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ORIGINAL PAPER

A child with lower gastrointestinal bleeding – aetiology and diagnostic procedure

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ABSTRACT

Introduction: Lower gastrointestinal bleeding (LGIB) is not a rare clinical problem in children. The aetiology of LGIB varies according to age. Likewise, experiences in different countries reflect the disparities in the frequency of various causes of LGIB in children. Although some cases can be diagnosed clinically, choosing the appropriate diagnostic methods in children is challenging. The aim of the study was to determine the aetiology of LGIB in children and analyse the diagnostic procedures needed to make a diagnosis.

Material and methods: The medical records of children with chronic LGIB admitted to the Paediatric Gastroenterology Department were reviewed. The diagnoses and diagnostic procedures were analysed according to age groups (< 5 with subgroups < 2 and 2–5, 5–10, and > 10 years old).

Results: 227 patients were enrolled in the study. The most important causes of LGIB among all patients were constipation associated with anal fissures (36.6%) and inflammatory bowel disease (IBD) (33.5%). According to age groups, the main causes of LGIB were: up to 5 years old – constipation (39.62%) and food allergy (28.3%), in the youngest age subgroup up to 2 years old – food allergy (52.38%), between 5 and 10 years old – constipation (44%) and ulcerative colitis (14%), over 10 years old – IBD ulcerative colitis (36.29%), Crohn's disease (13.71%), and constipation (32.26%). Patients with IBD were more likely to have anaemia and weight loss. The level of faecal calprotectin was significantly elevated in children with IBD and colorectal polyps.

Conclusions: Constipation is a common cause of LGIB in all age groups of children. Food allergy should be considered in infants and young children, but it is rarely seen in children over 5 years old. In children older than 5 years old, diagnostics for IBD should be carried out, especially in patients with weight loss, high levels of faecal calprotectin, and anaemia. Colorectal polyps and Meckel's diverticulum are less common causes of LGIB.

KEY WORDS:
children, aetiology, diagnostic procedure, lower gastrointestinal bleeding.

INTRODUCTION

In children, gastrointestinal bleeding (GIB) is not a rare condition, having a reported incidence of 6.4% [1]. Lower gastrointestinal bleeding (LGIB) in children is a common clinical problem; in fact, it is reportedly a complaint of about 0.3% of children in the emergency department [2]. In most cases, the LGIB is self-limiting and rarely requires intensive care. A wide range of these cases can be diagnosed and dealt with in primary care and do not require hospital admission. 80% of LGIB cases in the emergency department undergo routine discharge, suggesting that most cases involved non-life-threatening bleeds [3]. However, conditions such as Meckel's diver-

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ticulum, variceal haemorrhages, acute intestinal obstruction, or severe attack of ulcerative colitis (UC) are often present with life-threatening GIB [4].

Lower gastrointestinal bleeding is defined as bleeding distal to the ligament of Treitz (small bowel and colon). The most common symptoms of LGIB are hematochezia and melena [5]. Some patients have additional symptoms like abdominal tenderness or pain, diarrhoea, or constipation. In addition to GIB, patients may have abnormal blood or stool test results. Iron deficiency anaemia, high levels of inflammatory markers or faecal calprotectin, positive stool cultures, and positive allergy tests can play an important role in making a diagnosis [6].

Lower gastrointestinal bleeding may occur due to several reasons such as infectious colitis, anal fissures, colorectal polyps, food allergies (mainly cow's milk protein allergy), inflammatory bowel disease (IBD), Meckel's diverticulum, systemic diseases (e.g. hemolytic uremic syndrome, Schoenlein-Henoch disease), and malignancies. The aetiology of LGIB is age dependent. However, one of the leading factors for LGIB regardless of age remains gastrointestinal infections. In infants, allergic colitis and anorectal fissures represent common causes, while in toddlers and young children, colorectal polyps, perianal lesions, and infectious enterocolitis are the main reasons. In adolescents the predominant causes include anal fissures, infectious enterocolitis, colorectal polyps, and IBD [1]. Experiences in various countries and among different populations indicate differences in the prevalence of a variety of causes of LGIB in children [1, 7, 8]. For instance findings from the Iran study indicated that polyps, chronic nonspecific colitis and proctitis are the most prevalent causes of LGIB in children [7]. Another study shows that allergic colitis and anorectal fissures represent the most common causes in infants, while infectious enteritis and anorectal fissures are the most common causes in older children [9]. Differential diagnosis of LGIB in children varies with age. Timely and accurate diagnosis is necessary to reduce complications and mortality. Although some cases can be diagnosed clinically, choosing the appropriate diagnostic methods in children is challenging [8].

