



Assesment of Upper Gastrointestinal Bleeding in the Pediatric Emergency Department

Çocuk Acil Servisinde Üst Gastrointestinal Kanamalarının Değerlendirilmesi

İD Aysun Tekeli¹, İD Gülseren Şahin², İD Betül Öztürk³, İD Ferda Özbay Hoşnut², İD İlknur Bodur³, İD Ayla Akca Çağlar⁴,
İD Can Demir Karacan³, İD Nilden Tuğgun³

¹University of Health Sciences Turkey, Gülhane Training and Research Hospital, Clinic of Pediatric Emergency Medicine, Ankara, Turkey

²University of Health Sciences Turkey, Ankara Dr. Sami Ulus Children's Health and Diseases Training and Research Hospital, Clinic of Pediatric Gastroenterology, Ankara, Turkey

³University of Health Sciences Turkey, Ankara Dr. Sami Ulus Children's Health and Diseases Training and Research Hospital, Clinic of Pediatric Emergency Medicine, Ankara, Turkey

⁴Ankara Bilkent City Hospital, Clinic of Pediatric Emergency Medicine, Ankara, Turkey

Abstract

Introduction: Upper gastrointestinal bleeding is an important emergency problem that can occur at any age in childhood and requires urgent treatment for the underlying cause. Etiological causes of gastrointestinal bleeding vary by age and geographic region. In this study; we aimed to investigate the demographic characteristics, etiological causes, endoscopic intervention results, and the relationship between analgesic/antipyretic drug use and bleeding in patients admitted to the pediatric emergency department with upper gastrointestinal bleeding.

Methods: The records of patients aged 1 month to 18 years who presented to our pediatric emergency department with upper gastrointestinal bleeding between January 2017 and 2019 were retrospectively reviewed. Demographic features, complaints at admission, etiological reasons, endoscopy findings, diagnoses, and antipyretic/analgesic drug use were recorded.

Results: There were 108 patients presenting with upper gastrointestinal bleeding, and 53.7% of the patients were male. The mean age was 76.7±58.3 months. Hematemesis was present in 100 patients. Symptoms of the patients; vomiting was present in 82.4%, upper respiratory tract infection in 36.1%, fever in 29.6%, and abdominal pain in 25.9%. There were 52 patients with a history of antipyretic and/or analgesic drug use. An endoscopic examination was performed in 74 patients. In patients who underwent endoscopic examination; pathological changes were detected in 26 of 32 patients who used drugs and 30 of 42 patients who did not use drugs.

Öz

Giriş: Üst gastrointestinal kanama, çocukluk çağında her yaşta ortaya çıkabilen ve altta yatan nedene yönelik acil tedavi gerektiren önemli bir acil sorundur. Gastrointestinal kanamanın etiyolojik nedenleri yaşa ve coğrafi bölgeye göre değişir. Bu çalışmada; çocuk acil servisine üst gastrointestinal kanama ile başvuran hastaların demografik özellikleri, etiyolojik nedenleri, endoskopik girişim sonuçları ve analjezik/antipiretik ilaç kullanımı ile kanama arasındaki ilişkiyi araştırmayı amaçladık.

Yöntemler: Ocak 2017-2019 tarihleri arasında çocuk acil servisimize üst gastrointestinal kanama ile başvuran 1 ay-18 yaş arası hastaların kayıtları geriye dönük olarak incelendi. Demografik özellikler, başvuru şikayetleri, etiyolojik nedenler, endoskopi bulguları, tanıları, antipiretik/analjezik ilaç kullanımı kaydedildi.

Bulgular: Üst gastrointestinal kanama ile başvuran 108 hastanın %53,7'si erkekti. Ortalama yaş 76,7±58,3 aydı. Yüz hasta hematemez şikayeti ile başvurdu. Hastaların %82,4'ünde kusma, %36,1'inde üst solunum yolu enfeksiyonu bulguları, %29,6'sında ateş ve %25,9'unda karın ağrısı şikayeti vardı. Hastaların 52'sinde antipiretik ve/veya analjezik ilaç kullanım öyküsü mevcuttu. Yetmiş dört hastaya endoskopik inceleme yapıldı. Endoskopik inceleme yapılan hastalarda; ilaç kullanan 32 hastanın 26'sında ve kullanmayan 42 hastanın 30'unda patolojik değişiklik saptandı.

