Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE DOI: 10.53555/jptcp.v30i19.3687

RISK FACTORS IN NON-VARICEAL AND NON-MALIGNANCY UPPER GASTROINTESTINAL BLEEDING IN THE PATIENTS UNDERGOING SURGERY

Ahmed Taymour Algahiny¹, Ishan Antony², Fareeha Akram³, Abdullah Ahmed Almesri⁴, Iqra Zulfiqar^{5*}, Abdulhamid Diab⁶

1.6Royal College of Surgeons Ireland - Bahrain
 ²Lahey Hospital and Medical Center, Burlington, MA
 ³House Officer, Ayub Teaching Hospital, Abbottabad - Pakistan
 ⁴Royal College of Surgeons in Ireland
 ^{5*}Demonstrator Pharmacology, Mohi-ud-din Islamic Medical College, Mirpur - AJK

*Corresponding Author: Iqra Zulfiqar
*Demonstrator Pharmacology, Mohi-ud-din Islamic Medical College, Mirpur - AJK
Email: iqrazulfiqar980@gmail.com

ABSTRACT

Background and Aim: Upper gastrointestinal bleeding (UGIB) pertains to the occurrence of bleeding in the digestive tract above the flexor ligament and its remains a significant concern and challenges despite the development of advance treatment. The objective of the current investigation was to determine different risk factors associated with UGIB of non-variceal and non-malignant among patients undergoing surgery.

Patients and Methods: This retrospective analysis was conducted on 32 upper gastrointestinal bleeding patients who underwent surgery in the general surgery wards of several tertiary units in the United Kingdom. De-identified patient data was obtained in this multi-centric study from January 2020 to December 2021. Patients' details such as age, smoking status, gender, comorbidities, use of medication (NSAID), endoscopy findings, surgical procedures, and shock presence, duration of hospitalization, morbidity, and mortality rate were measured and recorded. Descriptive statistics was done using SPSS version 27.

Results: The overall mean age was 48.96 ± 17.8 years with an age range 19 to 80 years. There were 24 (75%) female and 8 (25%) male. Approximately 11 (34.4%) patients had used aspirin and 15 (46.9%) were smokers. Patients most frequently reported melena as their presenting complaint, accounting for 50% (n=16) of cases. The predominant comorbid problems observed were cardiovascular diseases, affecting 28.1% (n=9) of the patients. Shock signs were evident in 19 (59.4%) of the cases. The primary pathology responsible for bleeding in patients was identified as a duodenal ulcer in the majority, accounting for 68.8% (n=22). The most commonly employed surgical methods were Bilateral Truncal Vagotomy (BTV) and pyloroplasty, combined with ligation of the gastroduodenal artery, and these procedures were administered in 23 (71.9%) patients. Approximately 29.2% of patients, totaling 7 individuals, experienced complications, with pulmonary complications being the most prevalent among them. The mortality rate was 18.8% (n=6).

Conclusion: Factors influencing mortality in cases of varicose veins and non-malignant UGIB, which are unresponsive to endoscopy and necessitate surgery, include advanced age, male gender, comorbid diseases, excessive blood transfusions, shock, and a high Rockall score.

Keywords: Gastrointestinal bleeding, risk factors, mortality

INTRODUCTION

Upper gastrointestinal bleeding (UGIB) pertains to the occurrence of bleeding in the digestive tract above the flexor ligament. This encompasses the esophagus, stomach, duodenum, bile duct, and pancreatic duct. UGIB is commonly categorized into variceal upper gastrointestinal bleeding (VUGIB) and non-variceal upper gastrointestinal bleeding (NVUGIB) [1]. In numerous countries, the prevalence of NVUGIB is five times higher than that of VUGIB. Epidemiological studies indicate that the annual incidence of NVUGIB is estimated to range from 50 to 150 cases per 100,000 people, with a mortality rate varying between 2% and 14% [2-4]. A survey conducted in the UK revealed that 14% of NVUGIB patients were hospitalized due to non-digestive ailments, while 25% of them were individuals aged over 80 years. The mortality rate among NVUGIB patients in this survey was recorded at 33% [5]. Additionally, recent research has identified a positive correlation between the morbidity and mortality of NVUGIB and advancing age [6].

