SJIF Impact Factor: 5.464

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 4.
Issue: 6.
Page N. 01-08
Year: 2020

Original Article www.wjahr.com

ETIOLOGY AND ENDOSCOPIC FINDINGS OF GASTROINTESTINAL BLEEDING IN CHILDREN

[1]*Maria Adnan Naamah, [2]Zeina Alkilany, [3]Ali Ibrahim and [4]Ali Mohamed

[1,2]MD, Department of Pediatrics, Tishreen University hospital, Lattakia, Syria.
[3]Department of Pediatrics, Professor of Gastroenterology and Hepatology, Tishreen University hospital, Lattakia, Syria.
[4]Department of Pediatrics, Assistant Professor of Gastroenterology and Hepatology, Tishreen University hospital, Lattakia, Syria.

Received date: 25 August 2020 **Revised date:** 14 September 2020 **Accepted date:** 04 Oct 2020

***Corresponding author: Maria Adnan Naamah**

MD, Department of Pediatrics, Tishreen University hospital, Lattakia, Syria.

ABSTRACT

Background: Gastrointestinal (GI) bleeding in children, although uncommon, can be life-threatening. The purpose of the present study is to review the causes of gastrointestinal bleeding in pediatric patients according to age, determine the endoscopic findings in these children, and highlight of the important role of gastrointestinal endoscopy. **Methods:** A three-year prospective cross-sectional study included 150 children with upper or lower GI bleeding aged between 1 month and 14 years, who had referred to the pediatric gastrointestinal center at Tishreen University Hospital, Lattakia, Syria over 3 years from June 2017 to June 2020.Patients were categorized as infants, pre-school aged, school-aged, and adolescents. Each patient underwent an esophagogastroduodenoscopy and/or colonoscopy and several mucosal biopsies were taken. History and clinical information as well as endoscopy and pathology findings were reported. **Results:** The results showed that erosive gastritis was the most common upper endoscopic finding, and rectal colon polyp was the most common colonoscopic finding. HP related Gastritis and juvenile polyp were the most common causes of upper and lower gastrointestinal bleeding. Cow's milk protein intolerance was the most common cause of gastrointestinal bleeding in the younger age group (under 2 years), and Inflammatory Bowel Disease is becoming more common at younger ages. **Conclusion:** Causes of gastrointestinal bleeding in children are multiple, thus specific etiologies at different age groups should be kept in mind, while assessing pediatric patients with Gastrointestinal Bleeding.

KEYWORDS: gastrointestinal bleeding, children, endoscopic findings, esophagogastroduodenoscopy, colonoscopy.

INTRODUCTION

Gastrointestinal hemorrhage can be one of the most catastrophic events in childhood and requires prompt assessment, diagnosis, and treatment.[1]

Bleeding may occur anywhere along the gastrointestinal (GI) tract, which covers a large surface area and is highly vascularized.[2] In most patients, the clinical presentation indicates the level of bleeding. Hematemesis is the classic presentation of upper GI bleeding(UGIB). Bloody diarrhea and bright red blood mixed or coating normal stool are the classic presentations of lower GI bleeding(LGIB). Hematochezia, melena, or occult GI blood loss could represent upper or lower GI bleeding.[3]

There is a paucity of data in the literature concerning the epidemiology of GI bleeding in childhood. This condition is not rare, having a reported incidence of 6.4%.[4]

The etiology of GI bleeding varies with age but considerable overlap exists between the different age groups. The diagnostic approach for GIB should include extensive history-taking and examination including laboratory evaluations and application of the available and most appropriate diagnostic procedures.[4]

The initial diagnostic tests for identification of the bleeding source are typically esophagogastroduodenoscopy (EGD) and colonoscopy given the therapeutic potential.[5]

During endoscopy, diagnosis can be achieved via direct visualization of lesions with the endoscope, biopsy of

suspected lesions, rapid urease testing for H. pylori infection, and placement of capsule endoscopy for small bowel evaluation.[6] In the hands of the skilled endoscopist, EGD now can diagnose the etiology in 85–90% of cases.[7]