Sonuç: Çocuk acil servisine üst gastrointestinal kanama ile başvuran hastalarda kanama genellikle akut başlangıçlıdır ve kendi kendini sınırlar ancak acil tanı ve tedavi gerektirir. Çalışmamızdaki hastaların

Address for Correspondence/Yazışma Adresi: Aysun Tekeli, University of Health Sciences Turkey, Gülhane Training and Research Hospital, Clinic of Pediatric Emergency Medicine, Ankara, Turkey

E-mail: aysunnakay@yahoo.com.tr **ORCID ID:** orcid.org/0000-0002-3639-2224

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Conclusion: In patients presenting to the pediatric emergency department with upper gastrointestinal bleeding, the bleeding is usually acute and self-limiting, but requires prompt diagnosis and treatment. Approximately half of the patients in our study had a history of antipyretic/analgesic drug use in etiology. When the endoscopic findings of drug users and non-users were compared, no statistically significant difference was observed in terms of pathological findings.

Keywords: Bleeding, drug, upper gastrointestinal

Introduction

Upper gastrointestinal bleeding (UGB) is one of the important reasons for admission to the pediatric emergency department (PED). UGB is defined as bleeding anywhere between the upper part of the esophagus and the ligament of Treitz. It accounts for approximately 20% of all gastrointestinal bleeding.¹ The incidence of UGB is reported to be 6-25%.^{2,3}

It may develop due to various reasons ranging from self-limiting benign conditions to serious diseases that require urgent intervention. Therefore, it is very important to evaluate the etiological cause and the location of the bleeding site.

Its etiology varies according to geographical regions and age groups. There are several risk factors for UGB. The most important of these are drugs. Paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used for pain and fever control in children thanks to their antipyretic and analgesic effects and are generally considered safe. These drugs may cause gastrointestinal mucosal damage and cause complications such as peptic ulcer, bleeding and perforation. They also facilitate bleeding from pre-existing or new lesions.^{4,6} Detailed history and physical examination, early diagnosis, timely endoscopic intervention and appropriate treatment approach are important in the management of UGB.

In our study, we aimed to evaluate the demographic characteristics, laboratory findings, etiological reasons, endoscopic findings of patients who admitted to the PED with UGB, to investigate the place of analgesic and/or antipyretic drug use in etiology, and to investigate the relationship between bleeding and endoscopic findings in drug users and non-users.

Materials and Methods

Records of patients aged between 1 month and 18 years who applied to the PED of University of Health Sciences Turkey, Ankara Dr. Sami Ulus Children's Health and Diseases Training and Research Hospital, between January 2017 and January 2019 were analyzed retrospectively by using electronic data. Patients with chronic disease, long-term medication use, ingestion of corrosive substances or foreign bodies,

yaklaşık yarısının etiolojide antipiretik/analjezik ilaç kullanım öyküsü mevcuttu. Bu ilaçları kullanan grup ile ilaç kullanmayan grup karşılaştırıldığında patolojik endoskopik bulgularda istatistiksel olarak anlamlı fark gözlenmedi.

Anahtar Kelimeler: Kanama, ilaç, üst gastrointestinal

history of gastrointestinal surgery and missing data were excluded. Patients' age, gender, presentation complaints, laboratory findings, etiology of bleeding, antipyretic and/or analgesic drug use, endoscopic findings, and treatments were analyzed. Complete blood count and coagulation tests (prothrombin time, activated partial thromboplastin time, international normalized ratio) were evaluated. Esophagogastroduodenoscopy (EGD) records were also examined.

Ethical Approval

The study protocol was performed in accordance with the Helsinki Declaration of human rights. The study was reviewed and approved by the Keçiören Training and Research Hospital Ethics Committee (2012-KAEK-15/2020).

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) 23 program was used to analyze the data. Quantitative variables were presented as mean and \pm standard deviation, also categorical variables were presented as numbers and percentages. Student t-test was used for group comparison. Categorical data were analyzed using the χ^2 test and Fisher's Exact tests. A value of $p < 0.05$ was accepted as statistically significant.

Results

UGB was detected in 108 of 233,720 patients who applied to our PED in a 2-year period. Fifty-eight of them (53.7%) were male and the mean age was 76.7 ± 58.3 months (2-215 months). Forty-nine (45.4%) patients were under the age of five and 59 (54.6%) were over the age of five.

On admission to the PED; 100 of 108 (92.6%) patients presented with hematemesis, 7 (6.5%) with melena, and one with hematemesis and melena. The most common symptoms were vomiting 89 (82.4%), upper respiratory tract infection 39 (36.1%), fever 32 (29.6%) and 28 (25.9%) patients had complaints of abdominal pain.

The history of using NSAIDs, acetylsalicylic acid and paracetamol was presented in 52 of 108 patients (48.1%).

Most of the patients who used drugs, 27 (51.9%) were using both ibuprofen and paracetamol.

There were 15 patients under 2 years of age, 14 patients between the ages of 2-5, 15 patients between the ages of 5-10, 8 patients aged 10 and over using analgesic/antipyretic drugs. Thirty-two patients used antipyretic and 20 patients used analgesic drugs. In the physical evaluation-revealed pallor was detected in 5 patients, tachycardia, hypotension and shock were detected in 2 patients, and epigastric tenderness was detected in 8 patients.