Bleeding within the upper gastrointestinal tract (UGIS) encompasses bleeding originating from any segment of the gastrointestinal tract, including the proximal region of the ligament of Treitz. This type of bleeding typically presents as melena-hematemesis. The predominant etiological factor is commonly attributed to peptic ulcers, accounting for approximately 50% of cases [7]. The clinical presentation of UGIS bleeding varies widely, ranging from subtle, subclinical occult bleeding to severe manifestations such as massive bleeding or acute hypovolemic shock [8, 9]. Despite advancements in pharmacological and interventional treatment approaches, the mortality rate associated with UGI bleeding remains high, ranging from 0.6% to 40% [10-12]. Risk factors contributing to mortality include advanced age (typically >60), recurrent bleeding episodes, the presence of comorbid diseases, a history of peptic ulcer or prior surgical interventions, manifestation with hematemesis, and the presence of shock symptoms [13, 14]. As of now, there is no universally accepted scoring standard for predicting high-risk populations for upper gastrointestinal bleeding. Additionally, the existing scoring systems have not been revised to accommodate changes in clinical characteristics. Therefore, the objective of the current investigation was to determine different risk factors associated with UGIB of non-variceal and non-malignant among patients undergoing surgery.

METHODOLOGY

This retrospective analysis was conducted on 32 upper gastrointestinal bleeding patients who underwent surgery in the general surgery wards of several tertiary units in the United Kingdom. Deidentified patient data was obtained in this multi-centric study from January 2020 to December 2021. Patients' details such as age, smoking status, gender, comorbidities, use of medication (NSAID), endoscopy findings, surgical procedures, and shock presence, duration of hospitalization, morbidity, and mortality rate were measured and recorded. The study excluded cases involving esophageal and gastric varices, as well as upper gastrointestinal (UGI) bleeding caused by malignancies. The recorded parameters included the Rockall risk score, surgical procedures undertaken, length of hospital stay, as well as morbidity and mortality rates. Following admission, patients were transferred to the intensive care unit where they underwent blood and fluid replacement, along with nasogastric decompression. Continuous monitoring of central venous pressure, urine output, and vital signs was conducted, and treatments were adjusted accordingly. For patients receiving conservative treatment, which included antiulcer therapy for UGI bleeding, endoscopic intervention for bleeding was implemented, with a focus on identifying the bleeding source. The endoscopic findings were documented based on the Forrest classification [14].

Comorbidities such as cardiovascular diseases (CVD), respiratory diseases (RH), diabetes mellitus (DM) and renal failure were recorded.

In cases where bleeding persisted despite conservative and endoscopic interventions, surgical intervention was undertaken. The Rockall risk score was calculated based on the findings recorded on the day of surgery [15]. Patients with a Rockall risk score below 5 were categorized as the low-risk group, while those with a score exceeding 5 were designated as the high-risk group. Indications for surgery included: 1) Presence of bleeding and shock unresponsive to resuscitation, 2) Inability to halt bleeding through endoscopic means, 3) Abundant bleeding hindering endoscopic imaging and treatment, 4) Lack of response to treatment despite two endoscopies in low-risk patients, and 5) In high-risk patients, failure of treatment despite a single endoscopy. Preoperative prophylactic antibiotic treatment was administered to all patients and continued for 24 hours postoperatively. Laparotomy through a median incision was performed on all patients, with the type of surgery determined based on the causative pathology, the patient's overall condition, and the surgeon's discretion. Helicobacter Pylori (HP) eradication treatment was initiated for patients with ulcers following discharge.

Descriptive statistics was done using SPSS version 27. Quantitative data were presented as mean \pm standard deviation. Group comparisons involved the use of the Student-t test for analyzing parametric data, while the chi-square test was employed to assess various categorical data. A significance level of P<0.05 was deemed significant for all variables.

RESULTS

The overall mean age was 48.96±17.8 years with an age range 19 to 80 years. There were 24 (75%) female and 8 (25%) male. Approximately 11 (34.4%) patients had used aspirin and 15 (46.9%) were smokers. Patients most frequently reported melena as their presenting complaint, accounting for 50% (n=16) of cases. The predominant comorbid problems observed were cardiovascular diseases, affecting 28.1% (n=9) of the patients. Shock signs were evident in 19 (59.4%) of the cases. The primary pathology responsible for bleeding in patients was identified as a duodenal ulcer in the majority, accounting for 68.8% (n=22). The most commonly employed surgical methods were Bilateral Truncal Vagotomy (BTV) and pyloroplasty, combined with ligation of the gastroduodenal artery, and these procedures were administered in 23 (71.9%) patients. Approximately 29.2% of patients, totaling 7 individuals, experienced complications, with pulmonary complications being the most prevalent among them. The mortality rate was 18.8% (n=6). The patients in our study had an average Rockall score of 5.79±1.84, ranging from 3 to 10. Based on the Rockall scores, 10 patients (31.2%) were classified as low risk, while 22 patients (68.8%) were classified as high risk. Following endoscopic intervention, the bleeding focus could not be determined in 4 patients due to intense bleeding that filled the stomach. Among the remaining patients, the distribution of bleeding foci was as follows: Forrest 1a in 13 patients (40.6%), Forrest 1b in 7 patients (21.9%), Forrest 2a in 5 patients (15.6%), Forrest 2b in 2 patients (6.3%), and Forrest 2c in 1 patient (3.1%). Table-I represent the Rockall risk scoring system. Demographic and clinical details of patients are shown in Table-II. Figure-1 depicts the etiological pathologies of patients. Surgical procedures performed are illustrated in Table-III. Complications are demonstrated in Figure-2.