In this study, we aimed to investigate the aetiology of chronic LGIB in children referred to the Paediatric Gastroenterology Department in the University Hospital. The second goal was to analyse comorbid symptoms in hospitalized children and the diagnostic procedures needed to reach a diagnosis.

MATERIAL AND METHODS

The study was approved by the Medical University Ethics Committee.

In the study, the samples comprised children less than 18 years old, who were admitted for the first time to the Paediatric Gastroenterology Department from June 2017 to June 2020 because of mild to severe chronic LGIB. Children with a previously established diagnosis of LGIB were excluded from the study.

The medical records of the patients were retrospectively reviewed. After performing diagnostic procedures, a checklist containing all necessary information including demographic data, patient history, physical examination results, laboratory tests results, and endoscopy and imaging findings were collected. In all patients, we analysed the following data:

- duration of bleeding before admission,
- clinical presentation (type of bleeding, additional symptoms such as abdominal pain, diarrhoea, constipation, and weight loss),
- laboratory tests (haemoglobin – Hb, C-reactive protein – CRP, faecal calprotectin, stool cultures, allergen-specific IgE, skin prick tests),
- endoscopy (with histology) and scintigraphy findings.

Proctosigmoidoscopy was used as a first-line procedure in the event of suspicion of colonic polyps, anal fissure, anal varices, allergic colitis, or IBD. The indications for performing a complete colonoscopy were the presence of alarm symptoms (weight loss, anaemia, chronic diarrhoea, perianal changes) and suspected IBD or polyps. Anaemia was defined as Hb concentration below the 5th percentile for age and gender. Weight loss was defined as any history of weight loss reported by patients and caregivers due to symptoms. The normal ranges for CRP were 0–5.0 mg/dl and for faecal calprotectin 0–50.0 μg/g.

Final diagnoses were made based on all the mentioned diagnostic procedures. The diagnosis of a food allergy was established by the physicians based on clinical manifestation, trial elimination diet, oral food challenge, and additional tests such as skin prick tests and allergen-specific IgE concentrations in the serum.

The final diagnoses and results of diagnostic procedures were analysed according to age groups (< 5, 5–10, and > 10 years old). The group of children up to 5 years old was further divided into 2 subgroups: up to 2 years old and between 2 and 5 years old.

The quantitative study was conducted using the Statistica 13.1 PL package. Basic descriptive statistics were calculated for quantitative variables and frequencies of variants of qualitative variables. Differences between groups were tested using the non-parametric ANOVA Kruskal-Wallis test with a post hoc test (multiple comparison tests) because of non-normality of distribution of variables. Differences in the distributions of qualitative variables were sought by using multivariate (contingency) tables with Pearson's χ^2 or χ^2 NW test, applied according to the expected numbers. For the entire study, a level of $p < 0.05$ was taken as the cut-off for not rejecting the null hypothesis.

RESULTS

A total of 227 patients with chronic LGIB admitted the first time to the Department of Paediatrics, Gastro-

enterology, and Nutrition of the University Hospital in Wroclaw between June 2017 and June 2020 were enrolled in the study. That represents 3.44% of the total number of hospitalizations in the department at that time. The median patient age was 10.08 years (IQR: 15.17–5.08), and 117 (51.5%) were female patients. The average duration of bleeding before admission was about 4.85 months. Almost all patients (97.4%) presented hematochezia. Most patients reported additional symptoms such as abdominal pain (56.0%), diarrhoea (42.3%), constipation (39.6%), and weight loss (19.0%). Weight loss was mostly seen in children over 10 years old (27.42% of patients) compared to younger children (7.55% of children up to 5 years old, 10.0% of children between 5–10 years old), and the difference was statistically significant ($p = 0.00099$). The results of laboratory tests: Hb concentration, CRP, and faecal calprotectin were also analysed, taking into account the age of patients. Patients from the oldest group had significantly higher faecal calprotectin levels (672.36 vs. 419.77 and 222.67 μg/g, respectively) and more often anaemia (32.26% vs. 22.0% and 13.46%, respectively) than younger children, and the differences between the oldest and youngest groups were statistically significant ($p = 0.047$, $p = 0.021$). Differences in CRP level were not significant between age groups.

