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A survey on rectal bleeding in children, a report from Iran

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Background/aim: Studies on the epidemiology of rectal bleeding in children are limited in Iran. Our aim was to assess etiologies of rectal bleeding in children in Iran.

Materials and methods: We enrolled 730 children with rectal bleeding. All the patients underwent colonoscopy, and 457 were further evaluated with histopathology.

Results: According to colonoscopy and histopathology, respectively, inflammatory bowel disease (IBD) (29.4%, 15.8%), nodular hyperplasia (NH) (24.9%, 10%), and juvenile polyposis (JP) (12.6%, 9.9%) were the most common causes of rectal bleeding. Other conditions were solitary rectal ulcer (5.3%), chronic colitis (4.6%), allergic colitis (3.3%), focal colitis (1.3%), and infectious colitis (1.1%). In colonoscopy, there were no significant differences in the distribution of pathologies regarding sex, while the youngest and oldest mean ages were found for patients with NH (4.6 ± 3.9 years, $P < 0.0001$) and those with normal appearance (8.1 ± 4.4 years, $P < 0.0001$) respectively. Based on histopathologic reports, the youngest patients were diagnosed with infectious colitis (4.6 ± 2.8 years), while patients with chronic colitis were the oldest (9.2 ± 4.6 years, $P = 0.003$).

Conclusion: JP, NH, and IBD constituted the most common etiologies of rectal bleeding in our patients. It is recommended to perform a complete diagnostic approach to accurately assess rectal bleeding in children.

Key words: Colitis, hematochezia, inflammatory bowel disease, juvenile polyp, nodular hyperplasia, rectal bleeding

1. Introduction

Lower gastrointestinal (GI) bleeding is a common clinical presentation in children. Rectal bleeding can result from inflammation of the GI mucosa, a condition known as colitis. Pediatric colitis may be associated with multiple factors such as infection, allergy, immune deficiency, or infections. Other common etiologies include inflammatory bowel disease (IBD), juvenile polyposis (JP), and nodular hyperplasia (NH) (1). The majority of conditions associated with intestinal inflammation in children are self-limited and require no treatment. However, those patients diagnosed with IBD may need to be referred to a pediatric gastroenterologist for further evaluation.

The epidemiology of IBD in children is variable, and its incidence has increased over the past decade (2). It has been estimated that pediatric IBD constitutes one-fourth of all IBD cases (2–5). The etiology of IBD in children is multifactorial. A history of IBD in siblings has been known as a traditional risk factor (6). There is a shortage of large population studies in pediatric IBD, and most available data on this come from adult onset IBD.

Clinical symptoms of IBD (such as rectal bleeding, excessive abdominal pain, constipation, and food abstinence) are related to poorer quality of life in IBD patients (7). Abdominal pain, as a common feature in pediatric patients with digestive disorders, accompanied with lower GI bleeding may be the sole presentation of IBD and JP (8–10). Hematochezia (fresh rectal bleeding) is a feature of JP and this condition should be evaluated in children with painless rectal bleeding (9,11,12). Discrimination of various causes of rectal bleeding requires specific, reliable, and accurate diagnostic methods. Among

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biochemical, serologic, and enzymatic evaluations, the sensitivity of which is controversial, colonoscopic and histologic examination are acceptable procedures (13).

There are few studies addressing a complete spectrum of etiologies of rectal bleeding in a large cohort of the pediatric population. In the present study, we assessed 730 children and adolescents with lower GI bleeding with colonoscopy and histopathology to provide a comprehensive picture on the differential diagnosis of this problem.

2. Materials and methods

In this two-center study, pediatric patients (0–18 years old) who presented with rectal bleeding with or without clinical presentations such as abdominal pain and digestive problems underwent colonoscopy and histopathological examinations within 2010–2016.

2.1. Patients

The children had been referred to the Pediatric Gastroenterology Center at Nemazee Hospital, affiliated with Shiraz University of Medical Science, and the pediatric ward at Amir-Al-Momenin Hospital, associated with Zabol University of Medical Sciences. Informed consent was acquired from parents and the goal of the research was clearly explained to them. The study was approved by the research ethics committee of Zabol University of Medical Sciences.

