reported rates [10]. Rubin, et al. [23] have suggested that the risk of rebleeding is not affected by antithrombotic. However, aspirin continuation seems to be associated with its increased risk of rebleeding.

Aspirin use was a predictor for short length of hospital stay in our study, which is consistent with a better overall outcome for those patients. This is different from what has been reported, which might be due to varied study designs [11] or the patients included in the study (both PUD and non-PUD-related UGIB) [16]. Taha, et al. [19] suggested that patients having UGIB with aspirin use had a longer length of hospital stay, but the study included those with variceal bleeding.

Abu Daya, et al. [24] determined the impact of aspirin and anticoagulants on the clinical outcomes of patients who were admitted to hospital and hospitalized due to PUD-related UGIB and investigated the etiology of death in patients who had a fatal outcome.

CONCLUSION

Our study suggested that aspirin intake might be associated with favorable clinical outcomes in PUD-related UGIB, while anticoagulants seem to be associated with worse outcomes.

Further investigations are needed to validate these findings. Furthermore, if aspirin is found to improve outcomes in such patients, clinicians should be informed whether and when to resume aspirin in patients taking it for primary prophylaxis.

REFERENCES

- Palmer K. Acute upper gastrointestinal hemorrhage. *Br Med Bull.* 2007; 83: 307-324. <https://goo.gl/1dxKGx>
- Laine L, Jensen DM. Management of patients with ulcer bleeding. *Am J Gastroenterol.* 2012; 107: 345-360. <https://goo.gl/DVH5pW>
- Nutescu EA, Shapiro NL, Chevalier A, Amin AN. A pharmacologic overview of current and emerging anticoagulants. *Cleve Clin J Med.* 2005; 72: 1-6. <https://goo.gl/r4NUVE>
- Jennings LK. Role of platelets in atherothrombosis. *Am J Cardiol.* 2009; 103: 4-10. <https://goo.gl/oR6quB>
- Newsome LT, Weller RS, Gerancher JC, Kutcher MA, Royster RL. Coronary artery stents. II. Perioperative considerations and management. *Anesth Analg.* 2008; 107: 570-590. <https://goo.gl/e4qFJK>
- Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of Acute Coronary Syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 2011; 32: 2999-3054. <https://goo.gl/iqQFYg>
- Camm AJ, Lip GY, De Caterina R, et al. Focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation-developed with the special contribution of the European Heart Rhythm Association. *Europace.* 2012; 14: 1385-1413.
- Wang YR, Richter JE, Dempsey DT. Trends and outcomes of hospitalizations for peptic ulcer disease in the United States, 1993 to 2006. *Ann Surg.* 2010; 251: 51-58. <https://goo.gl/TBrk6L>
- Marmo R, Koch M, Cipolletta L, Capurso L, Pera A, Bianco MA, et al. Predictive factors of mortality from non-variceal upper gastrointestinal hemorrhage: a multicenter study. *Am J Gastroenterol.* 2008; 103: 1639-1647. <https://goo.gl/WN452E>
- Hearnshaw SA, Logan RF, Lowe D, Travis SP, Murphy MF, Palmer KR. Acute upper gastrointestinal bleeding in the UK: Patient characteristics, diagnoses, and outcomes in the 2007 UK audit. *Gut.* 2011; 60: 1327-1335. <https://goo.gl/MQkohY>
- Sung JJ, Lau JY, Ching JY, Wu JC, Lee YT, Chiu PW, et al. Continuation of low-dose aspirin therapy in peptic ulcer bleeding: a randomized trial. *Ann Intern Med.* 2010; 152: 1-9. <https://goo.gl/gdtJqt>
- Theocharis GJ, Thomopoulos KC, Sakellariopoulos G, Katsakoulis E, Nikolopoulou V. Changing trends in the epidemiology and clinical outcome of acute upper gastrointestinal bleeding in a defined geographical area its Greece. *J Clin Gastroenterol.* 2008; 42: 128-133. <https://goo.gl/dkwvsm>
- Garcia Rodriguez LA, Lin KJ, Hernandez-Diaz S, Johansson S. Risk of upper gastrointestinal bleeding with low-dose acetylsalicylic acid alone and in combination with clopidogrel and other medications. *Circulation.* 2011; 123: 1108-1115. <https://goo.gl/uD6gnE>
- Sostres C, Lanas A. Should prophylactic low-dose aspirin therapy be continued in peptic ulcer bleeding? *Drugs.* 2011; 71: 1-10. <https://goo.gl/srjCp>
- Sung JJ, Lau JY, Ching JY, Wu JC, Lee YT, Chiu PW, et al. Continuation of low-dose aspirin therapy in peptic ulcer bleeding: A randomized trial. *Ann Intern Med.* 2010; 152: 1-9. <https://goo.gl/hxChyA>
- Ortiz V, Ortuno J, Rodriguez Soler M, Iborra M, Garrigues V, Ponce J. Outcome of non-variceal acute upper gastrointestinal bleeding in patients with antithrombotic therapy. *Digestion.* 2009; 80: 89-94. <https://goo.gl/y7tNK>
- Lanas A, Aabakken L, Fonseca J, Mungan ZA, Papatheodoridis GV, Piessevaux H, et al. Clinical predictors of poor outcomes among patients with non-variceal upper gastrointestinal bleeding in Europe. *Aliment Pharmacol Ther.* 2011; 33: 1225-1233. <https://goo.gl/t19hXH>
- Ahlberg K, Hoglund P, Stael von Holstein C. Mortality from peptic ulcer



