

Original Article
Pediatrics



Potential Utility of Fecal Calprotectin in Discriminating Colorectal Polyps From Other Major Etiologies in Children Presenting With Isolated Hematochezia

Yu Bin Kim ^{1*}, Ju Young Kim ^{2*}, Sujin Choi ³, Hyun Jin Kim ⁴, Yoo Min Lee ⁵, Yoon Lee ⁶, Hyo-Jeong Jang ⁷, Eun Hye Lee ⁸, Kyung Jae Lee ⁹, Soon Chul Kim ¹⁰, So Yoon Choi ¹¹, Yunkoo Kang ¹², Dae Yong Yi ¹³, You Jin Choi ¹⁴, Byung-Ho Choe ³ and Ben Kang ³

OPEN ACCESS

Received: Nov 17, 2021

Accepted: Jan 26, 2022

Published online: Feb 28, 2022

Address for Correspondence:

Ben Kang, MD

Department of Pediatrics, School of Medicine, Kyungpook National University, 680 Gukchaebosang-ro, Jung-gu, Daegu 41944, Republic of Korea.
Email: benkang@knu.ac.kr

*Yu Bin Kim and Ju Young Kim contributed equally to this work.

© 2022 The Korean Academy of Medical Sciences.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

Yu Bin Kim
<https://orcid.org/0000-0001-6325-6191>
Ju Young Kim
<https://orcid.org/0000-0002-4406-2428>
Sujin Choi
<https://orcid.org/0000-0001-8894-8127>
Hyun Jin Kim
<https://orcid.org/0000-0003-0279-7925>
Yoo Min Lee
<https://orcid.org/0000-0003-3554-6559>
Yoon Lee
<https://orcid.org/0000-0001-9521-3575>
Hyo-Jeong Jang
<https://orcid.org/0000-0003-1496-5754>

¹Department of Pediatrics, Ajou University Medical Center, Suwon, Korea

²Department of Pediatrics, Eulji University Hospital, Daejeon, Korea

³Department of Pediatrics, School of Medicine, Kyungpook National University, Daegu, Korea

⁴Department of Pediatrics, Chungnam National University Hospital, Daejeon, Korea

⁵Department of Pediatrics, Soonchunhyang University Bucheon Hospital, Soonchunhyang University College of Medicine, Bucheon, Korea

⁶Department of Pediatrics, Korea University Anam Hospital, Seoul, Korea

⁷Department of Pediatrics, Dongsan Medical Center, Keimyung University School of Medicine, Daegu, Korea

⁸Department of Pediatrics, Nowon Eulji Medical Center, Eulji University School of Medicine, Seoul, Korea

⁹Department of Pediatrics, Hallym University College of Medicine, Chuncheon, Korea

¹⁰Department of Pediatrics, Jeonbuk National University Medical School and Hospital, Jeonju, Korea

¹¹Department of Pediatrics, Kosin University Gospel Hospital, Kosin University College of Medicine, Busan, Korea

¹²Department of Pediatrics, Yonsei University Wonju College of Medicine, Wonju, Korea

¹³Department of Pediatrics, Chung-Ang University Hospital, College of Medicine, Chung-Ang University, Seoul, Korea





¹⁴Department of Pediatrics, Inje University Ilsan Paik Hospital, Goyang, Korea

ABSTRACT

Background: Colorectal polyps are the most common cause of isolated hematochezia in children, which requires a colonoscopy for diagnosis. We aimed to investigate the potential utility of fecal calprotectin (FC) in assessing colorectal polyps detected by colonoscopy among children presenting with isolated hematochezia.

Methods: Pediatric patients of the age of < 18 years who had undergone both colonoscopy and FC tests for isolated hematochezia from June 2016 to May 2020 were included in the present multicenter, retrospective, cross-sectional study. Comparative analysis was conducted between major causes of isolated hematochezia and FC cut-offs for discriminating colorectal polyps were explored.

