RESEARCH

# Incidence and risk factors for gastrointestinal bleeding among patients admitted to medical intensive care units

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## ABSTRACT

**Objectives** To identify incidence and risk factors for new-onset gastrointestinal bleeding (GIB) in a medical intensive care unit (ICU), a topic for which there is a paucity of recent studies.

**Design** Retrospective cohort study.

**Setting** Medical ICUs at our tertiary-care hospital, from 2007 to 2013.

**Patients** Patients who developed clinically significant GIB after entering the ICU.

**Interventions** Univariable and multivariable analyses.

**Main outcome measures** Incidence and risk factors for development of GIB.

**Results** 4439 patients entered the medical ICU without a pre-existing GIB and 58 (1.3%) developed GIB while in the ICU. Risk factors included length of ICU stay (OR per additional day 1. 06; 95% CI 1.04 to 1.09) and elevated creatinine on ICU admission (OR 2.35; 95% CI 1.18 to 4.68, p=0.02). Elevated bilirubin on ICU admission (OR 2.08; 95% CI 0.97 to 4.47, p=0.06), and elevated aspartate transaminase (AST) on ICU admission (OR 2.20; 95% CI 0.96 to 5.03, p=0.06) trended towards increased risk of GIB that did not meet statistical significance. Age, gender, admission coagulation studies and mechanical ventilation were not predictive of GIB. Among those patients with new-onset GIB in the ICU, 47% died during that hospitalisation, as compared with those 30% of those without a GIB, p<0.01.

**Conclusions** Onset of GIB is now an infrequent occurrence in the ICU setting; however those with elevated bilirubin, AST and creatinine upon admission, and with longer length of ICU stay appear at increased risk and may benefit from closer monitoring.

## INTRODUCTION

Gastrointestinal bleeding (GIB) in patients with critical illness is a major source of morbidity and mortality. GIB can occur from stress-related mucosal damage, leading to an acute erosive gastropathy in patients after surgery and during organ failure, sepsis and respiratory failure.[1 2] These episodes can result in haemodynamic instability, decreased haemoglobin and the need for transfusion.[2 3] When severe, GIB can be associated with hypotension, organ failure and death.[3–5] Mortality increases with the severity of the stress-related insult, and severe GIB can result in mortality as high as 80%.[6]

The pathophysiology of bleeding in patients with critical illness is related to the severe systemic disease process and the critical care therapies themselves. Stress ulcer-related bleeding occurs as a consequence of gut ischemia in the context of multiorgan failure.[6 7] In patients with critical illness who have bouts of hypotension—and therefore hypoperfusion—with resultant ischaemia to multiple organ systems, GIBs are considered a manifestation of the entire disease process.[6] Even when systemic circulation is maintained, there could still be intestinal hypoperfusion.[8 9] Common medications used in intensive care units (ICUs) have been implicated as contributing to GIB: opiates and sedatives for intubated patients are associated with decreases in gut motility and venous return, as are vasopressors.[10 11]

The incidence of clinically significant GIBs in patients with critical illness has

been widely studied, and there appeared to be a decline in GIB incidence over the last few decades, with reported incidences of 16% in the mid-1980s, 12.4% in 1990 and 2% in the mid-1990s.[12–14] Recently, however, there have been few large observational studies regarding the incidence of GIB in ICU patients. The two most recent publications we identified were (1) a study evaluating the incidence of GIB during the period 2004–2007, with reported incidence of 7.4% and (2) a study published in 2015 reporting a 2.6% incidence for bleeds over a period of 7 days.[15 16] Moreover, these publications have noted the paucity of newer data on the incidence of GIB; as it is, much of the currently available data (which are used to guide decisions on prophylaxis, among other critical care tools) are dated, prompting the present study.[1 17]

Previous studies have also identified risk factors for GIB in patients with critical illness (including recent surgery, burns, trauma, liver or renal dysfunction, sepsis, hypotension, coagulopathy and respiratory failure/mechanical ventilation for over 48 hours). However, these studies tend to be older, clustered in the 1990s and early 2000s.[3 6 18–21] Given the improvements in critical care and the selective administration of prophylactic therapy in such patients, we aimed to identify the incidence of and risk factors for developing clinically significant GIB in patients entering a medical ICU over a more recent time period, and to evaluate any significant changes in trends of incidence or risk factors for this outcome.

