International Journal of General Medicine

Dovepress

open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Gastrointestinal Bleeding in COVID-19 Infected Patients, and Management Outcomes

Amnah Al Hanaei[1], Fatima AlKindi[2], Aysha Alkhemeiri[2], Satish Chandrasekhar Nair[3]

[1]Division of Gastroenterology, Tawam Hospital, Al Ain, Emirate of Abu Dhabi, United Arab Emirates; [2]Department of Internal Medicine, Tawam Hospital, Al Ain, Emirate of Abu Dhabi, United Arab Emirates; [3]Department of Academic Affairs, Tawam Hospital & the College of Medicine UAE University, Al Ain, Emirate of Abu Dhabi, United Arab Emirates

Correspondence: Satish Chandrasekhar Nair, Department of Academic Affairs, Tawam Hospital, Al Ain, United Arab Emirates, Tel +97137074736, Email satchi2000@outlook.com

Introduction: Gastrointestinal bleeding in COVID-19-infection poses unique challenges to patients owing to the high risk of concomitant respiratory failure. However, endoscopic care providers are prone to transmission. This study aimed to understand the risk and management outcomes of gastrointestinal bleeding in COVID-19-infected patients.

Methods: Data were abstracted from electronic patient medical records, using ICD 10 codes, and demographic and clinical data were collected, for COVID-19-infected patients who developed gastrointestinal (GI) bleeding. Complications related to COVID-19 infection and management outcomes of GI bleeding were studied. Statistically, descriptive analysis was used because of the small sample size.

Results: Eighteen COVID-19-infected patients developed episodes of GI bleeding, yielding a prevalence of 0.45%. Their mean age was 74.8 years, 55.5% were female, and 66.6% of patients (n=12) had upper GI bleeding symptoms, predominantly melena (55.5%), followed by coffee ground nasogastric aspirates (n=2). Only two patients (11.11%) had episodes of lower GI bleeding, and the remaining four patients (22.2%) had recurrent acute anemia requiring blood transfusion. The Glasgow-Blatchford score (GBS) at presentation ranged between 6 to 16 (mean 8.8) and seven patients (38.8%) underwent endoscopic evaluation for GI bleeding. The predominant comorbid conditions included hypertension (22.2%), diabetes mellitus (27.7%), chronic kidney disease (50%), ischemic heart disease (33%), atrial fibrillation (11.1%), and peripheral vascular disease (11.1%). The median hospitalization was 24.6 days (range: 3–54 days). The 30-day mortality rate in our cohort was 22.2%, (4/18) mainly noted in older patients aged> 60 years with comorbid conditions and severe COVID-19 infection.

Conclusion: The prevalence of GI bleeding observed in our cohort was approximately 0.45%, significantly lower than the global prevalence observed, majority (66%) had upper GI bleeding. The exact reasons for the observed low prevalence of GI bleeding cannot be explained and will be the subject of future research.

Plain Language Summary: Stomach bleeding in COVID-19-infected patients is a significant threat to the patients. This study aimed to understand the risk and management of stomach bleeding in patients infected with COVID-19. Medical records were retrospectively screened using appropriate disease codes to identify patients and collect information about their demographics and complications. Only 18 patients with stomach bleeding presented to the public hospitals in Al Ain from a total of 4000 COVID-19 patients during the peak of the pandemic. Majority of the patients had upper stomach bleeding (66%); the mean age of the patients was 78 years, majority of them being female (55.5%). The major comorbidity among the patients was chronic kidney disease (50%). The average duration of hospital stay was less than 25 days and the 30-day mortality was 22%. A higher mortality rate was observed in elderly patients with severe infections. The stomach bleeding observed in our patients was far less (0.45%) that in other COVID-19 patients globally, the reasons for which are not unknown.

Keywords: pandemic, Gulf, United Arab Emirates, endoscopy, medical therapy, Middle East