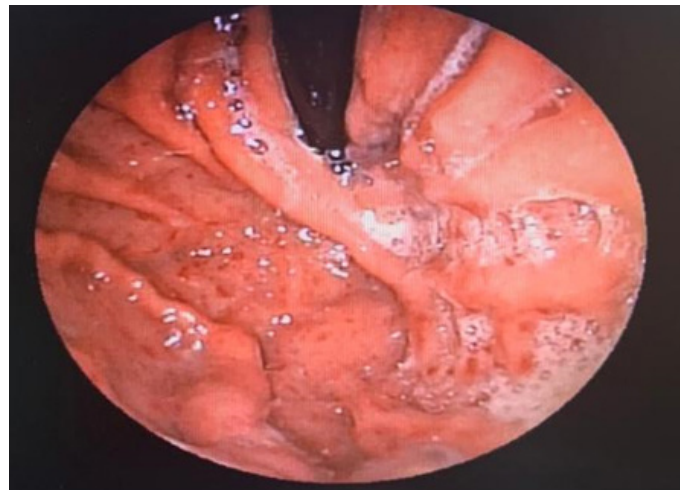
The demographic characteristics, symptoms and findings, and laboratory findings of the patients are presented in Table 1.

Table 1. Characteristics of children presenting with upper gastrointestinal bleeding	
Age (months) (mean ± SD)	76.7±58.3 (2-215)
Age group (n, %)	
1 month-2 years	24 (22.2%)
2-5 years	25 (23.1%)
5-10 years	35 (32.4%)
10-18 years	24 (22.2%)
Gender (n, %)	
Male	58 (53.7%)
Female	50 (46.3%)
Symptoms (n, %)	
Hematemesis	100 (92.6%)
Melena	7 (6.5%)
Hematemesis and melena	1 (0.9%)
Associated symptoms (n, %)	
Vomiting	89 (82.4%)
Upper respiratory tract infection	39 (36.1%)
Fever	32 (29.6%)
Abdominal pain	28 (25.9%)
Acute gastroenteritis	15 (13.9%)
Weakness	3 (2.7%)
Dizziness	3 (2.7%)
Using analgesic/antipyretic (n, %)	
Ibuprofen and paracetamol	27 (51.9%)
Paracetamol	14 (26.9%)
Ibuprofen	7 (13.5%)
Other NSAIDs	3 (5.8%)
Acetylsalicylic acid	1 (1.9%)
Physical examination findings (n, %)	
Epigastric tenderness	8 (7.4%)
Pallor	5 (4.6%)
Tachycardia	2 (1.8%)
Hypotension	2 (1.8%)
Laboratory findings	
Hemoglobin (gr/dL) (mean ± SD) (min-max)	12.7±1.78 (5.9-16.3)
Hematocrit (%) (mean ± SD) (min-max)	38±5.24% (17.5-48.5)
Platelet (UI) mean ± SD (min-max)	326,000±103,800 (113,000-673,000)
aPTT (sn) mean ± SD (min-max)	26.1±3.3 (17.5-34.9)
PT (sn) (mean ± SD) (min-max)	13.2±1.28 (10.9-17)
INR (mean ± SD) (min-max)	1.0±0.1 (0.9-1.4)
NSAIDs: Non-steroidal anti-inflammatory drugs, PT: Prothrombin time, aPTT: Partial thromboplastin time, INR: International normalized ratio, SD: Standard deviation	

Endoscopic examination was performed in 74 (68.5%) patients. Thirty eight (51.3%) of them were male. The endoscopic results of the patients were given in Table 2. Endoscopic examination images are presented (Pictures 1-4).

Table 2. Endoscopy reports of the patients

Pathological lesion	n (%)
Gastric erosion	27 (36.5%)
Gastritis	7 (9.5%)
Gastric ulcer	7 (9.5%)
Esophageal erosion	5 (6.8%)
Gastric erosion + esophagitis	3 (4%)
Esophagitis	2 (2.7%)
Gastric erosion + duodenal ulcer	2 (2.7%)
Gastric ulcer + esophagitis	1 (1.3%)
Ulcer in the esophagus	1 (1.3%)
Duodenal ulcer	1 (1.3%)
Normal	18 (24.3%)
Total	74 (100%)