Colonoscopy has a diagnostic yield between 48% and 90% in the setting of LGIB.[5]

If an EGD and colonoscopy (after bowel preparation) fail to identify the bleeding source, a small bowel source of bleeding should be sought.[5]

Methods and Patients

A three-year prospective cross-sectional study was performed on 150 children (aged 1 month- 14 years)with upper or lower GI bleeding and underwent endoscopy, who were referred to the pediatric gastrointestinal center at Tishreen University Hospital, Lattakia, Syria from June 2017 to June 2020, and underwent endoscopy . Clinical data included age, sex, type of bleeding, the appearance of vomitus (red bloody, coffee-ground), the appearance of stool (red or maroon stool, melena, bloody diarrhea), history of consumption of medications that predispose the patients to GI bleeding, underlying disease and the therapeutic management were recorded. Each patient underwent an EGD and/or colonoscopy and several mucosal biopsies were taken. History and clinical information as well as endoscopy and pathology findings were reported. Patients were categorized as infants, pre-school aged, school-aged children, and adolescents. The findings were reported separately in each group.

All data were analyzed using the Statistical Package for Social Sciences (SPSS Version 20). Data were presented in simple measures of frequency, percentage, mean, standard deviation.

RESULTS

The study included 150 children with upper or lower gastrointestinal bleeding, 94 (62,7%) were males and 56(37,3%) were females (Sex Ratio(M:F=1.6:1) with an average age of 5 years (1 month- 14 years). There were 48 children presented with UGIB,87 with LGIB ,and 15 with a positive occult blood test (POBT)in stool.
There was 32 (21.3%) infant, 54 (36%) pre-school aged, 55 (36.7%) school-aged, and 9 (6%) adolescents.

In total, the bleeding source can be identified in 91.6% of patients with UGIB(%) and 80.3% of patients with LGIB.

✓ **Upper Gastrointestinal Bleeding**

The main clinical presentations included hematemesis in 36 patients (75%), melena in 4 patients (8.4%), and hematemesis with melena in 8 patients (16.7%). The most common upper endoscopic finding in our patients was Erosive gastritis, followed by Erosive esophagitis. The endoscopic findings of patients according to the type of bleeding are summarized in **Table 1**.

Table 1: Upper endoscopic findings according to the type of bleeding.

		Type of bleeding	
Upper endoscopic findings	**LGIB(87)**	**UGIB(48)**	**POBT)15)**
Erosive Esophagitis, n(%)	0(0)	14(28.05)	2(13.4)
Esophageal Varices, n(%)	0(0)	3(6.25)	0(0)
Erosive Gastritis, n(%)	0(0)	17(35.3)	5(33.3)
Gastric ulcer, n(%)	1(1.1)	7(14.6)	0(0)
Duodenal ulcer, n(%)	2(2.3)	3(6.25)	0(0)
Erosive duodenitis, n(%)	0(0)	3(6.25)	0(0)
Nodular antritis, n(%)	0(0)	4(8.3)	1(6.7)

LGIB: lower gastrointestinal bleeding, **UGIB**: upper gastrointestinal bleeding, **POBT:** positive occult blood test.

In total, the most common cause of UGIB was HP related gastritis followed by reflux esophagitis. The causes of upper GIB are listed in **Figure 1**.