Results: A total 127 patients were included. Thirty-five patients (27.6%) had colorectal polyps, followed by anal fissure (14.2%), ulcerative colitis (UC; 12.6%), and others. A significant difference in FC levels was observed between patients with colorectal polyps (median, 278.7 mg/kg), anal fissures (median, 42.2 mg/kg), and UC (median, 981 mg/kg) ($P < 0.001$). According to receiver operating characteristic curve analysis, among patients diagnosed with colorectal polyp or anal fissure, the most accurate FC cut-off for discriminating colorectal polyps from anal fissures on colonoscopy was 225 mg/kg (sensitivity, 59.4%; specificity, 94.4%; positive predictive value [PPV], 95.0%; negative

Eun Hye Lee 
<https://orcid.org/0000-0002-9270-9783>
 Kyung Jae Lee 
<https://orcid.org/0000-0002-3969-384X>
 Soon Chul Kim 
<https://orcid.org/0000-0002-5947-4599>
 So Yoon Choi 
<https://orcid.org/0000-0002-7389-7678>
 Yunkoo Kang 
<https://orcid.org/0000-0003-1712-2138>
 Dae Yong Yi 
<https://orcid.org/0000-0002-4168-7131>
 You Jin Choi 
<https://orcid.org/0000-0002-6882-3877>
 Byung-Ho Choe 
<https://orcid.org/0000-0001-9899-9120>
 Ben Kang 
<https://orcid.org/0000-0002-8516-9803>

Funding

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (No. 2021R1A2C1011004).

Disclosure

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Kim YB, Kim JY, Kang B.
 Data curation: Kim YB, Kim JY, Choi S, Kim HJ, Lee YM, Lee Y, Jang HJ, Lee EH, Lee KJ, Kim SC, Choi SY, Kang Y, Yi DY, Choi YJ, Choe BH, Kang B.
 Formal analysis: Kim YB, Kim JY, Kang B.
 Funding acquisition: Kang B.
 Investigation: Kim YB, Kim JY, and Kang B.
 Writing - original draft: Kim YB, Kim JY, Choi S, Kim HJ, Lee YM, Lee Y, Jang HJ, Lee EH, Lee KJ, Kim SC, Choi SY, Kang Y, Yi DY, Choi YJ, Choe BH, Kang B.
 Writing - review & editing: Kim YB, Kim JY, Choi S, Kim HJ, Lee YM, Lee Y, Jang HJ, Lee EH, Lee KJ, Kim SC, Choi SY, Kang Y, Yi DY, Choi YJ, Choe BH, Kang B.

predictive value [NPV], 56.7%; area under the curve [AUC], 0.8; 95% confidence interval [CI], 0.678–0.923; $P < 0.001$), while among patients diagnosed with colorectal polyp or UC, the most accurate FC cut-off for discriminating colorectal polyps from UC on colonoscopy was 879 mg/kg (sensitivity, 81.2%; specificity, 56.2%; PPV, 78.8%; NPV, 60.0%; AUC, 0.687; 95% CI, 0.521–0.852; $P < 0.001$).

Conclusion: FC may assist in assessing the cause of lower gastrointestinal tract bleeding in children who present with isolated hematochezia.

Keywords: Fecal Calprotectin; Colorectal Polyp; Anal Fissure; Ulcerative Colitis; Hematochezia

INTRODUCTION

Colorectal polyps are the most common cause of isolated hematochezia in children.¹⁻⁴ However, in clinical settings, anal fissures may also present with isolated hematochezia. Therefore, distinguishing colorectal polyps from anal fissures may often be difficult, especially when the findings of anal inspection and digital rectal exam are negative. Ulcerative colitis (UC) may also present with isolated hematochezia, especially in those whose lesions are confined to the rectum.⁵ In these cases of isolated hematochezia, a colonoscopy or sigmoidoscopy is required. However, there are limitations in performing endoscopy in pediatric patients, especially in infancy or childhood.

Fecal calprotectin (FC) is a surrogate marker that is popularly used for assessing intestinal inflammation in patients with inflammatory bowel disease.^{6,7} However, consensus has not been established for the clinical use of FC in colorectal polyps due to the lack of baseline data.⁸ Meanwhile, recent studies have shown that FC may have a role in detecting and furthermore monitoring recurrence in colorectal polyps.⁹⁻¹² Considering the aforementioned conditions of children presenting with isolated hematochezia, FC may be able to discriminate colorectal polyps from different diseases and conditions before conducting an endoscopy.

