

ORIGINAL ARTICLE

Very Early-Onset Ulcerative Colitis Manifesting as Acute Rectal Prolapse and Persistent Hematochezia in a Three-Year-Old Child: An Observational Analytic Case Study of Diagnostic Trajectory and Multimodal Intervention

Revika¹, Neni Sumarni², Galih Widiyanto³

¹ Faculty of Medicine, Universitas Tarumanagara, Jakarta, Indonesia
² Department of Pediatrics, K.R.M.T. Wongsonegoro Regional Hospital, Semarang, Indonesia
³ Department of Pediatric Surgery, K.R.M.T. Wongsonegoro Regional Hospital, Semarang, Indonesia

ARTICLE INFO	ABSTRACT
ARTICLE TYPE Original Article ARTICLE HISTORY Received: August 19, 2026 Revised: September 15, 2026 Accepted: October 10, 2026 Available online: October 20, 2026 Published: October 22, 2026 KEYWORDS Colonoscopy; Hematochezia; Mesalazine; Rectal prolapse; Very early-onset ulcerative colitis CORRESPONDING AUTHOR Revika E-mail: revika.406251008@stu.untar.ac.id DOI 10.59345/sjped.v4i2.373 LICENSE CC BY-NC-SA 4.0 COPYRIGHT © 2026 The Author(s). Published by Phlox Institute: Indonesian Medical Research Organization.	Background: Very early-onset ulcerative colitis (VEO-UC), diagnosed before six years of age, is uncommon and often presents atypically. In toddlers, severe proctitis with tenesmus can weaken pelvic floor support and cause full-thickness rectal prolapse, which can mimic solitary rectal ulcer syndrome, cow's milk protein allergy or primary rectal prolapse. Objective: To describe the diagnostic course, treatment and six-month outcome of a toddler with VEO-UC presenting with full-thickness rectal prolapse. Methods: A boy aged 3 years 3 months presented to K.R.M.T. Wongsonegoro Regional Hospital with persistent mucoid hematochezia, a 1-kg weight loss and full-thickness rectal mucosal prolapse. He was followed over seven epochs from baseline (T0) to month 6 (T6). Work-up comprised colonoscopy with biopsy, abdominal ultrasonography and serial inflammatory biomarkers. Treatment was a Thiersch anal cerclage with oral mesalazine induction (60–80 mg/kg/day). Results: Colonoscopy showed continuous hyperemia and multiple 2–6 mm ulcers with fibrinous exudate in the rectosigmoid and descending colon; ultrasonography found no mass or lymphadenopathy. After cerclage on hospital day 2 and mesalazine induction, the Pediatric Ulcerative Colitis Activity Index (PUCAI) fell from 45 at T0 to 0 at T5–T6. Hematochezia had resolved by week 4. Fecal calprotectin declined from 880 to 35 µg/g (–96.0%), and weight rose from 13.0 to 14.6 kg (+12.3%). The prolapse did not recur. Conclusion: Full-thickness rectal prolapse in early childhood can be the first sign of VEO-UC. Prompt colonoscopy and combined medical and surgical management were followed by anatomical stabilization and mucosal healing in this patient.

1. Introduction

Inflammatory bowel disease (IBD) is traditionally divided into ulcerative colitis (UC) and Crohn's disease (CD). It is a chronic immune-mediated disorder, and its hallmarks are mucosal inflammation, loss of epithelial barrier function and a relapsing-remitting course.¹ For a long time it was regarded as a disease of adolescents and young adults in Western industrialized countries. That has changed.² Over the past three decades incidence has risen quickly in newly industrialized regions, above all in Asia and the Pacific, where changing environmental exposures, westernized diets, urbanization and altered microbial colonization are the usual explanations.³ Large population-based studies from South Asia describe a steep increase in pediatric IBD, with prevalence reaching public health significance in multicultural metropolitan centers.⁴ Southeast Asia shows the same trend. Early-onset inflammatory enteropathy is becoming more common in young children.²

About 20% to 25% of all IBD is diagnosed before 18 years of age, and its clinical, phenotypic and genetic course differs clearly from that of adult-onset disease.⁵ Children with UC often have an aggressive, extensive illness. Pancolitis or subtotal colonic involvement is documented in more than 70% to 80% of them at presentation, against fewer than 30% to 40% of adults.⁶ Late diagnosis has serious consequences. If mucosal inflammation is not suppressed early, during this critical developmental window, children are exposed to rapid deterioration, steroid dependence,

growth failure, delayed puberty and considerable psychosocial morbidity.⁷

Very early-onset IBD (VEO-IBD) is IBD diagnosed before six years of age. It forms a distinct and demanding subgroup of pediatric gastroenterology, and infantile IBD, diagnosed before the first birthday, is a smaller subset within it.⁸ In older children and adults, polygenic risk loci interact with many environmental triggers. VEO-IBD differs in this respect: genetic and immunologic factors contribute far more, and a high-penetrance monogenic defect is often responsible. Such a defect may affect epithelial barrier integrity, hyperinflammatory phagocyte pathways, regulatory T-cell development or interleukin-10 (IL-10) receptor signaling.⁸ Presentations are heterogeneous and often atypical. Intractable tenesmus, severe mucoid hematochezia, refractory perianal fistulizing disease and isolated extraintestinal symptoms all occur, and they can mimic primary anorectal anomalies, congenital enteric dysmotility or infectious proctocolitis.⁹ In European registries, very young children with VEO-UC often have refractory proctocolitis and biomarker kinetics unlike those of adolescents.¹⁰ A single-center series from Australasia reports the same difficulty in toddler-onset IBD. The presenting signs are unusual.¹¹

Separating VEO-UC from non-IgE-mediated cow's milk protein allergy (CMPA) is one of the hardest diagnostic questions in early childhood. The allergic condition in question is food protein-induced allergic proctocolitis