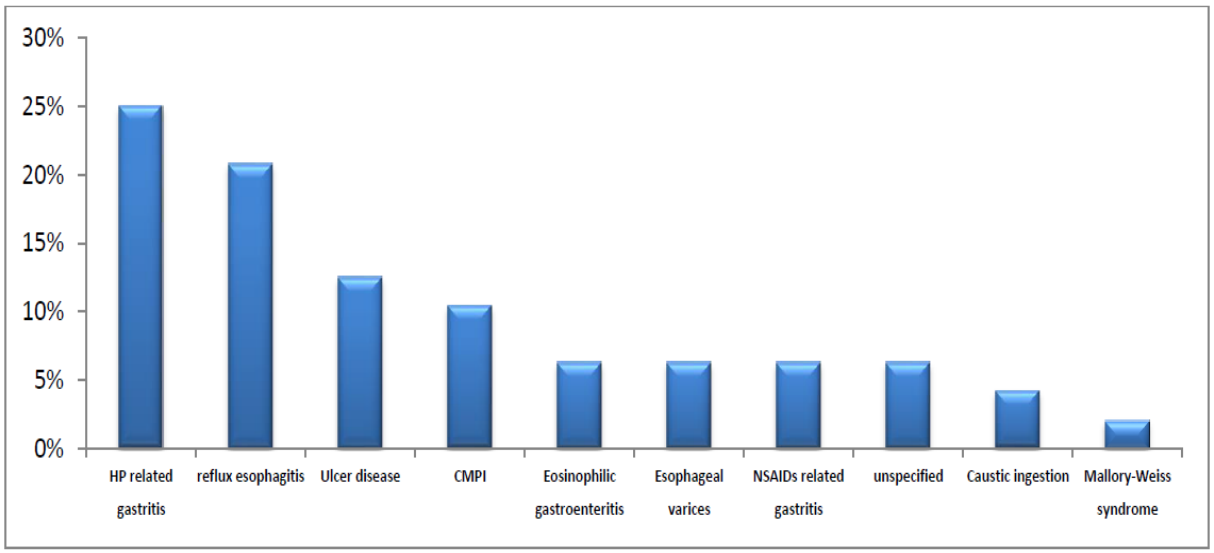

Figure 1: Causes of upper gastrointestinal bleeding.

UGIB: upper gastrointestinal bleeding, **HP:** helicobacter pylori, **NSAIDs:** nonsteroidal anti-inflammatory drugs.

CMPI: Cow's milk protein intolerance

Cow milk protein intolerance (CMPI) was the most common cause of UGIB among neonates, while the most common cause in children aged > 2 years was HP related gastritis. The causes of upper GI bleeding in different age groups are shown in **Table 2**.

Table 2: Causes of upper gastrointestinal bleeding in different age groups.

Age group				
UGIB causes	**>2**	**2-6**	**6-12**	**12<**
reflux esophagitis, n(%)	4(26.7)	3(20)	2(15.4)	1(20)
Esophageal varices, n(%)	2(13.3)	0(0)	1(7.7)	0(0)
Eosinophilic gastroenteritis, n(%)	1(6.7)	2(13.3)	0(0%)	0(0)
Ulcer disease, n(%)	2(13.3)	1(6.7)	2(15.4)	1(20)
Mallory-weiss syndrome, (%)	0(0)	1(6.7)	0(0)	0(0)
HP related gastritis, (%)	0(0)	3(20)	7(53.8)	2(40)
CMPI, (%)	5(33.3)	0(0)	0(0)	0(0)
NSAIDs related gastritis, n(%)	1(6.7)	2(13.3)	0(0)	0(0)
Caustic ingestion, n(%)	0(0)	1(6.7)	0(0)	1(20)
Unspecified, n(%)	0(0)	2(13.3)	1(7.7)	0(0)

UGIB: upper gastrointestinal bleeding, **HP:** helicobacter pylori, **NSAIDs:** non steroidal anti inflammatory drugs.
CMPI: Cow milk protein intolerance.

✓ **Lower Gastrointestinal Bleeding**

The presenting symptoms were hematochezia in 66 (75.8%), bloody diarrhea in 21 (24.1%). The most common colonoscopy finding in LGIB group was rectal polyps. **Table 3** summarizes the colonoscopy findings in patients according to the type of bleeding.

Table 3: Colonoscopic findings according to the type of bleeding.

