ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

DOI: 10.5336/medsci.2021-87373

Has the Number of Upper Gastrointestinal Bleeding Cases Presenting to the Emergency Department Decreased During the COVID-19 Pandemic?: A Single-Center Experience

COVID-19 Pandemisinde Acil Servise Başvuran Üst Gastrointestinal Kanamalı Hastaların Sayısı Azaldı mı?: Tek Merkez Deneyimi

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ABSTRACT Objective: In the period of the coronavirus disease-19 (COVID-19) pandemic, upper gastrointestinal endoscopy was either postponed or canceled, except for emergencies, due to the high risk of transmission. Our study aimed to evaluate the effect of the COVID-19 pandemic on patients with upper gastrointestinal bleeding presenting to the emergency department and to compare it with the data before the pandemic. **Material and Methods:** In this single-center, retrospective study, patients were divided into 2 groups: pre-COVID-19 (pre-C) (March 2019-March 2020) and post-COVID-19 (post-C) (March 2020-March 2021). Patients who presented to the emergency department with upper gastrointestinal bleeding during these periods and underwent endoscopic examination were included in the study. **Results:** Endoscopy for upper gastrointestinal bleeding was urgently performed in 125 patients in the pre-C period and in 89 (29% decrease) patients in the post-C period. The Glasgow-Blatchford Score was higher in the pre-C period (p=0.02). Peptic ulcers were the most common cause of bleeding in both groups. High-risk peptic ulcer (forrest 1a/1b/2a/2b), and malignancy were observed more frequently in the post-C period (p=0.003, p=0.04; respectively). Endoscopic combined treatment rate was higher in the post-C group (p<0.001). Re-bleeding ratios were similar for both the groups (p=0.48). **Conclusion: D**uring the post-C period, the number of upper gastrointestinal bleeding cases admitted to the emergency department decreased significantly. However, the rate of high-risk peptic ulcer and malignancy in the etiology of upper gastrointestinal bleeding increased in the post-C period.

Keywords: COVID-19; upper gastrointestinal bleeding; emergency department

ÖZET Amaç: Koronavirüs hastalığı-2019 [coronavirus disease-19 (COVID-19)] pandemisinde üst gastrointestinal sistem endoskopisi, bulaş açısından yüksek riskli olması nedeniyle acil vakalar dışında ertelenmiş veya iptal edilmiştir. Çalışmamızın amacı, COVID-19 pandemisinin acil servise başvuran üst gastrointestinal kanamalı hastalar üzerindeki etkisini, COVID-19 öncesi dönem ile karşılaştırarak değerlendirmektir. **Gereç ve Yöntemler:** Tek merkezli, retrospektif çalışmada hastalar COVID-19 öncesi (pre-C) (Mart 2019-Mart 2020) ve COVID-19 sonrası (post-C) (Mart 2020-Mart 2021) olmak üzere 2 dönem olarak gruplandı. Bu dönemlerde, acil servise üst gastrointestinal kanaması nedeniyle başvuran ve endoskopik inceleme yapılan hastalar çalışmaya dâhil edildi. **Bulgular:** Pre-C dönemde 125 hastada, post-C dönemde ise 89 (%29 azalma) hastaya üst gastrointestinal kanaması nedeniyle acil endoskopi uygulandı. Glasgow-Blatchford Skoru, pre-C döneminde daha yüksekti (p=0,02). Her iki grupta da en sık kanama nedeni peptik ülserdi. Kanama etiyolojisinde yüksek riskli peptik ülser (forest 1a/1b/2a/2b) oranı ve malignite oranı post-C dönemde daha fazlaydı (sırayla p=0,003, p=0,04). Endoskopik kombine tedavi oranı post-C grupta daha fazla fazlaydı (p<0,001). Tekrar kanama oranları her iki grup için benzerdi (p=0,48). **Sonuç:** Post-C döneminde acil servise başvuran üst gastrointestinal kanamalı hasta sayısı belirgin azalmıştır. Post-C dönemde üst gastrointestinal kanama etiyolojisinde yüksek riskli peptik ülser ve malignite oranı artmıştır.