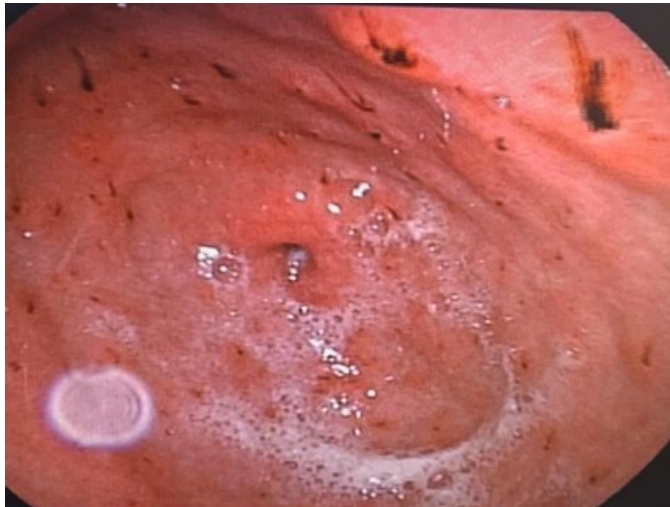
Picture 1. Superficial erosion of the fundus and bleeding areas



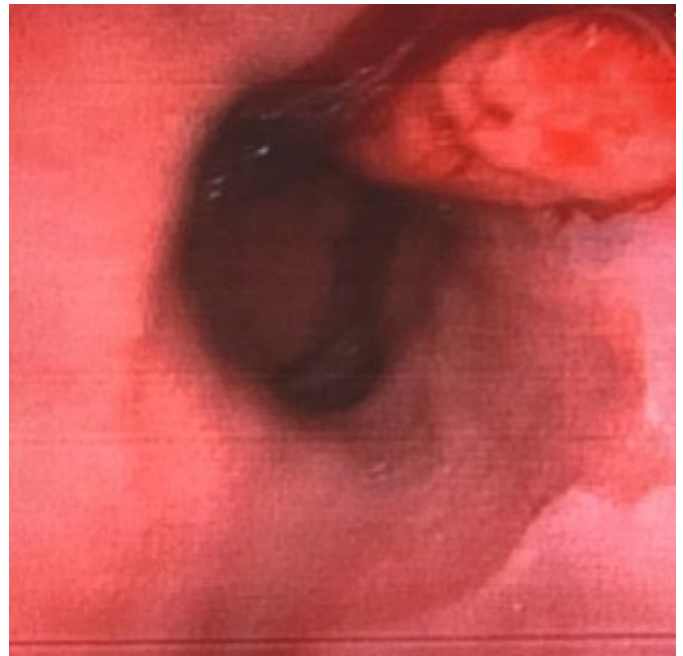
Picture 2. Ulcer in the stomach corpus

When patients were evaluated according to age groups, for children aged 1 month-2 years 56.2% of the patients stomach and 18.7% had esophageal changes; 61.5% had stomach and 30.8% had esophageal changes between 2-5 years old; 70.8% had stomach-duodenum and 4.2% had esophageal changes between 5-10 years old and 63.6% had stomach-duodenum and 22.7% had esophageal changes over 10 years old were observed.

Pathological changes were detected in the endoscopy in 26 (81.3%) out of 32 patients using drugs and in 30 (71.4%) out of 42 patients who did not. The endoscopy findings of patients using and not using drugs are shown in Figure 1.



Picture 3. Punctate bleeding areas in the stomach antrum



Picture 4. Distal esophagus erosion

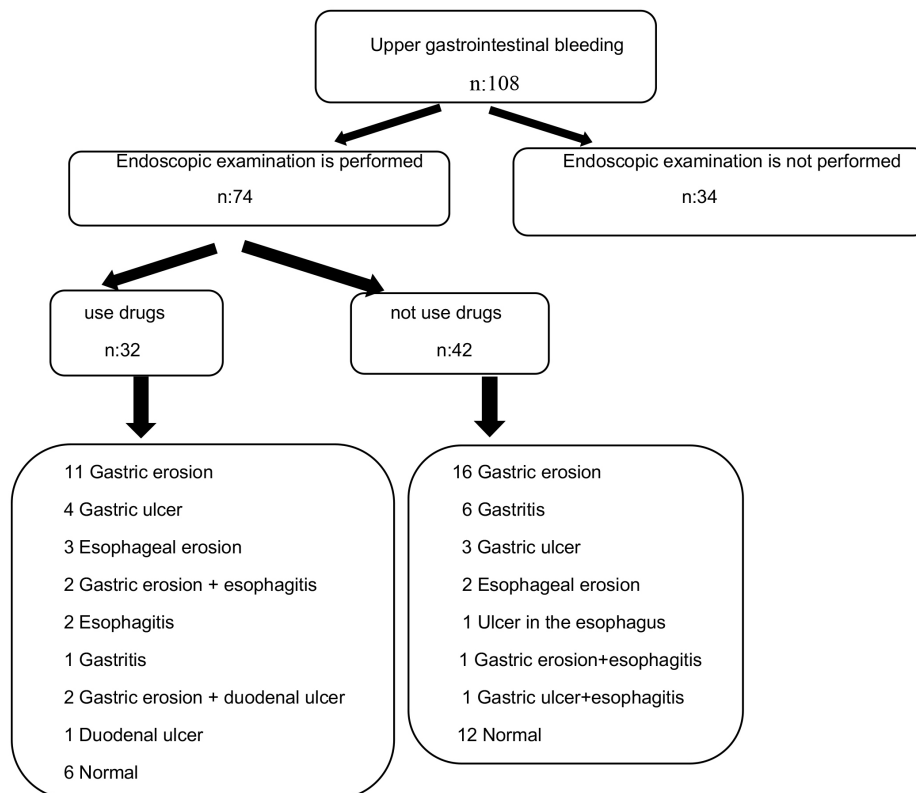


Figure 1. The endoscopy findings of the patients who use and do not use drugs are shown