Type of bleeding		
Lower endoscopic findings	**LGIB(87)**	**POBT)15)**
Diffuse ulcerative colitis, n(%)	9(10.3)	1(6.7)
Lymphatic follicular hyperplasia, n(%)	1(1.1)	0(0)
Diverticular longitudinal ulcers in the ascending colon and cecum, n(%)	0(0)	2(13.3)
Congestion of colonic mucosa, n(%)	5(5.7)	0(0)
Loss of vascular markings and mucosal frangibility, n(%)	12(13.8)	0(0)
Hemorrhoidal tag, n(%)	10(11.5)	0(0)
Colonic polyp, n(%)	3(3.4)	0(0)
Rectal polyp, n(%)	20(22.9)	0(0)
Sigmoid polyp, n(%)	4(4.6)	0(0)
Anal fissure, n(%)	10(11.5)	0(0)
Rectal and sigmoid erosions, n(%)	8(9.2)	0(0)
Ilium ulcers, n(%)	1(1.1)	0(0)
nodularity in the rectum and colons, n(%)	2(2.3)	2(13.3)
Rectal ulcer, n(%)	1(1.1)	0(0)
Rectal and sigmoid ulcers, n(%)	3(3.4)	0(0)

LGIB: lower gastrointestinal bleeding, **POBT:** positive occult blood test.

In total, the most common cause of LGIB was juvenile polyps which located most in the rectum. The causes of lower GI bleeding are shown in **Figure 2**.

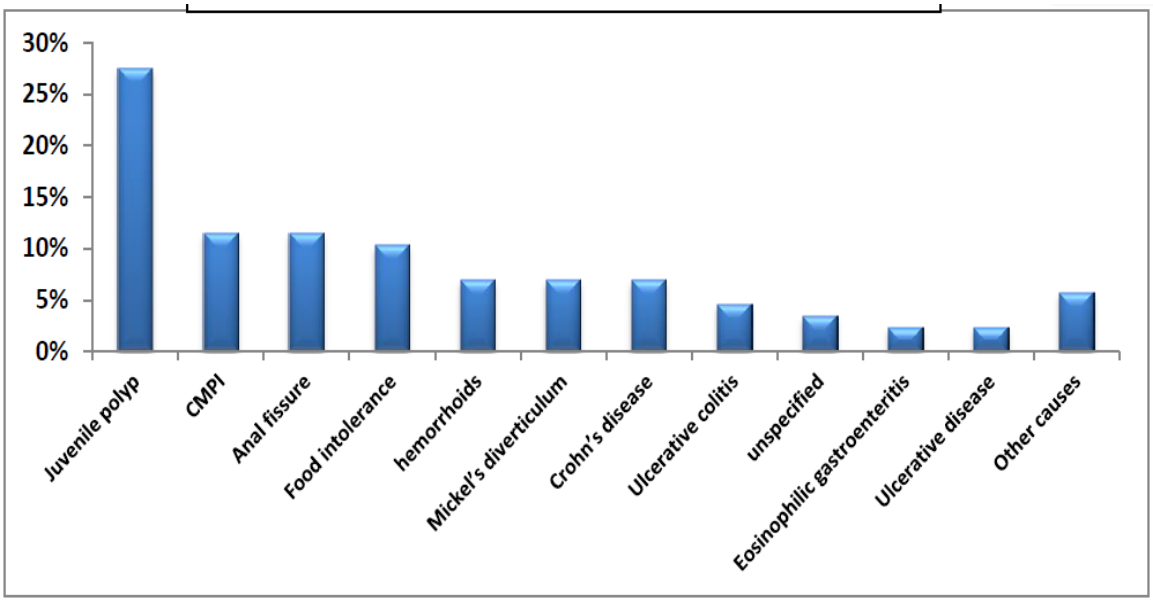

Figure 2: Causes of lower gastrointestinal bleeding.

LGIB: lower gastrointestinal bleeding, **POBT:** positive occult blood test.

Cow milk protein intolerance (CMPI) was the most common cause of LGIB among neonates, while the most common cause in pre-school and school-aged children was juvenile polyp. Causes of lower GI bleeding in different age groups are shown in **Table 4.**

Table 4: Causes of lower gastrointestinal bleeding in different age groups.