Received: 13 December 2023
Accepted: 13 March 2024
Published: 27 March 2024

Introduction

The global COVID-19 (SARS-CoV2) infection assumed a catastrophic public health crisis with significant morbidity and mortality that affected the world's population.[1] The clinical severity of COVID-19 infections varied from asymptomatic or mild disease to severe pneumonia, multi-organ failure, and death.[1] Respiratory distress indices predominated and largely determined patient prognoses. The incidence of Gastrointestinal (GI) manifestations in COVID-19 patients have been reported to between 3% and 61%, whereas GI bleeding contributes 1.1% to 13%, escalating patient morbidity and mortality.[2] Following hospital admission, GI bleeding was rated a significant component of multisystem infectious diseases. The three predominant reported characteristics of GI bleeding are a) that it is often from mucosal inflammation and erosions leading to mild bleeding, b) severe GI bleeding from peptic ulcer disease or severe gastritis from COVID-19 pneumonia, and c) lower GI bleeding resulting from ischemic colitis associated with thrombosis and hyper coagulopathy from COVID-19 infection.[3] Despite the anticipated risk of contracting COVID-19 from GI endoscopy performed on COVID-19-infected patients, the actual risks reported do not indicate it to be high.[3] The widespread use of sanitization techniques, personal protective equipment, and the advent of vaccinations against the virus have gradually enhanced the safety and frequency of performing GI endoscopy in COVID-19-infected patients. GI bleeding in COVID-19 patients presented as a major healthcare system challenge due to the rise in the number of cases and the introduction of newer viral variants.[4] The gastrointestinal SARS CoV 2 involvement can range from enteritis, acute hepatitis, acute pancreatitis, acute acalculous cholecystitis, and colitis to a lesser degree gastrointestinal bleeding. Performing endoscopic therapy for acute GI bleeding in COVID-19-infected patients has risks and benefits, and medical therapy may be an alternative approach.[5] Despite global data, limited COVID-19-related GI bleeding has been reported in the Middle East, particularly in the UAE. Therefore, the purpose of our study was to identify the risk factors, management outcomes (endoscopic or medical), and mortality rates associated with GI bleeding in COVID-19 infected patients.

Materials and Methods

Data were extracted from the electronic patient medical records of Tawam and Al Ain Hospitals, Joint Commission-accredited academic medical centers in the eastern region of the emirate of Abu Dhabi.[1] Both hospitals were the designated referral centers for COVID-19 and handled 90% of all the COVID-19 cases in the Al Ain region.[1] Ethical approval (#828) was obtained from the Central Research Ethics Committee for COVID19 Research, Department of Health- Abu Dhabi, United Arab Emirates. Retrospective review of patient medical charts did not require patient consent, provided no patient identifiers are collected for the study, and that patients have consented to using their anonymized health information for research purposes, upon initial visit to the hospital. The study was conducted according to the principles of the International Conference for Harmonization and Good Clinical Practice, per the Declaration of Helsinki. Data confidentiality and patient privacy were adhered to per local, and international regulations. The medical records were abstracted using ICD 10 codes, by physician researchers blinded to the study hypothesis, following approval by the Human Research Ethics Committee. The study duration was one year, from March 2021 to March 2022. Adult patients aged above 18 years, positive for COVID-19 infection confirmed by RT-PCR (polymerase chain reaction), and episodes of gastrointestinal (GI) bleeding during hospitalization, constituted the inclusion criteria. Patients younger than 18 years of age, those with bleeding from non-GI sources, and those with bleeding episodes following discharge from COVID-19 infection were excluded. Demographic and clinical data regarding COVID-19 infection were collected, including age, sex, comorbidities, presenting signs and symptoms, the clinical and radiological severity of COVID-19, and laboratory results. Complications related to COVID-19 infection such as sepsis, the need for critical care admission, the requirement of oxygen therapy or noninvasive or invasive ventilation methods, inotropic support, acute kidney injury with the need for renal replacement therapy, and thrombotic events requiring anticoagulation were also recorded. Gastrointestinal (GI) episodes are classified as upper or lower GI sources depending on the symptoms. All charts of patients with potential GI bleeding identified by the ICD-19 codes were manually reviewed to confirm the diagnosis.[1] An upper GI bleeding was defined as the presence of hematemesis or melena.[6] A lower GI bleeding was defined as hematochezia.[7] Risk factors for GI bleeding, anticoagulant use, and the duration of COVID-19 diagnosis were also recorded. The Glasgow-Blatchford score was calculated at the onset of signs of low-risk upper GI bleeding.[8] The management outcomes were classified into

two groups based on endoscopic intervention or medical therapy with an intravenous proton pump (PPI) inhibitor used as either a bolus twice daily dose or infusion. All patients received initial resuscitation with intravenous fluids, blood, and blood product transfusion as needed to maintain hemoglobin levels above 8 mg/dl and to hold anticoagulation. Endoscopic findings from esophagogastroduodenoscopy (EGD) and colonoscopy have been previously reported. The 30-day hospital mortality rate was recorded. Statistically, descriptive analysis was used because of the small sample size. Data are expressed as means, medians with interquartile IQ ranges, and percentages, as appropriate.