(FPIAP).¹² FPIAP usually appears in the first six months of life, in breastfed or formula-fed infants. Rectal bleeding is mild, the stools are loose and blood-streaked, and there is little systemic upset.¹² The likelihood shifts when bleeding continues beyond infancy into the toddler years or is accompanied by progressive weight loss and marked mucosal ulceration. Chronic inflammatory disease is then much more likely.¹³ The ESPGHAN and World Allergy Organization Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) guidelines stress that a correct diagnosis depends on matching the response to dietary protein elimination with endoscopic and histopathologic findings, because otherwise chronic autoimmune enteropathy may be mislabeled as simple dietary hypersensitivity.^{12,14,15} A toddler with atypical allergic proctocolitis symptoms who has not improved within four to eight weeks needs repeat endoscopic assessment.¹³ A diagnostic algorithm for pediatric lower gastrointestinal bleeding makes the same point. Early discrimination between self-limiting allergic colitis, mechanical lesions and progressive IBD is advised.¹⁶

Acute full-thickness rectal prolapse is an exceptionally rare and alarming presentation of pediatric VEO-UC.¹⁷ The term means circumferential protrusion of every layer of the rectal wall through the anal sphincter. In young children it usually reflects an immature pelvic floor: a vertically oriented sacrococcygeal spine, no sacral promontory to support the rectum and loose submucosal connective tissue.^{18–20} Chronic exudative proctitis changes the picture. Relentless mucosal inflammation, shear stress and crypt necrosis cause chronic tenesmus, tenesmus leads to repeated Valsalva straining, and the pelvic floor is eventually exhausted.^{19,21,22} Attributing this secondary prolapse to solitary rectal ulcer syndrome (SRUS), chronic idiopathic constipation or benign mucosal redundancy has real costs: inappropriate manual maneuvers, a long diagnostic delay and progressive colonic damage.^{23,24}

The European Crohn's and Colitis Organisation (ECCO) and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) recommend oral 5-aminosalicylic acid (5-ASA, mesalazine) as the mainstay of induction and maintenance therapy in mild-to-moderate pediatric UC. A toddler who also has acute full-thickness rectal prolapse needs closely coordinated multidisciplinary care.^{20,25} Medical induction cannot relieve strangulation at the anal outlet immediately, whereas transabdominal rectopexy carries considerable morbidity in a malnourished and inflamed small child.²⁰ Formulation, delivery vehicle and dose schedule matter most for non-invasive mucosal healing in young children.^{26,27} In pediatric cohorts with active distal colonic disease, weight-adjusted mesalazine dosing reaches tissue concentrations sufficient to suppress mucosal cytokine transcription.^{27,28}

Longitudinal observational documentation of VEO-UC that presents as acute rectal prolapse in a toddler remains very scarce in the global literature. Few reports describe the diagnostic course, the high-resolution colonoscopic ulcer features, the pelvic floor biomechanics and the combined medical-surgical treatment together.^{17,20} This observational analytic case study aims to address that gap. It reports an epoch-based investigation of a boy aged 3 years 3 months who presented with acute full-thickness rectal prolapse and persistent hematochezia at K.R.M.T. Wongsonegoro Regional General Hospital, Semarang, Indonesia. Biostatistical trajectory modeling, algorithmic causal probability matrices and benchmarking against the published literature are used to examine how mucosal

immunopathology and pelvic floor mechanics interact in very early-onset pediatric UC.

2. Methods

Study design and setting

This was an observational analytic case study with an intensive longitudinal prospective-tracking protocol. It followed the clinical, endoscopic, ultrasonographic, biomarker and therapeutic course of VEO-UC presenting atypically with acute full-thickness rectal mucosal prolapse. The design follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines, adapted for a single-subject analytic framework, and the CARE (CAse REports) consensus guidelines. The setting was the Department of Pediatrics and the Department of Pediatric Surgery of K.R.M.T. Wongsonegoro Regional General Hospital, Semarang, Central Java, Indonesia. The hospital is a tertiary referral center for pediatric gastroenterology and pediatric surgical emergencies in the region.

Participants and eligibility criteria

The participant was evaluated and enrolled against predefined diagnostic criteria for pediatric IBD. These were the ESPGHAN Revised Porto Criteria,²⁹ the Paris Classification of Pediatric IBD^{6,30} and the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) VEO-IBD consensus statement.⁸ Four conditions had to be met. Age at symptom onset had to be under six years, in line with the consensus definition of VEO-IBD. Lower gastrointestinal bleeding had to persist, with hematochezia lasting more than seven consecutive days. Colonoscopy had to show continuous mucosal hyperemia, loss of the normal vascular pattern, friability and discrete ulceration. Comprehensive microbiological screening had to show no enteric bacterial, viral or parasitic infection.

Exclusions were isolated non-inflammatory anatomical causes of rectal bleeding, such as solitary juvenile polyps, Meckel's diverticulum or congenital arteriovenous malformations without mucosal inflammation. Acute infectious dysentery confirmed by stool culture or multiplex polymerase chain reaction was also excluded, as were primary immunodeficiency syndromes with systemic opportunistic infections and classical early infantile cow's milk protein allergy that resolved with dairy elimination within seven days.^{12,14}

Variables and outcome measures

Clinical disease activity was scored at every epoch with the validated Pediatric Ulcerative Colitis Activity Index (PUCAI). It has six items: abdominal pain (0–10), rectal bleeding (0–30), stool consistency (0–10), stool frequency per 24 hours (0–15), nocturnal stools (0–10) and activity limitation (0–10). Totals range from 0 to 85 points.³¹ Severity categories were set in advance: remission below 10 points, mild disease 10 to 34, moderate disease 35 to 64, severe disease 65 or more.³¹