Age groups				
LGIB causes	**2>**	**2-6**	**6-12**	**12<**
Eosinophilic gastroenteritis, n(%)	1(6.7)	0(0%)	1(2.8%)	0(0%)
Ulcerative disease, n(%)	0(0%)	0(0%)	2(5.6%)	0(0%)
CMPI, n(%)	9(60%)	1(3%)	0(0%)	0(0%)
Hemorrhoids, n(%)	0(0%)	2(6.1%)	5(13.9%)	0(0%)
Juvenile polyp, (%)	0(0%)	13(39.4%)	11(30.6%)	0(0%)
Familial hereditary polyposis, n(%)	1(6.7%)	0(0%)	0(0%)	0(0%)
Anal fissure, (%)	1(6.7%)	4(12.1%)	4(11.1%)	1(33.3%)
Crohn's disease, n(%)	0(0%)	2(6.1%)	2(5.6%)	2(66.7%)
Infectious enterocolitis(yersinia), n(%)	1(6.7%)	0(0%)	0(0%)	0(0%)
Ulcerative colitis, n(%)	0(0%)	3(9.1%)	1(2.8%)	0(0%)
Mickel's diverticulum, n(%)	0(0%)	3(9.1%)	3(8.3%)	0(0%)
Unspecified, n(%)	0(0%)	1(3%)	2(5.6%)	0(0%)
Solitary rectal ulcers, n(%)	0(0%)	0(0%)	1(2.8%)	0(0%)
Food intolerance, n(%)	2(13.3%)	4(12.1%)	3(8.3%)	0(0%)
Intestinal lymphoma, n(%)	0(0%)	0(0%)	1(2.8%)	0(0%)

LGIB: lower gastrointestinal bleeding, **CMPI:** Cow milk protein intolerance.

DISCUSSION

Causes of gastrointestinal bleeding in children are multiple and can be grouped according to the involved portion of the digestive tract and age.[8] Specific etiologies at different ages should be kept in mind while assessing pediatric patients.[7] The fact that etiologies of pediatric GI bleeding vary among different geographical regions and ethnic groups necessitates the investigation of the epidemiology and characteristics of this disorder in each region.[9] There is no detailed information about the characteristics and etiology of GIB in children in Syria ,thus we did this research.

We found that UGIB most commonly presented with hematemesis which was similar to other studies such as Dehghani et al (50%), Yu et al (59%), and Shahraki et al.[2-10-11]

Malena in this study had a lower rate in presentation(8.4%). This finding was nearly similar to that observed by other researches.[2-10-12] This can by explained by the fact that hematemesis raises parents' attention more and prompts them to seek immediate medical advice, in contrast to melena, which is usually not noticeable by parents, especially in older children; besides hematemesis usually precedes melena.

In the study of Zahmatkeshan et al, LGIB cases manifested as hematochezia in 80% of the cases and bloody diarrhea in 18%,[9] and this is close to what we found in the current study.

Erosive gastritis was the most common upper endoscopic finding in the current study in all age groups (35.3% of cases) and that was similar to other studies; Dehghani et al (28%), Huang et al (44.6%), Elmouzan et al (44%) and Yu et al (33%).[2-12-13-10]

Erosive esophagitis accounted for 28% of the upper endoscopic findings, with a variable ratio between the different studies, reaching 30.4% in Huang et al, 36% in Elmouzan et al, and 24% in Mittal et al.[12-13-18], while the percentage decreased to 1.7% in Dehghani et al[2] and 4.6% in Hassoun et al.[12] Peptic ulcers accounted for 14% of cases as well in Yu et al (9%), Dehghani et al (8.5%), and Hassoun et al (9.7%).[10-2- 12]

Rectal polyps accounted for 22% of the lower endoscopic findings, followed by Loss of vascular markings and mucosal frangibility 14%, and anal fissures and hemorrhoids in 11.5% of cases for each, while Zahmatkeshan found in his study that sigmoid polyp was the most abundant lower endoscopic finding followed by descending colon petechia; nonetheless loss of vascular markings and anal fissures accounted only for 2.8% and 0.8% of cases respectively.[9]

Although HP gastritis was the most common cause of UGIB in our study (25%), which was similar to the findings of Rafeay et al(19%)[15] and Hassoun et al(19.6%)[12], the prevalence of HP in our study sample was less than previous studies (46-65%)[15] and this may be explained by the frequent random use of antibiotics in our country.