Results

A total of 4000 COVID-19 infected patients were admitted to both hospitals during the study period. Interestingly, eighteen COVID-19-infected patients (0.45%) developed episodes of GI bleeding. The mean age was 74.8 years, 55.5% were females and half of patients were UAE nationals (55.5%). Among the patients with GI bleeding, 66.66% of patients (n=12) had upper GI bleeding symptoms, predominantly melena (55.5%), followed by coffee ground nasogastric aspirates (n=2). While only two patients (11.11%) had episodes of lower GI bleeding (hematochezia), and the remaining four patients (22.2%) had recurrent acute anemia requiring blood transfusion. The Glasgow-Blatchford score (GBS) at presentation ranged between 6 to 16 (mean 8.8). The comorbid conditions in our cohort included hypertension (22.2%, 4/18), diabetes mellitus (27.7%, 5/18)), chronic kidney disease (50%, 9/18)), ischemic heart disease (33%, 8/18)), atrial fibrillation (11.1%, 2/18)), and peripheral vascular disease (11.1%). 2/18), interstitial lung disease (11.1% 2/18)), chronic liver disease (5.5%, 1/18), kidney transplant 5.5%, 1/18), pulmonary embolism 5.5%, 1/18), immune thrombocytopenic purpura (ITP) (5.5%.1/18) and Von Willebrand disease 5.5% (1/18). The chronic use of anticoagulation or antiplatelet therapy was identified in 13 patients (72.2%) such as aspirin (55.5%), clopidogrel (5.55%), and apixaban (11.1%). No previous episodes of GI bleeding were observed in our cohort (Table 1).

Table 1 Clinical Characteristics and Demographic Data of COVID-19-Infected Patients Who Developed Gastrointestinal Bleeding (n=18)

Baseline Characteristics of Study Participants	Number (%)
Patients	N = 18
Mean age	74.8 years
Male	8 (44.4)
Female	10 (55.5)
Comorbid conditions	
Diabetes mellitus	5 (27.7)
Hypertension	4 (22.2)
Ischemic heart disease	8 (33.0)
Chronic kidney disease	9 (50.0)
Peripheral vascular disease	2 (11.1)
Atrial fibrillation	2 (11.1)
Interstitial lung disease	2 (11.1)
Pulmonary embolism	1 (5.5)
Immune thrombocytopenic purpura (ITP)	1 (5.5)
Von Willebrand disease	1 (5.5)
Kidney transplant	1 (5.5)

(*Continued*)

Table 1 (Continued).

Baseline Characteristics of Study Participants	Number (%)
GI bleeding symptoms	
Melena	10 (55.5)
Coffee-ground nasogastric aspirates	2 (11.1)
Lower GI bleeding	2 (11.1)
Recurrent anemia	4 (22.2)
Anticoagulation	
Aspirin	10 (55.5)
Clopidogrel	1 (5.5)
Warfarin	0 (0)
Apixaban	2 (11.1)
Low molecular weight heparin for COVID-19	17 (94.4)

The diagnosis of COVID-19 was confirmed by two positive PCR results. The presenting symptoms in our cohort were predominantly fever and respiratory symptoms, whereas diarrhea, vomiting, and loss of taste were reported in less than 20% of patients. The severity of COVID-19 infection based on CT chest scores ranged from mild 38.8%, 7/18), moderate (22.2%, 2/18), severe pneumonia (16.6%, 3/18), and only 4 patients 22.22%) had normal initial radiological presentation. Initial laboratory investigations revealed a mean hemoglobin level (6.8 g/L), platelet level (277.9 x10^9/L), ferritin level (941 mcg/L), lactate dehydrogenase LDH (318.4 IU/L), and D Dimer (5.5 mg/L). The majority of the patients (66.6%, 12/18) had hypoxia related to COVID-19 pneumonia and required supplemental oxygen via high flow cannula (27.7%), non-invasive pressure ventilation (11.1%), and five patients (27.7%) developed acute respiratory failure managed with mechanical ventilation. Critical care admission was required in 44.4% of patients (8/18) with complications related to severe infection, including acute respiratory distress syndrome (44.4%), septic shock with secondary nosocomial infection (27.7%), acute kidney injury (16.6%) requiring renal replacement therapy (11/1%), and cytokine storm (5.55%). In our cohort, the majority of COVID-19-infected patients (94.4%) were on anticoagulation with low molecular weight heparin (LMWH), except one patient who had Von Willebrand disease and immune thrombocytopenia (Table 2). The median interval between an episode of GI bleeding and admission was 13.1 days and most patients had upper GI bleeding (66.6%). The mean decrease in the hemoglobin was 3.7 gm/L. All patients received initial resuscitation with intravenous fluids, blood, and blood product transfusion as needed to maintain hemoglobin levels above 8 mg/dl and to hold anticoagulation. All patients received intravenous proton pump inhibitors in the form of either an infusion or bolus twice daily.