In this study, we aimed to investigate the potential utility of FC in assessing colorectal polyps detected by colonoscopy among children presenting with isolated hematochezia.

METHODS

Patients and study design

The present study was a multicenter, retrospective, cross-sectional study conducted in 15 medical centers in South Korea; Kyungpook National University Children's Hospital affiliated with Kyungpook National University Chilgok Hospital, Ajou University Medical Center, Eulji University Hospital, Chungnam National University Hospital, Soonchunhyang University Bucheon Hospital, Korea University Anam Hospital, Keimyung University Dongsan Hospital, Nowon Eulji Medical Center, Hallym University Sacred Heart Hospital, Jeonbuk National University Medical School, Kosin University Gospel Hospital, Wonju Severance Christian Hospital, Kyungpook National University Hospital, Chung-Ang University Hospital, and Inje University Ilsan Paik Hospital. Pediatric patients of the age of < 18 years who had undergone a colonoscopy for isolated hematochezia from June 2016 to May 2020 were included. Medical charts were reviewed and those with symptoms other than hematochezia, or who were

previously diagnosed with a gastrointestinal tract disease were excluded. Additionally, those who had not conducted FC tests within 1 month before the colonoscopy were also excluded to control for alteration of FC levels owing to disease progression. The etiologies of isolated hematochezia were investigated. Thereafter, those with the diagnosis of colorectal polyps, anal fissures, and UC were ultimately included for statistical analysis.

Baseline clinicodemographics including sex, diagnosis age, family history of colorectal polyps, growth indicators, serum laboratory test results, and fecal test results including FC and fecal immunochemistry test (FIT) were investigated in all the patients with available data. FC level was analyzed using an enzyme-linked immunosorbent assay in 3 centers, while fluorescence immunoassay was conducted in 12 centers. Patients were divided according to diseases, and variables were compared between the following three diseases; colorectal polyps, anal fissure, and UC. Furthermore, FC level cut-off levels that could possibly discriminate colorectal polyps from anal fissures and UC were investigated.

Statistical analysis

For statistical comparison between the three groups, analysis of variance test and post-hoc Bonferroni t test was used for continuous variables, and chi square test or Fisher's exact test was used for categorical variables. Wilcoxon's rank-sum test was used for the comparison of FC levels between two groups. Comparative data for continuous variables are reported as median (interquartile range) or mean \pm SD. Receiver operating characteristic (ROC) curve analysis was performed to derive the most accurate FC cut-off points associated with the diagnosis of colorectal polyps. The results were expressed as area under the curve (AUC) with 95% confidence interval (CI), and sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. Data were considered to be statistically significantly different if $P < 0.05$. Statistical analyses were conducted using R version 3.2.3 (<http://www.r-project.org>).

Ethics statement

The present study was conducted with approval from 16 participating institutions including the Institutional Review Board (IRB) of Kyungpook National University Chilgok Hospital (IRB No. 2020-07-017), and informed consent was waived due to the retrospective nature of the study.

RESULTS

Patients

Among 1,036 children during the study period, 909 patients were excluded leaving 127 patients for inclusion. Colorectal polyp was the most common etiology of isolated hematochezia, comprising 27.6% of all etiologies followed by anal fissure (14.2%), and UC (12.6%) (**Table 1**).

Comparison of findings between groups of colorectal polyp, anal fissure, and UC

A total 69 patients with colorectal polyp, anal fissure, and UC were divided into three groups. Two patients with auto-amputated polyps were additionally excluded, ultimately leaving 67 patients for statistical analysis (**Fig. 1**). Clinicodemographic findings and laboratory test results were statistically compared between the three groups. Comparison between groups revealed statistically significant differences between the three groups in age at diagnosis, eosinophil count, C-reactive protein, serum albumin, proportion of patients with a positive