## MATERIALS AND METHODS

We performed a retrospective cohort study of all adults entering the two medical ICUs (totalling 28 beds) at our tertiary-care hospital between 1 January 2007 and 31 December 2013, to determine risk factors for GIB. The two medical ICUs are physically located on different floors on the same hospital, with identical inclusion criteria.

We queried the electronic medical records of all patients admitted to the medical ICU during the above dates. In addition to age, gender, ethnicity, race and length of stay (both in the ICU and if not directly admitted to the ICU, hospital stay prior to ICU admission), we recorded whether mechanical ventilation (endotracheal intubation) of any duration was used at any point or acid suppression medications (proton pump inhibitors (PPIs) or histamine 2 (H2) receptor blockers) were administered during the first 24 hours of ICU admission. We also recorded the following first laboratory values available within 24 hours of ICU admission: haematocrit, albumin, total and direct bilirubin, aspartate transaminase (AST), alanine transaminase (ALT) alkaline phosphatase, creatinine, partial thromboplastin time and international normalised ratio (INR).

We identified all patients who were admitted to the medical ICU in our specified date range, then excluded all patients whose GIB clinically predated their admission to the ICU. Of the remaining patients, we identified those with clinically suspected GIB, using billing diagnoses and indications in our endoscopy database. Suspected GIB was confirmed by chart review. Thus, for the purposes of this study, our end point was defined as suspected GIB in a patient not admitted with an apparent GIB.

We performed univariable analysis to determine predictors of incident GIB in this population, using the $\chi^2$ test for categorical variables and the unpaired t-test for continuous variables. We then performed multivariable logistic regression to identify independent predictors of GIB among patients admitted to the ICU, reporting ORs and corresponding 95% CI.

We used SAS V.9.4 (Cary, North Carolina, USA) for analyses. All recorded p values are two-sided.

## RESULTS

We identified 4439 patients admitted to the medical ICUs within the time frame specified above free of a pre-existing GIB. Table 1 shows these patient characteristics. The majority (53%) was male, with median age 60.7 years. Of 4439 patients, 58 (1.3%) developed a new-onset GIB while in the ICU. Of those who developed bleeding, 57, (98%) underwent endoscopy or colonoscopy (table 2). An upper gastrointestinal source was suspected or confirmed in 40 (69%), a lower gastrointestinal source was noted in 6 (10%) and 11 (19%) had no identifiable source. Of the 19 total patients who did not have a source confirmed on initial endoscopy, one underwent a bleeding scan without an identified source, and two required angiography identifying and treating the GIB. In total, 15 of the 58 (26%) patients had recurrent bleeding in the ICU.

Univariable analysis is shown in table 3. There is a trend towards increased GIB among older patients, especially those in the 50–59 years and 60–69 years age groups, with bleeding rates of 1.8% and 2%, respectively, compared with those aged 40–49 years (1.3%) or those above aged 70 years, who bled at a rate of 0.9% ($p=0.04$). White race was associated with increased risk of GIB as well, with a bleeding rate of 1.8%, compared with 1% of black patients and 0.9% with other/unknown listed ($p=0.03$). Length of ICU stay also had a noted association with increased risk of GIB: patients with 11+ ICU days had a 5% risk of GIB, versus those with 1–5 days' stays (0.4%) and those with 6–10 days' length of stays (1.5%) ($p<0.01$). ICU admission laboratory values predictive of GIB included elevated total bilirubin (those with bilirubin >2.5 mg/dL had a 3.1% risk GIB, vs 1% risk for lower levels, $p<0.01$), elevated direct bilirubin (where direct bilirubin >1.5 mg/dL bled at a rate of 3.2%, vs 1.1% for lower levels, $p<0.01$) and elevated creatinine (more than twice the upper limit of normal