Approximately two-thirds of patients (61.1%, 11/18) were treated conservatively, and only seven patients (38.8%) underwent endoscopic evaluation for GI bleeding. Five patients (5/7) underwent both upper and lower endoscopy performed and two patients underwent upper endoscopy only. The endoscopic findings of seven upper EGD performed were reflux esophagitis grade B (2), grade 1 esophageal varices (1), and gastric ulcer (3) with Forrest class IIa, Ib, III, and two normal studies. (Figures 1–3) Endoscopic therapeutic intervention using injection (adrenaline injection + APC) and clips was required in two patients. Colonoscopy procedures performed in five patients revealed diverticular bleeding (n = 1), internal hemorrhoids (n = 2), rectal ulcer (n = 1), and one normal study. (Figure 2) One patient required interventional radiological IR embolization. Some endoscopic procedures were performed after negative COVID-19 PCR results and discharge from the hospital in three patients (Figures 1–3). The median hospitalization was 24.6 days (range: 3–54 days). The 30 days mortality rate in our cohort was 22.2%, 4/18) mainly noted in older patients aged> 60 years with comorbid conditions and severe COVID-19 infection.

Table 2 Laboratory and Clinical Findings of COVID-19-Infected Patients

Laboratory and Clinical Findings of COVID-19-Infected Patients	n (%)
Severity of COVID-19 infection	**n=18**
Mild COVID-19	6 (33.3)
Moderate	4 (22.2)
Severe	8 (44.4)
Laboratory results	Mean
Hemoglobin level	6.8 g/L
Platelet level	277.9 x109/L
Ferritin level	941 mcg/L
D Dimer	5.5 mg/L
Lactate dehydrogenase LDH	318.4 IU/L
COVID-19 oxygen oxygen pneumonia/oxygen	
Supplemental oxygen via high-flow cannula	5 (27.7)
Non-invasive pressure ventilation	2 (11.11)
Mechanical ventilation	5 (27.7)
Extra-pulmonary complications	
Septic shock	5 (27.7)
Acute kidney injury	3 (16.6)
Renal replacement therapy	2 (11/1)
Cytokine storm	1 (5.55)
Secondary nosocomial infection	5 (27.7)
30-day mortality rate	4 (22.2)

Discussion

In our cohort of COVID1-19 hospitalized patients, 18 had gastrointestinal bleeding. The risk factors varied and included chronic use of anticoagulation for atrial fibrillation, antiplatelet therapy for ischemic heart disease, use of anticoagulation during hospitalization, and severity of COVID-19 infection. Two-thirds of the total patients (11/18) were managed conservatively with blood transfusion and intravenous PPI, and had comparable outcomes to seven patients who underwent endoscopic evaluation. The predominant GI bleeding etiologies identified by EGD were esophagitis and gastric ulcers, whereas rectal ulcers and internal hemorrhoids were identified by colonoscopy.

It is reported that in the gastrointestinal tract, the SARS CoV2 virus infects the intestinal epithelial cells via angiotensin-converting enzyme ACE2 receptors leading to replication and various manifestation of the disease.[9] Interestingly, GI biopsies of COVID-19-infected patients with GI bleeding detected the SARS CoV2 RNA in gastric, duodenal, and rectal tissues.[3] In addition, the risk of thromboembolic events and coagulopathy associated with COVID-19 has been well recognized, and recent guidelines support the use of anticoagulation therapy in critically ill COVID-19 infected patients.[10] Ischemic colitis in COVID-19 patients is associated with hypercoagulation.[11] The etiology of GI bleeding in COVID-19-infected patients is multifactorial, and identifying potential risk factors and predictive tools is essential. In our cohort, 72.2% of patients were on chronic antiplatelet therapy or anticoagulation, and 94.4% were started on anticoagulation using low molecular weight heparin (LMWH) per local COVID-19 infection therapy protocol. In

