

Risk factors and outcomes of upper gastrointestinal bleeding in hospitalized patients in a tertiary care hospital

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Abstract

Objective: To determine different aetiologies and outcomes of upper gastrointestinal bleeding in hospitalised patients.

Method: The retrospective cohort study was conducted at the Aga Khan University Hospital, Karachi, and comprised data from December 2019 to April 2021 related to adult patients of either gender with non-gastrointestinal illnesses who developed bleeding at least 24 hours after admission. Data was reviewed for clinical characteristics, cause of bleeding and clinical outcome. Data was analysed using SPSS 23.

Results: Among 47,337 hospitalised patients, upper gastrointestinal bleeding was identified in 147(0.3%); 98 (66.7%) males and 49 (33.3%) females. The overall mean age was 62.73±14.81 years (range 20-95 years). Of the total, 125(85%) presented with overt bleeding and 22(15%) with a drop in haemoglobin level. There were 34(23%) patients on aspirin, 36(24%) on dual anti-platelets, 41(28%) on therapeutic anticoagulation, and 81(55%) on prophylactic anticoagulation. There were 7(5%) patients having a history of non-steroidal anti-inflammatory drugs (NSAIDs), and 12(8%) were on steroids. In terms of associated medical conditions, pneumonia, stroke, and acute coronary syndrome were commonly seen with frequency of 29.9%, 8.1% and 7.4% respectively. Overall, 36(24.4%) patients underwent endoscopy, 8(5.4%) had therapeutic measures to control bleeding, 14(9.5%) had bleeding for >48 hours, 89(60.5%) were stepped up to special care. Mortality was seen in 36(24.5%) cases.

Conclusion: Hospital acquired gastrointestinal bleeding was found to be uncommon, and there were several risk factors for such bleeding events.

Key Words: Gastrointestinal haemorrhage, Melena, Hematemesis.

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Introduction

Upper gastrointestinal (GI) bleeding, defined as bleeding arising from the oesophagus, stomach or duodenum¹, is an important complication in hospitalised patients. These bleeding events significantly increase mortality in patients during hospital stay. The incidence of hospital-acquired GI bleeding varies from 0.17% to 5%². The common causes of such bleeding are ulceration and stress-related mucosal disease^{3,4}. Clinically important stress ulcers occur in ~1% of patients, but its severity and outcome are important issues⁵.

The reason behind such ulcers is impaired blood flow to gastric mucosa due to haemodynamic instability caused by either systemic causes, like hypotension, or local causes, like low visceral blood flow in mechanically ventilated patients. Causes also include anticoagulation therapy, renal insufficiency, burns, neurological insults

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like stroke and postoperative stress⁶. GI bleeding in non-critical patients in hospital is uncommon and carries a low risk of morbidity and mortality.

Stress ulcer prophylaxis (SUP) are acid-suppressive medications, such as histamine-2 (H2) receptor antagonists, sucralfate, or proton pump inhibitors (PPIs)⁷. Studies have demonstrated that these medications reduce the incidence of clinically significant nosocomial GI bleeding in hospitalised patients, both in and outside of the intensive care unit (ICU), with relative risk reduction ranging from 29% to 61%².

SUP is recommended in international guidelines and considered a standard of care in the ICU setting in critically ill patients, but guidelines recommend against its routine use in patients outside of the ICU⁸. However, there may be certain subsets of non-critically ill patients in whom the risk of nosocomial GI bleeding is high enough that prophylactic use of acid-suppressive medication may be warranted⁹. Indications for initiating SUP vary considerably. These inconsistencies in the initiation of SUP may be explained by sparse research data and variable recommendations. They are prescribed in an indiscriminate fashion in patients admitted to hospitals,

suggesting that physician preference dictates the practice.