**Table 1** Characteristics of patients admitted to the medical intensive care unit (ICU) free of pre-existing GIB (n=4439)

| | Number of patients (%) |
|---|---|
| Age (years) | |
| Mean/median | 59.1/60.7 |
| 18–39 | 791 (18) |
| 40–49 | 528 (12) |
| 50–59 | 823 (19) |
| 60–69 | 940 (21) |
| 70+ | 1357 (31) |
| Sex | |
| Male | 2361 (53) |
| Female | 2078 (47) |
| Race | |
| White | 1790 (40) |
| Black | 625 (14) |
| Other/unknown | 2024 (46) |
| Ethnicity | |
| Hispanic | 1028 (23) |
| Non-Hispanic | 2023 (46) |
| Unknown | 1388 (31) |
| Length of hospital stay (no. days) prior to ICU admission | |
| Mean/median | 5/1 |
| 0 | 1835 (41) |
| 1–5 | 1662 (37) |
| 6–10 | 329 (7) |
| 11+ | 613 (14) |
| Length of ICU stay (no. days) | |
| Mean/median | 6/3 |
| 0–5 | 2941 (66) |
| 6–10 | 802 (18) |
| 11+ | 696 (16) |
| Haematocrit* | |
| Normal to 2% below | 1440 (33) |
| 1.99–5% below LLN | 653 (15) |
| 5.01–8% below LLN | 660 (15) |
| ≤8.01% below LLN | 1551 (36) |
| Albumin (g/dL) | |
| ≥3.5 | 1192 (29) |
| 2.5–3.4 | 1948 (47) |
| <2.5 | 1037 (25) |
| Total bilirubin (mg/dL) | |
| ≤1.3 | 3044 (73) |
| 1.4–2.5 | 499 (12) |
| >2.5 | 638 (15) |
| Direct bilirubin (mg/dL) | |
| ≤0.4 | 2898 (69) |
| 0.5–1.5 | 746 (18) |
| >1.5 | 538 (13) |
| AST (U/L) | |
| <39 | 2315 (55) |
| 39–99 | 1133 (27) |
| 100–499 | 539 (13) |
| ≥500 | 199 (5) |
| ALT (U/L) | |
| <42 | 2946 (70) |
| 42–99 | 720 (17) |
| 100–499 | 365 (9) |
| ≥500 | 150 (4) |
| Alkaline phosphatase (U/L) | |
| ≤130 | 3079 (74) |
| 131–499 | 989 (24) |
| ≥500 | 118 (3) |
| Creatinine | |
| Normal† | 1819 (42) |
| 1–2× ULN | 1271 (30) |
| ≥2×ULN | 1204 (28) |
| INR | |
| <1.5 | 2928 (70) |
| 1.5–2.5 | 896 (21) |
| >2.5 | 368 (9) |
| aPTT (seconds) | |
| ≤35.7 | 2296 (57) |
| 35.8–71.4 | 1548 (38) |
| ≥71.5 | 216 (5) |
| Mechanical ventilation | |
| Yes | 1894 (43) |
| No | 2545 (57) |
| Gastrointestinal protective medications | |
| None | 934 (21) |
| PPI PO | 1.468 (33) |
| PPI IV | 1314 (30) |
| H2RA PO | 411 (9) |
| H2RA IV | 312 (7) |
| Developed GIB in ICU | 58 (1.31) |

*Normal values for haematocrit: 36.8% for men, 35.4% for women.
†Normal values for creatinine: 1.2 mg/dL for men, 0.9 mg/dL for women.
aPTT, partial thromboplastin time; ALT, alanine transaminase; AST, aspartate transaminase; GIB, gastrointestinal bleeding; H2RA, histamine 2 receptor antagonist; INR, international normalised ratio; IV, intravenous; LLN, lower limit of normal; PO, orally administered; PPI, proton pump inhibitor; ULN, upper limit of normal.

bled at rate of 2.4%, vs normal or creatinine less than twice the upper limit of normal, who bled at 0.9%, p<0.01). Those with an AST of 100–499 U/L bled at a rate of 2.6%, those with AST >500 U/L bled at a rate of 2%, those with AST 39–90 U/L bled at a rate of 1.6%, and for patients with normal AST (<39 U/L) the bleeding rate was 0.9% (p<0.01). Included subjects with an INR of >2.5 had a bleeding rate of 2.4%, as compared with a normal INR (1.1%) and a slightly elevated INR (1.5–2.5), which bled 1.8%, p=0.04. Mechanical ventilation was associated with GIB, with intubated patients bleeding at a rate of 2.1% vs 0.7% for non-intubated patients (p<0.01).

Regarding prophylaxis, GIB occurred in 2.6% of those receiving intravenous PPI, 1.2% receiving oral PPI and 0.2% who did not receive PPIs (p<0.01).