Table-I Rockall risk scoring system

Parameters and Responses	Grading (score)	
Age (years)		
<60	0	
60-79	1	
>80	2	
Shock		
No shock	0	
Tachycardia (SBP>100 mm Hg)	1	
Hypertension (SBP<100 mm Hg)	2	

Co-morbidity	
Nil	0
Cardiac Failure	2
Renal Failure	3
Diagnosis	
Mallory Weiss tears	0
Other diagnosis	1
Malignancy of UGI	2

Table-II Demographic and clinical details of patients (N=32)

Parameters	Value Mean ± SD N (%)
Age (years)	48.96±17.8
Gender	
Male	8 (25%)
Female	24 (75%)
History of Medicine Used	
Aspirin	11 (34.4%)
NSAID	17 (45.9%)
Anticoagulants	4 (12.5%)
Smoking status	15 (46.9%)
Comorbidities	
Cardiovascular	9 (28.1%)
Respiratory	8 (25%)
Diabetes	4 (12.5%)
Renal failure	2 (6.3%)
Clinical symptoms	
Melena	16 (50%)
Hematemesis	11 (34.4%)
Hematochezia	1 (3.1%)
Melena + Hematemesis	4 (12.5%)
Laboratory Investigations	
Leukocytes (/mm³)	15196.64±5892.45
Hemoglobin (mg/dl)	6.8±0.9
Creatinine (mg/dl)	1.4 ± 1.0
No. of Blood transfusion (unit)	6.4±2.8
Mortality	6 (18.8%)

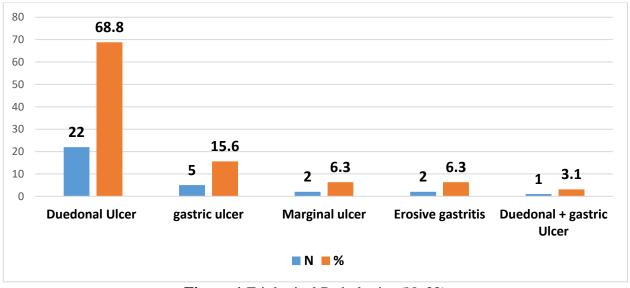


Figure-1 Etiological Pathologies (N=32)

Table-III Surgical Procedures (N=

Procedures	N (%)
Bilateral Truncal Vagotomy (BTV)+ pyloroplasty + ligation of the gastroduodenal artery	23 (71.9%)
Primary suture	4 (12.5%)
BTV+ gastrojejunostomy+ Anastmosis of Braun	2 (6.3%)
Wedge resection	2 (6.3%)
Exploratory laparotomy	1 (3.1%)

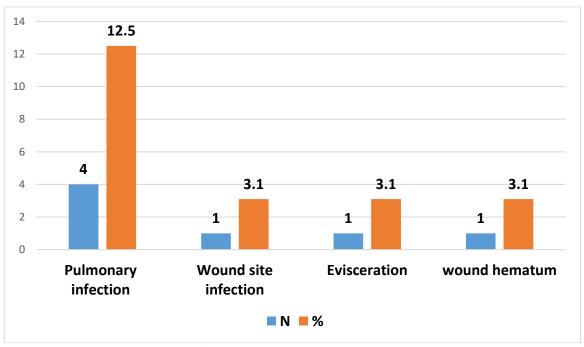


Figure-2 Complications (N=32)

DISCUSSION

Upper gastrointestinal bleeding refers to bleeding resulting from disorders affecting the gastrointestinal tract above the ligament of Trevor. This encompasses bleeding from the pancreatic or bile duct, as well as bleeding originating from conditions near the anastomotic stoma following gastro-jejunostomy [16]. Advancements in medical and endoscopic treatments, the hospitalization rate for upper gastrointestinal bleeding has witnessed a 20% decline over the past decade, with the mortality rate decreasing from 4.5% to approximately 2.1% [17]. Despite the reduction in hospitalization and case fatality rates, the absolute number of affected individuals remains significant given the larger population base. Notably, patients experiencing variceal bleeding are identified as a specific high-risk group [18].

