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The Management of Colonic Polyps in Children: A 13-Year Retrospective Study

--Manuscript Draft--

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Abstract:	The aim of this study was to describe the frequency, major symptoms and characteristics of colonic polyps in a cohort of children. A retrospective chart review of patients aged ≤18 years who were diagnosed with colonic polyp(s) from 2006 to 2019 in a tertiary hospital were included. Data collected included: demographics; clinical presentation; interval of time between the onset of symptoms and the endoscopic diagnosis of colonic polyps; family history; characteristics of the polyp and associated lesions. Over the study period, 35 Caucasian children were diagnosed with juvenile colonic polyps. Twenty-three patients (65.7%) were males. Lower gastrointestinal bleeding of a mean duration of 5.3 ± 4.9 months was the presenting symptom in nearly all cases (n = 34, 97%), and it was isolated in 17 patients. Clinical presentation did not significantly vary according to the age or the location or size of the polyp (p = 0.262, p = 1.000 and p = 0.149, respectively). The polyps were mainly located in the left colon (n = 29, 83%). Right colonic polyps were significantly larger than left colonic polyps (p = 0.037). Conclusion: Lower gastrointestinal bleeding represents the most common presentation of colonic polyps in children. Right-sided colonic polyps occur, and may be even larger than left-sided ones. A total colonoscopy is therefore mandatory for all cases of suspected colonic polyps. This study represents a real-life contribution and it can help improve the management strategies of this condition in childhood.

Revision paper ID EJPE-D-20-01757 entitled " **The Management of Colonic Polyps in Children: A 13-Year Retrospective Study"**

Dear Editor, we thank the Member of the Editorial Board and the Reviewers for all the important comments. We have revised the manuscript in accordance with the indications. Changes in the text are written in red.

Below there are our point-by-point answers to the Member of the Editorial Board and the Reviewers.

Member of the Editorial Board:

1. We have concluded that the paper is suitable for publication with MAJOR REVISE, provided that you revise it thoroughly taking into account the referees' comments and criticism.

Reply: We tried to address all the reviewers' comments and criticism.

2. Conflict of Interest: Authors must indicate whether or not they have a financial relationship with the organization that sponsored the research. This note should be added in a separate section before the reference list if you have not done so already.

Reply: The authors do not have any conflict of interest to declare. We added a "Conflict of Interest" statement before the reference list.

Reviewers' Comments:

Reviewer: 1

1. The main misdiagnosis of the causes of hematochezia should be noted: Constipation and fissures, hemorrhoids...

Reply: We mentioned it in the Discussion section.

2. page 3 Line 43: I would prefer the following It is important to differentiate between.....

Reply: We modified the sentence, as suggested.

3. page 4; line 74: Did the patients or the parents give consent to the study or the procedure??

Reply: We clarified the sentence.

4. page 5: line 83: pediatric gastroenterologist??

Reply: Either pediatric gastroenterologists or gastroenterologists performed endoscopy, and we modified the sentence accordingly.

5. line 104: Colo-Colonic intussusception is very rare and should be mentioned. Or was this case Ileo-colonic intussusception due to Polyp of terminal ileum (then it has to be excluded from the analysis - furthermore if it was seen by the surgeon which is not in line with the methodology in section 2.

Reply: It was a colo-colonic intussusception, and the polyp was first seen with abdominal ultrasound. We mentioned it is a very rare complication of colonic polyps.

6. line 105: What were the findings in the patient with positive family history??

Reply: We reported the characteristics of the polyp found in this patient ("In the patient with a positive family history of colonic polyps, an isolated, sessile polyp, located in the right colon, was found The histological examination was compatible with juvenile polyp").

7. Concerning the signs and symptoms I miss mentioning the protrusion of a rectal polyp via the anus (which we see quite often and get the photos from the parents). Furthermore, it would be worthwhile to mention the "triad of symptoms" of polyps mentioned in the textbooks (hematochezia, normal stool consistency, no pain on defecation). How often did the patients fulfill the criteria??

Reply: None of our patients presented with the polyp protruding from the anus. However, we mentioned this possibility in the Discussion section. We also reported that 15 patients fulfilled the classic triad of presenting symptoms.

8. In my opinion, injection of epinephrine or clipping is not necessary in the large majority of cases: I have been removing juvenile polyps for more than 30 years and never saw significant bleeding, and we do clipping only in less than 10%. There is one exception: large polyps of Peutz-Jeghers-Syndrome are more susceptible for bleeding. I recommend analyzing the literature concerning bleeding risk and prevention of bleeding.