Anahtar Kelimeler: COVID-19; üst gastrointestinal kanama; acil servis

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Peer review under responsibility of Turkiye Klinikleri Journal of Medical Sciences.

Received: 04 Dec 2021 ***Received in revised form:*** 09 Jun 2022 ***Accepted:*** 10 Jun 2022 ***Available online*:** 07 Jul 2022

Although it has been 18 months since the World Health Organization declared coronavirus disease-19 (COVID-19) a pandemic on March 11, 2020, the effects of COVID-19 are still observed worldwide.[1] During this period, quarantine measures were implemented in Türkiye, as in many countries, to prevent the spread of the virus.[2]

Upper gastrointestinal bleeding (UGIB) is one of the most important emergencies in gastroenterology and causes significant morbidity and mortality. UGI endoscopy is very important in the diagnosis and treatment of UGIB.[3] The majority of patients who are hospitalized with UGIB undergo endoscopy, because endoscopic findings predict risk and guide management. However, the timing of endoscopy is debatable.[3]

According to the guidelines updated due to the COVID-19 pandemic, UGI endoscopic procedures have been postponed or canceled in Türkiye moreover in other countries in the world, except in case of emergencies.[2,4] COVID-19 lockdown increased the instant concern that some people may be harmed by not having access to treatment. The significant decrease in the frequency of patients who applied to our emergency department with UGIB during the COVID-19 period compared to the previous year worries us in this regard. In the literature, there is limited knowledge about the detection and treatment of patients with UGIB in the post-COVID-19 (post-C) period. The aim of our study is to analyze the data of patients who presented to the emergency department with UGIB during the post-C period and compare it with that in the pre-COVID-19 (pre-C) period.

MATERIAL AND METHODS

Patients who presented to the emergency department of our hospital between March 2019-March 2021 with UGIB (hematemesis, melena, or both) and underwent endoscopic examination were included in this study. Patients younger than 18 years of age, those who could not undergo endoscopic examination, those who had COVID-related pneumonia and those with known UGI system malignancy were excluded from the study. The patients were divided into 2 groups as pre-C (March 2019-March 2020) and post-C (March 2020-March 2021). Demographic data, drug use, endoscopic findings and treatments, histopathological results, hospitalization duration, number of transfusions, length of intensive care unit stay, and 30-day mortality rates were recorded for all patients. Written consent to participate in the study was taken from all of the patients. This study was approved by the Health Sciences University Kanuni Training and Research Hospital Ethics Committee (date: May 03, 2021, no: 2021/80). This study was performed in accordance with the Helsinki Declaration.

A pantoprazole 8 mg/hour intravenous infusion therapy after 80 mg bolus was administered to patients with suspected non-variceal bleeding.[5] Vasoactive treatment (terlipressin) and antibiotic (cefotaxime) treatment were administered to patients with suspected varicose bleeding.[6]

Endoscopic examination was recommended for all patients with UGIB, except those with respiratory problems (patients who needed oxygen) in the post-C period. Polymerase chain reaction (PCR) test and risk assessment for COVID-19 infection was performed in all patients in the post-C group before endoscopy.[7] All procedures were performed after PCR test in patients in the low-risk group (no symptoms or history of contact with a COVID-19-positive patient, no history of traveling to or staying in a place with COVID-19 cases in the last 14 days, or PCR test negativity) and asymptomatic patients in the high-risk group (history of contact with a COVID-19-positive person or travel to or accommodation in a place with COVID-19 cases in the last 14 days). Symptomatic patients in the high-risk group (presence of cough, fever, or shortness of breath) were followed-up with conservative treatment. All endoscopic examinations in the post-C group were performed using personal protective equipment.[4]

The Glasgow Blatchford Score (GBS) was used to predict the risk of re-bleeding and mortality at the time of admission.[8] Forrest classification was used for classifying the re-bleeding risk in patients diagnosed with peptic ulcers.[9] Forrest 1a, 1b, 2a, and 2b were grouped as high-risk peptic ulcers.[5]

The primary endpoint of our study was the numerical change in patients presenting to the emer-

gency department with UGIB. Secondary endpoints were endoscopy findings (etiology of bleeding, incidence of high-risk peptic ulcer, incidence of malignancy, and endoscopic treatment requirement rates), *Helicobacter pylori* (HP) positivity, hospitalization durations, transfusion frequency, re-bleeding rates, angiographic or surgical treatment rates, and the 30-day mortality rates.