Diagnostic and follow-up colonoscopies followed international pediatric endoscopy guidelines from ESPGHAN and the European Society of Gastrointestinal Endoscopy (ESGE).³² Colonoscopy is safe in toddlers and gives a definitive view of mucosal inflammation.^{33,34} Endoscopic severity was graded with the Mayo Endoscopic Subscore (MES). Its levels are 0, normal or inactive disease; 1, mild disease with erythema, reduced vascular pattern and mild friability; 2, moderate disease with marked erythema, absent vascular pattern, friability and erosions; and 3,

severe disease with spontaneous bleeding and extensive ulceration. The Ulcerative Colitis Endoscopic Index of Severity (UCEIS) scores vascular pattern [1–3], bleeding [1–4] and erosions or ulcers [1–4], for a total of 3 to 11 points.³⁵ Four international diagnostic frameworks were applied to establish the diagnosis with certainty and to exclude competing anorectal and allergic conditions. First, phenotype was classified with the Paris Pediatric IBD Classification, which records age at onset, maximal extent of inflammation and initial severity.^{6,30} Second, the ESPGHAN Porto Criteria and the revised consensus on pediatric IBD diagnosis confirmed the diagnosis by separating continuous colonic inflammation from the granulomatous or transmural pattern of Crohn's disease.²⁹ Third, the World Allergy Organization DRACMA and ESPGHAN cow's milk protein allergy algorithms were used to judge the timeline of symptoms and dietary exposure. This covered symptom onset relative to dietary protein introduction, the response to maternal dietary elimination and the typical infantile age at onset.^{12,14,15} Fourth, mechanical and ischemic anorectal disorders were assessed against the established diagnostic criteria for SRUS. Those criteria distinguish multifocal continuous colonic ulceration from a localized anterior rectal wall ischemic lesion with fibromuscular obliteration of the lamina propria.^{23,36}

Data collection and measurement

The child was followed over a standardized seven-epoch timeline that covered six months, from emergency presentation to the primary endpoint. At baseline (T0, day 0) he had emergency triage, a full systemic and anorectal examination, baseline hematologic and biochemical panels and emergency bedside ultrasonography. In the acute stabilization phase (T1, days 1 to 3) he underwent diagnostic pediatric colonoscopy under general anesthesia. A modified Thiersch anal cerclage followed on hospital day 2. Oral 5-ASA induction was started. Early outpatient recovery was assessed two weeks after discharge (T2), covering wound healing, suture-site complications, stool frequency and a repeat blood count. Induction was reviewed at week 4 (T3, day 28), when serial fecal calprotectin, C-reactive protein and erythrocyte sedimentation rate were measured together with weight velocity. At month 2 (T4, day 60) the mesalazine dose was stepped down. Pelvic floor integrity was checked, and diet was normalized. Month 3 (T5, day 90) brought repeat non-invasive biomarkers and a check of suture retention, to appraise mid-term stability. The primary endpoint came at month 6 (T6, day 180). It comprised surveillance colonoscopy to confirm mucosal healing, final calculation of catch-up growth and review of relapse risk.

Laboratory follow-up used high-sensitivity C-reactive protein (hs-CRP; reference < 5.0 mg/L), erythrocyte sedimentation rate (ESR; Westergren method; reference < 15 mm/h), complete blood counts on an automated hematology analyzer (Sysmex XN-1000) and quantitative fecal calprotectin by enzyme-linked immunosorbent assay (ELISA; Bühlmann Laboratories; reference < 50 µg/g). Calprotectin above 100 µg/g was taken to indicate active mucosal inflammation, and above 250 µg/g moderate-to-severe activity.^{37,38}

Statistical analysis

All longitudinal physiologic, biomarker and anthropometric data were entered into a relational database and analyzed with R version 4.3.2 and the Python NumPy and SciPy libraries. Continuous variables are given as absolute values, as mean ± standard deviation (SD), or as median with interquartile range (IQR) where appropriate.

Relative percentage change (Δ%) at each epoch was calculated as:

$$\Delta\% = [(Value_Tx - Value_T0) / Value_T0] \times 100\%$$

Clinical response velocity was defined as the absolute fall in PUCAI score per week. Changes between baseline (T0) and the follow-up endpoints (T3, T6) were tested with the non-parametric Wilcoxon signed-rank test for paired ordinal indices (PUCAI, bleeding score). Two-tailed Student's t-tests were used for continuous hematologic variables. The significance threshold was $\alpha = 0.05$, fixed in advance. Somatic growth was benchmarked against the World Health Organization (WHO) Child Growth Standards (2006) for weight-for-age, height-for-age and body mass index (BMI)-for-age Z-scores.

Ethical considerations

The protocol was approved by the CMHC Research Center Ethics Committee, Indonesia (protocol approval reference 2026/7482). All clinical, diagnostic, endoscopic, surgical and therapeutic procedures followed the World Medical Association Declaration of Helsinki (amended 2013) and the International Council for Harmonisation Good Clinical Practice (ICH-GCP) guidelines. The child's biological parents and legal guardians gave full written informed consent. They did so before enrollment and before endoscopy and surgery. The consent document explicitly allowed collection, scientific analysis and open-access publication of the child's de-identified clinical data, longitudinal biomarker profiles, ultrasonograms, endoscopic recordings and clinical photographs. Privacy and confidentiality were protected throughout, in line with the patient anonymization requirements of the International Committee of Medical Journal Editors (ICMJE) and the Committee on Publication Ethics (COPE).

3. Results

Participant flow and baseline characteristics

The patient was a boy of Javanese ethnicity, aged 3 years 3 months (39 months). He came to the Emergency Department of K.R.M.T. Wongsonegoro Regional General Hospital, Semarang, with a persistent, painful anal mass and recurrent bloody defecation over the previous two weeks. His parents described fresh red blood dripping into the toilet bowl and coating the stool after bowel movements. A large amount of glistening mucus was mixed in. Stools were soft and unformed, 3 to 4 times per 24 hours.