**Table 2** Gastrointestinal (GI) bleeding that occurred in the medical intensive care unit (ICU) (n=58)

| | Number of patients (%) |
|---|---|
| Upper GI bleeding | 40 (69) |
| Gastric or duodenal ulcer | 7 (12) |
| Gastropathy | 6 (10) |
| Erosions | 6 (10) |
| Oesophagitis | 3 (5) |
| Variceal haemorrhage | 4 (7) |
| Mallory Weiss or other oesophageal tear | 2 (3) |
| Vascular (angioectasia, Dieulafoy's) | 3 (5) |
| Tumour | 1 (2) |
| No source identified, but suspected upper GI | 8 (14) |
| Lower GI bleeding | 6 (10) |
| Colitis | 1 (2) |
| Colonic ulcers | 2 (3) |
| Diverticular bleeding | 1 (2) |
| Rectal artery | 1 (2) |
| Friable mucosa | 1 (2) |
| GI bleeding, source not identified but underwent endoscopy | 11 (19) |
| GI bleeding noted clinically, no EGD or workup | 1 (2) |
| Total | 58 |

Of these, 57 patients underwent endoscopy for gastrointestinal bleeding (GIB) workup.
EGD, esophagoduodenoscopy.

The results of the multivariable logistic regression model are shown in table 4. We omitted the laboratory values of direct bilirubin, ALT and alkaline phosphatase from the multivariable model because of collinearity with total bilirubin and AST. We were also unable to perform multivariable analysis of gastrointestinal prophylaxis given the small numbers of patients on H2 blockers, which made the model unstable. Black race had borderline statistical significance associated with lower risk of GIB (OR 0.39, 95% CI 0.15 to 1.02, p=0.05). Length of stay in the ICU was strongly associated with the risk of GIB, (OR for 6–10 days vs 1–5 days: 3.94; 95% CI 1.60 to 9.72; OR for 11+ days vs 1–5 days: 14.78; 95% CI 6.37 to 34.30). When measuring the length of ICU stay as a continuous variable, the OR was 1.06 (95% CI 1.04 to 1.09, p<0.01), indicating a 6% increase in risk of GIB per each additional ICU day. Elevated creatinine significantly increased risk of GIB (for creatinine >twice the upper limit of normal: OR 2.35 (95% CI 1.18 to 4.68, p=0.02). Elevated bilirubin on ICU admission (OR 2.08; 95% CI 0.97 to 4.47, p=0.06) and elevated AST on ICU admission (OR 2.20; 95% CI 0.96 to 5.03, p=0.06) both trended towards increased risk of GIB that did not meet statistical significance. Age, length of hospital stay prior to ICU admission, haematocrit, albumin, coagulation factors and mechanical ventilation did not have significant effects on GIB risk in our multivariable model.

Among those patients with new-onset GIB in the ICU, 47% died during that hospitalisation, as compared with those without a GIB, whose inhospital mortality was 30%, p<0.01.

## DISCUSSION

In our study, the overall incidence for new-onset GIB in the medical ICU was low, 1.3%. This value is lower than the rate reported in the only other study we encountered over the last 5 years (2.6%).[15] In addition, we found that length of ICU stay and increased creatinine were significantly associated with increased risk of GIB, and elevated bilirubin and AST were borderline statistically significant for increased risk of GIB.

Elevated bilirubin was found to be associated with GIB with borderline significance. While on univariable analysis both total and direct were associated with increased bleed risk, we studied only total bilirubin in our multivariable analysis given collinearity. It is likely that the bilirubin serves as a marker for liver disease and can lead to GIB through known sequelae such as portal hypertension (varices, portal hypertensive gastropathy) or synthetic dysfunction (coagulopathy). Among 25 patients with GIB who had an elevated total bilirubin on ICU admission, 13 (52%) had an elevated total bilirubin at baseline, suggesting some pre-existing hepatic dysfunction, whereas 48% had a normal or lower value. Elevated AST reflects liver injury, and is similarly associated with GIB (also of borderline significance). Creatinine reflecting both acute and chronic kidney injury, was significantly associated with GIB. Among 40 patients with GIB who had an elevated creatinine on ICU admission, 23 (58%) had an elevated creatinine at baseline, suggesting pre-existing renal dysfunction, whereas 42% had a normal or lower value. Patients on renal replacement therapy or with marked kidney injury have qualitative platelet defects, predisposing them to bleeding.