Table 1. Etiologies of isolated hematochezia

| Etiologies | Values (N = 127) |
|--|------------------|
| Colorectal polyp | 35 (27.6) |
| Juvenile polyp | 28 (22.0) |
| Auto-amputated polyp | 2 (1.6) |
| Familial adenomatous polyposis | 2 (1.6) |
| Peutz-Jeghers syndrome | 2 (1.6) |
| Juvenile polyposis syndrome | 1 (0.9) |
| Anal fissure | 18 (14.2) |
| Ulcerative colitis | 16 (12.6) |
| Nodular lymphoid hyperplasia of the rectum | 12 (9.4) |
| Eosinophilic gastrointestinal disease | 8 (6.3) |
| Rectal erosion | 5 (3.9) |
| Allergic proctocolitis | 2 (1.6) |
| Pseudomembranous colitis | 2 (1.6) |
| Solitary rectal ulcer | 2 (1.6) |
| Angiodysplasia | 1 (0.8) |
| Hemorrhoids | 1 (0.8) |
| Meckel's diverticulum | 1 (0.8) |
| Miscellaneous | 24 (18.9) |

Values are presented as number (%).

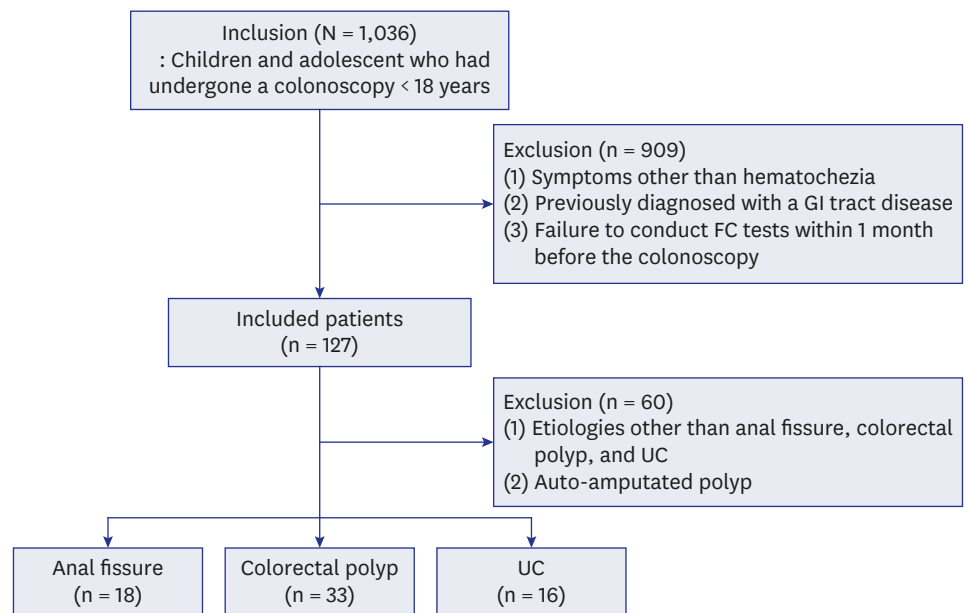


Fig. 1. Patient inclusion and exclusion.

GI = gastrointestinal, FC = fecal calprotectin, UC = ulcerative colitis.

FIT, and FC levels (**Table 2, Fig 2**). According to the post-hoc Bonferroni t test, significant differences in FC levels were observed between the anal fissure group and the colorectal polyp group ($P = 0.048$), and between the anal fissure group and the UC group ($P = 0.002$).

Cut-off level for the discrimination between colorectal polyps and other major etiologies

According to ROC curve analysis, the most accurate FC cut-off level for the discrimination between colorectal polyp and anal fissure was 225 (AUC, 0.8; 95% CI, 0.678–0.923; sensitivity, 59.4%; specificity, 94.4%; PPV, 95.0%; NPV, 56.7%; $P < 0.001$) (**Fig. 3A**).