In a study conducted by Lakatos et al. [19], a comparison was made between patients undergoing emergency endoscopy and those undergoing regular gastroscopy. The study revealed notable differences in mortality rates, blood transfusion volumes, and the necessity for clinical intervention. Therefore, the early identification of high-risk upper gastrointestinal bleeding (UGIB) patients and prompt enhancement of endoscopy can contribute to further improvements in patient prognosis. Currently, various scoring systems are in clinical use to evaluate the risk of upper gastrointestinal bleeding. Each of these systems exhibits distinct levels of specificity, sensitivity, and predictive value for clinical observation indicators [20].

Upper gastrointestinal (UGI) bleeding constitutes a significant portion of emergency department presentations, occurring at a frequency of approximately 40–150 cases per 100,000 individuals annually and contributing to about 1% of all hospitalizations [21]. While 80% of UGI bleedings tend to halt spontaneously, 2% experience persistent or recurrent bleeding. In cases of persistent or

recurrent bleeding, surgery becomes necessary in 10-60% of instances, and the associated mortality rates can rise to 25-40% [22, 23].

Advances in identifying Helicobacter pylori (HP) and implementing eradication therapy have led to a reduction in bleeding attributed to peptic ulcers. Furthermore, it has been observed that endoscopy detects bleeding in 98% of cases, with endoscopic intervention successfully achieving bleeding control in 94% of instances, thereby reducing the need for emergency surgical intervention [24]. Despite these advancements, reports indicate that patients admitted to the hospital for acute UGI bleeding tend to be older, with higher usage of nonsteroidal anti-inflammatory drugs (NSAIDs), and mortality rates remain elevated [25].

The global rise in the elderly population has led to an increased incidence and mortality of upper gastrointestinal (UGI) bleeding, a condition more frequently reported in older age groups. Acute UGI bleeding is reported to be 2.4-3.3 times more common in adults than in women [26]. Literature indicates that 37-48% of UGI bleeding cases involve individuals over the age of 60 [27]. In the present study, the average age of the patients was 51 years, and the male-to-female ratio was 4.7:1. Notably, 33.8% of the patients were aged 60 years or older. This demographic shift highlights the significance of addressing UGI bleeding in the context of an aging global population.

Klebl et al. [28] assert that upper gastrointestinal (UGI) bleeding tends to be more severe, with a higher mortality rate, in patients of advanced age and those with existing medical conditions. Phang et al. [29] discovered that 25.6% of patients had comorbidities, and 1.8% of patients succumbed to these concurrent diseases. Clarke et al. [30] reported comorbidities in 58.4% of their patients. In our study, 47.3% of patients had comorbidities, with cardiovascular disease (CVD) being the most prevalent. It is well-established that comorbid diseases have a detrimental impact on tissue oxygenation, wound healing, and the coagulation mechanism. Consequently, recognizing the higher risk of mortality in patients with concurrent health issues, as observed in our study, emphasizes the importance of not delaying necessary surgical interventions when indicated.

In our study, the most frequently performed surgical procedure involved ligating the gastroduodenal artery in conjunction with bilateral total vagotomy (BTV) and pyloroplasty. We believe that, especially in high-risk patients, a collaborative evaluation by gastroenterology and surgery clinics through a multidisciplinary approach is crucial. This collaborative effort helps promptly determine surgical indications and avoids unnecessary delays in surgery, ultimately preventing the development of mortality.

In a study by Aldemir et al. [31], the reported morbidity rate was 31.1%, with eventration being the most common complication. In our study, the morbidity rate was slightly lower at 24.3%, and lung complications were the most frequently observed. We attribute these pulmonary complications to the advanced age and comorbidities prevalent in our patient population. This underscores the importance of considering the unique health profile of each patient when anticipating and managing postoperative complications.

CONCLUSION

Factors influencing mortality in cases of varicose veins and non-malignant UGIB, which are unresponsive to endoscopy and necessitate surgery, include advanced age, male gender, comorbid diseases, excessive blood transfusions, shock, and a high Rockall score.