We found that length of stay in the ICU was associated with an increased risk of GIB on both univariable and multivariable analysis. Longer ICU stays can serve as a proxy for severity of illness, and thus increase the risk of GIB. This association may be due to increased time in which patients were at risk for the outcome of GIB; we were unable to perform time-to-event analysis due to the relatively rare outcome of GIB in this population.

Mechanical ventilation is a known risk factor for GIB, and in univariable analysis was associated with GIB. On multivariable analysis, this association was no longer significant. Existing literature identifies mechanical ventilation as a risk factor for GIB, but the risk emanates from undergoing mechanical ventilation for >48 hours.[3 22] Due to limitations in data retrieval, we could not uniquely identify patients only on ventilators for >48 hours, and therefore, we included patients who were on any given duration of mechanical ventilation in this category.

**Table 3** Univariable analysis of predictors of GIB in patients admitted to the intensive care unit (ICU)

| | Number (%) with new-onset GIB in ICU (n=58) | p Value |
|---|---|---|
| Age (years) | | |
| 18–39 | 5 (0.6) | 0.04 |
| 40–49 | 7 (1.3) | |
| 50–59 | 15 (1.8) | |
| 60–69 | 19 (2) | |
| 70+ | 12 (0.9) | |
| Sex | | 0.57 |
| Male | 33 (1.4) | |
| Female | 25 (1.2) | |
| Race | | 0.03 |
| White | 33 (1.8) | |
| Black | 6 (1) | |
| Other/unknown | 19 (0.9) | |
| Ethnicity | | 0.21 |
| Hispanic | 10 (1) | |
| Non-Hispanic | 33 (1.6) | |
| Unknown | 15 (1.1) | |
| Length of hospital stay (no. days) prior to ICU admission | | |
| Mean/median | 4/1 | 0.24 |
| 0 | 18 (1) | |
| 1–5 | 26 (1.6) | |
| 6–10 | 7 (2.1) | |
| 11+ | 7 (1.1) | |
| Length of ICU stay (no. days) | | <0.01 |
| Mean/ median | 15/12 | |
| 0–5 | 11 (0.4) | |
| 6–10 | 12 (1.5) | |
| 11+ | 35 (5) | |
| Haematocrit* | | 0.62 |
| Normal to 2% below | 16 (1.1) | |
| 1.99–5% below LLN | 8 (1.2) | |
| 5.01–8% below LLN | 12 (1.8) | |
| ≤8.01% below LLN | 21 (1.4) | |
| Albumin (g/dL) | | 0.41 |
| ≥3.5 | 14 (1.2) | |
| 2.5–3.4 | 31 (1.6) | |
| <2.5 | 11 (1.1) | |
| Total bilirubin (mg/dL) | | <0.01 |
| ≤1.3 | 31 (1) | |
| 1.4–2.5 | 5 (1) | |
| >2.5 | 20 (3.1) | |
| Direct bilirubin (mg/dL) | | <0.01 |
| <0.4 | 31 (1.1) | |
| 0.5–1.5 | 8 (1.1) | |
| >1.5 | 17 (3.2) | |
| AST (U/L) | | <0.01 |
| <39 | 20 (0.9) | |
| 39–90 | 18 (1.6) | |
| 100–499 | 14 (2.6) | |
| ≥500 | 4 (2) | |
| ALT (U/L) | | 0.08 |
| <42 | 31 (1.1) | |
| 42–99 | 15 (2.1) | |
| 100–499 | 8 (2.2) | |
| ≥500 | 2 (1.3) | |
| Alkaline phosphatase (U/L) | | 0.41 |
| ≤130 | 38 (1.2) | |
| 131–499 | 15 (1.5) | |
| ≥500 | 3 (2.5) | |
| Creatinine | | <0.01 |
| Normal† | 16 (0.9) | |
| 1–2× ULN | 11 (0.9) | |
| ≥2× ULN | 29 (2.4) | |
| INR | | 0.04 |
| <1.5 | 31 (1.1) | |
| 1.5–2.5 | 16 (1.8) | |
| >2.5 | 9 (2.4) | |
| aPTT (seconds) | | 0.51 |
| ≤35.7 | 27 (1.2) | |
| 35.8–71.4 | 25 (1.6) | |
| ≥71.5 | 3 (1.4) | |
| Mechanical ventilation | | <0.01 |
| Yes | 39 (2.1) | |
| No | 19 (0.7) | |
| Gastrointestinal protective medications | | <0.01 |
| None | 2 (0.2) | |
| PPI PO | 17 (1.2) | |
| PPI IV | 34 (2.6) | |
| H2RA PO | 3 (0.7) | |
| H2RA IV | 2 (0.6) | |

