Pediatr Gastroenterol Hepatol Nutr. 2022 Jan;25(1):52-60
https://doi.org/10.5223/pghn.2022.25.1.52
pISSN 2234-8646·eISSN 2234-8840

Pediatric Gastroenterology, Hepatology & Nutrition
pghn

Original Article

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Juvenile Polyps in Bangladeshi Children and Their Association with Fecal Calprotectin as a Biomarker

Subarna Rani Das, A S M Bazlul Karim, Md RukonUzzaman, Md Wahiduzzaman Mazumder, Rubaiyat Alam, Md Benzamin, Parisa Marjan, Mst. Naznin Sarker, Hazera Akther, and Mohuya Mondal

Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh

OPEN ACCESS

Received: Jun 8, 2021
Revised: Sep 15, 2021
Accepted: Oct 3, 2021
Published online: Jan 7, 2022

Correspondence to
Subarna Rani Das
Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka 1000, Bangladesh.
Email: dr.subarna13@gmail.com

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ORCID iDs
Subarna Rani Das
https://orcid.org/0000-0002-5690-8080
A S M Bazlul Karim
https://orcid.org/0000-0002-8899-9052
Md RukonUzzaman
https://orcid.org/0000-0003-0330-5080
Md Wahiduzzaman Mazumder
https://orcid.org/0000-0001-6947-9572
Rubaiyat Alam
https://orcid.org/0000-0002-6140-7571
Md Benzamin
https://orcid.org/0000-0002-8239-6541
Parisa Marjan
https://orcid.org/0000-0003-4795-1914
Mst. Naznin Sarker
https://orcid.org/0000-0003-1338-8991

ABSTRACT

Purpose: Colonoscopy is considered the most reliable method for the diagnosis of juvenile polyps. However, colonoscopic screening is an invasive and expensive procedure. Fecal calprotectin (FCP), a marker of intestinal inflammation, has been shown to be elevated in patients with polyps. Therefore, this study aimed to evaluate FCP as a screening biomarker for the diagnosis of juvenile polyps.
Methods: This cross-sectional, observational study was conducted at the Pediatric Gastroenterology and Nutrition Department, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. For children with polyps, colonoscopic polypectomy and histopathology were performed. FCP levels were analyzed before and 4 weeks after polypectomy in all patients. Information was recorded in a datasheet and analyzed using the computer-based program SPSS.
Results: The age of the children was between 2.5 and 12 years. Approximately 93% of the polyps were found in the rectosigmoid region. Children with juvenile polyps had elevated levels of FCP before polypectomy that subsequently normalized after polypectomy. The mean FCP levels before and after polypectomy were 277±247 μg/g (range, 80–1,000 μg/g) and 48.57±38.23 μg/g (range, 29–140 μg/g) (p<0.001), respectively. The FCP levels were significantly higher in patients with multiple polyps than in those with single polyps. Moreover, mean FCP levels in patients with single and multiple polyps were 207.6±172.4 μg/ g and 515.4±320.5 μg/g (p<0.001), respectively.
Conclusion: Colonic juvenile polyps were found to be associated with elevated levels of FCP that normalized after polypectomy. Therefore, FCP may be recommended as a noninvasive screening biomarker for diagnosis of colonic juvenile polyps.

Keywords: Juvenile polyp; Per rectal bleeding; Child

INTRODUCTION

In day-to-day medical practice, rectal bleeding is a common problem in children. Chronic cases of minor lower gastrointestinal (GI) tract bleeding may produce significant anemia; thus, localization of the source of bleeding is important in the management of such children. In addition to a careful history, inspection of the perianal area, digital rectal examination,

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Hazera Akther
https://orcid.org/0000-0003-0059-3048
Mohuya Mondal
https://orcid.org/0000-0001-5328-2599

Conflict of Interest
The authors have no financial conflicts of interest.

and a stool test, several other techniques, such as endoscopy, radiology, ultrasonography, technetium-labeled red blood cell scans, and angiography are available for diagnosis [1].

Colorectal polyps are common during childhood and affect 1.1% of preschool and school-aged children [2]. The reported prevalence ranges between 0.08% and 3.7% in children, and it is most frequently diagnosed in children, especially boys, aged 3–10 years [3].