Studies in the ICU setting investigating risk factors for nosocomial GI bleeding have consistently identified mechanical ventilation and coagulopathy as significant independent predictors¹⁰, both of which confer high enough risk to warrant prophylactic acid-suppressive medication in this particular patient population¹¹. Whether similar risk factors exist in non-critically ill patients has not been well examined. Such information is crucial to aid clinicians and to provide a better understanding regarding more appropriate use of acid-suppressive medication. PPIs remain the mainstay as the chemoprophylaxis, but the cost and adverse effect of nosocomial diarrhoea remain a limitation^{12,13}. Patients with sufficiently low risk of bleeding may not need prophylaxis. To the best of our knowledge, a systematic study on GI bleeding occurring in hospitalised patients admitted for non-GI disorders has not been conducted. The current study was planned to fill the gap by determining different aetiologies and outcomes of upper GI bleeding in hospitalised patients.

Materials and Methods

The retrospective cohort study was conducted at the Aga Khan University Hospital (AKUH), Karachi, and comprised patient data from December 2019 to April 2021. After approval from the institutional ethics review committee, data was retrieved related to adult patients of either gender with non-GI illnesses who developed upper GI bleeding at least 24 hours after admission. Data was excluded for patients aged <18 years, patients with documented GI bleeding complaint at the time of the index admission, patients with lower GI bleed, and those presenting with haematochezia during hospitalisation.

Demographic data was extracted by chart review. Data on comorbid conditions, including hypertension (HTN), diabetes mellitus (DM), dyslipidaemia, arthritis, liver cirrhosis, congestive heart failure (CHF), coronary artery disease (CAD), cerebrovascular accidents (CVAs) and chronic kidney disease (CKD), was also recorded. Prior medication usage history, presenting complaint, and non-GI diagnosis from the initial hospitalisation were noted. Daily progress notes were reviewed to determine the event of upper GI bleeding, significant laboratory investigations in the form of haemoglobin (Hb) level, activated prothrombin time (PT), platelet (Plt), partial thromboplastin time (PTT), medical management, endoscopic evaluation, need for advanced techniques to control bleeding (therapeutic endoscopy or angiography with embolisation) were also noted. The end point of the

study was to identify mortality rate in the targetted patient population.

Medical records were reviewed to identify patients who had overt GI bleeding or a significant drop in Hb level during hospitalisation. Overt manifestations of bleeding were in the form of haematemesis or melena. Patients with drop in Hb level had nasogastric tube lavage positive for coffee-ground aspirate or clotted or altered blood.

Upper GI endoscopy had been done by trained personnel in the Gastroenterology Unit. Endoscopic findings were categorised by the nature of the visualised lesions, and if multiple lesions were noted, the endoscope technician's impression of the most likely bleeding site was used to define the source of bleeding. Forrest classification was used to evaluate the ulcers¹⁴. Findings include spurting haemorrhage (Forrest Ia), oozing haemorrhage (Forrest Ib), a nonbleeding visible vessel (Forrest IIa), an adherent clot (Forrest IIb), a pigmented spot on ulcer base (Forrest IIc) and a clean ulcer base (Forrest III).

Data was analysed using SPSS 23. Data was presented as frequencies and percentages for categorical variables and as mean \pm standard deviation (SD) for continuous variables.

Results

Among 47,337 hospitalised patients, upper gastrointestinal bleeding was identified in 147(0.3%); 98 (66.7%) males and 49 (33.3%) females. The overall mean

Table-1: Demographic data.

Variables	Frequency/Percentage
Age (year)	Min: 20 Max: 95 Mean: 62
Gender	
Male	98 (66.7%)
Female	49 (33.3%)
Medical History	
Hypertension	96 (65.3%)
Diabetes	67 (45.6%)
Ischaemic Heart Disease	47 (32%)
CKD	20 (13.6%)
Chronic Liver Disease	17 (11.6%)
CVA	13 (8.8%)
Carcinoma	13 (8.8%)
COPD	7 (4.8%)
Arthritis	65 (44.2%)
Arrhythmia	6 (4.1%)
Dyslipidaemia	84 (57.1%)

CKD: Chronic kidney disease, CVA: Cerebral vascular accident, COPD: Chronic obstructive pulmonary disease.

Table-2: Primary complaints.