*Normal values for haematocrit: 36.8% for men, 35.4% for women.
†Normal values for creatinine: 1.2 mg/dL for men, 0.9 mg/dL for women.
For some patients' lab values, there were missing values. In these instances, the categories may not sum to the total n.
aPTT, partial thromboplastin time; ALT, alanine transaminase; AST, aspartate transaminase; GIB, gastrointestinal bleeding; histamine 2 RA, H2 receptor antagonist; INR, international normalised ratio; IV, intravenous; LLN, lower limit of normal; PPI, proton pump inhibitor; PO, orally administered; ULN, upper limit of normal.

Paradoxically, patients on a PPI (orally administered or intravenous) had increased risk of GIB in our univariable model. We were unable to perform a multivariable analysis due to the small numbers creating an unstable model, but our univariable results are likely due to reverse causality and confounding by indication, wherein patients with a high underlying risk of GIB were given the most aggressive prophylactic therapy. That is, those patients that received early PPIs may have had previous GIB or other comorbidities we were unable to capture that were likely to predispose them to bleeding.

We had hypothesised that elevated INR (from anticoagulation or pre-existing hepatic dysfunction) would

**Table 4** Multivariable logistic regression identifying independent variables associated with GIB

| | OR (95% CI) | p Value |
|---|---|---|
| Age (years) | | |
| 18–39 | 1.0 | |
| 40–49 | 1.63 (0.49 to 5.45) | 0.42 |
| 50–59 | 1.98 (0.67 to 5.83) | 0.21 |
| 60–69 | 2.14 (0.74 to 6.20) | 0.16 |
| 70+ | 1.45 (0.48 to 4.37) | 0.51 |
| Sex | | |
| Male | 1.0 | |
| Female | 0.84 (0.48 to 1.50) | 0.56 |
| Race | | |
| White | 1.0 | |
| Black | 0.39 (0.15 to 1.02) | 0.05 |
| Other/unknown | 0.57 (0.24 to 1.38) | 0.21 |
| Ethnicity | | |
| Non-Hispanic | 1.0 | |
| Hispanic | 0.66 (0.30 to 1.47) | 0.30 |
| Unknown | 0.83 (0.31 to 2.20) | 0.71 |
| Length of hospital stay (no. days) prior to ICU admission | | |
| 0 | 1.0 | |
| 1–5 | 1.64 (0.86 to 3.14) | 0.14 |
| 6–10 | 1.32 (0.48 to 3.62) | 0.58 |
| 11+ | 0.94 (0.35 to 2.53) | 0.90 |
| Length of ICU stay (no. days) | | |
| 1–5 | 1.0 | |
| 6–10 | 3.94 (1.60 to 9.72) | <0.01 |
| 11+ | 14.78 (6.37 to 34.30) | <0.01 |
| Haematocrit* | | |
| Normal to 2% below | 1.0 | |
| 1.99–5% below LLN | 0.74 (0.28 to 1.91) | 0.53 |
| 5.01–8% below LLN | 1.00 (0.43 to 2.30) | 0.99 |
| ≤8.01% below LLN | 0.76 (0.35 to 1.64) | 0.48 |
| Albumin (g/dL) | | |
| ≥3.5 | 1.0 | |
| 2.5–3.4 | 1.09 (0.55 to 2.18) | 0.81 |
| <2.5 | 0.62 (0.26 to 2.02) | 0.29 |
| Total bilirubin (mg/dL) | | |
| ≤1.3 | 1.0 | |
| 1.4–2.5 | 0.74 (0.27 to 2.02) | 0.55 |
| >2.5 | 2.08 (0.97 to 4.47) | 0.06 |
| AST (U/L) | | |
| <39 | 1.0 | |
| 39–99 | 1.67 (0.83 to 3.39) | 0.15 |
| 100–499 | 2.20 (0.96 to 5.03) | 0.06 |
| ≥500 | 2.62 (0.74 to 9.23) | 0.13 |
| Creatinine | | |
| Normal† | 1.0 | |
| 1–2× ULN | 0.91 (0.40 to 2.08) | 0.83 |
| ≥2×ULN | 2.35 (1.18 to 4.68) | 0.02 |
| INR | | |
| <1.5 | 1.0 | |
| 1.5–2.5 | 1.16 (0.53 to 2.53) | 0.71 |
| >2.5 | 1.51 (0.57 to 4.01) | 0.41 |
| aPTT (seconds) | | |
| ≤35.7 | 1.0 | |
| 35.8–71.4 | 0.70 (0.35 to 1.40) | 0.31 |
| ≥71.5 | 0.75 (0.20 to 2.80) | 0.67 |
| Mechanical ventilation | | |
| Yes | 1.14 (0.58 to 2.27) | 0.71 |
| No | 1.0 | |