In children, juvenile polyps usually present with painless, intermittent, and fresh rectal bleeding with or without associated symptoms, including recurrent abdominal pain, prolapse through the anus, diarrhea, anemia (haemoglobin [Hb] <10 gm/dL), and anal mass [4]. When left untreated for a long time, they cause significant anemia due to occult blood loss and apparent bleeding from the rectum [5].

Juvenile polyps are the most common type of colorectal polyps in children and are generally considered benign [6]. However, recent studies have reported cases of adenomatous changes in juvenile polyps, indicating their neoplastic potential [7,8]. Additionally, cases of colorectal adenocarcinoma arising from juvenile polyps have been found in children [9,10]. Thus, early detection of polyps may significantly improve patient's quality of life and overall health.

Calprotectin is a 36-kDa calcium- and zinc-binding protein found in human neutrophils, monocytes, and macrophages [11,12]. It has well-known antimicrobial activity as it competes for zinc and inhibits zinc-dependent enzymes [13,14]. Calprotectin, with its iron-binding capacity, functions as a component of the innate immune response and inhibits bacterial proliferation [15]. Elevated concentrations of calprotectin in the plasma, synovial fluid, urine, saliva, and feces indicate recruitment of neutrophils and inflammatory response [16,17]. In the presence of active intestinal inflammation, polymorphonuclear neutrophils migrate from the circulation to the intestinal mucosa. Any disturbance to the mucosal architecture due to inflammatory process leads to leakage of neutrophils, and thus, calprotectin is secreted into the lumen and is subsequently excreted in feces [18]. Therefore, fecal calprotectin (FCP) is used as a noninvasive biomarker for intestinal inflammation, especially active inflammatory bowel disease (IBD) [19].

Juvenile polyps are composed of inflammatory cells, including many neutrophils, and the mucosal surface is often friable. Exfoliation of these cells into the stool may lead to increased levels of fecal inflammatory markers [20].

Until now, only a few conditions other than IBD have been reported with elevated FCP. No diagnostic noninvasive markers have been evaluated for screening individuals with juvenile polyps, and only sporadic case studies and a recent study have been published on children with solitary juvenile polyps and elevated levels of FCP [21].

Colonoscopic evaluation is often uncomfortable and expensive. It is still not easily available even at tertiary healthcare facilities in Bangladesh. Moreover, colonoscopic screening requires highly skilled expertise, and colonoscopies are difficult to perform in children.

Therefore, as other invasive procedures, such as colonoscopy, are unavailable at most clinics, FCP, a noninvasive screening biomarker, would be a valuable tool in clinical practice for detecting juvenile polyps.

MATERIALS AND METHODS

This prospective, cross-sectional, observational study was conducted between January 2018 and July 2019. Forty children aged 1–18 years with juvenile polyps (detected with colonoscopy), who attended the Pediatric Gastroenterology and Nutrition Department at the Bangabandhu Sheikh Mujib Medical University, Dhaka, were selected consecutively. Informed written consent was obtained from their guardians, and ethical clearance was obtained from the Institutional Review Board of the University (IRB number: BSMMU/2017/12017). Forty-two patients with rectal bleeding were initially enrolled in the study. However, two patients failed to qualify the inclusion criteria of the study (other than the juvenile polyp). Thus, 40 cases with juvenile polyps were finally included in the study. The study objectives were explained to the parents. Patient history, physical examination findings, and initial investigation reports were recorded in a standard datasheet. Colonoscopy was performed using Pantex video scopes instruments (A Division of PENTAX of America, Inc., Montvale, NJ, USA) in the Pediatric Gastroenterology and Nutrition Department, Bangabandhu Sheikh Mujib Medical University, under sedation after ensuring normal coagulation profiles and platelet counts, and after ensuring bowel preparation as per the protocol. After diagnosis, polyps were removed by colonoscopic polypectomy and immediately placed in formalin for transportation to the Pathology Laboratory for histopathology. Estimation of FCP levels was performed before and 4 weeks after polypectomy.