A week before admission the parents had noticed a fleshy, reddish-purple mass protruding through the anus, mainly during straining. At first they could push it back gently by hand. Over the last 48 hours it had stayed outside, become exquisitely tender and could no longer be reduced at home; the child complained of distressing anal pain on defecation, rated 6/10 on the Wong-Baker FACES Pain Rating Scale. His weight had fallen by 1.0 kg over the 14-day illness, from 14.0 kg to 13.0 kg (7.1% acute loss). The parents denied fever, chills, vomiting, hematemesis, epistaxis, macroscopic hematuria and purpuric rash.

He was born at term (38 weeks) by uncomplicated spontaneous vaginal delivery, with a birth weight of 3,100 g. Development was age-appropriate. His basic immunizations, including BCG, hepatitis B, pentavalent (DTP-HB-Hib), polio and measles-rubella, were complete and on schedule. He was exclusively breastfed from birth to six months, and complementary foods began at six months. He never received cow's milk formula in infancy or early toddlerhood, and he had no commercial formula until after two years of age. There was no documented adverse reaction, eczema or wheezing. Three generations of his

family had no early-onset IBD, celiac disease, autoimmune thyroiditis, rheumatoid disease or early-onset colorectal cancer.

At admission (T0) the boy was alert and oriented but moderately distressed by anal discomfort (Glasgow Coma Scale 15, E4M6V5). He was hemodynamically stable. Pulse was 100 beats per minute, regular and of good volume. Respiratory rate was 22 breaths per minute without retractions, axillary temperature 36.5 °C and transcutaneous oxygen saturation (SpO₂) 99% on room air. Weight was 13.0 kg, height 92.0 cm and body mass index (BMI) 15.36 kg/m². The weight-for-height Z-score was

−0.34 and the height-for-age Z-score −0.62 on WHO standards, which indicates normal nutritional status despite the recent weight loss. Examination of the head, neck, heart and lungs was unremarkable; the abdomen was soft and not distended, with normal bowel sounds. There was no localized tenderness, rebound, guarding or organomegaly. All baseline sociodemographic, physiologic, anthropometric and clinical data are listed in Table 1.

Table 1. Baseline Sociodemographic, Anthropometric, and Initial Clinical-Biomarker Characteristics of the Pediatric Patient (T0).

Parameter / Clinical Domain	Baseline Observation (T0)	Reference Range / Standard	Clinical Interpretation
Chronological Age	3 years 3 months (39 months)	—	Toddler age cohort (VEO-IBD spectrum: < 6 years)
Sex / Gender	Male	—	Consistent with pediatric UC demographics
Body Weight (kg)	13.0 kg	12.0 – 16.5 kg (50th percentile: 14.3 kg)	Documented 1.0 kg acute weight loss over 14 days (~7.1%)
Body Height / Length (cm)	92.0 cm	90.5 – 98.0 cm (50th percentile: 94.5 cm)	Normal linear stature (Height-for-age Z-score: −0.62)
Body Mass Index (BMI, kg/m ²)	15.36 kg/m ²	14.2 – 16.8 kg/m ²	Normal weight-for-height index (BMI-for-age Z-score: −0.34)
Glasgow Coma Scale (GCS)	15 (E4M6V5)	15	Alert, active, no encephalopathy or systemic toxic state
Heart Rate (beats/min)	100 bpm	80 – 120 bpm	Normocardic, stable baseline hemodynamics
Respiratory Rate (breaths/min)	22 breaths/min	20 – 28 breaths/min	Eupneic, absence of respiratory distress
Axillary Temperature (°C)	36.5 °C	36.5 – 37.5 °C	Afebrile, absence of overt systemic sepsis
Oxygen Saturation (SpO ₂ , %)	99% on ambient room air	≥ 95%	Adequate peripheral microvascular oxygenation
Chief Presenting Complaint	Reddish-purple protruding anal mass & bloody stool	Absent	Protrusion present for 7 days; hematochezia for 14 days
Defecation Frequency	3 – 4 episodes / 24 hours	1 – 2 soft formed stools / day	Increased bowel frequency, soft stools mixed with mucus
Hematochezia Characteristics	Fresh red blood dripping post-defecation + mucus	Absent	Active lower gastrointestinal bleeding from rectosigmoid
Anal Pain Severity (Wong-Baker FACES)	6 / 10 (Moderate pain)	0 / 10	Pain aggravated by defecation straining and tenesmus
Nutritional History	Exclusive breastfeeding 0-6 mo; no cow formula < 2 yr	—	Negates typical early infantile cow's milk protein allergy
Family & Autoimmune History	Negative for IBD, celiac disease, CRC, or polyposis	Negative	Sporadic presentation; monogenic panel indicated

BMI: Body mass index; CRC: Colorectal cancer; GCS: Glasgow Coma Scale; IBD: Inflammatory bowel disease; SpO₂: Peripheral oxygen saturation; UC: Ulcerative colitis; VEO-IBD: Very early-onset inflammatory bowel disease.

With the child in the left lateral position, inspection of the perianal area showed a prominent, round, full-thickness rectal mass projecting about 2.5 to 3.0 cm beyond the external anal sphincter verge (clinical photograph in Figure 1). The mass bore concentric circular mucosal rings. These are typical of complete rectal prolapse or intussusception and quite unlike the radial sulci of mucosal prolapse or prolapsed internal hemorrhoids. Its surface was intensely hyperemic, edematous and reddish-purple, moist and glistening, with a thin coat of serosanguinous and yellowish

fibrinous exudate. At the dependent lower margin (6 o'clock) there was active mucosal oozing on gentle palpation. Sphincter tone was intact, with no anatomical ring defect. Manual reduction under topical 2% lidocaine gel was easy. The mucosa prolapsed again as soon as the child cried or strained. No facial features appear in any clinical image.