REFERENCES

- 1. Önder A, Kapan M, Taşkesen F, Aliosmanoğlu İ, Arıkanoğlu Z, Gül M. Risk factors in non-variceal and non-malignancy upper gastrointestinal system bleedings in the patients undergoing surgery. Turk J Surg. 2011;27(4):216.
- 2. Kim MS, Moon HS, Kwon IS, Park JH, Kim JS, Kang SH, Sung JK, Lee ES, Kim SH, Lee BS and Jeong HY. Validation of a new risk score system for non-variceal upper gastrointestinal bleeding. BMC Gastroenterol 2020; 20: 193.

- 3. Samuel R, Bilal M, Tayyem O and Guturu P. Evaluation and management of non-variceal upper gastrointestinal bleeding. Dis Mon 2018; 64: 333-343.
- 4. Mullady DK, Wang AY and Waschke KA. AGA clinical practice update on endoscopic therapies for non-variceal upper gastrointestinal bleeding: expert review. Gastroenterology 2020; 159: 1120-1128.
- 5. Mujtaba S, Chawla S and Massaad JF. Diagnosis and management of non-variceal gastrointestinal hemorrhage: a review of current guidelines and future perspectives. J Clin Med 2020; 9: 402.
- 6. Sasaki Y, Abe T, Kawamura N, Keitoku T, Shibata I, Ohno S, Ono K and Makishima M. Prediction of the need for emergency endoscopic treatment for upper gastrointestinal bleeding and new score model: a retrospective study. BMC Gastroenterol 2022; 22: 337.
- 7. Lanas A, Dumonceau JM, Hunt RH, Fujishiro M, Scheiman JM, Gralnek IM, Campbell HE, Rostom A, Villanueva C and Sung JJY. Non-variceal upper gastrointestinal bleeding. Nat Rev Dis Primers 2018; 4: 18020.
- 8. Poddar U. Diagnostic and therapeutic approach to upper gastrointestinal bleeding. Paediatr Int Child Health 2019; 39: 18-22
- 9. Kärkkäinen JM, Miilunpohja S, Rantanen T, Koskela JM, Jyrkkä J, Hartikainen J and Paajanen H. Alcohol abuse increases re-bleeding risk and mortality in patients with non-variceal upper gastrointestinal bleeding. Dig Dis Sci 2015;60: 3707-3715.
- 10. Ozel F, Yorulmaz E, Yorulmaz H, Davutoglu C, Guven A. The Evalation of Risk Scorings in Non-variceal Upper Gastrointestinal Bleedings/Varis Disi Ust Gastrointestinal Kanamalarda Risk Skorlamalarmin Degerlendirilmesi. Bagcilar Medical Bulletin. 2021 Jun 1;6(2):183-90.
- 11. Yamaguchi D, Sakata Y, Tsuruoka N, Shimoda R, Higuchi T, Sakata H, Fujimoto K and Iwakiri R. Characteristics of patients with non-variceal upper gastrointestinal bleeding taking antithrombotic agents. Dig Endosc 2015; 27: 30-36.
- 12. Yamaguchi D, Sakata Y, Yoshida H, Furukawa NE, Tsuruoka N, Higuchi T, Watanabe A, Shimoda R, Tsunada S, Iwakiri R and Fujimoto K. Effectiveness of endoscopic hemostasis with soft coagulation for non-variceal upper gastrointestinal bleeding over a 12-year period. Digestion 2017; 95: 319-326.
- 13. Dango S, Beißbarth T, Weiss E, Seif Amir Hosseini A, Raddatz D, Ellenrieder V, Lotz J, Ghadimi BM and Beham A. Relevance of surgery in patients with non-variceal upper gastrointestinal bleeding. Langenbecks Arch Surg 2017;402: 509-519.
- 14. Forgerini M, Lucchetta RC, Urbano G, de Nadai TR and de Carvalho Mastroianni P. Genetic polymorphisms associated with upper gastrointestinal bleeding: a systematic review. Pharmacogenomics J 2021; 21: 20-36.
- 15. Rockall TA. Management and outcome of patients undergoing surgery after acute upper gastrointestinal haemorrhage. JR Soc Med 1998;91:518-523.
- 16. Hajiagha Mohammadi AA and Reza Azizi M. Prognostic factors in patients with active nonvariceal upper gastrointestinal bleeding. Arab J Gastroenterol 2019; 20: 23-27.
- 17. Abougergi MS, Peluso H and Saltzman JR. Thirty-day readmission among patients with nonvariceal upper gastrointestinal hemorrhage and effects on outcomes. Gastroenterology 2018; 155: 38-46.
- 18. Liu BX, Wang XZ, Yan YL, Xiao X, Yang L and Luo XF. Efficacy analysis of transcatheter arterial embolization in acute non-variceal upper gastrointestinal bleeding. Sichuan Da Xue Xue Bao Yi Xue Ban 2022; 53: 398-403.
- 19. Lakatos L, Gonczi L, Lontai L, Izbeki F, Patai A, Racz I, Gasztonyi B, Varga-Szabo L, Ilias A and Lakatos PL. Incidence, predictive factors, clinical characteristics and outcome of non-variceal upper gastrointestinal bleeding a prospective population-based study from hungary. J Gastrointestin Liver Dis 2021; 30: 327-333.