In 150 of the children in the study (66.1%) an endoscopic examination of the lower gastrointestinal tract was performed – proctosigmoidoscopy and/or complete colonoscopy, and in some patients both procedures were used. Proctosigmoidoscopy or complete colonoscopy was performed in 100 (80.65%) patients > 10 years old, in 31 (62.00%) patients between 5 and 10 years old, and in 19 (35.85%) children under 5 years old. Based only on the sigmoidoscopy, 4 cases of rectal polyps, 2 cases of UC, and 3 cases of perianal changes (anal fissure, inflammation) were diagnosed. Ninety-two (40.5%) children underwent a full colonoscopy. Six colonoscopies were performed in the children up to 5 years old, 17 in the group 5–10 years old, and 69 in children over 10 years old. The diagnosis rate for colonoscopy (Crohn's disease – CD, UC, or colonic polyps) was 83.7%. No abnormalities were found in 16.3% of cases. The number of patients who underwent an endoscopy in each group of diagnoses is shown in Table 1. Nuclear scintigraphy, due to suspicion of Meckel's diverticulum, was performed in 8 children in the study group (3.52%). In 4 cases the presence of Meckel's diverticulum was confirmed.

TABLE 1. The number of patients who underwent endoscopy

Diagnosis (*n*)	Proctosigmoidoscopy, *n* (%)	Colonoscopy, *n* (%)
Food allergy (16)	4/25	0
Crohn's disease (23)	8/34.78	23/100.00
Ulcerative colitis (53)	19/35.85	51/96.25
Constipation (83)	33/39.76	8/9.64
Infections (7)	1/14.29	0
Meckel's diverticulum (4)	0	0
Colorectal polyps (7)	4/57.14	3/42.86
Cause unknown (28)	15/53.57	5/17.86

The results of the study showed that the most common reasons for LGIB among all admitted patients were constipation (36.6%), UC (23.3%), and CD (10.1%). In 12.3% of cases the cause of rectal bleeding could not be determined. The patients were divided into 3 groups according to their age. In children up to 5 years old (53 patients) the main causes of LGIB were food allergy (28.3%) and constipation (39.6%). In the youngest age subgroup (up to 2 years old, 21 patients) food allergy was diagnosed in 52.38% of cases, and the second cause of LGIB was constipation, found in 19.05% of children. In children between 2 and 5 years old (32 patients) constipation was the first cause of LGIB (53.13% of patients), and food allergy was diagnosed as second cause, found in 12.5% of patients. In a group of children between 5 and 10 years old (50 patients) the main causes were constipation (44.0%) and UC (14.0%). Among the patients over 10 years old (124 patients), IBD

TABLE 2. The aetiology of lower gastrointestinal bleeding according to age

Aetiology	Patient age				
	Subgroup < 2 years old, *n* = 21 (%)	Subgroup 2–5 years old, *n* = 32 (%)	< 5 years old, *n* = 53 (%)	5–10 years old, *n* = 50 (%)	> 10 years old, *n* = 124 (%)
Food allergy	11 (52.38)	4 (12.50)	15 (28.30)	1 (2.00)	0 (0)
Crohn's disease	1 (7.76)	1 (3.13)	2 (3.77)	4 (8.00)	17 (13.71)
Ulcerative colitis	0 (0)	1 (3.13)	1 (1.89)	7 (14.00)	45 (36.29)
Constipation	4 (19.05)	17 (53.13)	21 (39.62)	22 (44.00)	40 (32.26)
Infections	2 (9.53)	0 (0)	2 (3.77)	3 (6.00)	2 (1.61)
Meckel's diverticulum	2 (9.52)	0 (0)	2 (3.77)	0 (0)	2 (1.61)
Colorectal polyps	0 (0)	3 (9.38)	3 (5.66)	3 (6.00)	1 (0.81)
Cause unknown	1 (4.76)	3 (9.38)	4 (7.55)	9 (18.00)	15 (12.10)