All patients were followed hospitalization and 77 (71.3%) of them were followed in the PED, 28 (25.9%) of them were followed up in the pediatric wards, and 3 (2.8%) of them were followed up in the intensive care unit. Nasogastric lavage was applied to all patients, their oral intake was discontinued and medical treatment was initiated. Endoscopic treatment was applied to 10 patients with active bleeding. None of the patient died from bleeding.

Discussion

Pediatric UGB is one of the important conditions that require urgent intervention. Although most of the cases are benign serious and life-threatening bleeding should be diagnosed treated quickly.⁷ There is insufficient data on the frequency of UGB in outpatient admissions and most of the studies have been conducted in pediatric intensive care units. In a study conducted in France, UGB was reported to be seen in 1-2 of 10,000 children per year and the ratio of female to male in UGB was 1.2:1.⁸ In our study, 108 (0.046%) of the 233,720 patients who were admitted to the PED in a two-year period were presented with UGB and the male to female ratio of the patients was 1.16.

Hematemesis and melena are the main symptoms of upper GIB. Hematemesis refers to vomiting of either red blood or coffee-ground emesis. Melena is defined as black, tarry stools that appear a few hours after the bleeding episode. In studies, the complaints at presentation of patients were reported at the rate of 63-96.6% with hematemesis, 15-20% with melena and 2.8% with hemorrhagic shock.⁹⁻¹² Similar to the other studies, hematemesis was the most common symptom in our study. The reduced rate of melena may be due to the fact that it is not noticed by the patient and their family.

Causes of UGB in children vary according to the age and geographical region. While the most common cause in Eastern countries is varicose bleeding due to portal hypertension, non-varicose causes such as gastric and duodenal ulcers have been reported most frequently in the west.^{13,14} It has been shown that the most common cause of non-varicose bleeding in childhood was gastro-duodenal diseases. Gastric erosion, gastritis and gastric ulcer were found most common ones. In various studies, this rate ranges from 35% to 69%.^{10,15-21} Esophagitis ranks second among the causes of UGB, with a rate varying between 7.1% and 36% in the literature.^{11,16,17,20} Similar to the literature, gastro-duodenal diseases constituted the most common cause of bleeding in this study group, while esophageal diseases were in the second place. Studies have reported that reduced erosive gastritis, increased gastric and duodenal ulcers with age.^{10,22,23} Similarly, gastric erosion was common in young children, while the frequency of duodenal ulcers increased in older children in this study.

NSAIDs and viral infections are important risk factors for the development of UGB. Gastrointestinal bleeding can be seen due to the use of NSAIDs such as ibuprofen, which is commonly used in childhood.²⁴ It is reported that it can cause bleeding by causing gastric mucosal damage.²⁵⁻²⁸ However, data on the gastrointestinal complications of these drugs in children are limited; evidence is based on case reports and case series.^{8,29-32} NSAIDs are reported to be used in approximately 20-50% of patients with UGB.^{19,33,34} Approximately half of the patients in this study had a history of drug use and 37 (71.1%) of these patients used NSAIDs. UGB has also been reported after using paracetamol, which is frequently used for fever and pain control and is usually considered to be safe. Unal et al.²⁴ reported that the bleeding was developed in 26.6% of the patients due to the drug and 32.5% of them used paracetamol. No difference was found in the studies comparing the rate of gastrointestinal complications secondary to paracetamol and ibuprofen use.^{35,36} There were 14 patients who used only paracetamol in this study.

Thirty-two (43.2%) of the patients who undergone endoscopy used NSAIDs and/or paracetamol and pathological changes were detected in 26 of them. No significant difference was found in terms of pathological changes in endoscopy of the patients who used antipyretic and/or analgesic drugs and those who did not. Although the role of drugs in the etiology of UGB is known, it should be kept in mind that our patients had an infection like upper respiratory tract infection or gastroenteritis during this period, and these infections may increase the sensitivity of the gastric mucosa and increase the effect of antipyretic/analgesics on gastrointestinal damage. In a pediatric study, viral infections were found to be the most common cause of non-variceal UGB.³⁷ In our study, 26 patients with upper respiratory tract infection and gastroenteritis underwent endoscopy, and 19 (73.1%) had pathological changes. In addition, some of the patients used these drugs for abdominal pain, and it is unknown whether the patients had gastrointestinal pathologies before bleeding.