- 20. Park HW and Jeon SW. Clinical outcomes of patients with non-ulcer and non-variceal upper gastrointestinal bleeding: a prospective multicenter study of risk prediction using a scoring system. Dig Dis Sci 2018; 63: 3253-3261.
- 21. Luo PJ, Lin XH, Lin CC, Luo JC, Hu HY, Ting PH and Hou MC. Risk factors for upper gastrointestinal bleeding among aspirin users: an old issue with new fndings from a population based cohort study. J Formos Med Assoc 2019; 118: 939-944.
- 22. Lu Y, Adam V, Teich V and Barkun A. Timing or dosing of intravenous proton pump inhibitors in acute upper gastrointestinal bleeding has low impact on costs. Am J Gastroenterol 2016;111: 1389-1398.
- 23. Ito N, Funasaka K, Furukawa K, Kakushima N, Hirose T, Muroi K, Suzuki T, Suzuki T, Hida E, Ishikawa T, Yamamura T, Ohno E, Nakamura M, Kawashima H, Miyahara R and Fujishiro M. A novel scoring system to predict therapeutic intervention for non-variceal upper gastrointestinal bleeding. Intern Emerg Med 2022; 17:423-430.
- 24. Cho SH, Lee YS, Kim YJ, Sohn CH, Ahn S, Seo DW, Kim WY, Lee JH, Lim KS. Outcomes and Role of Urgent Endoscopy in High-Risk Patients With Acute Nonvariceal Gastrointestinal Bleeding. Clin Gastroenterol Hepatol. 2018 Mar;16(3):370-377
- 25. Oguri N, Ikeya T, Kobayashi D, Yamamoto K, Yoshimoto T, Takasu A, Okamoto T, Shiratori Y, Okuyama S, Takagi K, Nakamura K, Fukuda K. Effectiveness of risk scoring systems in predicting endoscopic treatment in colonic diverticular bleeding. J Gastroenterol Hepatol. 2020 May;35(5):815-820.
- 26. Elsebaey MA, Tawfik MA, Ezzat S, Selim A, Elashry H, Abd-Elsalam S. Endoscopic injection sclerotherapy versus N-Butyl-2 Cyanoacrylate injection in the management of actively bleeding esophageal varices: a randomized controlled trial. BMC Gastroenterol. 2019 Feb 4;19(1):23.
- 27. Wuerth BA, Rockey DC. Changing Epidemiology of Upper Gastrointestinal Hemorrhage in the Last Decade: A Nationwide Analysis. Dig Dis Sci. 2018 May;63(5):1286-1293.
- 28. Klebl F, Bregenzer N, Schöfer L, et al. Risk factors for mortality in severe upper gastrointestinal bleeding. Int J Colorectal Dis 2005; 20:49-56. doi:10.1007/s00384-004-0624-2 http://dx.doi. org/10.1007/s00384-004-0624-2 doi:10.1007/s00384-004-0642-0 http://dx.doi. org/10.1007/s00384-004-0642-0
- 29. Phang TS, Vornik V, Stubbs R. Risk assessment in upper gastrointestinal haemorrhage: implications for resource utilisation. NZ Med J 2000;113:331-333.
- 30. Clarke CS, Afifi AY. Impact of blood transfusion on outcome in patients admitted for gastrointestinal hemorrhage. Current Surg 2000; 57: 493–496. doi:10.1016/S0149-7944(00)00311-1 http://dx.doi.org/10.1016/S0149-7944(00)00311-1
- 31. Aldemir M, Yılmaz G, Öztürk A, et al. Surgical treatment for upper gastrointestinal system bleeding. Journal of Contemporary Surgery 2002;16:72-77