For estimation of FCP, <1 g of native stool was collected in plain tubes. The sample was stored in a refrigerator at 2–8°C. for at least 6 days. The extracts remained stable for at least 7 days at 2–8°C. and for at least 24 months at ≤20°C. The samples were collected without any chemical or biological additives in the collection container. FCP levels were measured using the Buhlmann Quantum Blue kit (BUHLMANN Diagnostics Corp., Amherst, NH, USA). Briefly, fecal samples were placed in an extraction tube and diluted 1:16 using extraction buffer to provide quantitative results from 30 to 1,000 μg/g. The mixture was vortexed for 1 minutes and centrifuged for 5 minutes. Following a predetermined dilution, large particles were allowed to settle, and the supernatant was assayed for 12 minutes. The high FCP concentration was assayed for 15 minutes using a calibrated Buhlmann Quantum Blue Reader. The color intensity was directly proportional to FCP concentration in the test samples. A cutoff FCP level >50 μg/g was considered positive as per the manufacturer's instructions. No separate cutoff levels were provided for children. This test was performed at the Department of Microbiology.

Data processing and analysis

After collection, data was checked manually and analyzed using a computer-based SPSS software (ver. 22.0; IBM Co., Armonk, NY, USA). Paired *t*-test was used to compare means of two dependent sample groups, and unpaired *t*-test was used to compare means of two independent sample groups. Results are expressed as mean±standard deviation, number, or percentage. The results of the statistical analysis are presented in the tables and charts.

A paired *t*-test was performed to compare the levels of FCP before and after polypectomy, and the relationship between FCP levels and the number of polyps was determined using unpaired *t*-test. For all statistical tests, $p<0.05$ was considered to be statistically significant.

https://doi.org/10.5223/pghn.2022.25.1.52

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RESULTS

Table 1 showing age wise distributions of study populations. The ages of the 40 children ranged from 2.5 to 12 years. The male-to-female ratio was 1.5:1. The duration of symptoms varied from 1 to 36 months. The mean symptom duration was 8.2±7.6 months (range, 1–36 months). All patients had hematochezia, and all patients had painless defecation. One patient (2.5%) experienced abdominal pain. Two patients (5.0%) had history of (H/O) constipation. There were no recent H/O drug use in the participants. In the physical findings, pallor was absent in all patients, the digital rectal examination polyp was palpated in 10 (25%) patients, and anal fissure and skin tag were absent. Laboratory investigations indicated mean Hb of 11.26±0.99 g/dL, ranging 9.2 to 13.4 g/dL. The mean erythrocyte sedimentation rate was 18.89±14.5 mm in the 1st hour, ranging 5 to 65 mm. The mean C-reactive protein was 2.27±1.4 mg/L, ranging 0.14 to 6.7 mg/L. Three (7.5%) patients had red blood cells and one (2.5%) patient had white blood cells in the stool on routine microscopic examination. No microscopic growth was observed in any (100%) patient stool culture. **Table 2** showing distribution of the patients by polyps. Further, it was observed that 31 (77.5%) patients had a single polyp. Of these, 22 (55%) polyps were located in the rectum. Additionally, 32 (80.0%) were pedunculated polyps. Histologically, all patients (100.0%) had juvenile polyps. In all the patients, 55% and 37.5% of juvenile polyps were found in the rectum and sigmoid colon, respectively. **Table 3**, **Table 4**, and **Fig. 1** showing change of FCP before and after polypectomy. The children with juvenile polyps had strongly elevated levels of FCP before polypectomy that subsequently normalized or significantly decreased to levels close to normal after polypectomy. The mean FCP levels before and after polypectomy were 277±247 μg/g (range, 80–1,000 μg/g) and 48.57±38.23 μg/g (range, 30–140 μg/g), respectively (p<0.001). **Table 5** showing relation of FCP level with number of polyps (n=40). The FCP levels were significantly higher in patients with multiple polyps than in those with single polyps. FCP levels in single polyps were 207.6±172.4 μg/g and in multiple polyps were 515.4±320.5 μg/g (p<0.001).

Table 1. Characteristics of the patients (n=40)

Age (y)	Value
≤5	25 (62.5)
6–10	14 (35.0)
>10	1 (2.5)
Mean±standard deviation	5.28±2.4
Range (min–max)	2.5–12

Values are presented as number (%).