Laboratory tests are not helpful in determining the cause of gastrointestinal bleeding, but may be helpful in differential diagnosis and follow-up of patients. Complete blood count, kidney and liver function and coagulation tests should be assessed.³⁸ A complete blood count should be repeated in terms of ongoing bleeding. Two of our patients had anemia, and the other two had a decrease in hemoglobin in serial complete blood count tests.

The primary diagnostic method for the evaluation of UGB is EGD. Endoscopy allows the identification of the source of bleeding, determination of risk factors for the possibility of ongoing bleeding and therapeutic intervention. Most of the bleeding stops spontaneously and endoscopic intervention is not required urgently. An endoscopic examination within

the first 24-48 hours is useful for diagnosis and treatment in patients presenting with UGB. In addition, early EGD has a high probability of determining the location of bleeding, and the etiology of bleeding can be determined in 82% of patients.^{38,39} The cause of bleeding cannot be clarified by endoscopy in 28-34% of the patients who were admitted to the PED with UGB.^{4,40} Similarly, endoscopic examination was performed in 74 (68.5%) of the patients within the first 48 hours and the location of bleeding was determined in 56 (75.7%) patients in this study.

In the treatment of UGB, firstly the hemodynamic stabilization should be provided and then the medical and endoscopic treatments can be applied secondly.⁴¹ Nasogastric aspiration and saline lavage should be performed to confirm the presence of gastric bleeding, to determination of the amount, to control ongoing or recurrent bleeding, to empty the stomach for endoscopic intervention and to prevent aspiration from gastric contents.^{42,43} For medical therapy acid suppression and vasoactive agents are used in patients. Coagulation, band ligation, sclerosing or adrenaline injection, and clip treatments can be applied endoscopically.^{44,45} In this study, all patients underwent nasogastric aspiration and lavage with saline, and acid suppression therapy was applied. As an endoscopic treatment, adrenaline injection was applied to 10 patients with active bleeding and clips were applied to one patient.

UGB, which usually has a good prognosis in childhood, stops without any for intervention. However, there is always a risk of potentially serious and life-threatening hemorrhagic shock.⁴⁶ In our study, 2 (1.8%) patients presented with hemorrhagic shock. The mortality rate varies between 1-21% depending on age, etiology, severity of bleeding, patient stabilization, diagnosis and treatment approach.^{46,47} In our study, no patients died from bleeding.

Study Limitations

It was a retrospective cross-sectional study, the frequency, duration and dose compliance of families could not be determined. It is not known whether the patients had gastrointestinal pathologies before bleeding and how long after bleeding they applied to the PED.

Conclusion

UGB in children is usually self-limited, but children may present to the PED with severe life-threatening bleeding. The physician should first provide hemodynamic stabilization of the patient and then consider endoscopic evaluation within 24 hours to identify and treat the etiologic causes and source of the bleeding. Pediatric emergency physicians should plan the management and treatment of the patient together with the gastroenterologist. Approximately half of our

patients had a history of antipyretic/analgesic drug use in the etiology. However, no significant difference was observed in pathological findings in endoscopy between drug users and non-users. More studies are needed to determine the use of antipyretic and/or analgesic drugs and other possible risk factors in children with UGB.

Ethics

Ethics Committee Approval: The study protocol was performed in accordance with the Helsinki Declaration of human rights. The study was reviewed and approved by the Keçiören Training and Research Hospital Ethics Committee (2012-KAEK-15/2020).

Informed Consent: The study was designed retrospectively, no written informed consent form was obtained from patients.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.T., G.Ş., F.Ö.H., Concept: A.T., C.D.K., N.T., Design: A.T., G.Ş., N.T., Data Collection or Processing: A.T., G.Ş., B.Ö., İ.B., A.A.Ç., Analysis or Interpretation: A.T., G.Ş., C.D.K., N.T., Literature Search: A.T., B.Ö., F.Ö.H., İ.B., A.A.Ç., Writing: A.T., G.Ş.