Primary Complaint	F (%)
Dyspnoea	49 (33.3%)
Fever	34 (23.1%)
Drowsiness	21 (14.3%)
Limb weakness	11 (%)
Abdominal distention	2 (1.4%)
Abdominal pain	7 (4.8%)
Chest pain	7 (4.8%)
Diarrhoea	6 (4.1%)
Seizures	3 (2.0%)
Unconsciousness	3 (2.0%)
Fall	2 (1.4%)
Jaundice	1 (0.7%)
Limb pain	1 (0.7%)

age was 62.73 ± 14.81 years (range 20-95 years). There were 96(65.3%) patients with a history of HTN, 67(45.6%) DM, 84(57.1%) dyslipidaemia, 17(11.6%) chronic liver disease, 20(13.6%) CKD, 7(4.8%) chronic obstructive pulmonary disease (COPD), 65(44.2%) arthritis, 47(32.0%) ischaemic heart disease (IHD), 13(8.8%) CVAs, 6(4.1%) arrhythmia and 13(8.8%) patients had carcinoma (Table 1). The most common primary complaint at presentation was dyspnoea 49(33.3%), followed by fever 34(23.1%), drowsiness or altered mentation 21(14.3%), upper or

lower limb weakness 11(7.5%), abdominal distention 2(1.4%), abdominal pain 7(4.8%), chest pain 7(4.8%), diarrhoea 6(4.1%), seizures 3(2.0%), unconsciousness 3(2.0%), fall 2(1.4%), jaundice 1(0.7%) and limb pain 1(0.7%) (Table 2).

Of the total, 125(85%) presented with overt bleeding; 59(47.21%) haematemesis, 49(39.2%) melena and 17(13.6%) having both haematemesis and melena. The remaining 22(15%) patients presented with a drop in Hb level.

The primary diagnosis for which the patients were admitted were pneumonia 44(29.9%), stroke 12(8.1%), acute coronary syndrome (ACS) 11(7.4%), encephalopathy 10(6.8%), septic shock 10(6.8%), severe sepsis secondary to urinary tract infection (UTI) 8(5.4%), acute kidney injury (AKI) 7(4.7%), cardiogenic shock 5(3.4%), dengue fever (DF) 5(3.4%), enteric fever 5(3.4%), acute gastroenteritis 4(2.7%), ascites 3(2.0%), epilepsy 3 (2.0%), carcinoma 3(2.0%), cellulitis 3(2.0%), peritonitis 2(1.4%), intestinal obstruction 2(1.4%), pancreatitis 2(1.4%), pulmonary embolism 2(1.4%), fracture 2(1.4%), diabetic foot 2(1.4%), septic arthritis 1(0.7%), and tumour infection 1(0.7%). Amongst patients with pneumonia, 26(59%) had coronavirus disease-2019 (COVID-19) pneumonia.