Cases of HP gastritis are more common in school-aged and adolescents groups, where mixing with peers and eating fast and contaminated foods may have a role in raising the rates of HP infection.

The prevalence of GERD has increased recently in children, due to many reasons, including the increase in obesity rates and the consumption of fatty junk food, spices, chocolate, and caffeine.[16]

Reflux esophagitis was the second most common cause

of UGIB (~ 21% of cases) with a higher rate than previous studies in western and eastern populations.[17]

This may be explained by selection bias, as 40% of GERD patients had a hiatal hernia, 30% of them were under the age of two years, and 10% had complaints of bad psychomotor development. Cases of reflux esophagitis were most common in the infant group (26%) and this correlates with other studies.[17] Ulcerative disease accounted for 12.5% of the causes of UGIB, similar to Cleveland et al[17], but less than other studies, as its prevalence as a cause of bleeding was 23% in previous studies on Eastern populations and 43% in Western studies. The researcher explained this by improving antacid treatments as well as the recognition of HP and the development of effective treatments against it.[17]

According to the findings of our study, there would be a small increased risk of gastric lesions associated with NSAIDs (6.25%), which confirms that these drugs account for only a small proportion of UGIB. This was close to the results of Elmouzan et al(6.8%) and Yu et al(11%).[14-10] The cases of NSAIDs related gastritis were more common in the preschool-aged group.

The incidence of varices (6.25%) in our population was closer to that of the developed countries such as Cleveland et al (7.1%) and Huang et al (10.7%)[17-13], while it was more common in studies done in developing countries such as Mittal et al(39%) and Hassoun et al (40%).[18-12] UGIB associated with esophageal varices was more common among the infant group, whereas most cases were among children > 2 years in Hassoun et al and Dehghani et al studies.[12-2] This may be due to the geographical differences in diseases resulting in varices bleeding, that extrahepatic biliary obstruction was the main cause in our study whereas bleeding due to extrahepatic portal venous obstruction was the most common cause in other studies.

Juvenile polyps are the most common causes of LGIB and they are usually single and located in the rectum and sigmoid colon, especially at ages> 2 years. Our current study showed that juvenile polyp is the most common cause of LGIB (27.5% of cases) in children aged 2-12 years and this was also found by Zahmatkeshan et al[9] and Leung et al[19] in their research, while other studies found that anal fissures were the most common cause of LGIB[1-19], which was the second most common cause in our study.

The current study also showed that cow's milk protein intolerance is an important cause of LGIB (11.5%), especially at ages <2 years, where it was the most common cause, followed by anal fissures. This was similar to the findings by Fox et al[21] and Nambu et al.[22] However, CMPI was seen only in a small percentage in studies done in Iran (1.9%) and India[2-18], and the researcher explained this by the high prevalence of parental breastfeeding in these countries.

LGIB is the main symptom in most patients with ulcerative colitis and 25% of Crohn's patients.[19] In the current study, IBD accounted for 9.2% of all patients. Although this was similar to the percentage in Zahmatkeshan et al study (10.2%), it was higher compared with previous studies from Western populations.[9] That may be explained by selection bias , as the current study included patients reviewing our tertiary center. Future studies should be population-based in order to avoid this type of bias. We found that IBD was more common in the preschool-aged group(2-6 years) and it was mostly ulcerative colitis. This correlates with Leung et al, who showed an increase in the incidence of the disease in ages <6 years recently.[19] However, Crohn's disease was the most common cause among adolescents in our study and this doesn't correlate with other studies that listed anal fissure as the most common cause at this age.[4-19] This may be due to the limited number of patients included in our study from this age group.

Endoscopy is the method of choice for evaluating UGIB and LGIB, after stabilization and resuscitation, and within 24 h of presentation.[4]

The overall yield of EGD in our patients as a diagnostic procedure of UGIB causes was 91.6% which is similar to that in many reports such as Prolla et al(85-90%)[23] and Huang et al (90%)[13], but higher than that recorded by Yu et al(~ 76%), Elmouzan et al (75%) and Dehghani et al (~ 79%).[10-14-2] The researchers attributed this to the delay in performing EGD which gives a high false negative[12], while it was performed within 24 hours in our study and by expert hands.