According to ROC curve analysis, the most accurate FC cut-off level for the discrimination

Table 2. Comparison of clinicodemographic, laboratory factors between anal fissures, juvenile polyps, and UC

| Factors | Anal fissure (n = 18) | Colorectal polyp (n = 35) | UC (n = 16) | P value |
|--------------------------------------|-----------------------|---------------------------|---------------------|---------|
| Male, sex | 11 (61.1) | 20 (60.6) | 8 (50.0) | 0.747 |
| Age at diagnosis, yr | 11.5 ± 4.6 | 9.5 ± 5.7 | 15.1 ± 4.0 | 0.003 |
| Family history of colorectal polyp | 0 (0.0) | 5 (15.2) | 0 (0.0) | 0.070 |
| Height Z-score | 0.3 ± 0.9 | 0.0 ± 0.8 | 0.1 ± 1.0 | 0.513 |
| Weight Z-score | 0.5 ± 1.7 | 0.0 ± 1.1 | -0.1 ± 1.6 | 0.417 |
| BMI Z-score | 0.4 ± 1.6 | 0.0 ± 1.1 | -0.2 ± 1.7 | 0.391 |
| WBC count, /μL | 7,310 (5,180–8,680) | 7,355 (5,965–9,885) | 8,145 (5,435–9,595) | 0.760 |
| Eosinophil count, /μL | 141 (90–269) | 133 (64.3–243.4) | 374 (221–1,015) | 0.001 |
| Hemoglobin, g/dL | 13.2 (12.2–14.1) | 12.7 (11.8–14.1) | 12.8 (11.4–13.6) | 0.490 |
| Hematocrit, % | 38.8 ± 3.6 | 37.8 ± 4.6 | 36.3 ± 6.5 | 0.340 |
| MCV, fL | 83.4 ± 4.8 | 80.2 ± 6.8 | 83.0 ± 4.7 | 0.137 |
| MCH, pg | 28.4 (27.3–30.2) | 27.3 (25.8–28.8) | 28.9 (27.2–29.5) | 0.118 |
| Platelet count, ×10 ³ /μL | 304 (270–372) | 348 (300–392) | 313 (295–370) | 0.258 |
| CRP, mg/dL | 0.02 (0.01–0.05) | 0.08 (0.03–0.14) | 0.05 (0.04–0.25) | 0.008 |
| ESR, mm/hr | 4 (2–9) | 11 (2–15) | 12 (2.0–22) | 0.414 |
| Total protein, g/dL | 7.3 ± 0.5 | 7.0 ± 0.7 | 7.2 ± 0.6 | 0.243 |
| Albumin, g/dL | 4.7 (4.6–4.8) | 4.5 (4.3–4.8) | 4.3 (4.3–4.5) | 0.004 |
| PT, sec | 12.0 ± 0.9 | 12.0 ± 0.8 | 12.4 ± 0.9 | 0.339 |
| PT, INR | 1.02 ± 0.07 | 1.04 ± 0.07 | 1.03 ± 0.04 | 0.730 |
| aPTT, sec | 28.5 (27.4–30.6) | 31.2 (28.0–34.0) | 31.8 (31.8–34.1) | 0.116 |
| Positive FIT (n = 44) | 1 (7.1) | 13 (54.2) | 6 (100.0) | < 0.001 |
| FC, mg/kg | 42.2 (20–70.1) | 278.7 (63.5–665.9) | 981 (294.6–2,000) | < 0.001 |

Data are expressed as means ± SD for continuous variables that showed normal distribution, and median (interquartile range) or number (%) for continuous variables that did not show normal distribution, unless otherwise indicated.

UC = ulcerative colitis, BMI = body mass index, WBC = white blood cell, MCV = mean corpuscular volume, MCH = mean corpuscular hemoglobin, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, PT = prothrombin time, INR = International Normalized Ratio, aPTT = activated partial thromboplastin time, FIT = fecal immunochemistry test, FC = fecal calprotectin.

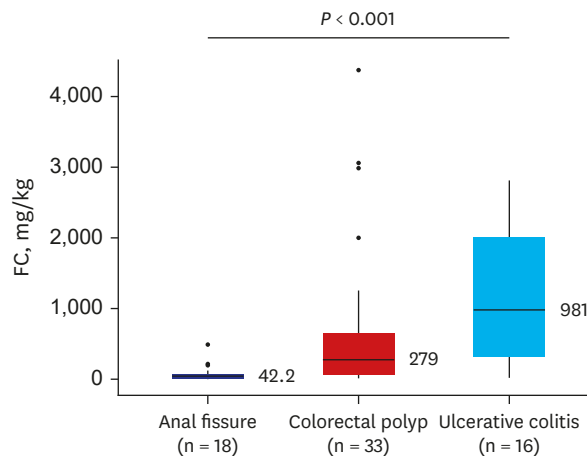


Fig. 2. Significant FC level differences between major etiologies of isolated hematochezia. FC = fecal calprotectin.

between colorectal polyp and anal fissure was 879 (AUC, 0.687; 95% CI, 0.521–0.852; sensitivity, 81.2%; specificity, 56.2%; PPV, 78.8%; NPV, 60.0%; $P < 0.001$) (Fig. 3B).