TABLE 3. Mean C-reactive protein and faecal calprotectin concentration values and the incidence of anaemia and weight loss depending on the diagnosis

Diagnosis	CRP [mg/l]*	Calprotectin [μg/g]**	Anaemia, *n* (%)***	Weight loss, *n* (%)
Food allergy	1.26	90.76	3/18.75	1/6.25
Crohn's disease	14.5	1264.19	13/56.52	12/52.17
Ulcerative colitis	5.37	1171.49	24/45.28	19/35.85
Constipation	1.24	43.67	10/12.05	5/6.02
Infections	2.26	402.95	0/0	1/14.29
Meckel's diverticulum	5.5	36.30	3/75.00	0/0
Colorectal polyps	0.58	721.23	1/14.29	0/0
Cause unknown	0.90	100.68	4/14.81	4/14.29
p-value	0.0003	0.0000	0.0004	0.00071

CRP – C-reactive protein
**Normal range 0–5.0 mg/dl. **Normal ranges 0–50.0 μg/g. ***Hb concentration less than the 5th percentile for age and gender.*

dominated (UC in 36.29% and CD in 13.71%) accompanied by constipation (32.26%). The aetiology of LGIB in children in various age groups is presented in Table 2.

Patients with IBD were statistically significantly more likely to have anaemia and weight loss compared to children with other diagnoses. A higher average CRP serum concentration was noted in children with CD than in children with other diagnoses. The level of faecal calprotectin was significantly higher in children with IBD and colorectal polyps. The mean values of CRP and faecal calprotectin and the incidence of anaemia and weight loss depending on the diagnosis are indicated in Table 3.

DISCUSSION

Gastrointestinal bleeding is considered an alarming sign in any age group that requires diagnostic work-up to determine the cause and implement appropriate therapy. Lower gastrointestinal bleeding in children may have several aetiologies that can be categorized by age group (Table 4) [1, 2]. In the paediatric population, certain pathologies leading to LGIB may occur more frequently in specific age groups such as allergic colitis in infants, polyps in preschool age children, or IBD in adolescents [1].

Experience from different countries shows differences in the prevalence of the most common causes of LGIB in children. The aetiology of LGIB may differ depending on the studied population and the diagnostic methods used [7, 9–12]. Differences may be due to various reasons, including lifestyle, dietary habits, ethnicity, and geographic conditions. Regional epidemiological data should be available to help clinicians better manage these patients. The fact that the aetiology of LGIB in children varies across geographic regions and ethnic groups requires an investigation of the epidemiology and characteristics of these disorders in each region. In our study the main cause of LGIB was constipation, found in 36.6% of patients (39.62% in children younger than 5 years old, 44.00% in children between 5 and 10 years old, and 32.26% in the oldest group). Most previous reports have also revealed that constipation was the most common reason for rectal bleeding in toddlers and school-aged children [10, 13]. Constipation is one of the most common reasons for patient visits to paediatric gastroenterology departments, and as many as 25% of referrals to paediatric gastroenterology are related to constipation. Constipation can cause various gastrointestinal problems such as abdominal pain, anal pruritus, painful defecation, and anorexia or non-gastrointestinal complications such as urinary problems. It is also commonly associated with the presence of anal fissure and rectal bleeding [14]. Rectal bleeding was reported in 4.0–42.0% of constipated patients depending

TABLE 4. Causes of lower gastrointestinal bleeding in children of different age groups (authors' modification based on [1, 2])