Table 2. Distribution of the patients by polyps (n=40)

Polyp	Value
No. of polyps	
Single	31 (77.5)
Multiple	9 (22.5)
Location of polyp	
Rectum	22 (55.0)
Sigmoid colon	15 (37.5)
Rectum+sigmoid colon	2 (5.0)
Cecum	1 (2.5)
Type of polyp	
Pedunculated polyp	32 (80.0)
Sessile polyp	1 (2.5)
Both pedunculated and sessile polyp	7 (17.5)
Histopathological types	
Juvenile polyp	40 (100)
Others	0

Values are presented as number (%).

https://doi.org/10.5223/pghn.2022.25.1.52

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Table 3. Distribution of the patients by FCP before and after polypectomy (n=40)

FCP level (μg/g)	Before polypectomy (n=40)	After polypectomy (n=40)	*p*-value
≤50	0	32 (80.0)	
>50	40 (100)	8 (20.0)	
Mean±standard deviation	277±247	48.57±38.23	0.001*
Range (min–max)	80–1,000	29–140	

Values are presented as number (%).
p-value reached using paired *t*-test.
FCP: fecal calprotectin.
*Significant.

Table 4. FCP levels in individuals with multiple polyps before and after polypectomy

Serial No.	No. of polyps	FCP (μg/g) before polypectomy	FCP (μg/g) after polypectomy
1	2	966	87
2	4	560	130
3	2	310	<30
4	3	519	130
5	2	115	<30
6	4	1,000	132
7	4	510	85
8	2	569	<30
9	2	95	<30

FCP: fecal calprotectin.

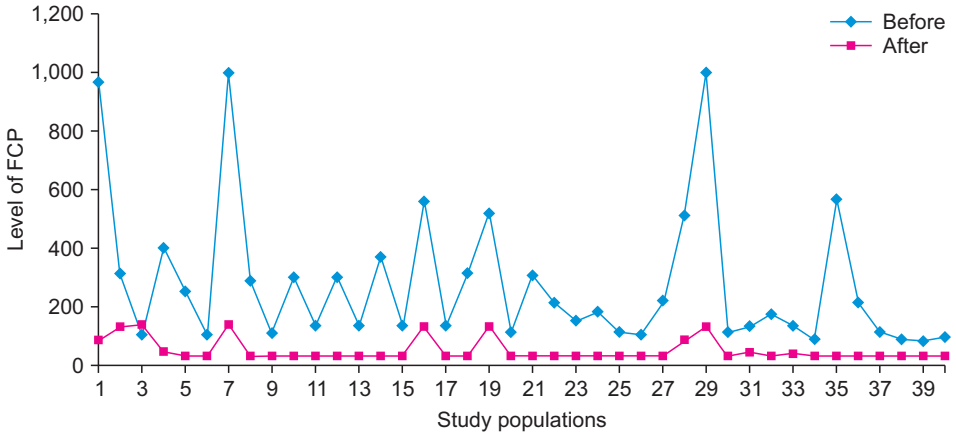

Fig. 1. Line chart of fecal calprotectin (FCP) levels before and after polypectomy. Patient number 3 had higher FCP levels after polypectomy. It may be due to regrowth of polyp after polypectomy. In this particular case we missed follow up.

Table 5. Relation of FCP level with number of polyps (n=40)

FCP levels in polyps	Single polyp (n=31)	Multiple polyps (n=9)	*p*-value
Mean±standard deviation	207.6±172.4	515.4±320.5	0.001*
Range (min–max)	80–1,000	95–1,000	

p-value reached using unpaired *t*-test.
FCP: fecal calprotectin.
*Significant.

DISCUSSION

Calprotectin is an antimicrobial protein in the cytoplasm of granulocytes, monocytes, and macrophages in the stool and plasma [22]. This protein is released due to cell disruption and death [23]. FCP is strongly associated with active IBD and is moderately elevated in GI bleeding, gastroenteritis, celiac disease, microscopic colitis, nonsteroidal antiinflammatory drug enteropathy, and in diverticular diseases and colonic polyps in adults [15,24]. However,

https://doi.org/10.5223/pghn.2022.25.1.52

there are very few published studies (mainly in the form of case reports/case series) that describe the association between FCP and juvenile polyps in children.