DISCUSSION

This is the first multicenter study to evaluate the value of FC in assessing colorectal polyps detected by colonoscopy among children presenting with isolated hematochezia. A significant difference in FC levels was observed between patients with colorectal polyps and

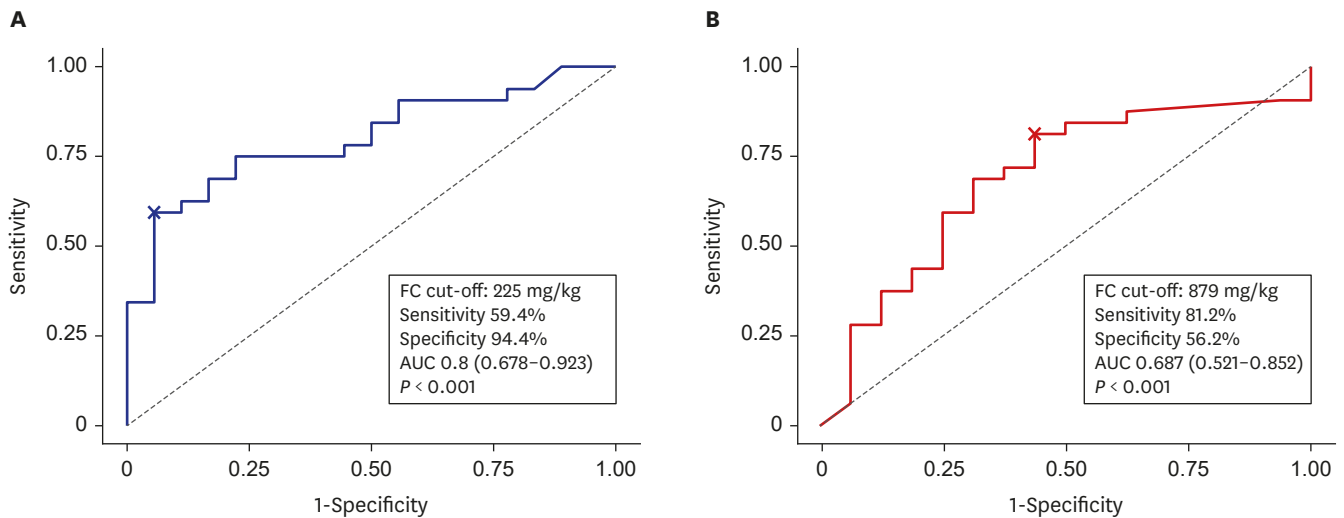


Fig. 3. ROC curve analysis for the discrimination between colorectal polyp and other major etiologies. **(A)** ROC curve analysis for the discrimination between colorectal polyp and anal fissure. **(B)** ROC curve analysis for the discrimination between colorectal polyp and ulcerative colitis. FC = fecal calprotectin, AUC = area under the curve; ROC = receiver operating characteristic.

other major etiologies, such as anal fissures, and UC. Furthermore, we were able to identify FC cut-off levels for discriminating between colorectal polyps and anal fissures and colorectal polyps and UC.

In our study, the most common cause of isolated hematochezia was colorectal polyps (27.6%), which are in line with previous studies of 19.5–44.1%.^{1,11,13} However, unlike previous studies we were also capable of identifying a relatively high proportion of patients with anal fissures (14.2%). Although, anal fissures can be observed by inspection and a history of constipation, there are uncertain cases in which the fissures are located in the anal canal or cases of an insufficient physical exam owing to the unwillingness of the child to cooperate. Moreover, it is hard to discriminate only by history taking if the child's history of constipation is acute or if the child does not have hardened stool. In these indefinite cases, a colonoscopy or sigmoidoscopy is required to evaluate the cause of hematochezia, and to rule out the possibility of a colorectal polyp.