Figure 1. Clinical perianal presentation of full-thickness rectal mucosal prolapse in a 3-year-3-month-old child. Note the prominent, exteriorized reddish-purple cylindrical mass with characteristic concentric mucosal rings and serosanguinous-fibrinous exudate, distinguishing full-thickness prolapse from radial mucosal hemorrhoidal folds. No facial features are shown.

Diagnostic work-up

Emergency laboratory tests at T0 showed no overt anemia. Hemoglobin was 11.6 g/dL, hematocrit 35.1%, mean corpuscular volume (MCV) 78.4 fL and mean corpuscular hemoglobin (MCH) 26.2 pg. The white blood cell count was $7.8 \times 10^3/\mu\text{L}$ (neutrophils 56%, lymphocytes 36%, monocytes 6%, eosinophils 2%), with no toxic granulation or left shift. The platelet count of $312 \times 10^3/\mu\text{L}$ argued against reactive thrombocytosis. Serum electrolytes were preserved: sodium (Na^+) 135 mmol/L, potassium (K^+) 3.6 mmol/L, chloride 101 mmol/L and ionized calcium (Ca^{2+}) 1.31 mmol/L. Renal and hepatic function were normal. Blood urea nitrogen (BUN) was 11.2 mg/dL, creatinine 0.38 mg/dL, AST 24 U/L, ALT 18 U/L, total bilirubin 0.42 mg/dL and albumin 3.8 g/dL. Hepatitis B surface antigen (HBsAg) was non-reactive.

Systemic inflammatory markers were mildly to moderately raised: ESR 28 mm/h (reference < 15 mm/h) and hs-CRP 8.5 mg/L (reference < 5.0 mg/L). Fecal calprotectin was markedly elevated at 880 $\mu\text{g/g}$ (reference < 50 $\mu\text{g/g}$). This indicates substantial neutrophil migration and active inflammation of the lower gastrointestinal mucosa. Fresh stool specimens were examined by darkfield microscopy, bacterial culture (Salmonella, Shigella, Campylobacter and Yersinia species), Clostridioides difficile toxin A/B enzyme immunoassay and ova and parasite concentration. All were negative. Acute infectious enterocolitis was excluded. The baseline blood counts, electrolytes, inflammatory markers and microbiology are summarized in the diagnostic panel in Table 2.

Table 2. Multimodal Diagnostic Panel: Comprehensive Laboratory, Ultrasonographic, Endoscopic, and Histopathological Metrics at Baseline.

Diagnostic Modality	Specific Target / Measured Parameter	Patient Finding	Standard Clinical Reference	Diagnostic Significance
Complete Blood Count	Hemoglobin (Hb)	11.6 g/dL	11.5 – 13.5 g/dL	Absence of severe microcytic anemia at initial presentation
Complete Blood Count	Hematocrit (Ht)	35.1%	34.0 – 40.0%	Adequate circulating red cell mass preserved
Complete Blood Count	White Blood Cells (WBC)	$7.8 \times 10^3/\mu\text{L}$	$5.5 - 15.5 \times 10^3/\mu\text{L}$	Absence of peripheral leukocytosis or acute bacterial shift
Complete Blood Count	Platelet Count	$312 \times 10^3/\mu\text{L}$	$150 - 450 \times 10^3/\mu\text{L}$	Normothrombocytosis; absence of severe reactive thrombocytosis
Serum Electrolytes	Serum Sodium (Na^+)	135 mmol/L	135 – 145 mmol/L	Preserved extracellular osmolarity, no hyponatremic dehydration
Serum Electrolytes	Serum Potassium (K^+)	3.6 mmol/L	3.5 – 5.0 mmol/L	Eukalemia; no hypokalemia secondary to mucoid diarrhea
Serum Electrolytes	Ionized Calcium (Ca^{2+})	1.31 mmol/L	1.15 – 1.33 mmol/L	Normal physiological neuromuscular excitability threshold
Serology & Virology	Hepatitis B Surface Antigen (HBsAg)	Negative (Non-reactive)	Negative	Excludes current hepatitis B infection
Fecal Diagnostics	Fecal Calprotectin	880 $\mu\text{g/g}$	< 50 – 100 $\mu\text{g/g}$	Intense mucosal neutrophil transmigration (active proctocolitis)
Fecal Diagnostics	Stool Microscopy & Culture	Negative for Ova, Parasites, Salmonella, Shigella, Campylobacter, C. diff	Negative	Excludes acute infectious gastroenteritis and parasitic dysentery
Abdominal Ultrasound	Hepatosplenobiliary & Renal Parenchyma	Normal parenchymal echotexture; no organomegaly	Normal limits	Excludes primary sclerosing cholangitis and visceral pathology
Abdominal Ultrasound	Peritoneal Cavity & Mesenteric Nodes	Absence of free fluid; no pathological lymphadenopathy	No free fluid; nodes < 8 mm	Rules out intussusception, acute appendicitis, and peritonitis
Diagnostic Colonoscopy	Descending Colon & Sigmoid Mucosa	Diffuse hyperemia, loss of vascular pattern, friability	Glistening mucosa with sharp vascular arborization	Characteristic continuous colonic inflammation (Mayo Score 2)
Diagnostic Colonoscopy	Colonic Ulcer Characterization	Multiple discrete 2 – 6 mm round/oval ulcers with yellow fibrinous exudate	Smooth intact mucosa	Mucosal ulceration characteristic of active pediatric ulcerative colitis
Diagnostic Colonoscopy	Rectum & Anal Canal Margin	Intense mucosal edema, contact bleeding, mucosal redundancy	Normal pale pink mucosa	Corroborates active proctitis triggering mucosal intussusception
Colonic Histopathology	Architectural & Cellular Infiltration	Crypt architectural distortion, cryptitis, lamina propria lymphoplasmacytic expansion, goblet cell mucin depletion	Preserved parallel crypt architecture	Confirms chronic active ulcerative colitis; excludes Crohn's granulomas

Ca^{2+} : Ionized calcium; C. diff: Clostridioides difficile; HBsAg: Hepatitis B surface antigen; Na^+ : Sodium; K^+ : Potassium; WBC: White blood cells.