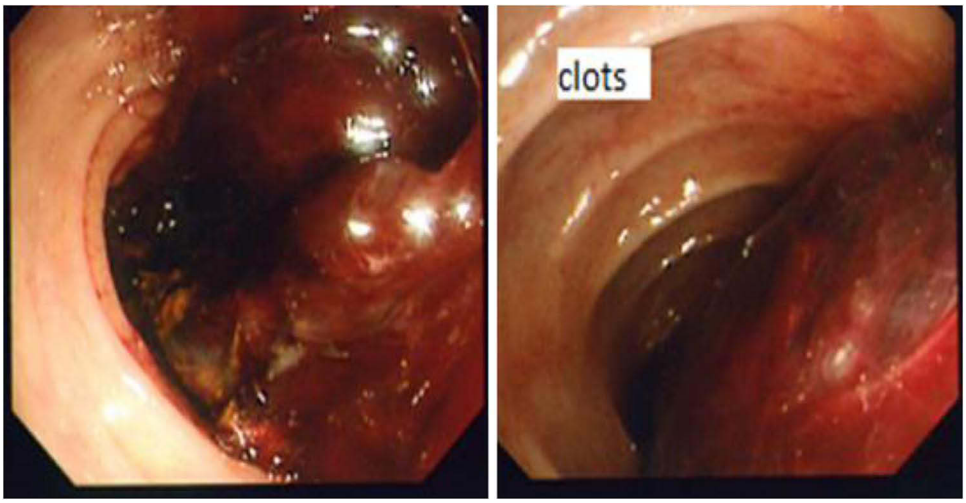

Figure 1 Findings for the source of GI bleeding in COVID-19 patients, sigmoidoscopy indicating huge clots and fresh blood more than 40 cm from the anal verge.

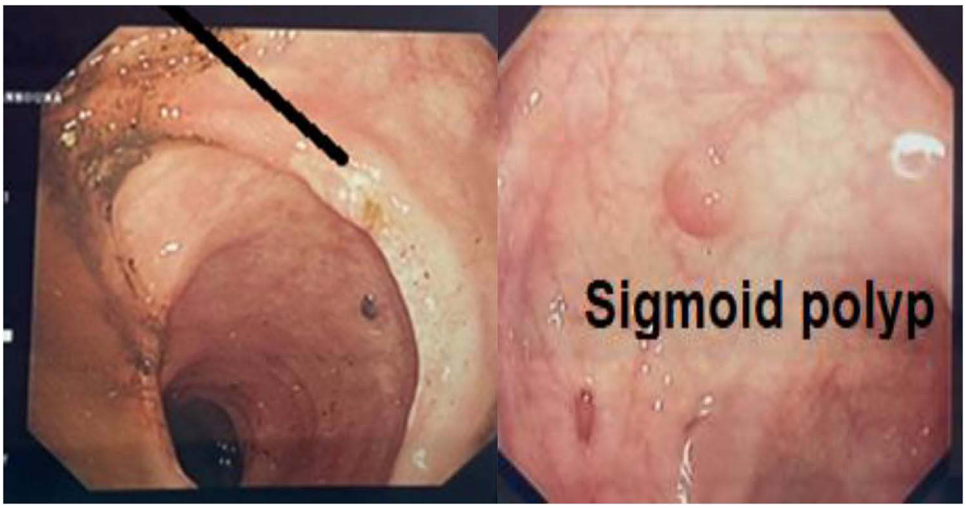

Figure 2 Findings for the source of GI bleeding in COVID-19 patients, colonoscopy indicating solitary rectal ulcer circular at 7 cm from anal verge and one 5mm sessile sigmoid polyp.

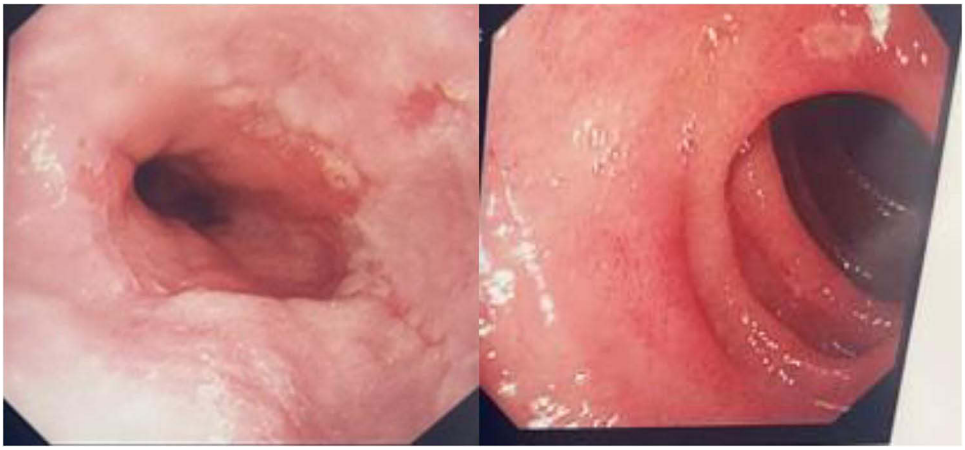

Figure 3 Findings for the source of GI bleeding in COVID-19 patients, esophagogastroduodenoscopy showing Esophageal erosions and reflux disease, duodenal bulbitis with fibrinous ulcers in healing phase.