FC is a neutrophil-derived substance released during cell disruption and death in the gastrointestinal tract, and is widely used as a screening test for inflammatory bowel disease (IBD), colorectal cancer, celiac disease, and necrotizing enterocolitis of newborns.^{14,15} It is also popularly used for monitoring disease activity in patients with IBD.^{6,7,16} Several previous studies have proposed the potential role of FC in identifying colorectal polyps. In a case series of 4 patients with juvenile polyps, pre-polypectomy FC levels were increased to a median 1,800 mg/kg (range, 534–2,500 mg/kg), while post-polypectomy FC levels decreased to normal in all 4 of these cases.⁹

In another study of 203 children who had undergone FC measurement and colonoscopy, median FC level was 844 mg/kg (range, 28–2,287 mg/kg) among 12 cases with colorectal polyps.¹⁰ That finding of elevated FC was significantly higher than the 83 cases who revealed normal findings on colonoscopy (median, 130 mg/kg; range, < 20–2,443 mg/kg; $P < 0.0001$). However, no significant difference was observed between the colorectal group and 108 patients with IBD (median, 962 mg/kg; range, < 20–7,780 mg/kg; $P = 0.630$). Meanwhile, we

identified a significant difference in FC levels between patients with colorectal polyps and those with UC. This difference may be due to the larger number of patients with colorectal polyps in our study, as well as the difference in patient characteristics. We included those with isolated hematochezia, while the aforementioned study included those who had undergone a combined colonoscopy and FC, irrespective of symptoms. Meanwhile, in another prospective study in 59 children with lower gastrointestinal bleeding, FC was increased in all 26 cases with polyps (median, 685 mg/kg; range, 220–2,736 mg/kg). Furthermore, FC revealed a strong discriminative power showing a PPV of 92.8% and NPV of 100% in differentiating from the normal colonoscopy group.¹¹

The underlying mechanism of FC elevation in colorectal polyps is yet to be elucidated. However, it is known that juvenile polyps exhibit an ulcerated surface due to auto-infarction macroscopically, while dilated cysts filled with mucin, and abundant lamina propria with prominent inflammatory infiltration are observed microscopically.¹⁷ Although there are limitations in stating whether histologically consistent characteristics exist in the different pediatric polyposis, however, depending on its unregulated growth rate, causes imbalance of blood supply, and ischemia mediates cellular injury and neutrophil recruitment. Increased calprotectin release into alimentary tract may be elucidated in this process.

Our study has some limitations and thus results should be interpreted with caution. First, this was a retrospective study and patients who did not have FC results were excluded. Therefore, selection bias may have been introduced in this process. Second, the number of patients in each group was not large. Third, we did not investigate the outcomes of post-polypectomy in our studies due to the small number of patients with such data. Fourth, differences in FC tests among centers may have affected the results. However, it has been reported that the accuracy in the FC measurement is comparable between enzyme-linked immunosorbent assay and fluorescence immunoassay.¹⁸

Future large-scaled prospective longitudinal studies may better elucidate the results of our study.

In conclusion, FC levels were capable of discriminating between colorectal polyps and other major etiologies presenting with isolated hematochezia in children. FC may assist in assessing the cause of lower gastrointestinal tract bleeding in children who present with isolated hematochezia.

REFERENCES

1. Silbermintz A, Matar M, Assa A, Zevit N, Glassberg YM, Shamir R. Endoscopic findings in children with isolated lower gastrointestinal bleeding. *Clin Endosc* 2019;52(3):258-61.
[PUBMED](#) | [CROSSREF](#)
2. Lee YJ, Park JH. The most common cause of lower gastrointestinal bleeding without other symptoms in children is colonic polyp: is total colonoscopy needed? *Clin Endosc* 2019;52(3):207-8.
[PUBMED](#) | [CROSSREF](#)
3. Lee BG, Shin SH, Lee YA, Wi JH, Lee YJ, Park JH. Juvenile polyp and colonoscopic polypectomy in childhood. *Pediatr Gastroenterol Hepatol Nutr* 2012;15(4):250-5.
[PUBMED](#) | [CROSSREF](#)
4. Kim DY, Bae JY, Ko KO, Cheon EJ, Lim JW, Song YH, et al. Juvenile polyp associated with hypovolemic shock due to massive lower gastrointestinal bleeding. *Pediatr Gastroenterol Hepatol Nutr* 2019;22(6):613-8.
[PUBMED](#) | [CROSSREF](#)