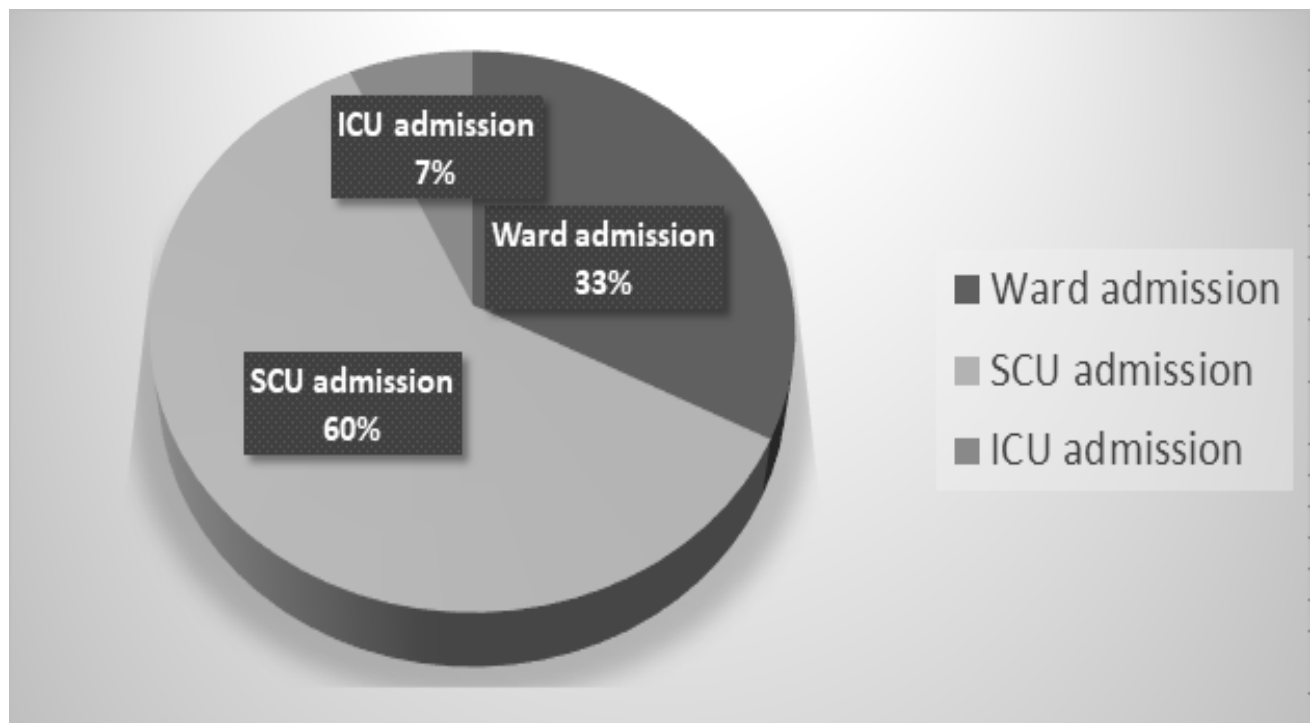


Figure: Severity of the primary disease.
ICU: Intensive care unit, SCU: Special care unit.

Primary services provided were internal medicine 111(75.5%), general surgery 3(2.0%), cardiology 8(5.4%), cardiothoracic surgery 2(1.4%), neurology and neurosurgery 6(4.1%), orthopaedics 2(1.4%), gastroenterology 5(3.4%) and oncology 10(6.8%).

There were 34(23%) patients on aspirin, 3(2.0%) on clopidogrel, 36(24%) on dual anti-platelets, 41(28%) on therapeutic anticoagulation, 81(55%) on prophylactic anticoagulation. There were 7(5%) patients having a history of non-steroidal anti-inflammatory drugs (NSAIDs), and 12(8%) were on steroids. Transfusion was done in 105(71.4%) patients.

Majority of the patients 144(97.9%) were on intravenous (IV) omeprazole 40mg once daily as prophylaxis since the time of admission. After the development of upper GI bleed, 9(6.1%) patients remained on once daily dosage, while 39(26.5%) were managed with 40mg 12 hourly and 99(67.3%) were given infusion at 8mg per hour.

A total of 36(24.5%) patients underwent upper GI endoscopy, which revealed that 21(14.3%) patients had ulcers, 6(4.1%) had varices, 3(2.0%) had gastric erosions, 2(1.4%) had ulcerated mass and 4(2.7%) had moderate to severe gastritis or duodenitis.

Among patients with gastric ulcers, 17(81%) had Forrest class III ulcers, 2(9.5%) Forrest class IIa and 2(9.5%) Forrest class IIb. Those with Forrest class IIa ulcer underwent sclerotherapy with adrenaline injection and argon plasma coagulation (APC).

Of the patients with varices, 3(50%) with oesophageal varices underwent variceal band ligation, and in 1(16.66%) patient with gastric varix, histoacryl was injected.

Of the patients with ulcerated mass, 1(50%) patient had it infiltrating into the duodenum which, on imaging, was found to be peri-ampullary mass. Besides, 1(50%) patient had a gastric mass which was later found on biopsy to gastrointestinal stromal tumour (GIST).

A total of 8(5.4%) patients had had therapeutic measures to control bleeding. Duration of bleeding was <24 hours in 86(58.5%) patients, 24-48 hours in 25(17.0%) and >48 hours in 14(9.5%). Out of 147 patients, 111 (75.5%) were discharged while 36 (24.5%) patients died.