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References

1. Rodgers BM. Upper gastrointestinal hemorrhage. *Pediatr Rev.* 1999;20:171-4.
2. Barnert J, Messmann H. Diagnosis and management of lower gastrointestinal bleeding. *Nat Rev Gastroenterol Hepatol.* 2009;6:637-46.
3. Arora NK, Ganguly S, Mathur P, Ahuja A, Patwari A. Upper gastrointestinal bleeding: etiology and management. *Indian J Pediatr.* 2002;69:155-68.
4. Titchen T, Cranswick N, Beggs S. Adverse drug reactions to nonsteroidal anti-inflammatory drugs, COX-2 inhibitors and paracetamol in a paediatric hospital. *Br J Clin Pharmacol.* 2005;59:718-23.
5. Kalyoncu D, Urganci N, Cetinkaya F. Etiology of upper gastrointestinal bleeding in young children. *Indian J Pediatr.* 2009;76:899-901.
6. Orbis PC, Laguna CB, Miguel LS, Mallada GH, Arbeloa ALS. Non-variceal upper gastrointestinal hemorrhage. *Gut.* 2020;13:136-44.
7. Friedlander J, Mamula P. Gastrointestinal hemorrhage. In: Wyllie R, Hyams JS, Kay M (eds). *Pediatric Gastrointestinal and Liver Disease*, fourth edition. Philadelphia: Elsevier Saunders. 2011:146-53.
8. Grimaldi-Bensouda L, Abenheim L, Michaud L, Mouterde O, Jonville-Béra AP et al. Clinical features and risk factors for upper gastrointestinal bleeding in children: a case-crossover study. *Eur J Clin Pharmacol.* 2010;66:831-7.