SPSS software version 22 (IBM Corp., Chicago, IL, USA) was used for statistical calculations. The Shapiro-Wilk test was used to test for normality prior to the statistical calculations. Chi-square test, and the Mann-Whitney U test were used for categorical and continuous variables. A p value of <0.05 was considered statistically significant in all analysis.

RESULTS

There were signs of UGIB in 140 of 133,862 patients in the pre-C period and 98 of 42,504 patients in the post-C period who applied to the emergency department. In the pre-C group, conservative treatment was administered to 5 patients who did not accept endoscopic examination, 5 patients with high risk of anesthesia-related complications, and 5 patients with a known history of gastric cancer. In the post-C group, conservative treatment was administered to 4 patients who did not accept endoscopic examination, 3 patients who were at high risk for COVID-19 and were symptomatic, and 2 patients with a known history of gastric cancer. Thus, 125 patients in the pre-C period and 89 patients in the post-C period who underwent UGI endoscopy were included in the study. Of the patients in the post-C period, 82 were in the low-risk group and 7 were in the high-risk asymptomatic group. The PCR test was positive for COVID-19 in one low-risk and one high-risk asymptomatic patient.

According to the results, although there was a significant reduction in the number of patients with UGIB who presented to the emergency department during the post-C period (140 vs 98, 30.0%), a 2.3-fold increase in the incidence of UGIB [98/42,504 (0.0023%) vs 140/133,862 (0.001%), p<0.001] was observed. Demographic data were similar in both the periods. Melena was more common in the pre-C period (100.0% vs 65.2%, p<0.001), and syncope was more common in the post-C period (31.5% vs 8.9%, p<0.001). Although the use of non-steroidal anti-inflammatory drug and anticoagulants was similar in both the groups (p=0.35 and p=0.13; respectively), antiaggregant use was more common in the post-C period (36.0% vs 22.4%, p=0.03). The number of American Society of Anesthesiologists (ASA) 4 patients was higher in the pre-C period (p=0.001) (Table 1). GBS of patients was higher in the pre-C period [pre-C: 13 (1-19) vs post-C: 11 (3-19), p=0.02]. Although bleeding was mostly seen in the stomach and bulbus, no difference was observed between the 2 periods [gastric (pre-C: 32.0% vs post-C: 41.6%, p=0.56)] [bulbus (pre-C: 36.8% vs post-C: 38.2%, p=0.83)]. The most common cause of bleeding was peptic ulcer, and no difference was observed between the 2 periods (pre-C: 60.1% vs post-C: 71.9%; p=0.09). However, high-risk peptic ulcers were more common in the post-C period (44.9% vs 24.0%, p=0.003; 22.5% vs 8.9%, p=0.005, respectively) (Table 2). Although the incidence of varicose bleeding was proportionally higher in the pre-C period, no statistically significant difference was observed between the 2 periods (20.0% vs 11.2%, p=0.09). The rate of endoscopic combined treatment was higher in the post-C group (36.0% vs 18.4%, p<0.001). The rates of thermal therapy (40.4% vs 12.0%, p<0.001) and endoclip therapy (28.1% vs 12.8%, p=0.005) were higher in the post-C period. Endoscopic examination of 2 COVID-19-positive patients in the post-C period revealed that the cause of bleeding was gastric ulcer (Forrest-2a) and Dieulafoy lesion. Both patients were discharged with full recovery after endoscopic combined treatment. Re-bleeding rates, transfusion frequency, angiographic treatment rates, surgical treatment requirement, length of hospital stay, intensive care unit admission, and 30-day mortality rates were similar for both the groups (p=0.48, p=0.18, p=0.24, p=0.94, p=0.17, p=0.15, and p=0.31; respectively) (Table 2). HP positivity was more common in the post-C period (43.8% vs 16.8%, p<0.001). The incidence of malignant peptic ulcers was higher in the post-C period (11.2% vs 4.0%, p=0.04) (Table 3).