With respect to severity of the primary disease, 48(32.7%) patients were admitted to the ward, 89(60.5%) to special care units (SCUs) and 10(6.8%) to ICUs. All patients in ICU were intubated and were on mechanical ventilators. Out of 147 patients, 111 (75.5%) were discharged, while 36 (24.5%) died.

Discussion

The current study aimed at identifying the frequency and aetiology of nosocomial GI bleeding in patients with non-GI illness on admission. It looked at various parameters, including age, gender, comorbidities, risk factors, primary complaint, presentation of bleeding, primary care provided, disease severity, treatment modalities, duration of bleeding and patient outcome.

Mean age of the patients who developed nosocomial GI bleeding was 62.78 years, and males (66.7%) were more likely to develop nosocomial GI bleeding compared to females (33.3%). The findings were comparable to a study conducted by Herzig et al., who found that the incidence of GI bleeding was greater in those aged 60 and above, and the male gender was more likely to be affected⁹.

Comorbidities that had the most significant impact on nosocomial GI bleeding included HTN (65.3%), dyslipidaemia (57.1%), DM (45.6%) and arthritis (44.2%). HTN and DM were also listed as considerable comorbidities by Qadeer et al².

The most significant primary complaints in the current study were dyspnoea (33.3%), fever (23.1%) and drowsiness (14.3%). These primary complaints can be explained by the fact that approximately one-fourth of the participants were seeking care for pneumonia mainly caused by COVID-19. Occurrence of GI bleeding in such patients has been reported by recent studies¹⁵.

The leading presentation was overt GI bleed; haematemesis (40.1%) and melena (33.3%). Since in the current study only nosocomial bleeding was included, which is acute, a decrease in Hb level due to occult bleeding was observed in fewer patients.

In terms of primary care service provided, majority of the patients were treated by the department of internal medicine (75%), followed by oncology (6.8 %) and cardiology (5.4%).

Primary disease severity in the study warranted SCU admissions in 60.5% of patients, ward admission in 32.7%, and ICU admissions in 6.8% of patients. This goes to show that disease severity did not predetermine the likelihood of a nosocomial GI bleed in the patients.

In patients who developed ulcers, gastric ulcers were more common than duodenal. The least common were oesophageal ulcers. Among those with gastric and duodenal ulcers, the highest percentage had Forrest class III ulcers.

The most common treatment modality offered to the

patients was blood transfusion (71.4%), followed by infusion of omeprazole (67.3%). Majority of the patients (97.9%) were on IV omeprazole 40mg once daily as prophylaxis since the time of admission. After the development of upper GI bleed, an infusion was given. Omeprazole as an effective treatment modality was also reported earlier².

Patients with risk factors owing to the use of NSAIDs, anti-platelet drugs, anti-coagulants, and steroids were included in the current study. This shows that a significant study population was at risk of developing a GI bleed.

Most patients enrolled in the study (58.5%) bled for <24 hours. This is attributable to the prompt treatment offered. Further, 9.5% patients bled for >48 hours, and such cases were more likely to be fatal.

The outcome included 75.5% patients who were discharged after treatment and 24.5% deaths due to bleeding-related complications.

Approximately all the patients were on PPI since the time of admission. Despite the absence of evidence of any benefit of the use of prophylactic acid blockade outside the ICU, this practice is common. It also creates an unnecessary economic burden. Similar finding were reported by a recent study done in Karachi¹⁶. This suggests that relevant international guidelines for prescribing stress ulcer prophylaxis are not followed in majority of tertiary care centres in the country. Unnecessary use of PPIs shall be discontinued in most hospitalised patients.

The current study has limitations owing to a small sample size from a single centre spanning only 2 years. Comprehensive studies are required to assess the incidence of GI bleed in patients receiving SUP in low-and middle-income countries (LMICs).

Conclusion

The incidence of nosocomial upper GI bleeding was low, but it is important to evaluate its parameters and risk factors. This will allow for greater vigilance and prompt treatment of the condition.

Disclaimer: An abstract of the text has been presented at a few conferences in the form of a poster presentation.

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Author's Contributions

OP: Study concept, supervision and finalized.

ZS: Interpretation and data analysis.

FB: Data collection, compilation and writing.