Reply: Thank you for the comment and for sharing your experience. In our Centre we greatly rely on ESGE guidelines, that suggest (Recommendation3) "… polipectomy (with or without submucosal injection) for removal of sessile polyps 10 – 19 mm in size. In most cases deep thermal injury is a potential risk and thus submucosal injection prior to HSP should be considered. (Low quality evidence, strong recommendation.)", and recommend (Statement 4) "…to prevent bleeding in pedunculated colorectal polyps with head ≥ 20 mm or a stalk ≥ 10 mm in diameter, […] pretreatment of the stalk with injection of dilute adrenaline and/or mechanical hemostasis. (Moderate quality evidence, strong recommendation.)" (Endoscopy 2017; 49(03): 270-297). We added this reference.

9. some new Publications are missing:

Ibrahimi N, Septer SS, Lee BR, Garola R, Shah R, Attard TM. Polyp Characteristics of Nonsyndromic and Potentially Syndromic Juvenile Polyps: A Retrospective Cohort Analysis. J Pediatr Gastroenterol Nutr. 2019 Dec;69(6):668-672. doi: 10.1097/MPG.0000000000002477. PMID: 31765335; PMCID: PMC6882539.

Kay M, Eng K, Wyllie R. Colonic polyps and polyposis syndromes in pediatric patients. Curr Opin Pediatr. 2015 Oct;27(5):634-41. doi: 10.1097/MOP.0000000000000265. PMID: 26208235.

Reply: We added these references, as suggested.

Reviewer: 3

1. In the introduction, line 44 you should change "latter" for second or last one, so it could be clearer.

Reply: We modified the sentence, thank you.

2. The presenting symptom was lower gastrointestinal bleeding in 34 cases, of these 13 patients had hematochezia and 13 melena, what happened in the rest.

Reply: Twenty-one patients presented with hematochezia. We corrected this finding in the Results section.

3. One patient had multiple polyps but no more than 5. It is important to know exactly how many polyps this patient had.

Reply: The patient had 2 polyps. We added this information in the text.

4. It could be useful to include two tables, one with the demographic and clinical characteristics and another one with the polyp's characteristics.

Reply: We added 2 tables, as suggested.

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Article Title: The Management of Colonic Polyps in Children: A 13-Year Retrospective Study

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Abstract: The aim of this study was to describe the frequency, major symptoms and characteristics of colonic polyps in a cohort of children. A retrospective chart review of patients aged ≤18 years who were diagnosed with colonic polyp(s) from 2006 to 2019 in a tertiary hospital were included. Data collected included: demographics; clinical presentation; interval of time between the onset of symptoms and the endoscopic diagnosis of colonic polyps; family history; characteristics of the polyp and associated lesions. Over the study period, 35 Caucasian children were diagnosed with juvenile colonic polyps. Twenty-three patients (65.7%) were males. Lower gastrointestinal bleeding of a mean duration of 5.3 ± 4.9 months was the presenting symptom in nearly all cases (n = 34,

97%), and it was isolated in 17 patients. Clinical presentation did not significantly vary according to the age or the location or size of the polyp ($p = 0.262$, $p = 1.000$ and $p = 0.149$, respectively). The polyps were mainly located in the left colon (n = 29, 83%). Right colonic polyps were significantly larger than left colonic polyps ($p = 0.037$). *Conclusion:* Lower gastrointestinal bleeding represents the most common presentation of colonic polyps in children. Right-sided colonic polyps occur, and may be even larger than left-sided ones. A total colonoscopy is therefore mandatory for all cases of suspected colonic polyps. This study represents a real-life contribution and it can help improve the management strategies of this condition in childhood.

Keywords: colonic polyps; colonoscopy; lower gastrointestinal bleeding; children

List of Abbreviations: N/A

What is Known

- Colonic polyps are quite common in children.
- The majority of pediatric colonic polyps are solitary, benign and located in the left colon,

What is New

- Right-sided colonic polyps occur, and may be even larger than left-sided ones.
- A total colonoscopy is mandatory for all cases of suspected colonic polyps.

Author Declarations

Funding: No financial or nonfinancial benefits have been received or will be received from any party related directly or indirectly to the subject of this article.

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Ethics approval: The study was approved by the local ethical committee.

Consent to participate: N/A

Consent for publication: N/A

Availability of data and material: N/A

Code availability: N/A

Authors' contributions: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Valeria Dipasquale, Mauro Iannelli and Claudio Romano. The first draft of the manuscript was written by Valeria Dipasquale and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