The mean age of the patients was 5.28±2.4 years. Similar results were also observed in studies conducted by Mandhan et al. [25] in Pakistan and Ko et al. [26] in Taiwan. A majority of the children were boys and aged between 2.5 and 12 years. A similar preponderance of boys was observed by Mandhan et al. [25], Ko et al. [26], Poddar et al. [7], and Thakkar et al. [27]. This is probably because parents are more concerned about boy child.

In the present study, 55% and 37% of the juvenile polyps were found in the rectum and sigmoid colon, respectively. These findings are similar to those of studies conducted by Latt et al. [28], Olafsdottir et al. [3], Pillai and Tolia [29], Poddar et al. [7], and Wei et al. [30]. This typical localization explains why a majority of the children clinically presented with hematochezia. Therefore, while a majority of the children had solitary polyps in the rectosigmoid area, a significant number had multiple and proximally located polyps; this result emphasizes the need for total colonoscopy in all children with rectal bleeding [7].

In the present study, 80.0% of the patients had pedunculated polyps. Similar data were found in other studies conducted by Mandhan [25] and Rathi et al. [31]. The percentages of pedunculated polyps in their studies were 70% and 88%, respectively. In the present study, 22.5% of the patients had multiple polyps, and the number of polyps ranged from 2 to 4, consistent with findings of another study conducted by Poddar et al. [7] in India.

In the present study, we found that children with juvenile polyps had strongly elevated levels of FCP before polypectomy that subsequently normalized after polypectomy. These findings are similar to those of another study conducted by Olafsdottir et al. [3], and of another study conducted by Pezzilli et al. [15], in which the average patient age was 60 years.

The associations between FCP and juvenile polyps have also been described in children with juvenile polyps in a few case studies; these also reported that elevated levels of FCP were subsequently normalized or significantly decreased to levels close to normal after polypectomy [25,32-34].

The histology was consistent with juvenile polyps in 100% of the cases in the present study. The histological features of a solitary juvenile polyp showed typical non-adenomatous structures containing dilated cystic spaces, exuberant lamina propria with marked vascularity, areas of ulcerations, and increased numbers of inflammatory cells, including neutrophilic granulocytes [15,24]. Considering inflammatory characteristics of the histological features of juvenile polyps that typically show crypt-filled mucus rich in neutrophils and eosinophils and a surface layer that is covered with intraepithelial neutrophils, it is not surprising why patients with solitary juvenile polyps also show high concentrations of FCP [3]. Therefore, the levels of FCP generally decrease to normal post excision of all polyps.

In the present study, the detection limit for FCP was 30–1,000 μg/g, and the cutoff for a positive value was set to >50 μg/g. Follow-up FCP assessment after polypectomy was performed after 4 weeks; the analyses showed that the FCP levels decreased in all patients except one, and 20% of patients had FCP levels >50 μg/g after polypectomy. The decrease in calprotectin in the patients in the present study after polypectomy is consistent with polyp

https://doi.org/10.5223/pghn.2022.25.1.52

removal. However, non-normalization may represent residual polyps that are not visible at colonoscopy, regrowth of polyps after polypectomy, incomplete healing of the polypectomy site with associated mucosal inflammation, or a generalized mucosal inflammatory state present in the children, who had numerous polyps, or it may be due to the very small duration of follow-up [34]. Follow up of FCP was performed at the 8th week, 12th week, and 24th week after polypectomy in other studies conducted by Olafsdottir et al. [3] and Khan et al. [33], respectively.

The relationship between FCP levels and the number of polyps was also evaluated in the present study; the analyses suggested that FCP levels were significantly increased in patients with multiple polyps than in those with single polyps. This suggests that inflammatory response is related to the number of polyps. However, these findings differed from those of another study conducted by Pezzilli et al. [15].

The study duration and resources were limited, the sample size was small, and the study was conducted at a specialized tertiary care hospital that may not be a true representation of all Bangladeshi children with juvenile polyps.