2.2. Colonoscopy and histopathology examination

Clinical suspicion was raised in adolescents referred with lower GI bleeding (3). Colonoscopy was performed under general anesthesia to examine the GI tract for any signs of inflammation. Biopsy specimens were obtained from different parts of the rectum and the colon (ascending, transverse, descending colon). Tissue sections were fixed in formalin and stained with hematoxylin and eosin. Tissue sections were evaluated for histological features by two independent histopathologists.

Diagnoses were made according to the guidelines of the European Society for Paediatric Gastroenterology Hepatology and Nutrition (14). A smooth and pink appearance of intestinal mucosa without any evidence of bleeding or abnormal structures in endoscopy and normal crypt and epithelial structures without any inflammatory cell infiltrations in microscopic findings was recognized as normal condition. JP was diagnosed in cases of presence of intestinal polyps in visual observations of intestine. NH was considered as the presence of multiple intestinal lymphocytic aggregates in histological observations. Chronic colitis was defined as mucosal inflammation of the intestine with distorted cryptic structures along with lymphoplasma cell infiltrations. Allergic colitis was defined as eosinophilic infiltrations surrounding lymphoid nodules within the intestinal mucosa. Focal colitis was recognized as altered architecture of the lamina propria limited to surface epithelial lesions and infiltrated with neutrophils.

2.3. Statistical analysis

Data were entered into SPSS 19. Normality of the data was checked by the Kolmogorov–Smirnov test. Frequencies and means ± standard deviations were used to present data. The chi-square test was utilized to check significant associations between qualitative variables. One-way ANOVA was run to assess significant differences of means of ages between different pathologies.

3. Results

3.1. Demographic features

Of 730 patients, 434 (59.4%) were male and 296 (40.6%) were female. The mean age of the patients was 6.9 ± 4.5 years. Minimum and maximum ages were 1 and 18 years, respectively. Details on the age spectrum of the participants are presented in Table 1.

3.2. Colonoscopy findings

Based on colonoscopy, the majority of our patients (241, 33%) had normal intestinal morphology without any evidence of inflammation. The pathologies identified in colonoscopy were IBD (29.4%), NH (24.9%), and

Table 1. Age spectrum of 730 pediatric subjects with gastrointestinal symptoms.

Parameter		Number	Percentage
Age categories (years)	<2	110	15
	3–5	227	31
	6–8	146	20
	9–12	145	19.8
	>13	102	13.2
Total		730	100

JP (12.6%). Overall, male subjects predominated in all inflammatory conditions; however, the association between sex and these conditions was not statistically significant (P = 0.1, Table 2).

3.3. Histological evaluation

Of 730 patients who underwent colonoscopy, biopsy specimens were obtained from 457 patients with abnormal intestinal appearance. Based on histologic examination, the majority of these (219, 47.7%) had no abnormality in histological sections. Of 93 patients who were diagnosed with JP appearance in colonoscopy, 72 cases were confirmed in histopathology. Common recognized histologic pathologies were JP (15.8%), NH (10%), IBD (9.9%), solitary rectal ulcer (5.3%), chronic colitis (4.6%), and allergic colitis (3.2%) (Table 3).

3.4. Distribution of pathologies among age groups

There was a significant difference between mean age of the patients regarding different colonoscopy or histologic diagnoses. In patients who underwent colonoscopy, the lowest mean age was found for those with NH (4.6 ± 3.9 years, P < 0.0001). Participants with normal colonoscopy appearance were significantly older than other colonoscopic groups (8.1 ± 4.4 years, P < 0.0001). Based on 457 patients who had histopathologic reports, the youngest patients were diagnosed with infectious colitis (4.6 ± 2.8 years), while patients with chronic colitis were the oldest (9.2 ± 4.6 years, P = 0.003, Table 4).