Infants	Pre-school age	Adolescents
Non-specific colitis Anal fissures Food allergy Hirschsprung's disease Infectious enterocolitis Intussusception Developmental malformations (intestinal duplication)	Polyps (juvenile polyps) Anal fissures Infectious enterocolitis Intussusception Meckel's diverticulum Haemorrhagic diseases Schoenlein-Henoch disease Hemolytic uremic syndrome Toxins Inflammatory bowel disease	Anal fissures Inflammatory bowel disease Infectious enterocolitis Polyps (familial polyposis juvenile polyps) Schoenlein-Henoch disease Hemolytic uremic syndrome

on the study site [15, 16]. In most cases, constipation is functional, and patients do not present other alarm symptoms [17]. Similarly, in our study, the incidence of analysed alarm symptoms such as anaemia and weight loss were reported to be low, and CRP and calprotectin levels were within normal ranges. Diagnosis of constipation is usually based on accurate history-taking, physical examination, including digital rectal examination, and basic laboratory tests. Endoscopic examination of the lower GI tract is not recommended as a first-line assessment in these cases [18]. Among our constipated patients, about 40% underwent proctosigmoidoscopy, and less than 10% had indications for a full colonoscopy. The indications for endoscopy in these patients were the presence of alarm symptoms, suspected rectal polyps, or vascular lesions and a failure to improve after initial treatment of constipation.

In the discussed group of 227 patients with LGIB, endoscopic examination was necessary in 66.1% of them. IBD was one of the most common pathologies leading to bleeding (33.4%) – it was found in only 5.7% of the youngest children, while in adolescents it was found in 50%, which is consistent with some previous observations in the paediatric population [2, 12, 19–21].

Inflammatory bowel disease comprises chronic diseases of the gastrointestinal tract, with unclear aetiology, in which genetic, environmental, and immunological factors play a role. They include UC and CD. In nearly 20% of patients, the first symptoms of these diseases occur during childhood – most are below 15 years of age. In UC, the predominant symptom is bleeding from the lower gastrointestinal tract, while in CD the symptoms are less characteristic and most often include abdominal pain, anaemia, and weight loss [22]. In the diagnostics of both conditions, endoscopic examinations of the gastrointestinal tract, imaging studies, and laboratory tests are performed, in which, as well as inflammatory markers or total blood count, faecal calprotectin is determined [22, 23]. In the analysed group of patients with evidence of LGIB, IBD was the cause of bleeding in 33.4% of patients, including more than 23% with UC. In adolescents, UC was the cause of as many as 36.3% of cases of symptomatic GIB, and CD about 14%, indicating the need for endoscopic testing in the diagnosis of bleeding, especially in this age group. High levels of faecal calprotectin, found in both UC and CD children from the study group, similarly to children diagnosed with colorectal polyps, confirm the usefulness of this marker, especially in case of GIB, when planning further invasive diagnostic procedures. However, the exclusion of gastrointestinal infections should be considered, because in these cases (as our observations show) the faecal calprotectin concentration may also be increased. On the other hand, weight loss, anaemia, and high inflammatory markers were found only in patients with inflammatory bowel disease, especially in CD.

In several studies, the most common cause of asymptomatic LGIB in children was colorectal polyps, especially in the Middle East, found in 25.1–41.6% of children undergoing colonoscopy [1, 7, 8, 24]. They are less commonly found in Western populations [10, 12, 13]. In a multicentre study in the USA it was reported that polyps were detected in 6.1% of all children who underwent colonoscopy and in 12% of children with LGIB [25]. Therefore, suspected bleeding from a polyp in a child serves as an indication for colonoscopy [18]. In our study group the incidence of polyps was 3.1%. The highest prevalence of adolescent polyps was found in preschool and early school-aged children (11.7% in total), as compared to adolescents (0.8%). The typical age of diagnosis for juvenile polyps is between 2 and 5 years old, with a predominance of males and non-Caucasians [20]. In our subgroup of children aged between 2 and 5 years old polyps were diagnosed in 9.38% of patients, which was the third most common cause of LGIB in this group. The incidence of polyps in children under 10 years of age in our study is similar to that observed in studies from European countries and the USA. It appears that polyps are much more common than is clinically recognized because many of them become ischaemic with growth and undergo autoamputation with moderate and painless hematochezia [8].

In 83.7% of performed colonoscopies, the diagnoses (UC, CD, or juvenile polyp) were confirmed. In 12.3% patients, despite colonoscopy, the cause of the LGIB could not be determined. Similar results in children who underwent colonoscopy for rectal bleeding are reported by de Ridder *et al.* [19]. The percentage of diagnoses for the colonoscopy (IBD and colorectal polyps) was 80%, and no abnormalities were found in 20.4% of patients, either in colonoscopy or histopathology.