addition, 50% of the recruited patients had chronic kidney disease with considerable risk of platelet dysfunction and bleeding.

A remarkable reduction in the number of endoscopic procedures performed during the first wave of the COVID-19 pandemic was observed.[2] Several reports indicated a reduction in upper endoscopy studies performed for GI bleeding episodes during the peak of the contagion, that ranging from 40.7% in Austria to 73.4% in China.[12–14] Upper endoscopy is an aerosol-generating procedure that carries the risk of COVID-19 infection. The implementation of infection control measures is fundamental to reducing the risk of COVID-19 transmission among healthcare providers and patients in endoscopy units. International endoscopy societies have published and updated guidelines for performing endoscopy during the COVID-19 pandemic.[15–17] Only seven patients in our cohort who did not respond to medical therapy underwent endoscopic evaluation of the etiology of GI bleeding with a predominant Upper GI source. This retrospective matched 1:2 case-control study included forty-one COVID-19 infected patients with GI bleeding, thirty-one, and ten, with lower GI bleeding.[5] Further the same report indicated that peptic ulcer disease and rectal ulcers from rectal tubes were the most common etiologies identified.[5] Similar to our cohort, only 36.5%of patients underwent endoscopic procedures, and remaining were managed conservatively. Therapeutic endoscopic interventions were required for four patients with upper GI bleeding, and three patients required rectal packing for bleeding rectal ulcers. There was no difference in in-hospital mortality rates between COVID-19 patients with and without GI bleeding.[5] Consistently, the mortality rate in our cohort at 30 days was 22.2% owing to septic shock and severe COVID-19 infection, with no direct relationship with GI bleeding.

Another report described the course of four patients with severe COVID-19 infection and upper GI bleeding, of whom two were on anticoagulation for acute pulmonary embolisms. EGD of the four cases revealed variable degrees of ulcerations in the gastric mucosa or esophagus, and endoscopic intervention was required in three patients.[18] In comparison with our cohort, anticoagulation was used in all admitted COVID-19-infected patients per our local protocol. It is considered a therapeutic option for COVID-related hyper-coagulation and at the same time may simultaneously exacerbate the risk of GI bleeding in vulnerable patients. Interestingly, a propensity score-matched cohort study that included more than three-hundred COVID-19 patients with GI bleeding showed that the use of anticoagulants, steroids, or antiplatelet therapy was not associated with GI bleeding in hospitalized COVID-19 patients.[19] The same study indicated that the prevalence of GI bleeding in hospitalized COVID-19 patients was 3%; the majority was upper GI bleeding in 68% of cases, 104 patients developed GIB on admission (33.2%), and endoscopy was performed in 6% of patients.[19] The mortality was higher in GI bleeding patients, ICU care was required for 45% of the patients, and PPI had a limited role in protection against GI bleeding.[19]

In addition, Cavaliere et al reported favorable outcomes of conservative management for upper GI bleeding in six COVID-19-infected patients without performing endoscopies.[20] Higher Glasgow-Blatchford bleeding scores of 7 and 11 on admission translated to high-risk GIB with a need for intervention.[20] In our study, the Glasgow–Blatchford bleeding score for upper GI bleeding ranged from 6 to 16. Of the 18 patients, 11 responded to conservative management with careful monitoring of hemodynamic parameters, fluid resuscitation, blood transfusion, and medical therapy with PPI, as recommended by the international GI guidelines. Several other case reports and case series have described the causes of GI bleeding in COVID-19 patients, endoscopic findings, and management outcomes.[21] A few COVID-19 patients with GI bleeding require elective intubation for endoscopy. Interventional radiology with selective angioembolization has been reported in rare massive GI bleeding cases.[3] Further studies are needed to ascertain whether COVID-19 infection carries an independent risk for GI bleeding, which will help in developing a risk-stratification model for complications.