Colonoscopy had a high diagnostic yield too (80.3%) and this finding is similar to previous results be Lissey et al(80% of cases).[24]

Finally, we should mention that the current study included patients who underwent gastrointestinal endoscopy only, which made us overlook patients with cases that do not constitute an endoscopic indication, such as infectious gastroenteritis. We did not neither include patients who required emergency surgery, such as patients with malrotation and intussusception.

However, this study was the first in our region to study the endoscopic findings and causes of gastrointestinal bleeding according to age and to determine the effectiveness of endoscopic procedures and their potential in diagnosing the cause of GIB.

CONCLUSION

It’s important to perform an endoscopy in children with gastrointestinal bleeding in order to establish a causal diagnosis as a step towards directing specific treatment .Investigating for H. pylori sepsis in children with upper

gastrointestinal bleeding and Encouraging breastfeeding in infants are recommended.

Abbreviations
GIB: Gastrointestinal bleeding.
UGIB: upper gastrointestinal bleeding.
LGIB: lower gastrointestinal bleeding.
EGD: esophagogastroduodenoscopy.
CMPA: cow's milk protein intolerance.
HP: helicobacter pylori.
IBD: Inflammatory Bowel Diseases.
POBT: positive occult blood test.
NSAIDs: non-steroidal anti-inflammatory drugs.
GERD: gastro-esophageal reflux disease.

Declarations
Ethics approval and consent to participate.
All parents whose children were studied gave informed consent for the sharing of this research. Ethical clearance for this study was obtained from the Ethical Committee of Tishreen University Hospital.

Consent for publication
All parents whose children were studied gave informed consent for publication of the research.

Availability of data and materials.
We can't share patient data due to our hospital's privacy policy, which concerns with maintaining patient confidentiality and refuses to publish or share data. Also, the informed consent signed by parents to participate in the study prevents the sharing of information with the unknown researchers.

Competing interests: Not applicable. Funding: Not applicable.

Author Contributions: Both authors developed and carried out sample collection. Literature review was done by Dr. Maria Naamah, and both authors did data analysis and read through the final data.

Acknowledgments: We wish to thank the medical officer, doctors in the pediatric department, and Tishreen University Hospital gastroenterology center who worked with us in reviewing the patients and doing the Endoscopic procedures. We want to thank Dr Leen Doya for technical help. We want to thank the parents, the patients for their consent to participate in this study.