The Management of Colonic Polyps in Children: A 13-Year Retrospective Study

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Abstract

The aim of this study was to describe the frequency, major symptoms and characteristics of colonic polyps in a cohort of children. A retrospective chart review of patients aged ≤18 years who were diagnosed with colonic polyp(s) from 2006 to 2019 in a tertiary hospital were included. Data collected included: demographics; clinical presentation; interval of time between the onset of symptoms and the endoscopic diagnosis of colonic polyps; family history; characteristics of the polyp and associated lesions. Over the study period, 35 Caucasian children were diagnosed with juvenile colonic polyps. Twenty-three patients (65.7%) were males. Lower gastrointestinal bleeding of a mean duration of 5.3 ± 4.9 months was the presenting symptom in nearly all cases (n = 34, 97%), and it was isolated in 17 patients. Clinical presentation did not significantly vary according to the age or the location or size of the polyp (p = 0.262, p = 1.000 and p = 0.149, respectively). The polyps were mainly located in the left colon (n = 29, 83%). Right colonic polyps were significantly larger than left colonic polyps (p = 0.037). *Conclusion:* Lower gastrointestinal bleeding represents the most common presentation of colonic polyps in children. Right-sided colonic polyps occur, and may be even larger than left-sided ones. A total colonoscopy is therefore mandatory for all cases of suspected colonic polyps. This study represents a real-life contribution and it can help improve the management strategies of this condition in childhood.

Keywords: colonic polyps; colonoscopy; lower gastrointestinal bleeding; children

1. Introduction

Colonic polyps are quite common in childhood, reported in about 6% of all pediatric colonoscopies and in 12-15% of those performed for lower gastrointestinal bleeding [1-4]. The majority of pediatric colonic polyps are solitary and located in the left colon, even if an increasing number of children are found with polyps located proximal to the splenic flexure. Colonic polyps are usually of benign nature in children and have a typical inflammatory or hamartomatous histology with a minimal risk of developing dysplasia or malignancy [5,6]. These polyps are classified as "juvenile polyps." Juvenile polyps are the most common intestinal polyps in children, accounting for 70-80% of pediatric colonic polyps removed endoscopically [7,8]. Juvenile polyps are more frequently diagnosed in non-Caucasian boys, at 2-5 years of age [7,8]. It is important to differentiate between isolated juvenile polyps and juvenile polyposis syndrome, because the second one is associated with an increased risk of development of recurrent polyps and dysplasia, in approximately 17% and 3.9% of cases, respectively [6,9]. Nonetheless, the polyposis syndromes are quite rare, ranging between 12% and 17% [8,10,11].

Data on clinical and endoscopic spectrum of colonic polyps are limited. In this study, we retrospectively reviewed the clinical presentation and macroscopic and histopathological features of colonic polyps in a cohort of children over a 13-year period, in order to determine their frequency, major symptoms and predominant characteristics.

2. Materials and methods

2.1. Study population and data collection

Medical records of children with colonic polyps were retrospectively reviewed from January 2006 to December 2019 in a tertiary care center of Messina, Italy. Patients with age of presentation less than or equal to 18 years were included in the study. Patients diagnosed with pseudopolyps caused by intestinal inflammatory disease or polyps of infectious etiology, as well as those whose medical procedures and search for data were incomplete were excluded. The following demographic, clinical, and endoscopic data were collected: gender; indication for the procedure; signs and symptoms; age at identification of the polyp; interval of time between the onset of symptoms and the endoscopic diagnosis of colonic polyps; family history; size, number, location, morphological (sessile/pedunculated) and histological types of the polyp, and associated lesions; and complications during endoscopic treatment. Polyps were anatomically categorized as left colonic (if found in the splenic flexure and distal colon), right colonic (if found proximal to the splenic flexure), and pan-colonic (if found both distal and proximal to the splenic flexure). Anemia was defined by age and sex [12]. Polyposis syndrome was diagnosed if more than 5 polyps were seen in the colon. For statistical purposes, polyps were classified according to diameter size into small (< 25 mm) and large (≥ 25 mm). This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Human Investigation Committee (IRB) of University of Messina approved this study. All patients provided written informed consent to the study.

2.2. Management protocol

All patients underwent bowel preparation with polyethylene glycol (PEG)-based solutions the day before the procedure. Colonoscopy was considered to be complete if it included an examination of the cecum or terminal ileum. Total colonoscopy with a standard pediatric endoscope was performed in the operating room under general anesthesia or with intravenous sedation with mask anesthesia. Polyps were removed with a polypectomy hot snare. Prophylactic epinephrine injection (1:10,000 final concentration) and/or hemostatic clip application were performed in order to prevent post-polypectomy bleeding [5,13]. All endoscopies were performed by either pediatric gastroenterologists or gastroenterologists. Surgical specimens were evaluated by pathologists who were aware of the clinical information.

2.3. Statistical analysis

Continuous variables were reported as means with standard deviations (SD) and categorical variables as frequencies and percentages. $\chi 2$ tests (or Fisher's exact tests, where needed) were used to assess dependence between categorical variables. All statistical analyses were performed using R version 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria) (14). Results were considered statistically significant when $p \leq 0.05$.