TABLE 1: Clinical characteristics data of patients with upper gastrointestinal bleeding in the 2 groups.

Parameters	Pre-COVID-19 group (n=125)	Post-COVID-19 group (n=89)	p value
Age (median, minimum-maximum)	66.5 (56-84)	64 (22-88)	0.64
Male gender (n, %)	93 (74.4)	64 (71.9)	0.69
Symptom (n, %)			
Hematemesis	52 (41.6)	44 (49.4)	0.26
Melena	125 (100.0)	58 (65.2)	<0.001
Syncope	11 (8.9)	28 (31.5)	<0.001
Drugs (n, %)			
NSAID	18 (14.4)	9 (10.1)	0.35
Antiaggregant	28 (22.4)	32 (36.0)	0.03
Anticoagulant	18 (14.4)	20 (22.5)	0.13
GBS	13 (1-19)	11 (3-19)	0.02
Hemoglobin (median, minimum-maximum)	8 (5-16.7)	9 (4-14)	0.39
ASA score (n, %)			
I	12 (9.6)	7 (7.9)	0.66
II	25 (20.0)	25 (28.1)	0.17
III	51 (40.8)	47 (52.8)	0.08
IV	33 (26.4)	8 (9.0)	0.001
NA	4 83.2)	2 (2.2)	0.68

COVID-19: Coronavirus disease-2019; NSAID: Non-steroidal anti-inflammatory drug; ASA: American Society of Anesthesiologists; GBS: Glasgow Blatchford Score.

TABLE 2: Endoscopic findings of patients who underwent endoscopy for upper gastrointestinal bleeding.

Parameters	Pre-COVID-19 group (n=125)	Post-COVID-19 group (n=89)	p value
Bleeding site (n, %)			
Esophagus	29 (23.2)	13 (14.6)	0.12
Stomach	47 (37.6)	37 (41.5)	0.56
Duodenum	47 (37.6)	35 (35.8)	0.82
Anastomosis line	1 (0.8)	5 (5.6)	0.04
Na	1 (0.8)	0	0.40
Etiology (n, %)			
Variceal bleeding	25 (20.0)	10 (11.2)	0.09
Non-variceal bleeding	100 (80.0)	79 (88.8)	
Ulcer	76 (60.1)	64 (71.9)	0.09
Erosion	11 (8.8)	3 (3.3)	0.11
Ulcerated GIST	1 (0.8)	1 (1.1)	0.81
MWS	1 (0.8)	2 (2.2)	0.38
Dieulafoy lesion	8 (6.4)	8 (8.9)	0.48
Angiodysplasia	2 (1.6)	2 (2.2)	0.73
GAVE	0	1 (1.1)	0.24
Na	1 (0.8)	0	0.40
Peptic ulcer classification (n, %)			0.003
High risk (1a/1b/2a/2b)	30 (24.0)	40 (44.9)	
Low risk (2c/3)	46 (36.8)	22 (24.7)	
Na	49 (39.2)	27 (30.3)	
Endoscopic treatment (n, %)			<0.001
Mono therapy	37 (29.6)	34 (38.2)	
Combined therapy	23 (18.4)	32 (36.0)	
Na	65 (28)	23 (25.8)	
Other treatments (n, %)			0.24
Angiography	0	1 (1.1)	0.94
Surgery	3 (2.4)	2 (2.2)	
Re-bleeding (n, %)	12 (9.6)	9 (10.1)	0.48
ES Tx (median, minimum-maximum)	2.5 (0-4)	2 (0-11)	0.18
LOS (median, minimum-maximum)	4.5 (1-23)	4 (1-8)	0.17
30-day mortality (n, %)	10 (8)	4 (4.4)	0.31

COVID-19: Coronavirus disease-2019; GIST: Gastrointestinal stromal tumor; MWS: Mallory Weiss syndrome; GAVE: Gastric antral vasculary ectasia; ES Tx: Erythrocyte suspension transfusion; LOS: Length of stay.