REFERENCES

1. HILLEMEIER, C.; GRYBOSKI, J. D. Gastrointestinal bleeding in the pediatric patient. *The Yale Journal of Biology and Medicine*, 1984; 57.2: 135.
2. Dehghani, Haghighat, Imanieh, and Tabebordbar. Upper Gastrointestinal Bleeding in Children in Southern Iran. Indian Journal of Pediatrics, Indian J Pediatr, 2009; 76(6): 635-638.DOI:10.1007/s12098-009-0092-3.
3. Boyle JT. Gastrointestinal Bleeding in Infants and Children. Pediatrics in Review, 2008; 29: 39. DOI: 10.1542/pir.29-2-39.
4. Romano C, Oliva S, Martellossi S, Miele E, Arrigo S, Graziani MG, Cardile S, Gaiani F, de'Angelis GL, Torroni
5. F. Pediatric gastrointestinal bleeding: Perspectives from the Italian Society of Pediatric Gastroenterology. World Gastroenterol, 2017; 23(8): 1328-1337. DOI: 10.3748/wjg.v23.i8.1328.
6. Sahn B, Bitton S. Lower Gastrointestinal Bleeding in Children. Gastrointst Endoscopy Clin N Am, 2016; 26: 75–98. DOI: 10.1016/j.giec.2015.08.007.
7. Monroe EJ, Slowik V, Shin DS. Pediatric Nonvariceal Gastrointestinal Hemorrhage.Digestive Disease Interventions, 2018; 2.03: 266-275. DOI:10.1055/s-0038-1667316.ISSN 2472-8721.
8. Singhi S, Jain P, Jayashree M, Lal S.Approach to a Child with Upper Gastrointestinal Bleeding. Indian Journal of Pediatrics, 2013; 80(4): 326–333. DOI :10.1007/s12098-013-0987-x.
9. Genel S, Lucia SM, Daniel SG, Emanuela F .Gastrointestinal Bleeding in Children can have Many Causes. Pharmceutica Analitica Acta, 2016; 7: 2 e184. DOI:10.4172/21532435.1000e184.
10. Zahmatkeshan M, Fallahzadeh E, Najib KS, Geramizadeh B, Haghighat M, Imanieh MH. Etiology of Lower Gastrointestinal Bleeding in Children: A Single-Center Experience from Southern Iran. Middle East Journal of Digestive Diseases, 2012; 4: 216-23.
11. Yu Y, Wang B, Yuan L, Yang H, Wang X, Xiao Y, Mei H, Xu C. Upper Gastrointestinal Bleeding in Chinese Children: A Multicenter 10-Year Retrospective Study.Clinical Pediatrics, 2015; 1-6. DOI:10.1177/0009922815611642.
12. Shahraki T, Shahraki M, Miri-Aliabad G. The Importance of Endoscopy as a Useful Method for Diagnosis of Upper Gastrointestinal Bleeding in Children. Journal of Comprehensive Pediatrics, 2018; 9(1): e55022.DOI:10.5812/compreped.55022
13. Hassoon AJ, AlMaeeni AA, Matloub HY.Upper Gastrointestinal Bleeding In Children. J Fac Med.Baghdad 2012; 54: 3.
14. Huang IF, Wu TC, Wang KS, Hwang B, Hsieh KS. Upper gastrointestinal endoscopy in children with uppergastrointestinal bleeding. *J Chin Med Assoc*, 2003; 66: 271-275.
15. EL Mouzan MI, Abdullah AM, AI- Mofleh IA. Yield of endoscopy in children with hematemesis. *TropGastroenterol*, 2004; 25: 44-46.
16. Rafeey M, Shoaran M, Majidy H. Diagnostic Endoscopy and Clinical Characteristics of Gastrointestinal Bleeding in Children: a 10-Year Retrospective Study. Iranian Red Crescent Medical Journal. 2013; 15(9): 794-7. DOI:10.5812/ircmj.7075.
17. Leung AKC, Hon KL. Gastroesophageal reflux in children: an updated review. Drugs in Context, 2019; 8: 212591. DOI: 10.7573/dic.212591.

18. Cleveland K, Ahmad N, Bishop P, Nowicki M. Upper gastrointestinal bleeding in children: an 11-year retrospective endoscopic investigation. World Journal of Pediatrics, 2012; 8(2): 123-128. DOI: 10.1007/s12519-012-0350-8.
19. Mittal SK, Kalra KK, Aggarwal V. Diagnostic upper GI endoscopy for hematemesis in children: experience from a pediatric gastroenterology center in north India. *Indian J Pediatr*, 1994; 61: 651-654.
20. Leung AK, Wong AL. Lower gastrointestinal bleeding in children. Pediatr Emerg Care, 2002; 18: 319-23.
21. Rayhorn N, Thrall C, Silber G. A review of the causes of lower gastrointestinal tract bleeding in children. Gastroenterol Nurs, 2001; 24: 77–82.
22. Fox VL. Gastrointestinal bleeding in infancy and childhood. Gastroenterol Clin North Am, 2000; 29: 37–66.
23. Nambu et al. Current role of colonoscopy in infants and young children: a multicenter study. BMC Gastroenterology, 2019; 19: 149. DOI:10.1186/s12876-019-1060-7.
24. Prolla JC, Diehl AS, Bemvenuti GA, Loguercio SV, Magalhaes DS, Silveira TR. Upper gastrointestinal fiberoptic endoscopy in pediatric patients. Gastrointest Endosc, 1983; 29: 279–81.
25. de Ridder L, van Lingen AV, Taminiau JA, Benninga MA. Rectal bleeding in children: endoscopic evaluation revisited. Eur J Gastroenterol Hepatol, 2007; 19: 317–20.