Gastroenteritis and GI infections are considered as relatively prevalent causes of LGIB in any age group. In our report, infections were found infrequently (3.1%) while in other studies they have been classified as the first or second most common causes of LGIB in children [1, 10, 26]. The small numbers of infection-related bleeding cases possibly resulted from selection bias because we included patients with chronic rectal bleeding who were referred to our centre.

Food allergy is considered as one of the most common causes of LGIB in infants [1, 26]. In our study, food allergy was the second cause of LGIB following constipation in the entire group of children under 5 years old. However, in the subgroup of children below 2 years old, allergy was the first cause of LGIB and accounted for 52.38% of cases. In older age groups, we found very few cases of allergy; therefore, it should not be considered in older children as a cause of LGIB. In severe cases, food allergy may lead to malabsorption, protein-losing enteropathy, anaemia, and failure to thrive [27]. In our study sample, 18.75% of children diagnosed with food allergy had confirmed anaemia and 6.25% reported weight loss. In allergic patients, faecal calprotectin levels were only slightly elevated. In our study and in other reports, low

faecal calprotectin levels were observed in patients with food allergy manifested by gastrointestinal symptoms. On the other hand, many reports support a correlation between elevated calprotectin levels and food allergy in infants. In conclusion, the available data do not support making any recommendations concerning the use of faecal calprotectin in the diagnosis of food allergy [28]. Given the patient's age and favourable course in most food allergy cases, endoscopy with biopsy is not recommended for diagnosis, except in cases of unusual or severe symptoms, such as significant malnutrition, or severe rectal bleeding complicated by anaemia despite an elimination diet [27, 28].

In most LGIB cases, bleeding is mild and self-limiting, but significant bleeding can occur with Meckel's diverticulum [2].

Meckel's diverticulum complicated by LGIB is most associated with the existence of ectopic gastric mucosa. In patients with suspected Meckel's diverticulum, the diagnosis can be based on a ^{99m}Tc-pertechnetate scan, which can visualize Meckel's diverticulum because this tracer accumulates in certain tissues, such as ectopic gastric tissue [29]. We confirmed Meckel's diverticulum using this imaging modality in 4 patients, which represents 1.8% of our study group. These cases involved children under 5 years old as well as those over 10 years old. The incidence of Meckel's diverticulum associated with complications is higher in males, and it has been reported that more than 75% of cases occur under the age of 10 years [29]. In many cases, bleeding from Meckel's diverticulum can be profuse and lead to anaemia, which we found in 3 of our 4 patients. Meckel's diverticulum should be strongly suspected at any age if bleeding is massive and accompanied by both light and dark red stools and anaemia [2].

CONCLUSIONS

The findings of our study indicated that constipation, which is associated in many cases with anal fissure, is a common cause of LGIB in all age groups of children. Furthermore, food allergy should be taken into account in the diagnosis of LGIB in infants and young children, but it is rarely the cause of LGIB in children over 5 years old. In children above 5 years old, diagnostics for IBD should be carried out (including colonoscopy), especially in patients with weight loss, high level of faecal calprotectin, and anaemia. Colorectal polyps and Meckel's diverticulum are less common causes of LGIB.

Our study had some limitations. It was a retrospective, single-centre study that included children referred to a tertiary gastroenterology centre for chronic LGIB. This selection method may have resulted in selection bias because only patients with chronic bleeding, without infectious or surgical causes, e.g. intussusceptions, were referred to our centre. Future studies should also include general paediatrics and paediatric surgery centres where children with short-term or acute bleeding requiring surgical intervention are present, which could mitigate errors. Nevertheless, this is the first report from Poland on the characteristics of chronic LGIB in the paediatric population. We found that LGIB was more common among children above 10 years old. Hematochezia was the most common presentation, which is consistent with reports by other authors. The most common causes of LGIB were age-dependent, but constipation leading to rectal and/or anal bleeding was found very frequently and dominated among causes in children under 10 years old. In adolescents, IBD was the first cause of bleeding. Food allergy was only identified as the cause of LGIB in the youngest children.

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DISCLOSURE

The authors declare no conflict of interest.

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