Our study has several limitations, such as the small sample size, retrospective nature of the study design, and the interplay of other risk factors. The fact that the study was conducted at only two designated COVID-19 referral public hospitals catering to almost one million people, and that this is the first study from the UAE, contributes to the strengths of the study. Future research involving large multicenter randomized control trials may help understand the risk factors for GI bleeding in COVID-19-infected patients and their outcomes.

Conclusion

GI bleeding in COVID-19-infected patients is rare and multifactorial, with a predominance of upper GI sources. The prevalence of GI bleeding observed in our cohort was approximately 0.45%, significantly lower than the global prevalence observed. Majority (66%) had upper GI bleeding, despite 4000 patients being in COVID-19 care. The exact reason for the observed lower GI bleeding prevalence (0.45%) cannot be explained, although lower age of the patient population in the UAE may be a significant contributor, and other potential factor is the use of PPI prophylaxis in patient receiving anticoagulation. Such observation will be subject of future research.

Abbreviations

GI, gastrointestinal; COVID-19, Corona Virus Infection 2019; UAE, United Arab Emirates; GBS, Glasgow-Blatchford score; PPI, Proton pump inhibitors (PPIs); EGD, Esophagogastroduodenoscopy; IR, Interventional radiology; SARS CoV 2, Severe acute respiratory syndrome coronavirus 2; LMWH, Low molecular weight heparin; ITP, Immune thrombocytopenic purpura; ACE, Angiotensin-converting enzyme; ICU, Intensive care unit.

Ethics Approval and Informed Consent

Ethical approval (#828) was obtained from the Central Research Ethics Committee for COVID-19 Research, Department of Health- Abu Dhabi, United Arab Emirates. Retrospective review of patient medical charts did not require patient consent, provided no patient identifiers are collected for the study, and that patients have consented to using their anonymized health information for research purposes, upon initial visit to the hospital. The study was conducted according to the principles of the International Conference for Harmonization and Good Clinical Practice, per the Declaration of Helsinki.

Acknowledgment

The authors acknowledge Prof. Salah Gariballa, Internal Medicine Department at the College of Medicine and Health Sciences, UAE University, for reading the manuscript. The authors would like to thank the team members who contributed to patient care.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Nair SC, Gasmelseed HI, Khan AA, et al. Assessment of mortality from COVID-19 in a multicultural multi-ethnic patient population. *BMC Infect Dis*. 2021;21(1):1115. PMID: 34715808; PMCID: PMC8554744. doi:10.1186/s12879-021-06762-9
2. Kariyawasam JC, Jayarajah U, Riza R, Seneviratne SL. Gastrointestinal manifestations in COVID-19. *Trans R Soc Trop Med Hyg*. 2021;115(12):1362–1388. PMID: 33728439; PMCID: PMC7989191. doi:10.1093/trstmh/trab042
3. Cappell MS, Friedel DM. Gastrointestinal Bleeding in COVID-19-Infected Patients. *Gastroenterol Clin North Am*. 2023;52(1):77–102. PMID: 36813432; PMCID: PMC9622379. doi:10.1016/j.gtc.2022.10.004
4. Rana SS. Risk of COVID-19 transmission during gastrointestinal endoscopy. *J Dig Endosc*. 2020;11(1):27–30. PMCID: PMC7356654. doi:10.1055/s-0040-1712076
5. Martin TA, Wan DW, Hajifathalian K, et al. Gastrointestinal bleeding in patients with Coronavirus Disease 2019: a Matched Case-Control Study. *Am J Gastroenterol*. 2020;115(10):1609–1616. PMID: 32796176; PMCID: PMC7446989. doi:10.14309/ajg.0000000000000805