Colonic juvenile polyps are frequently found in pediatric patients who undergo colonoscopy for rectal bleeding. Colonic juvenile polyps are associated with increased levels of FCP that are normalized after polypectomy. Therefore, FCP may be used to assess the presence of polyps, assess the complete removal of all polyps, and also help detect polyp recurrence. Therefore, FCP may be recommended as a noninvasive screening biomarker for colonic juvenile polyps. This laboratory marker may also serve as a noninvasive measure instead of frequent colonoscopic procedures for detecting polyps.

REFERENCES

1. Yachha SK, Khanduri A, Sharma BC, Kumar M. Gastrointestinal bleeding in children. J Gastroenterol Hepatol 1996;11:903-7.
PUBMED | CROSSREF
2. Gelb AM, Minkowitz S, Tresser M. Rectal and colonic polyps occurring in young people. N Y State J Med 1962;62:513-8.
PUBMED
3. Olafsdottir I, Nemeth A, Lörinc E, Toth E, Agardh D. Value of fecal calprotectin as a biomarker for juvenile polyps in children investigated with colonoscopy. J Pediatr Gastroenterol Nutr 2016;62:43-6.
PUBMED | CROSSREF
4. Holgersen LO, Mossberg SM, Miller RE. Colonoscopy for rectal bleeding in childhood. J Pediatr Surg 1978;13:83-5.
PUBMED | CROSSREF
5. Cynamon HA, Milov DE, Andres JM. Diagnosis and management of colonic polyps in children. J Pediatr 1989;114:593-6.
PUBMED | CROSSREF
6. Park JH. Role of colonoscopy in the diagnosis and treatment of pediatric lower gastrointestinal disorders. Korean J Pediatr 2010;53:824-9.
PUBMED | CROSSREF
7. Poddar U, Thapa BR, Vaiphei K, Singh K. Colonic polyps: experience of 236 Indian children. Am J Gastroenterol 1998;93:619-22.
PUBMED | CROSSREF
8. Fox VL, Perros S, Jiang H, Goldsmith JD. Juvenile polyps: recurrence in patients with multiple and solitary polyps. Clin Gastroenterol Hepatol 2010;8:795-9.
PUBMED | CROSSREF