*Normal values for haematocrit: 36.8% for men, 35.4% for women.
†Normal values for creatinine: 1.2 mg/dL for men, 0.9 mg/dL for women.
aPTT, partial thromboplastin time; AST, aspartate transaminase; GIB, gastrointestinal bleeding; ICU, intensive care unit; INR, international normalised ratio; LLN, lower limit of normal; ULN, upper limit of normal.

lead to increased risk of GIB. The lack of statistical significance was likely related to low power, since only nine patients with an INR of >2.5 had a GIB. Additionally, the INR studied was obtained on ICU admission and not necessarily reflective of the ongoing state of coagulation during an ICU course, which could change considerably with reversal agents and blood products.

The inhospital mortality among those with new-onset GIB in the ICU was 47%, greater than those who did not have a GIB (30%), p<0.01. This is congruent with prior studies showing that GIB increases inhospital mortality.[19]

Our study has a number of limitations. This was a single-centre study of a tertiary-care setting, raising the question of generalisability. We lacked clinical information that could further inform underlying risk of GIB, like use of aspirin and antiplatelet agents, warfarin, heparin and other anticoagulant agents. Similarly, information regarding pre-existing hepatic and renal dysfunction or conditions predisposing to coagulopathy or bleeding was limited in this cohort.

Our end point was a suspected GIB, but was not always visually identified (see table 2). While other studies have used endoscopic confirmation or other modalities (such as nasogastric contents) to confirm bleeding, in this study we relied on the critical care team's assessment to determine this end point. A limitation is that this method excludes those who developed GIB but were missed by the ICU team. Alternatively, given that some patients were endoscoped without any source found, the number could be an overestimation.

## CONCLUSION

In summary, in this analysis of patients entering the medical ICUs of this tertiary-care referral centre, we found that 1.3% had a new-onset GIB and that ICU length of stay and elevated creatinine on ICU admission were associated with an increased risk of GIB. Elevated bilirubin and AST on ICU admission also reached near significant values for predicting a GIB in the ICU. Those patients who developed a GIB in the

ICU had markedly increased mortality. Patients with the above risk factors may benefit from increased vigilance for the development of this outcome, which, while decreasing in incidence, still affects a sizeable portion of the ICU population and carries additional morbidity and mortality.

## Significant of this study

**What is already known on this topic?**

Gastrointestinal bleeding (GIB) in patients with critical illness has been declining in incidence since the 1980s, when it was as high as 16% to 2–7% from the 1990s to 2000s. Risk factors include recent surgery, burns, trauma, liver or renal dysfunction, sepsis, hypotension, coagulopathy and prolonged mechanical ventilation.

**What this study adds?**

The incidence is lower than previously reported, and while liver dysfunction and renal dysfunction remain risk factors, other historical risk factors, such as mechanical ventilation, were no longer associated with GIB, suggesting improved prophylaxis adherence.

**How might it impact on clinical practice in the foreseeable future?**

Patients' elevated bilirubin, aspartate transaminase and creatinine upon admission, and patients with longer intensive care unit stay should be monitored for development of GIB.

**Contributors** All authors contributed to this project, meeting ICMJE recommendations for authorship. We can also assure there are no other contributors who have been excluded as authors.

**Competing interests** None declared.

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**Data sharing statement** Statistical analyses were performed by the authors, and all data are presented in the manuscript. For data analysis and models, please contact the authors.

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# Incidence and risk factors for gastrointestinal bleeding among patients admitted to medical intensive care units

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## Notes