3. Results

3.1. Demographic and clinical characteristics

Over the study period, 35 Caucasian children were diagnosed with colonic polyps. Main demographic and clinical characteristics are summarized in Table 1. They were 7% of all pediatric patients (n = 500) submitted to colonoscopies for lower gastrointestinal bleeding. At identification of the polyp, the mean age was 5.5 ± 3.3 years (range 1 – 14.5 years). Twenty-three patients (65.7%) were males. Lower gastrointestinal bleeding of a mean duration of 5.3 ± 4.9 months (range: 1 – 24 months) was the presenting symptom in nearly all cases (n = 34, 97%), either as hematochezia (n = 21) or rectorragia (n = 13). Lower gastrointestinal bleeding was isolated in 17 patients. In the remaining cases, other signs and symptoms were observed, such as abdominal pain, diarrhea, chronic constipation, and chronic iron deficiency anemia. Fecal calprotectin was available for 4 patients only, and all of them were reported to have elevated (> 100 mg/kg) levels. In one patient the finding of the colonic polyp was incidental, first seen during abdominal ultrasound for suspected intestinal intussusception. One patient only had a positive family history of colonic polyps.

3.2. Polyps characteristics

Main characteristics of colonic polyps are summarized in Table 2. The polyps were mainly located in the left colon (Figure 1). Data about the size of the polyps were missing in 4 cases. In the remaining 31 cases mean diameter size was 21.5 mm (range 5–50 mm). Right colonic polyps were significantly larger than left colonic polyps ($p = 0.037$). Clinical presentation (hematochezia or rectorragia) did not significantly vary according to the age or the location or size of the polyp ($p = 0.262$, $p = 1.000$ and $p = 0.149$, respectively). There was no significant difference in the ages regarding the location of the polyps ($p = 1.000$). Nearly all patients (n =

34, 97%) had a single polyp. One patient only had multiple (n = 2) polyps but no more than 5. The most commonly associated lesions found during colonoscopy examination were mucosal hyperemia and/or edema, lymphoid hyperplasia and rectal nodularity. Most polyps were pedunculated. Their histopathologic subtypes consisted of juvenile polyps in all cases, and there was no adenomatous change. Neither intra-procedural nor delayed bleeding was observed.

In the patient with a positive family history of colonic polyps, an isolated, sessile polyp, located in the right colon, was found The histological examination was compatible with juvenile polyp.

4. Discussion

The present study included 35 pediatric cases of colonic polyps over a 13-year period at a single center, and showed a 7% prevalence of colonic polyps in children undergoing colonoscopy for lower gastrointestinal bleeding. The lower prevalence in comparison to other reports [1-4] might be related to the lower number of cases studied. Lower gastrointestinal bleeding was the most common presentation in our study, as in most others [1,4,15-19]. Other symptoms included abdominal pain, diarrhea, chronic constipation, and iron deficiency anemia. Overall, 15 patients fulfilled the classically recognized "triad of symptoms" of colonic polyps (hematochezia, normal stool consistency, no pain on defecation) [3]. Notably, chronic constipation, together with anal fissures and/or hemorrhoids, may easily be a misdiagnosis of the cause of hematochezia. In one patient, a large pedunculated polyp led to a colo-colonic intussusception, a very rare complication, maybe because it was pushed distally by peristalsis. In none of the patient the polyp was seen protruding from the anus during the physical examination [4,6]. No signs of protein-losing enteropathy were identified [20]. Of interest, a small proportion of patients in our cohort were found to have raised levels of fecal calprotectin. Recently, fecal calprotectin combined with ultrasound and digital rectal examination has been proposed as a non-invasive screening test for detecting colonic polyps in children with isolated and sporadic rectal bleeding [4,20]. The prospective study by Di Nardo et al [4] showed that all children with juvenile polyps had elevated fecal calprotectin levels (> 100 mg/kg), which always normalized after polypectomy. Similarly, the study from Olafsdottir et al [20] showed higher levels of fecal calprotectin in children with juvenile polyps (median 844 mg/kg) compared with those with normal colonoscopies (median 130 mg/kg, $p < 0.0001$), and after polypectomy (median 49 mg/kg, $p < 0.0001$). However, further and more specific studies are needed to address this issue. Mean age and gender distribution of our patients were similar to those reported in other studies; the majority of patients were

less than 6 years old and were male [1,4,16,21]. Although polyps were usually solitary and located in the left colon or rectum in our series, 3% our children had multiple polyps and 14% had polyps proximal to the splenic flexure, which were even bigger than left-sided ones. Similarly, Haghi Ashtiani et al [16] found 6% of patients with multiple polyps, and 18.8% of right-sided polyps. Latt et al [22] and Roth et al [23] demonstrated that up to 53–58% of polyps were multiple and 30–60% of them were located proximal to the sigmoid colon. In another retrospective study [15], polyps were found to be isolated to left colon in nearly all (97%) patients in the non-polyposis group, but none in the polyposis syndrome group (juvenile polyposis syndrome, familial adenomatous polyposis, and Peutz-Jeghers syndrome) had only left colonic polyps. This was similar to the study done by Hoffenberg et al [10]. In contrast with previous reported series [20], and similarly to others [4], all patients underwent polipectomy without complications, neither for right-sided, larger polyps in our study, maybe due to the routine use of prophylactic methods before the standard polypectomy technique.