6. Wilkins T, Wheeler B, Carpenter M. Upper gastrointestinal bleeding in adults: evaluation and management. *Am Fam Physician*. 2020;101(5):294–300. Erratum in: Am Fam Physician. 2021 Jan 15;103(2):70. PMID: 32109037
7. Ghassemi KA, Jensen DM. Lower GI bleeding: epidemiology and management. *Curr Gastroenterol Rep*. 2013;15(7):333. PMID: 23737154; PMCID: PMC3857214. doi:10.1007/s11894-013-0333-5
8. Chatten K, Purssell H, Banerjee AK, Soteriadou S, Ang Y. Glasgow Blatchford Score and risk stratifications in acute upper gastrointestinal bleed: can we extend this to 2 for urgent outpatient management? *Clin Med*. 2018;18(2):118–122. PMID: 29626014; PMCID: PMC6303462. doi:10.7861/clinmedicine.18-2-118
9. Syed A, Khan A, Gosai F, Asif A, Dhillon S. Gastrointestinal pathophysiology of SARS-CoV2 - a literature review. *J Community Hosp Intern Med Perspect*. 2020;10(6):523–528. PMID: 33194122; PMCID: PMC7599006. doi:10.1080/20009666.2020.1811556
10. Gómez-Mesa JE, Galindo-Coral S, Montes MC, Muñoz Martin AJ. Thrombosis and Coagulopathy in COVID-19. *Curr Probl Cardiol*. 2021;46(3):100742. PMID: 33243440; PMCID: PMC7605852. doi:10.1016/j.cpcardiol.2020.100742
11. Krejčová I, Berková A, Kvasnicová L, et al. Ischemic colitis in a patient with severe COVID-19 pneumonia. *Case Rep Gastroenterol*. 2022;16(2):526–534. PMID: 36157607; PMCID: PMC9459627. doi:10.1159/000525840
12. Schmiderer A, Schwaighofer H, Niederreiter L, et al. Decline in acute upper gastrointestinal bleeding during COVID-19 pandemic after initiation of lockdown in Austria. *Endoscopy*. 2020;52(11):1036–1038. PMID: 32408356; PMCID: PMC7653543. doi:10.1055/a-1178-4656
13. Lantinga MA, Theunissen F, Ter Borg PCJ, Bruno MJ, Ouwendijk RJT, Siersema PD. Trans. IT foundation study group. Impact of the COVID-19 pandemic on gastrointestinal endoscopy in the Netherlands: analysis of a prospective endoscopy database. *Endoscopy*. 2021. 53(2):166–170. doi:10.1055/a-1272-3788. Erratum in: Endoscopy. 2021 Feb;53(2):C11. PMID: 33080630; PMCID: PMC7869035.
14. Duan Z, Duan Q, Liu K, Zhang X, Zhou S, Behalf O; Of Xingtai Society Of Digestive Endoscopy. Impact of the COVID-19 pandemic on Acute Upper Gastrointestinal Bleeding in Xingtai City. *Gastroenterol Res Pract*. 2021;2021:5586030. PMID: 33727916; PMCID: PMC7938257. doi:10.1155/2021/5586030
15. Gralnek IM, Hassan C, Beilenhoff U, et al. ESGE and ESGENA Position Statement on gastrointestinal endoscopy and COVID-19: an update on guidance during the post-lockdown phase and selected results from a membership survey. *Endoscopy*. 2020;52(10):891–898. PMID: 32643767; PMCID: PMC7520543. doi:10.1055/a-1213-5761
16. Repici A, Maselli R, Colombo M, et al. Coronavirus (COVID-19) outbreak: what the department of endoscopy should know. *Gastrointest Endosc*. 2020;92(1):192–197. PMID: 32179106; PMCID: PMC7102667. doi:10.1016/j.gie.2020.03.019
17. Chiu PWY, Ng SC, Inoue H, et al. Practice of endoscopy during COVID-19 pandemic: position statements of the Asian Pacific Society for Digestive Endoscopy (APSDE-COVID statements). *Gut*. 2020;69(6):991–996. PMID: 32241897; PMCID: PMC7211066. doi:10.1136/gutjnl-2020-321185
18. Pradhan F, Alishahi Y. Gastrointestinal bleeding and endoscopic outcomes in patients with SARS-CoV-2. *Clin Endosc*. 2021;54(3):428–431. PMID: 33652519; PMCID: PMC8182236. doi:10.5946/ce.2020.244
19. Trindade AJ, Izard S, Coppa K, Hirsch JS, Lee C, Satapathy SK; Northwell COVID-19 Research Consortium. Gastrointestinal bleeding in hospitalized COVID-19 patients: a propensity score matched cohort study. *J Intern Med*. 2021;289(6):887–894. PMID: 33341978. doi:10.1111/joim.13232
20. Cavaliere K, Levine C, Wander P, Sejpal DV, Trindade AJ. Management of upper GI bleeding in patients with COVID-19 pneumonia. *Gastrointest Endosc*. 2020;92(2):454–455. PMID: 32325065; PMCID: PMC7169931. doi:10.1016/j.gie.2020.04.028
21. Massironi S, Viganò C, Dioscoridi L, et al. Endoscopic findings in patients infected with 2019 novel Coronavirus in Lombardy, Italy. *Clin Gastroenterol Hepatol*. 2020;18(10):2375–2377. PMID: 32480008; PMCID: PMC7260560. doi:10.1016/j.cgh.2020.05.045