Patients diagnosed with JP and NH in colonoscopy were most commonly encountered in the age group of 3–5 years old (54.8% and 34.6%, respectively). Patients with an IBD diagnosis in colonoscopy also most commonly belonged to the age group of 3–5 years old (24.7%, Table 5). After histological examination and establishing the diagnoses, patients 6–8 years old were the most prevalent in the IBD group, while patients with JP were most commonly 3–5 years old (Table 6).

Table 2. Colonoscopy diagnoses in 730 children with rectal bleeding and gastrointestinal symptoms.

Colonoscopy diagnosis	n (%)	Male n (%)	Female n (%)	P
Normal	241 (33)	146 (60.1)	95 (39.9)	
Juvenile polyp	93 (12.6)	63 (67.7)	30 (32.3)	
IBD	214 (29.4)	126 (58.8)	88 (41.2)	0.1
Nodular hyperplasia	182 (24.9)	104 (57.1)	78 (42.9)	
Total	730 (100)	438 (60)	292 (40)	

IBD: Inflammatory bowel disease.

Table 3. Histopathologic findings in 457 pediatric patients with gastrointestinal symptoms.

Histological diagnosis	n (%)	Male n (%)	Female n (%)	P
NSPC	219 (47.7)	128 (58.4)	91 (41.6)	
Juvenile polyp	72 (15.8)	47 (65.2)	25 (34.8)	
IBD	46 (9.9)	21 (46.6)	24 (53.4)	
Nodular hyperplasia	47 (10)	26 (54.3)	21 (45.7)	
Solitary rectal ulcer	25 (5.3)	18 (70.8)	8 (29.2)	0.2
Chronic colitis	22 (4.6)	12 (52.4)	11 (47.6)	
Allergic colitis	15 (3.2)	8 (57.1)	6 (42.9)	
Focal colitis	6 (1.3)	3 (50)	3 (50)	
Infectious colitis	5 (1.1)	3 (60)	2 (40)	
Total	457 (100)	266 (58.2)	191 (41.8)	

NSPC: No specific pathological condition, IBD: inflammatory bowel disease.

Table 4. Mean ages of patients diagnosed with normal or different pathological appearance of gastrointestinal mucosa in colonoscopy or histopathology.

Diagnosis		Mean age (years) ± SD	Minimum	Maximum	P
Colonoscopy	Normal	8.1 ± 4.4	1	19	<0.0001*
	Juvenile polyp	6 ± 3.8	2	21	
	IBD	7.8 ± 4.6	1	18	
	Nodularity	4.6 ± 3.9	1	19	
Histology	NSPC	7 ± 4.6	1	19	0.003*
	Juvenile polyp	5.6 ± 3.6	1	16	
	IBD	7.9 ± 4.1	1	19	
	Nodular hyperplasia	5.5 ± 4.1	1	15	
	Solitary rectal ulcer	8.8 ± 4.9	1	17	
	Chronic colitis	9.2 ± 4.6	1	18	
	Allergic colitis	7.2 ± 5.9	1	18	
	Focal colitis	8.1 ± 3.7	2	13	
	Infectious colitis	4.6 ± 2.8	3	8	

NSPC: No specific pathological condition, IBD: inflammatory bowel disease, *: statistically significant.

Table 5. Age spectrum of pediatric patients diagnosed as either normal or having a clinical condition in colonoscopy.

Age spectrum (years)	Normal n = 241 n (%)	Juvenile polyposis n = 93 n (%)	IBD n = 214 n (%)	Nodularity n = 182 n (%)	P
<2	17 (7)	8 (8.6)	26 (12.1)	62 (34)	<0.0001*
3–5	58 (24)	51 (54.8)	53 (24.7)	63 (34.6)	
6–8	57 (23.7)	16 (17.4)	46 (21.5)	31 (17)	
9–12	65 (26.9)	13 (13.9)	48 (22.5)	13 (7.2)	
>13	44 (18.4)	5 (5.3)	41 (19.2)	13 (7.2)	

IBD: Inflammatory bowel disease, *: statistically significant.