9. Giardiello FM, Hamilton SR, Kern SE, Offerhaus GJ, Green PA, Celano P, et al. Colorectal neoplasia in juvenile polyposis or juvenile polyps. Arch Dis Child 1991;66:971-5.
PUBMED | CROSSREF
10. Mestre JR. The changing pattern of juvenile polyps. Am J Gastroenterol 1986;81:312-4.
PUBMED
11. Poullis A, Foster R, Mendall MA, Fagerhol MK. Emerging role of calprotectin in gastroenterology. J Gastroenterol Hepatol 2003;18:756-62.
PUBMED | CROSSREF
12. Fagerhol MK, Dale I, Andersson T. A radioimmunoassay for a granulocyte protein as a marker in studies on the turnover of such cells. Bull Eur Physiopathol Respir 1980;16 Suppl:273-82.
PUBMED | CROSSREF
13. Steinbakk M, Naess-Andresen CF, Lingaas E, Dale I, Brandtzaeg P, Fagerhol MK. Antimicrobial actions of calcium binding leucocyte L1 protein, calprotectin. Lancet 1990;336:763-5.
PUBMED | CROSSREF
14. Costa F, Mumolo MG, Bellini M, Romano MR, Ceccarelli L, Arpe P, et al. Role of faecal calprotectin as non-invasive marker of intestinal inflammation. Dig Liver Dis 2003;35:642-7.
PUBMED | CROSSREF
15. Pezzilli R, Barassi A, Morselli Labate AM, Finazzi S, Fantini L, Gizzi G, et al. Fecal calprotectin levels in patients with colonic polyposis. Dig Dis Sci 2008;53:47-51.
PUBMED | CROSSREF
16. Johne B, Fagerhol MK, Lyberg T, Prydz H, Brandtzaeg P, Naess-Andresen CF, et al. Functional and clinical aspects of the myelomonocyte protein calprotectin. Mol Pathol 1997;50:113-23.
PUBMED | CROSSREF
17. Bjerke K, Halstensen TS, Jahnsen F, Pulford K, Brandtzaeg P. Distribution of macrophages and granulocytes expressing L1 protein (calprotectin) in human Peyer's patches compared with normal ileal lamina propria and mesenteric lymph nodes. Gut 1993;34:1357-63.
PUBMED | CROSSREF
18. Røseth AG, Fagerhol MK, Aadland E, Schjønsby H. Assessment of the neutrophil dominating protein calprotectin in feces. A methodologic study. Scand J Gastroenterol 1992;27:793-8.
PUBMED | CROSSREF
19. Vrabie R, Kane S. Noninvasive markers of disease activity in inflammatory bowel disease. Gastroenterol Hepatol (N Y) 2014;10:576-84.
PUBMED
20. McMahon CW, Chhabra R. The role of fecal calprotectin in investigating digestive disorders. J Lab Precis Med 2018;3:19.
CROSSREF
21. Di Nardo G, Esposito F, Ziparo C, Strisciuglio C, Vassallo F, Di Serafino M, et al. Faecal calprotectin and ultrasonography as non-invasive screening tools for detecting colorectal polyps in children with sporadic rectal bleeding: a prospective study. Ital J Pediatr 2020;46:66.
PUBMED | CROSSREF
22. Vaos G, Kostakis ID, Zavras N, Chatzemichael A. The role of calprotectin in pediatric disease. BioMed Res Int 2013;2013:542363.
PUBMED | CROSSREF
23. Voganatsi A, Panyutich A, Miyasaki KT, Murthy RK. Mechanism of extracellular release of human neutrophil calprotectin complex. J Leukoc Biol 2001;70:130-4.
PUBMED | CROSSREF
24. Montalto M, Gallo A, Santoro L, D'Onofrio F, Landolfi R, Gasbarrini A. Role of fecal calprotectin in gastrointestinal disorders. Eur Rev Med Pharmacol Sci 2013;17:1569-82.
PUBMED
25. Mandhan P. Juvenile colorectal polyps in children: experience in Pakistan. Pediatr Surg Int 2004;20:339-42.
PUBMED | CROSSREF
26. Ko FY, Wu TC, Hwang B. Intestinal polyps in children and adolescents--a review of 103 cases. Zhonghua Min Guo Xiao Er Ke Yi Xue Hui Za Zhi 1995;36:197-202.
PUBMED | CROSSREF
27. Thakkar KH, Alsarraj A, Fong E, Gilger M, El-Serag H. M1575: the frequency and determinants of polyps in children: results from a national endoscopic database. Gastrointest Endosc 2010;71:AB258.
CROSSREF
28. Latt TT, Nicholl R, Domizio P, Walker-Smith JA, Williams CB. Rectal bleeding and polyps. Arch Dis Child 1993;69:144-7.
PUBMED | CROSSREF

29. Pillai RB, Tolia V. Colonic polyps in children: frequently multiple and recurrent. Clin Pediatr (Phila) 1998;37:253-7.
PUBMED | CROSSREF

30. Wei C, Dayong W, Liqun J, Xiaoman W, Yu W, Xiaohong Q. Colorectal polyps in children: a retrospective study of clinical features and the value of ultrasonography in their diagnosis. J Pediatr Surg 2012;47:1853-8.
PUBMED | CROSSREF

31. Rathi C, Ingle M, Pandav N, Pipaliya N, Choksi D, Sawant P. Clinical, endoscopic, and pathologic characteristics of colorectal polyps in Indian children and adolescents. Indian J Gastroenterol 2015;34:453-7.
PUBMED | CROSSREF

32. Pauley-Hunter RJ, Kunnath S, Wolff K, Vanderhoof JA. Fecal calprotectin and pediatric juvenile polyps. J Pediatr Gastroenterol Nutr 2015;60:e30-1.
PUBMED | CROSSREF

33. Khan F, Mani H, Chao C, Hourigan S. Fecal calprotectin as a future screening tool for large juvenile polyps. Glob Pediatr Health 2015;2:2333794X15623716.
PUBMED | CROSSREF

34. Teitelbaum JE, Adu-Darko MA. Fecal calprotectin in juvenile polyposis coli. J Clin Gastroenterol 2010;44:593.
PUBMED | CROSSREF