TABLE 3: Histopathological results of patients.

Parameters	Pre-COVID-19 group (n=125)	Post-COVID-19 group (n=89)	p value
Gastric ulcer histopathology (n, %)			0.04
Benign	33 (26.4)	30 (33.7)	
Malignant	5 (4.0)	10 (11.2)	
Na	87 (69.6)	49 (55)	
HP positivite (n, %)	21 (16.8)	39 (43.8)	<0.001

COVID-19: Coronavirus disease-2019; HP: Helicobacter pylori.

DISCUSSION

COVID-19 infection leads to a multisystem inflammatory syndrome with high morbidity and mortality.[10] Due to the large number of patients hospitalized because of this disease, COVID-19 has affected in both the number of patients with acute coronary syndrome admitted to the hospital and the number of emergency surgeries performed.[11,12] During this period, the number of endoscopic procedures in endoscopy units has decreased significantly.[13,14] It has been reported that one-third of patients with bleeding symptoms who were scheduled for elective endoscopic screening missed their appointment.[1] In addition, a 40% decrease was observed in the number of hospital admissions due to UGIB.[15] During the COVID-19 pandemic, guidelines recommended minimizing high-risk aerosol-generating procedures, such as UGI endoscopy.[2,4] The aim of our study is to examine the indirect effect of COVID-19 on patients with UGIB presenting to the emergency department. Unlike previous studies, 1-year periods before and after the pandemic were compared in this study for the first time in the literature.[1,13-15] According to the data of our single-center, retrospective study, a decrease of more than half (68.2%) was observed in the number of patients admitted to the emergency department over the post-C 1-year period compared to the pre-C 1-year period. A decrease of approximately one-third was observed in the number of patients who underwent emergency endoscopy for UGIB. We believe that various factors are responsible for this decrease. First of all, as our hospital is a reference hospital for COVID-19 in the Eastern Black Sea region, patients with symptoms other than COVID-19 may have presented to other centers for fear of virus transmission. Another factor is that the endoscopist who performed emergency consultation for UGIB may have acted defensively during the post-C period. Finally, serious restrictions such as curfews put in place to avert the transmission of COVID-19 may have reduced the frequency of hospital admissions of patients with UGIB. According to the results of the present study, although a significant decrease was observed in the number of patients who presented to the emergency department during the post-C period and the number of emergency endoscopy procedures performed for UGIB, there was an increase in the ratio of patients with UGIB among the patients who presented to the emergency department. It was believed that this proportional increase may be related to the decrease in the number of patients without serious problems admitting to the emergency department due to the pandemic rather than an increase in the number of UGIB admissions.

Guidelines for patients with UGIB, which is one of the most important emergencies in gastroenterology, recommend performing an endoscopy in the first 24 hours of the bleed.[5] In fact, for patients with suspected varicose bleeding, endoscopy within the first 12 hours is recommended.[6] There are a small number of studies on the management of UGIB in COVID-19-positive symptomatic patients, and these studies recommend conservative treatment instead of endoscopy.[16-20] In a study by Martin et al., only one-third of the COVID-19-positive patients with UGIB underwent endoscopy, and the remaining patients received conservative treatment.[21] Cavaliere et al. suggested that COVID-19-positive patients with UGIB should be followed primarily with conservative treatment in the first 24 hours, and endoscopy should be performed in case of no response.[20] In the present

study, all patients (except high-risk symptomatic patients) underwent endoscopic intervention in the first 24 hours both in the both periods. Conservative treatment was initially administered to high-risk COVID-19-positive symptomatic patients. None of the 3 patients in this group who were not included in the study required endoscopic intervention during follow-up. Therefore, the present study has shown that dividing patients into risk groups for COVID-19 facilitates treatment management during the post-C period.