Table 6. Age spectrum of pediatric patients diagnosed as either normal or having a clinical condition in histologic evaluation.

Age spectrum (years)	NSPC n = 219 n (%)	IBD n = 45 n (%)	Juvenile polyp n = 72 n (%)	Nodular hyperplasia n = 46 n (%)	Solitary rectal ulcer n = 24 n (%)	Chronic colitis n = 21 n (%)	Other n = 30 n (%)	P
<2	35 (15.9)	4 (8.8)	10 (13.8)	12 (26)	3 (12.5)	2 (9.5)	3 (10)	<0.003*
3–5	67 (30.7)	6 (13.4)	37 (51.4)	13 (28.5)	3 (12.5)	2 (9.5)	11 (36.6)	
6–8	44 (20)	15 (33.4)	11 (15.3)	12 (26)	3 (12.5)	6 (28.5)	6 (20)	
9–12	42 (19.3)	9 (20)	11 (15.3)	6 (13)	9 (37.5)	4 (19)	6 (20)	
>13	31 (14.1)	11 (24.4)	3 (4.2)	3 (6.5)	6 (25)	7 (33.5)	4 (13.4)	

NSPC: No specific pathological condition, IBD: inflammatory bowel disease, *: statistically significant.

4. Discussion

Rectal bleeding in ages <20 years old is a commonly encountered phenomenon. Etiologies related to this condition are heterogeneous. In the present study, an evaluation of 730 children referred to our centers because of lower GI bleeding, etiologies were sought using colonoscopy and histopathology. The most common causes identified by colonoscopy were IBD (214/730, 29.4%), NH (182/730, 24.9%), and JP (93/730, 12.6%). In addition, colonoscopy revealed normal GI mucosa in 33% of the cases. Furthermore, of 93 patients who were diagnosed with JP by colonoscopy, 72 cases were confirmed in histopathology, while 21 patients had other types of polyps. NH and IBD at 10% and 9.9% respectively were the other common entities in the histological examination.

IBD is a commonly encountered disease in patients with lower GI bleeding. In an Iranian study, IBD was detected in 20 (6.5%) of 309 children with rectal bleeding (15). The mean age of Iranian patients with IBD was 10.3 years in another Iranian study (16). The mean age of patients with IBD was 8.7 years in our study with the lowest and highest ratios of patients with IBD belonging to subjects <2 years old and >5 years old, respectively. In a study by Olafsdottir et al., 47% of 239 children with GI symptoms had IBD (17). In another study, IBD was documented in 22 (61%) of 36 patients with rectal bleeding (18). Likewise, 36% of 117 patients with rectal bleeding and other suggested intestinal symptoms were identified to have IBD disorders (19). Accordingly, IBD has been reported in 21%–62% of children with lower GI bleeding in other studies (20–23). Risk factors associated with IBD in children have been socioeconomic factors such as parents' educations and occupations, as well as nutritional factors including early (<6 month of age) gluten exposure (6). Life style is supposed to affect the risk of IBD development as IBD has been frequently associated with western culture (24). Vitamins deficiencies, especially vitamin D, may play a role in the development of IBD (25). Pediatric populations affected with IBD suffer from a compromised growth rate, and therefore timely and appropriate diagnostic and therapeutic measures play a substantial role in prognosis of IBD (16,24,26).

Studies on the prevalence and clinical features of JP in children are limited. Overall, we found 93/730 (12.6%) patients with JP in colonoscopy. Of these, 72 cases were confirmed as JP, while 21 patients showed nonjuvenile polyps in histological examination. JP in the colorectal area has been the most common etiology for GI bleeding in children (27). Frequency of JP among children with rectal bleeding is variable. In a study by Thakkar et al., JP was recognized in 6% of patients without rectal bleeding and 12% of those who had hematochezia using colonoscopy (8). In another study in France, 183 (12%) of 1533 children who underwent colonoscopy were identified with JP (28). In a study of 2117 children with rectal bleeding, JP was reported in 8.7% (12). In England, JP was identified in 4% of children who met the criteria for colonoscopy conduction (29). In the study by Olafsdottir et al., of 239 children with digestive symptoms, 4.5% had JP (17). Overall, JP is a common feature in children with rectal bleeding and should be considered in such patients.