The risk of malign transformation in a solitary juvenile polyp appears to be low. Nugent et al [24], in a review of 82 patients with solitary juvenile polyp, observed no increased risk of cancer or greater mortality related to the polyp. Fox et al [8] reported malignancy in 3.9% of their cohort. All of these cases involved patients with more than 5 polyps. In our study, there were no cases of neoplasia and no patients with more than 2 polyps. This difference may be explained by the difference in the composition of the cohorts and the absence of patients with more than 2 polyps [18]. However, the malignant potential of nonsindromic juvenile polyps, including solitary polyps [25], or the coexistence of adenomas with no characteristics of juvenile polyps, or even of adenocarcinoma associated with the presence of juvenile polyps (2%-15% of the cases of juvenile polyposis syndrome) have been reported [26,27].

Due to the possibility of multiple and/or right-sided polyps, and the occasional appearance of colonic polyps in the context of a hereditary polyposis disease characterized by significant morbidity, all children with suspected colonic polyps and/or recurrent lower gastrointestinal bleeding should undergo a total colonoscopy [4,25,27]. All polyps should be removed and submitted to histological examination for definitive diagnosis [1,4,27]. Based on clinical, endoscopic and histological information, the clinician will make more precise decisions about therapy and follow-up for the patients and their relatives.

The present study has some limitations. First, this was an observational, retrospective, single-center study, and the included cases and clinical management approaches were confounding variables. Additionally, the retrospective study design might have limited the clinical findings and management.

In conclusion, this retrospective, single-center study confirmed that colonic polyps are present in a considerable proportion of children undergoing colonoscopy for rectal bleeding. Indeed, lower gastrointestinal bleeding represent the most common presentation, alone or in combination with other signs or symptoms. Right-sided colonic polyps occur, and may be even larger than left-sided ones. A total colonoscopy is therefore mandatory for all cases of suspected colonic polyps, for a complete diagnosis and subsequent endoscopic treatment. This study represents a real-life contribution in this area and it can help improve the management strategies in childhood.

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Conflict of Interest: The Authors have no conflict of interest to declare.

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The Management of Colonic Polyps in Children: A 13-Year Retrospective Study

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Abstract

The aim of this study was to describe the frequency, major symptoms and characteristics of colonic polyps in a cohort of children. A retrospective chart review of patients aged ≤18 years who were diagnosed with colonic polyp(s) from 2006 to 2019 in a tertiary hospital were included. Data collected included: demographics; clinical presentation; interval of time between the onset of symptoms and the endoscopic diagnosis of colonic polyps; family history; characteristics of the polyp and associated lesions. Over the study period, 35 Caucasian children were diagnosed with juvenile colonic polyps. Twenty-three patients (65.7%) were males. Lower gastrointestinal bleeding of a mean duration of 5.3 ± 4.9 months was the presenting symptom in nearly all cases (n = 34, 97%), and it was isolated in 17 patients. Clinical presentation did not significantly vary according to the age or the location or size of the polyp (p = 0.262, p = 1.000 and p = 0.149, respectively). The polyps were mainly located in the left colon (n = 29, 83%). Right colonic polyps were significantly larger than left colonic polyps (p = 0.037). *Conclusion:* Lower gastrointestinal bleeding represents the most common presentation of colonic polyps in children. Right-sided colonic polyps occur, and may be even larger than left-sided ones. A total colonoscopy is therefore mandatory for all cases of suspected colonic polyps. This study represents a real-life contribution and it can help improve the management strategies of this condition in childhood.

Keywords: colonic polyps; colonoscopy; lower gastrointestinal bleeding; children

1. Introduction

Colonic polyps are quite common in childhood, reported in about 6% of all pediatric colonoscopies and in 12-15% of those performed for lower gastrointestinal bleeding [1-4]. The majority of pediatric colonic polyps are solitary and located in the left colon, even if an increasing number of children are found with polyps located proximal to the splenic flexure. Colonic polyps are usually of benign nature in children and have a typical inflammatory or hamartomatous histology with a minimal risk of developing dysplasia or malignancy [5,6]. These polyps are classified as "juvenile polyps." Juvenile polyps are the most common intestinal polyps in children, accounting for 70-80% of pediatric colonic polyps removed endoscopically [7,8]. Juvenile polyps are more frequently diagnosed in non-Caucasian boys, at 2-5 years of age [7,8]. It is important to differentiate between isolated juvenile polyps and juvenile polyposis syndrome, because the second one is associated with an increased risk of development of recurrent polyps and dysplasia, in approximately 17% and 3.9% of cases, respectively [6,9]. Nonetheless, the polyposis syndromes are quite rare, ranging between 12% and 17% [8,10,11].