Peptic ulcer is the most common etiology (19.4-57.0/100,000) in patients with UGIB.[22] In a reported case series, peptic ulcer was also the most frequent cause of etiology in COVID-19-positive patients.[21] In our case series, the etiology was found to be similar in both the groups. Although the number of patients with UGIB decreased in the post-C period, the incidence of high-risk peptic ulcers and malignant ulcers has increased markedly. Although the rate of high-risk bleeding increased in the post-C period, the need for angiographic or surgical treatment did not increase. The biggest reason for this is believed to be related to the success of endoscopic treatment. Soft-coagulation with monopolar hemostatic forceps, which we use in endoscopic treatment, especially in high-risk ulcer bleeding, eliminated the risk of re-bleeding or the need for further treatment in these patients. In addition, the more frequent use of endoscopic combined therapy in the post-C period may be another important factor for endoscopic treatment success.

During the post-C period, a remarkable decrease was observed in the number of patients in our hospital due to limitations in both gastroenterology outpatient services and routine endoscopic procedures. This has created difficulties in follow-up for those with chronic diseases, such as chronic liver disease. Unfollowed patients with chronic liver disease may have a risk for variceal UGIB. In a study by Schmiderer et al., no change was reported in the incidence of variceal bleeding in the post-C period.[15] In our study, no significant difference was observed in the incidence of variceal UGIB. Even though it was not statistically significant, a proportional decrease was observed in variceal bleeding in the post-C period. The requirement for intensive care hospitalization in variceal UGIB and the limited number of COVID-19-negative intensive care beds in our hospital may have contributed to a significant decrease in patient referral, thus keeping this rate low in the post-C period.

In the present study, GBS was found to be significantly lower in patients in the post-C period. The higher number of ASA 4 patients in the pre-C group may be the reason for this result. However, there was no significant difference between the 2 periods in terms of re-bleeding or 30-day mortality. According to the multicenter retrospective cohort study by Tavabie et al., a significant decrease was observed in the 30-day survival associated with UGIB during the COVID-19 pandemic (odds ratio: 0.25, 95% confidence interval 0.08-0.67, p=0.06).[13] The single-centered design of the present study and, as we mentioned above, our success in endoscopic treatment may be associated with this result.

There are certain limitations of the present study. First of all, the study is single-centered and retrospective. In addition, the fact that our hospital is one of the reference centers for COVID-19 may have also affected our results. Another shortcoming is that the number of COVID-positive patients with UGIB may have been underrepresented because the sensitivity of the COVID-19 PCR test is not 100%.[23] The fact that only patients with UGIB who applied to the emergency department were included in the present study is another important factor limiting the number of patients included in both the groups.

CONCLUSION

The number of UGIB cases admitted to the emergency department decreased significantly during the post-C period compared to the pre-C period. However, during the post-C period, the ratios of both patients with UGIB in the emergency department and malignancy in the etiology of UGIB significantly increased.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Abdullah Murat Buyrk, Ali Şenkaya, Seymur Aslanova, Elif Artut, Mustafa Çiçek;* ***Design:*** *Abdullah Murat Buyruk, Aydın Aktaş;* ***Control/Supervision:*** *Abdullah Murat Buyruk, Mustafa Çiçek, Aydın Aktaş;* ***Data Collection and/or Processing:*** *Abdullah Murat Buyruk, Elif Artut, Ayten Livaoğlu, Eser Bulut, Aydın Aktaş;* ***Analysis and/or Interpretation:*** *Abdullah Murat Buyruk, Ali Şenkaya, Aydın Aktaş;* ***Literature Review:*** *Abdullah Murat Buyruk, Ali Şenkaya, Seymur Aslanova;* ***Writing the Article:*** *Abdullah Murat Buyruk, Elif Artut, Ali Şenkaya, Seymur Aslanova, Mustafa Çiçek;* ***Critical Review: A****bdullah Murat Buyruk, Aydın Aktaş.*

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