Incidence of JP in a certain age spectrum and its association with male sex have been noted. Although we observed more males with JP in our study, there was no significant association between JP and sex of the participant. The mean age of our JP patients was 5.6 years old with most patients (54.8%) belonging to the 3–5 years category. In comparison, JP in children has been noted most commonly in the age group of 3–10 years (8). In a large population-based study in children, JP was associated with male sex and lower mean age respective to children with conditions other than this entity (8,12). The mean age of children with JP was 5.2 years in 129 Pakistani children (11). Likewise, a male predominance was also reported in that study (11). Male predominance and mean age of 5 years in pediatric JP has also been reported by other authors (27).

Although JP is considered to be benign, it needs prompt correction as there have been some reports of malignant transformation (30,31). JP is usually located in the distal portion of the colon with small dimensions (32). Colonoscopy is necessary to differentiate JP from IBD (17). In fact, colonoscopy is commonly performed to diagnose polyps in children presenting with suggesting signs and symptoms. It seems that male patients aged 3–5 years constitute the most susceptible pediatric cohort for JP. Considering the greater sensitivity of histological examination, the presence of JP should be established by microscopy.

In our study, 189/730 (24.9%) and 46/457 (10%) of children showed intestinal NH based on colonoscopy and histopathology, respectively. In comparison, NH was described with a frequency of 3% in a previous report (27). NH of the GI tract results from hyperproliferation of lymphoid cells as a result of immune stimulation. The clinical significance of NH in the lower GI tract is not certain. Lymphoid clusters are normally found throughout the mucosa surfaces of the GI tract; nevertheless, both the frequency and the size of these clusters are increased in NH (33). Clinical presentations of this condition are similar to other inflammatory conditions associated with GI bleeding (34). The role of food allergies has been proposed in the development of rectal NH, although this has not been established (34). NH is a reversible condition and its pathological nature is controversial, with debate in regard to requirements for therapeutic interventions.

A perfect approach for the diagnosis of this phenomenon necessitates performing colonoscopy supported by histological examinations.

In the present study, 75 of 457 patients who had been histologically evaluated for GI pathologies had inflammatory conditions including solitary rectal ulcer (5.3%), chronic colitis (4.6%), allergic colitis (3.2%), focal colitis (1.3%), and infectious colitis (1.1%). There are scare reports encompassing all of these conditions in the literature. In a study of 54 children with solitary rectal ulcer, Dehghani et al. stated a mean age of 10.4 years in these patients (35). Similarly, the majority (15, 58%) of our 24 patients identified with this condition had age higher than 9 years old with a mean age of 8.8 years. In another study of 207 children with signs of rectal bleeding who underwent colonoscopy, solitary rectal ulcer was reported in 3.5% (27). Histological examination is necessary for the discrimination of solitary rectal ulcer from IBD. The characterizing feature in the histological picture of solitary rectal ulcer is lamina propria fibrotic changes, which are different from the features seen in IBD (27). Regarding other etiologies of rectal bleeding, allergic colitis has been described in 1.5% of 239 children with digestive symptoms (17). Infections have been among the common causative factors for intestinal inflammation. The majority of organisms leading to infectious colitis have been bacteria; however, both parasitic and viral organisms can also be associated with the condition (36). Further studies are required to provide a clear picture of the frequencies of the mentioned conditions in children with lower GI bleeding.

Rectal bleeding etiologies are multifactorial in children. The most common causes identified here were IBD, NH, and JP. Other causes responsible for this included solitary rectal ulcer, chronic colitis, allergic colitis, focal colitis, and infectious colitis. Due to heterogeneous differential diagnosis of rectal bleeding in children, it is recommended to use highly sensitive and specific methods to confirm the diagnosis.

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