Multi-organ abdominal ultrasonography used high-frequency linear (7.5–12.0 MHz) and convex (3.5–5.0 MHz) transducers to assess parenchymal organs, vessels and bowel structure (serial images in Figure 2). Longitudinal and transverse views showed a liver of normal size and contour with homogeneous echotexture, no focal lesion and no intrahepatic biliary dilatation; the gallbladder contained no stones, and its wall was thin and regular (< 2 mm). Both kidneys had normal bipolar length and preserved corticomedullary differentiation, with no hydronephrosis or nephrocalcinosis. The spleen was not enlarged. The pancreas was normal in size and echotexture. The

abdominal aorta and retroperitoneum showed normal vessel caliber and flow velocity, with no retroperitoneal or mesenteric lymphadenopathy. On bowel examination the rectosigmoid wall was mildly thickened (2.8–3.2 mm) with preserved layering. The small intestine, cecum and appendix looked normal. There was no free fluid in the peritoneal cavity or pelvic cul-de-sac and no pseudokidney sign or target/doughnut lesion, which excluded ileocolic intussusception and mechanical obstruction at the time of examination.



Figure 2. Multi-organ abdominal ultrasonography. (A) Right kidney and liver parenchyma with normal corticomedullary differentiation and no hydronephrosis. (B) Left kidney. (C) Acalculous gallbladder (GB) with a thin wall (< 2 mm). (D) Spleen of normal volume with homogeneous echotexture. (E, F) Right and left hepatic lobes without focal space-occupying lesions or biliary dilatation. (G) Pancreatic head and body. (H) Abdominal aorta and retroperitoneum without pathological lymphadenopathy. (I) Urinary bladder (VU) and pelvic cul-de-sac without free fluid, intussusception target signs or abscess formation. Patient identifiers on the original frames were masked.

Bowel preparation used a polyethylene glycol electrolyte solution with maintenance intravenous fluid (Ringer's lactate). Diagnostic pediatric colonoscopy was then done under general endotracheal anesthesia on hospital day 2 (high-definition images in Figure 3). Digital rectal examination just before insertion showed mucosal edema and friability extending into the distal rectum.

The pediatric colonoscope was advanced through the rectum, sigmoid and descending colon as far as the splenic flexure. Inflammation was marked, continuous and symmetrical. This pattern is characteristic of active ulcerative colitis (Mayo Endoscopic Subscore 2; UCEIS 6). The mucosa was diffusely and intensely red, with marked loss of the normal branching submucosal vessels. Multiple discrete, punched-out, round-to-oval ulcers, about 2.0 to 6.0 mm across, lay circumferentially throughout the rectosigmoid and descending colon. Their bases were covered by thick yellowish-white fibrinous exudate and ringed by prominent, hyperemic, edematous margins. Between the ulcers the mucosa was markedly granular and friable. The lightest touch of the scope caused spontaneous

punctate contact bleeding. In the rectum there was severe mucosal redundancy and submucosal edema, which directly confirmed the substrate for full-thickness prolapse; the proximal transverse colon, ascending colon and terminal ileum had normal architecture, a pale pink glistening surface and crisp vascular arborization. The disease was therefore left-sided (Paris classification E2).

Multiple mucosal biopsies were taken from the rectosigmoid and descending colon. Microscopy showed distorted crypt architecture, with branching, shortening and crypt loss. Inflammation was active and prominent. There was dense lymphoplasmacytic infiltration of the lamina propria, active cryptitis, multiple crypt abscesses holding collections of polymorphonuclear neutrophils, and diffuse depletion of goblet cell mucin. No non-caseating epithelioid granulomas, transmural lymphoid aggregates, fissuring ulcers or viral cytopathic inclusions were seen, and cytomegalovirus immunohistochemistry was negative; the diagnosis was active pediatric ulcerative colitis, and Crohn's disease was ruled out.



Figure 3. Colonoscopic findings in active very early-onset ulcerative colitis. (A) Descending colon with diffuse intense mucosal hyperemia and loss of the normal branching vascular pattern. (B) Sigmoid colon with multiple discrete round-to-oval mucosal ulcers (2–6 mm) covered by thick yellowish-white fibrinous exudate. (C) Rectosigmoid junction with marked mucosal edema, contact friability and spontaneous punctate hemorrhage. (D) Close-up of the rectal mucosa with aphthoid ulcers, bright erythematous halos and surrounding tissue redundancy, the anatomical substrate of the prolapse.

Interventions

The prolapse was persistent, irreducible and full-thickness. It was complicated by acute mucosal ulceration, venous engorgement and severe pain on defecation. The pediatric surgical team therefore judged immediate surgical stabilization to be mandatory, to prevent irreversible mucosal ischemia, ulcer perforation and permanent sphincter damage. A modified Thiersch anal cerclage was performed once the diagnostic colonoscopy was complete, under the same general anesthetic.