Data on clinical and endoscopic spectrum of colonic polyps are limited. In this study, we retrospectively reviewed the clinical presentation and macroscopic and histopathological features of colonic polyps in a cohort of children over a 13-year period, in order to determine their frequency, major symptoms and predominant characteristics.

2. Materials and methods

2.1. Study population and data collection

Medical records of children with colonic polyps were retrospectively reviewed from January 2006 to December 2019 in a tertiary care center of Messina, Italy. Patients with age of presentation less than or equal to 18 years were included in the study. Patients diagnosed with pseudopolyps caused by intestinal inflammatory disease or polyps of infectious etiology, as well as those whose medical procedures and search for data were incomplete were excluded. The following demographic, clinical, and endoscopic data were collected: gender; indication for the procedure; signs and symptoms; age at identification of the polyp; interval of time between the onset of symptoms and the endoscopic diagnosis of colonic polyps; family history; size, number, location, morphological (sessile/pedunculated) and histological types of the polyp, and associated lesions; and complications during endoscopic treatment. Polyps were anatomically categorized as left colonic (if found in the splenic flexure and distal colon), right colonic (if found proximal to the splenic flexure), and pan-colonic (if found both distal and proximal to the splenic flexure). Anemia was defined by age and sex [12]. Polyposis syndrome was diagnosed if more than 5 polyps were seen in the colon. For statistical purposes, polyps were classified according to diameter size into small (< 25 mm) and large (≥ 25 mm). This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Human Investigation Committee (IRB) of University of Messina approved this study. All patients provided written informed consent to the study.

2.2. Management protocol

All patients underwent bowel preparation with polyethylene glycol (PEG)-based solutions the day before the procedure. Colonoscopy was considered to be complete if it included an examination of the cecum or terminal ileum. Total colonoscopy with a standard pediatric endoscope was performed in the operating room under general anesthesia or with intravenous sedation with mask anesthesia. Polyps were removed with a polypectomy hot snare. Prophylactic epinephrine injection (1:10,000 final concentration) and/or hemostatic clip application were performed in order to prevent post-polypectomy bleeding [5,13]. All endoscopies were performed by either pediatric gastroenterologists or gastroenterologists. Surgical specimens were evaluated by pathologists who were aware of the clinical information.

2.3. Statistical analysis

Continuous variables were reported as means with standard deviations (SD) and categorical variables as frequencies and percentages. $\chi 2$ tests (or Fisher's exact tests, where needed) were used to assess dependence between categorical variables. All statistical analyses were performed using R version 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria) (14). Results were considered statistically significant when $p \leq 0.05$.

3. Results

3.1. Demographic and clinical characteristics

Over the study period, 35 Caucasian children were diagnosed with colonic polyps. Main demographic and clinical characteristics are summarized in Table 1. They were 7% of all pediatric patients (n = 500) submitted to colonoscopies for lower gastrointestinal bleeding. At identification of the polyp, the mean age was 5.5 ± 3.3 years (range 1 – 14.5 years). Twenty-three patients (65.7%) were males. Lower gastrointestinal bleeding of a mean duration of 5.3 ± 4.9 months (range: 1 – 24 months) was the presenting symptom in nearly all cases (n = 34, 97%), either as hematochezia (n = 21) or rectorragia (n = 13). Lower gastrointestinal bleeding was isolated in 17 patients. In the remaining cases, other signs and symptoms were observed, such as abdominal pain, diarrhea, chronic constipation, and chronic iron deficiency anemia. Fecal calprotectin was available for 4 patients only, and all of them were reported to have elevated (> 100 mg/kg) levels. In one patient the finding of the colonic polyp was incidental, first seen during abdominal ultrasound for suspected intestinal intussusception. One patient only had a positive family history of colonic polyps.

3.2. Polyps characteristics

Main characteristics of colonic polyps are summarized in Table 2. The polyps were mainly located in the left colon (Figure 1). Data about the size of the polyps were missing in 4 cases. In the remaining 31 cases mean diameter size was 21.5 mm (range 5–50 mm). Right colonic polyps were significantly larger than left colonic polyps ($p = 0.037$). Clinical presentation (hematochezia or rectorragia) did not significantly vary according to the age or the location or size of the polyp ($p = 0.262$, $p = 1.000$ and $p = 0.149$, respectively). There was no significant difference in the ages regarding the location of the polyps ($p = 1.000$). Nearly all patients (n =

34, 97%) had a single polyp. One patient only had multiple (n = 2) polyps but no more than 5. The most commonly associated lesions found during colonoscopy examination were mucosal hyperemia and/or edema, lymphoid hyperplasia and rectal nodularity. Most polyps were pedunculated. Their histopathologic subtypes consisted of juvenile polyps in all cases, and there was no adenomatous change. Neither intra-procedural nor delayed bleeding was observed.