9. Romano C, Oliva S, Martellosi S, Miele E, Arrigo S, et al. Pediatric gastrointestinal bleeding: Perspectives from the Italian Society of Pediatric Gastroenterology. *World J Gastroenterol.* 2017;23:1328-37.
10. Huang IF, Wu TC, Wang KS, Hwang B, Hsieh KS. Upper gastrointestinal endoscopy in children with upper gastrointestinal bleeding. *J Chin Med Assoc.* 2003;66:271-5.
11. Akçam M, Yılmaz A, Artan Y. Evaluation of children underwent endoscopy due to upper gastrointestinal bleeding: a retrospective analysis of 54. *SDÜ Tıp Fak Derg.* 2006;13:22-6.
12. Cleveland K, Ahmad N, Bishop P, Nowicki M. Upper gastrointestinal bleeding in children: an 11-year retrospective endoscopic investigation. *World J Pediatr.* 2012;8:123-8.
13. Owensby S, Taylor K, Wilkins T. Diagnosis and management of upper gastrointestinal bleeding in children. *J Am Board Fam Med.* 2015;28:134-45.
14. Rodgers BM. Upper gastrointestinal hemorrhage. *Pediatr Rev.* 1999;20:171-4.
15. Mittal SK, Kalra KK, Aggarwal V. Diagnostic upper GI endoscopy for hematemesis in children: experience from a pediatric gastroenterology centre in north India. *Indian J Pediatr.* 1994;61:651-4.
16. El Mouzan MI, Abdullah AM, Al-Mofleh IA. Yield of endoscopy in children with hematemesis. *Trop Gastroenterol.* 2004;25:44-6.
17. Aydoğdu S, Levent RE, Selimoğlu MA, Kasırga E, Yağcı RV. Çocukluk çağı gastrointestinal sistem kanamalarında etioloji ve tanı: 5 yıllık gözlem. *Ege Tıp Dergisi.* 1999;38:9-12.
18. Erkan T, Kutlu T, Çullu F, Göksel S, Tümay GT. Üst gastrointestinal kanama ile getirilen hastaların retrospektif olarak değerlendirilmesi. *Çocuk Sağlığı ve Hastalıkları Dergisi.* 1998;41:355-60.
19. Eren M, Hekim S. Upper gastrointestinal system bleeding in children: Etiology and treatment. *Türkiye Klinikleri J Pediatr.* 2010;19:1-8.
20. Türe E, Yazar A, Akın F. Retrospective Evaluation of 47 Patients with Gastrointestinal Bleeding In Pediatric Emergency Clinic Sakarya Tıp Dergisi. 2017;7:196-203.
21. Srichand Talreja, Muhammad Nadeem Chohan, Deve Dass. Significance of Upper GI endoscopy for the detection of upper GI bleeding in children, *Rawal Medical Journal.* 2018;43.
22. Cardile S, Martinelli M, Barabino A, Gandullia P, Oliva S, et al. Italian survey on non-steroidal anti-inflammatory drugs and gastrointestinal bleeding in children. *World J Gastroenterol.* 2016;22:1877-83.
23. Yu Y, Wang B, Yuan L, Yang H, Wang X, et al. Upper Gastrointestinal Bleeding in Chinese Children: A Multicenter 10-Year Retrospective Study. *Clin Pediatr (Phila).* 2016;55:838-43.
24. Unal F, Şahin G, Ecevit ÇO, Semizel E, Cebe A, et al. Diagnostic and Therapeutic Endoscopic Approaches to Upper Gastrointestinal System Bleeding in Children *The Journal of Current Pediatrics.* 2012;10:1-8.
25. Lanza FL, Chan FK, Quigley EM; Practice Parameters Committee of the American College of Gastroenterology. Guidelines for prevention of NSAID-related ulcer complications. *Am J Gastroenterol.* 2009;104:728-38.
26. Dills R, Anderson LA, Pierce CA. The role of nonsteroidal anti-inflammatory drugs in pediatric patients. *Pharmacol Res.* 2012;65:5-8.
27. Etienney I, Beaugerie L, Viboud C, Flahault A. Non-steroidal anti-inflammatory drugs as a risk factor for acute diarrhoea: a case crossover study. *Gut.* 2003;52:260-3.
28. Wolfe MM, Lichtenstein DR, Singh G. Gastrointestinal toxicity of nonsteroidal antiinflammatory drugs. *N Engl J Med.* 1999;340:1888-99.
29. Berezin SH, Bostwick HE, Halata MS, Feerick J, Newman LJ, et al. Gastrointestinal bleeding in children following ingestion of low-dose ibuprofen. *J Pediatr Gastroenterol Nutr.* 2007;44:506-8.
30. Autret-Leca E, Bensouda-Grimaldi L, Maurage C, Jonville-Bera AP. Upper gastrointestinal complications associated with NSAIDs in children. *Therapie.* 2007;62:173-6.
31. Clarkson A, Choonara I. Surveillance for fatal suspected adverse drug reactions in the UK. *Arch Dis Child.* 2002;87:462-6.
32. Mulberg AE, Linz C, Bern E, Tucker L, Verhave M, et al. Identification of nonsteroidal antiinflammatory drug-induced gastroduodenal injury in children with juvenile rheumatoid arthritis. *J Pediatr.* 1993;122:647-9.
33. Boukthir S, Mazigh SM, Kalach N, Bouayhya O, Sammoud A. The effect of non-steroidal anti-inflammatory drugs and Helicobacter pylori infection on the gastric mucosa in children with upper gastrointestinal bleeding. *Pediatr Surg Int.* 2010;26:227-30.
34. Gultekinil A, Teksam O, Gulsen HH, Ates BB, Saltık-Temizel İN, et al. Risk factors associated with clinically significant gastrointestinal bleeding in pediatric ED. *Am J Emerg Med.* 2018;36:665-8.
35. Lesko SM, Mitchell AA. An assessment of the safety of pediatric ibuprofen. A practitioner-based randomized clinical trial. *JAMA.* 1995;273:929-33.
36. Lesko SM, Mitchell AA. The safety of acetaminophen and ibuprofen among children younger than two years old. *Pediatrics.* 1999;104:e39.
37. Yabe K, Kouchi K, Takenouchi A, Matsuoka A, Kudou W, et al. Current status and future challenges in the endoscopic management of non-variceal upper gastrointestinal bleeding in children. *Pediatr Surg Int.* 2020;36:1451-58.
38. Bachur R, Shaw K. *Fleisher&Ludwig'sTextbook of Pediatric Emergency Medicine.* 7th ed. Philadelphia: Wolters Kluwer. 2015;193-202.
39. Mougnot (F. Duche M. Hemorragies digestives. In: Navarro J. Schmitz J. eds. *Gastroenterologie Pédiatrique*, 2nd ed. Paris: Flammarion. 2000;612-21.
40. Wyllie R, Kay M. Gastrointestinal hemorrhage. In: Wyllie R, Hyams JS, Kay M, eds. *Pediatric Gastrointestinal and Liver Disease.* 3th ed. Philadelphia: ElsevierInc. 2006;203-15.
41. Poddar U. Diagnostic and therapeutic approach to upper gastrointestinal bleeding. *Paediatr Int Child Health.* 2019;39:18-2.
42. Singhi S, Jain P, Jayashree M, Lal S. Approach to a child with upper gastrointestinal bleeding. *Indian J Pediatr.* 2013;80:326-33.
43. Stanley AJ, Laine L. Management of acute upper gastrointestinal bleeding. *BMJ.* 2019;25:364-536.
44. Carvalho ED, Nita MH, Paiva LM, Silva AA. Hemorragia digestiva [Gastrointestinal bleeding]. *J Pediatr (Rio J).* 2000;76(Suppl 1):135-46.
45. Banc-Husu AM, Ahmad NA, Chandrasekhara V, Ginsberg GG, Jaffe DL, et al. Therapeutic Endoscopy for the Control of Nonvariceal Upper Gastrointestinal Bleeding in Children: A Case Series. *J Pediatr Gastroenterol Nutr.* 2017;64:88-1.
46. Peters JM. Management of Gastrointestinal Bleeding in Children. *Curr Treat Options Gastroenterol.* 2002;5:399-413.
47. Romano C, Oliva S, Martellosi S, Miele E, Arrigo S, et al. Pediatric gastrointestinal bleeding: Perspectives from the Italian Society of Pediatric Gastroenterology. *World J Gastroenterol.* 2017;23:1328-37.