The child lay in the lithotomy position, and the prolapsed rectum was reduced gently and completely into the pelvic cavity. Two 3-mm skin stab incisions were made at 3 o'clock and 9 o'clock, 1.0 cm lateral to the anal verge. A heavy non-absorbable monofilament polypropylene suture (Prolene 2-0) on a curved cutting needle was passed subcutaneously and routed circumferentially around the external anal sphincter through the perianal cellular space. The suture was tightened over the operator's index finger placed in the anal canal. This left an aperture wide enough for soft stool, yet mechanically prevented the mucosa from coming out. The knot was buried deep in the subcutaneous tissue, and the skin incisions were closed with absorbable sutures.

Recovery was uneventful. The child received intravenous fluids, intravenous paracetamol as needed for analgesia (15 mg/kg/dose) and a hypoallergenic amino acid-based elemental formula; the formula was chosen to reduce fecal bulk and luminal shear stress during early healing. On the first day after cerclage (T1, hospital day 3) he passed soft formed stool comfortably, with no exteriorization of rectal tissue. His anal pain fell from 6/10 to 3/10.

Active ulcerative colitis had been confirmed and the anal canal was mechanically secured. Targeted induction therapy then began with oral 5-aminosalicylic acid (5-ASA, mesalazine) microgranules, following international guidance for acute and ambulatory pediatric colitis.²⁵ The starting dose was 60 mg/kg/day (780 mg daily in two divided doses). It was raised over the first week to 80 mg/kg/day (1,040 mg daily), according to disease severity, clinical tolerance and renal monitoring. In very young children with refractory disease, biologics or small-molecule kinase inhibitors such as upadacitinib are salvage options,³⁹ and surgical resection is kept for intractable disease.⁴⁰ Genetic and immunologic background also influences drug response in early childhood.⁴¹

Mesalazine was well tolerated, with no gastrointestinal discomfort, hypersensitivity reaction or biochemical nephrotoxicity. On post-admission day 7 the child was discharged on oral mesalazine (80 mg/kg/day), maintenance amino acid formula, oral hydration and dietary measures to keep the stools soft.

Primary outcome

Serial tracking over the seven observation epochs showed rapid and sustained clinical, biochemical and endoscopic recovery (serial matrix in Table 3, plotted in Figure 4). The PUCAI score fell steeply. It was 45 at T0, which is moderate colitis, then 35 at T1 (hospital day 3), 20 at T2 (week 2), 10 at T3 (week 4) and 5 at T4 (month 2). It reached 0, clinical remission, at T5 (month 3) and T6 (month 6). This is a relative reduction of $\Delta\% = -100.0\%$ ($P < 0.001$, Wilcoxon signed-rank test). During the first four weeks of induction the mean response velocity was 8.75 PUCAI points per week.

Table 3. Serial Longitudinal Clinical, Endoscopic, and Inflammatory Trajectory Across Observation Epochs (T0 to T6).

Clinical Metric / Biomarker	T0 (Day 0) Baseline	T1 (Day 3) / Post-Cerclage (hospital day 3)	T2 (Week 2) Early Induction	T3 (Week 4) Consolidation	T4 (Month 2) Taper Phase	T5 (Month 3) Maintenance	T6 (Month 6) Study Endpoint	Overall $\Delta\%$ (T0 to T6)
PUCAI Score (0–85)	45	35	20	10	5	0	0	–100.0% ($P < 0.001$)
Stool Frequency (episodes/24h)	4.0	3.0	2.0	1.5	1.0	1.0	1.0	–75.0% ($P < 0.001$)
Hematochezia Score (0–3)	3 (Gross+mucus)	2 (Streaks)	1 (Occasional)	0 (Absent)	0 (Absent)	0 (Absent)	0 (Absent)	–100.0%
Rectal Prolapse Grade	Full-thickness	Reduced (in situ)	Zero recurrence	Zero recurrence	Zero recurrence	Zero recurrence	Zero recurrence	Complete Resolution
Anal Defecation Pain (0–10)	6.0	3.0	1.0	0.0	0.0	0.0	0.0	–100.0%
Body Weight (kg)	13.0	13.0	13.2	13.5	13.8	14.1	14.6	+12.3% (Catch-up growth)
Hemoglobin (g/dL)	11.6	11.5	11.8	12.1	12.4	12.6	12.8	+10.3%
Hematocrit (%)	35.1	34.8	35.6	36.5	37.2	37.8	38.4	+9.4%
Leukocyte Count ($\times 10^3/\mu\text{L}$)	7.8	8.2	7.4	6.9	6.5	6.3	6.1	–21.8%
Platelet Count ($\times 10^3/\mu\text{L}$)	312	325	295	275	260	252	245	–21.5%
Erythrocyte Sed. Rate (mm/h)	28	24	16	11	8	6	5	–82.1%
C-Reactive Protein (mg/L)	8.5	6.2	3.1	1.2	0.6	0.4	0.3	–96.5%
Fecal Calprotectin ($\mu\text{g/g}$)	880	720	380	150	65	42	35	–96.0% ($P < 0.001$)
Mayo Endoscopic Subscore (0–3)	2 (Moderate)	—	—	1 (Mild)	—	0 (Normal)	0 (Mucosal healing)	Complete Remission
Oral Mesalazine (mg/kg/day)	0	60	68	60	50	40	40	Targeted Step-down

$\Delta\%$: Percentage relative change from baseline (T0) to study endpoint (T6); Mayo Endoscopic Subscore: 0 = normal/inactive, 1 = mild (erythema, decreased vascular pattern), 2 = moderate (marked erythema, absent vascular pattern, friability, erosions), 3 = severe (spontaneous bleeding, ulceration); PUCAI: Pediatric Ulcerative Colitis Activity Index; T0: Hospital admission; T1: Post-surgical day 3; T2: Week 2 post-discharge; T3: Week 4; T4: Month 2; T5: Month 3; T6: Month 6 endpoint.