5. Sahn B, Bitton S. Lower gastrointestinal bleeding in children. *Gastrointest Endosc Clin N Am* 2016;26(1):75-98.
[PUBMED](#) | [CROSSREF](#)
6. D'Haens G, Ferrante M, Vermeire S, Baert F, Noman M, Moortgat L, et al. Fecal calprotectin is a surrogate marker for endoscopic lesions in inflammatory bowel disease. *Inflamm Bowel Dis* 2012;18(12):2218-24.
[PUBMED](#) | [CROSSREF](#)
7. Lee YM, Choi S, Choe BH, Jang HJ, Kim S, Koh H, et al. Association between fecal calprotectin and mucosal healing in pediatric patients with Crohn's disease who have achieved sustained clinical remission with anti-tumor necrosis factor agents. *Gut Liver* 2022;16(1):62-70.
[PUBMED](#) | [CROSSREF](#)
8. Koninckx CR, Donat E, Benninga MA, Broekaert JJ, Gottrand F, Kolho KL, et al. The use of fecal calprotectin testing in paediatric disorders: a position paper of the European Society for Paediatric Gastroenterology and Nutrition Gastroenterology Committee. *J Pediatr Gastroenterol Nutr* 2021;72(4):617-40.
[PUBMED](#) | [CROSSREF](#)
9. Pauley-Hunter RJ, Kunnath S, Wolff K, Vanderhoof JA. Fecal calprotectin and pediatric juvenile polyps. *J Pediatr Gastroenterol Nutr* 2015;60(4):e30-1.
[PUBMED](#) | [CROSSREF](#)
10. 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(1):43-6.
[PUBMED](#) | [CROSSREF](#)
11. 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(1):66.
[PUBMED](#) | [CROSSREF](#)
12. Das SR, Karim AS, RukonUzzaman M, Mazumder MW, Alam R, Benzamin M, et al. Juvenile polyps in Bangladeshi children and their association with fecal calprotectin as a biomarker. *Pediatr Gastroenterol Hepatol Nutr* 2022;25(1):52-60.
[PUBMED](#) | [CROSSREF](#)
13. Campbell AM, Sugarman I. Does painless rectal bleeding equate to a colonic polyp? *Arch Dis Child* 2017;102(11):1049-51.
[PUBMED](#) | [CROSSREF](#)
14. Jeong SJ. The role of fecal calprotectin in pediatric disease. *Korean J Pediatr* 2019;62(8):287-91.
[PUBMED](#) | [CROSSREF](#)
16. Yoo IH, Cho JM, Joo JY, Yang HR. Fecal calprotectin as a useful non-invasive screening marker for eosinophilic gastrointestinal disorder in Korean children. *J Korean Med Sci* 2020;35(17):e120.
[PUBMED](#) | [CROSSREF](#)
16. Cozijnsen MA, Ben Shoham A, Kang B, Choe BH, Choe YH, Jongsma MM, et al. Development and validation of the mucosal inflammation noninvasive index for pediatric Crohn's disease. *Clin Gastroenterol Hepatol* 2020;18(1):133-140.e1.
[PUBMED](#) | [CROSSREF](#)
17. Hyer W. Pediatric polyposis syndrome. In: Wyllie R, Hyams JS, Kay M, editors. *Pediatric Gastrointestinal and Liver Disease*. 5th ed. Philadelphia, PA, USA: Elsevier; 2016, 496-507.
18. Prell C, Nagel D, Freudenberg F, Schwarzer A, Koletzko S. Comparison of three tests for faecal calprotectin in children and young adults: a retrospective monocentric study. *BMJ Open* 2014;4(5):e004558.
[PUBMED](#) | [CROSSREF](#)