In the patient with a positive family history of colonic polyps, an isolated, sessile polyp, located in the right colon, was found The histological examination was compatible with juvenile polyp.

4. Discussion

The present study included 35 pediatric cases of colonic polyps over a 13-year period at a single center, and showed a 7% prevalence of colonic polyps in children undergoing colonoscopy for lower gastrointestinal bleeding. The lower prevalence in comparison to other reports [1-4] might be related to the lower number of cases studied. Lower gastrointestinal bleeding was the most common presentation in our study, as in most others [1,4,15-19]. Other symptoms included abdominal pain, diarrhea, chronic constipation, and iron deficiency anemia. Overall, 15 patients fulfilled the classically recognized "triad of symptoms" of colonic polyps (hematochezia, normal stool consistency, no pain on defecation) [3]. Notably, chronic constipation, together with anal fissures and/or hemorrhoids, may easily be a misdiagnosis of the cause of hematochezia. In one patient, a large pedunculated polyp led to a colo-colonic intussusception, a very rare complication, maybe because it was pushed distally by peristalsis. In none of the patient the polyp was seen protruding from the anus during the physical examination [4,6]. No signs of protein-losing enteropathy were identified [20]. Of interest, a small proportion of patients in our cohort were found to have raised levels of fecal calprotectin. Recently, fecal calprotectin combined with ultrasound and digital rectal examination has been proposed as a non-invasive screening test for detecting colonic polyps in children with isolated and sporadic rectal bleeding [4,20]. The prospective study by Di Nardo et al [4] showed that all children with juvenile polyps had elevated fecal calprotectin levels (> 100 mg/kg), which always normalized after polypectomy. Similarly, the study from Olafsdottir et al [20] showed higher levels of fecal calprotectin in children with juvenile polyps (median 844 mg/kg) compared with those with normal colonoscopies (median 130 mg/kg, $p < 0.0001$), and after polypectomy (median 49 mg/kg, $p < 0.0001$). However, further and more specific studies are needed to address this issue. Mean age and gender distribution of our patients were similar to those reported in other studies; the majority of patients were

less than 6 years old and were male [1,4,16,21]. Although polyps were usually solitary and located in the left colon or rectum in our series, 3% our children had multiple polyps and 14% had polyps proximal to the splenic flexure, which were even bigger than left-sided ones. Similarly, Haghi Ashtiani et al [16] found 6% of patients with multiple polyps, and 18.8% of right-sided polyps. Latt et al [22] and Roth et al [23] demonstrated that up to 53–58% of polyps were multiple and 30–60% of them were located proximal to the sigmoid colon. In another retrospective study [15], polyps were found to be isolated to left colon in nearly all (97%) patients in the non-polyposis group, but none in the polyposis syndrome group (juvenile polyposis syndrome, familial adenomatous polyposis, and Peutz-Jeghers syndrome) had only left colonic polyps. This was similar to the study done by Hoffenberg et al [10]. In contrast with previous reported series [20], and similarly to others [4], all patients underwent polipectomy without complications, neither for right-sided, larger polyps in our study, maybe due to the routine use of prophylactic methods before the standard polypectomy technique.

The risk of malign transformation in a solitary juvenile polyp appears to be low. Nugent et al [24], in a review of 82 patients with solitary juvenile polyp, observed no increased risk of cancer or greater mortality related to the polyp. Fox et al [8] reported malignancy in 3.9% of their cohort. All of these cases involved patients with more than 5 polyps. In our study, there were no cases of neoplasia and no patients with more than 2 polyps. This difference may be explained by the difference in the composition of the cohorts and the absence of patients with more than 2 polyps [18]. However, the malignant potential of nonsindromic juvenile polyps, including solitary polyps [25], or the coexistence of adenomas with no characteristics of juvenile polyps, or even of adenocarcinoma associated with the presence of juvenile polyps (2%-15% of the cases of juvenile polyposis syndrome) have been reported [26,27].

Due to the possibility of multiple and/or right-sided polyps, and the occasional appearance of colonic polyps in the context of a hereditary polyposis disease characterized by significant morbidity, all children with suspected colonic polyps and/or recurrent lower gastrointestinal bleeding should undergo a total colonoscopy [4,25,27]. All polyps should be removed and submitted to histological examination for definitive diagnosis [1,4,27]. Based on clinical, endoscopic and histological information, the clinician will make more precise decisions about therapy and follow-up for the patients and their relatives.

The present study has some limitations. First, this was an observational, retrospective, single-center study, and the included cases and clinical management approaches were confounding variables. Additionally, the retrospective study design might have limited the clinical findings and management.