- bleeding: The impact of comorbidity and the use of drugs that promote bleeding. *Aliment Pharmacol Ther.* 2010; 32: 801-810. <https://goo.gl/DFD2bF>
19. Taha AS, Angerson WJ, Knill-Jones RP, Blatchford O. Clinical outcome in upper gastrointestinal bleeding complicating low-dose aspirin and antithrombotic drugs. *Aliment Pharmacol Ther.* 2006; 24: 633-636. <https://goo.gl/wc5Kz3>
20. Marmo R, Koch M, Cipolletta L, Capurso L, Grossi E, Cestari R, et al. Italian registry on upper gastrointestinal bleeding (Progetto Nazionale Emorragie Digestive-PNED 2): Predicting mortality in non-variceal upper gastrointestinal bleeders: Validation of the Italian PNED score and prospective comparison with the Rockall score. *Am J Gastroenterol.* 2010; 105: 1284-1291. <https://goo.gl/7XhncC>
21. Wong GL, Wong VW, Chan Y, Ching JY, Au K, Hui AJ, et al. High incidence of mortality and recurrent bleeding in patients with *Helicobacter pylori*-negative idiopathic bleeding ulcers. *Gastroenterology.* 2009; 137: 525-531. <https://goo.gl/6f615r>
22. Marmo R, Del Piano M, Rotondano G, Koch M, Bianco MA, Zambelli A, et al. Mortality from non-ulcer bleeding is similar to that of ulcer bleeding on high-risk patients with non-variceal hemorrhage: A prospective database study in Italy. *Gastrointest Endosc.* 2012; 75: 263-272. <https://goo.gl/oVj8Jz>
23. Rubin TA, Murdoch M, and Nelson DB. Acute GI bleeding in the setting of the supratherapeutic international normalized ratio in patients taking warfarin: Endoscopic diagnosis, clinical management, and outcomes. *Gastrointest Endosc.* 2003; 58: 369-373. <https://goo.gl/19APKG>
24. Abu Daya H, Eloubeidi M, Tamim H, Halawi H, Malli AH, Rockey DC, et al. Opposing effects of aspirin and anticoagulants on morbidity and mortality in patients with upper gastrointestinal bleeding. *J Dig Dis.* 2014; 15: 283-292. <https://goo.gl/uAFsiG>