In conclusion, this retrospective, single-center study confirmed that colonic polyps are present in a considerable proportion of children undergoing colonoscopy for rectal bleeding. Indeed, lower gastrointestinal bleeding represent the most common presentation, alone or in combination with other signs or symptoms. Right-sided colonic polyps occur, and may be even larger than left-sided ones. A total colonoscopy is therefore mandatory for all cases of suspected colonic polyps, for a complete diagnosis and subsequent endoscopic treatment. This study represents a real-life contribution in this area and it can help improve the management strategies in childhood.

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Conflict of Interest: The Authors have no conflict of interest to declare.

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272 reference centers. Arq Gastroenterol. 2015;52:303-10.

Figure 1. Distribution of juvenile polyps in the colon

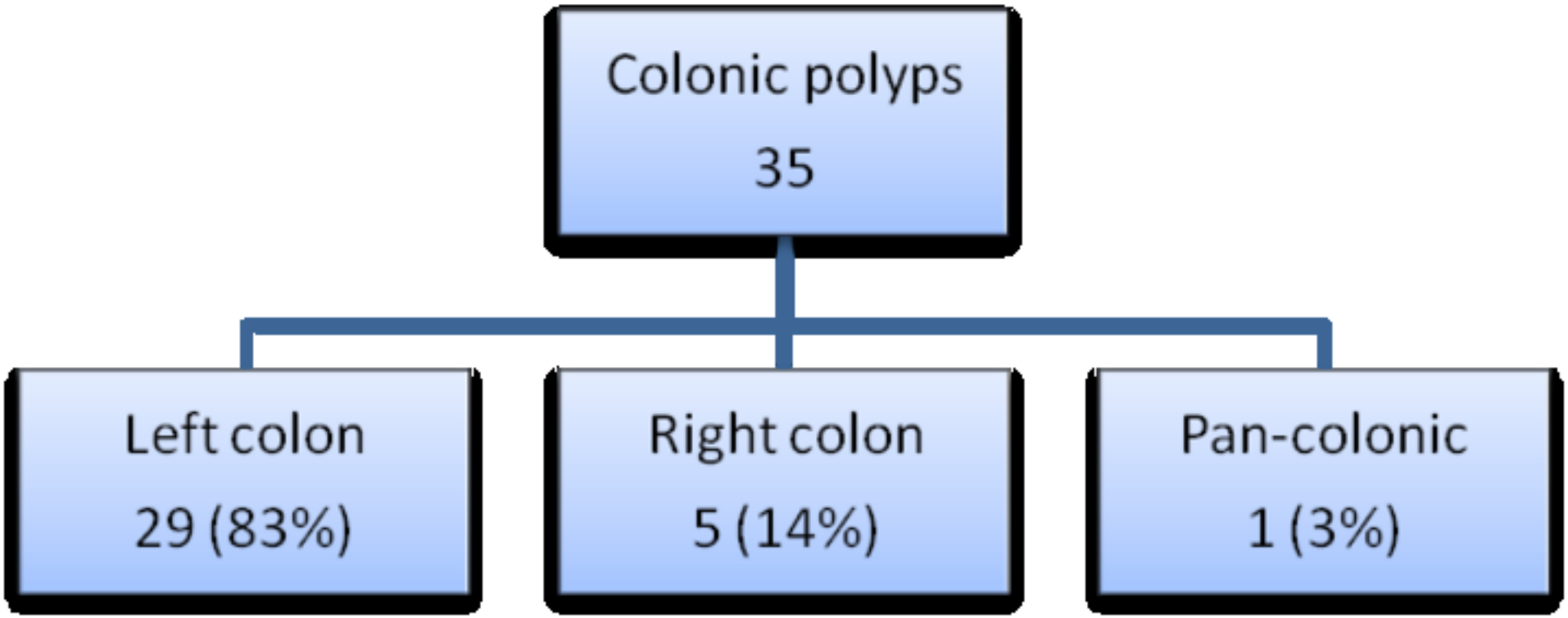

Table 1. Demographic and clinical characteristics of the patients

Variable	Number (%)
Sex	
Male	23 (66)
Female	12 (34)
Age, mean (years)	5.5 ± 3.3
Clinical presentation	
Lower gastrointestinal bleeding	34 (97)
Abdominal pain	8 (23)
Diarrhea	7 (20)
Chronic constipation	5 (14)
Chronic iron deficiency anemia	3 (8)
Positive family history	
No	34 (97)
Yes	1 (3)

Table 2. Main characteristics of colonic polyps at endoscopy

Variable	Number (%)
Number	
Single	34 (97)
Multiple	1 (3)
Size, mean (mm)*	21.5
Type	
Pedunculated	29 (83)
Sessile	5 (17)
Associated mucosal lesions**	
No	27 (77)
Yes	8 (23)
Hyperemia and/or edema	6
Lymphoid hyperplasia	5
Nodularity	1

*missing data