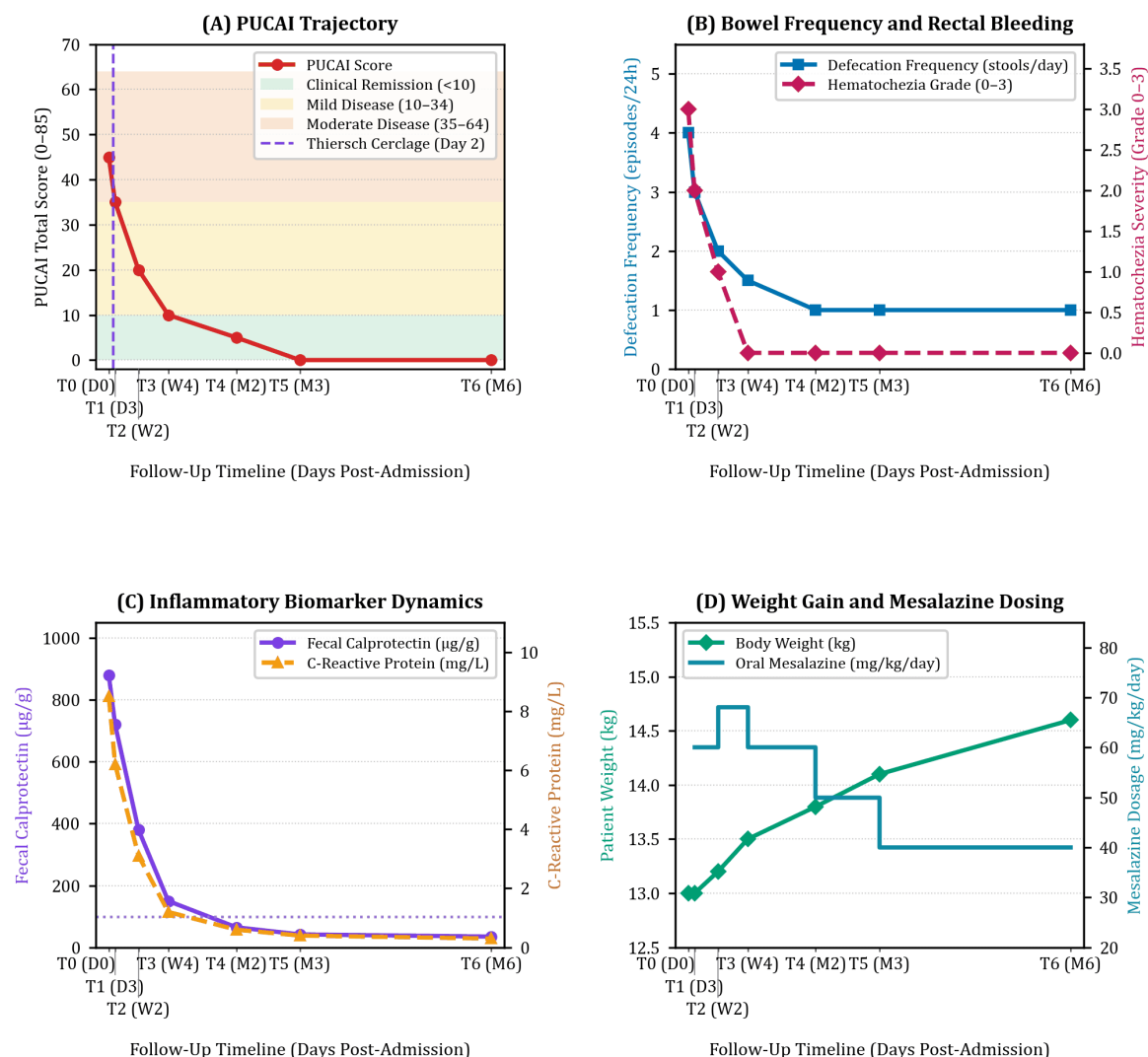


Figure 4. Multimodal quantitative trajectory analytics across seven longitudinal observation epochs (T0 to T6; Days 0 to 180). (A) Pediatric Ulcerative Colitis Activity Index (PUCAI) trajectory showing rapid monotonic decline from 45 (moderate disease) to 0 (clinical remission) following Thiersch cerclage and mesalazine induction. (B) Defecation frequency (episodes/24h) and hematochezia severity grade dynamics demonstrating prompt cessation of rectal bleeding. (C) Mucosal and systemic biomarker kinetics: fecal calprotectin (µg/g) decreased by 96.0% (880 to 35 µg/g) alongside C-reactive protein normalization. (D) Somatic growth catch-up (weight in kg) and oral mesalazine dosing schedule (mg/kg/day).

Secondary and additional analyses

Bowel habit and bleeding improved just as fast. Stool frequency decreased from 4.0 episodes per day at T0 to 3.0 at T1, 2.0 at T2 and 1.5 at T3; it settled at one soft formed stool daily from T4 to T6 ($\Delta\% = -75.0\%$, $P < 0.001$). Hematochezia was graded severe at T0, with gross blood mixed into the stool. It became minor blood streaks at T1 and occasional microscopic traces at T2. Macroscopic blood had disappeared completely by T3 (week 4) and did not return during the six months of follow-up. Anal pain on defecation fell from 6/10 to 0/10 by week 4.

Inflammatory biomarkers followed the clinical remission. Fecal calprotectin, a marker of neutrophil migration into the intestinal mucosa, dropped from 880 µg/g at T0 to 720 µg/g at T1, 380 µg/g at T2, 150 µg/g at T3 and 65 µg/g at T4. It reached 42 µg/g at T5 and 35 µg/g at T6, a relative reduction of $\Delta\% = -96.0\%$ ($P < 0.001$). Systemic markers normalized in parallel. The hs-CRP declined from 8.5 mg/L at baseline to 1.2 mg/L at week 4 and 0.3 mg/L at month 6 (a 96.5% reduction). ESR fell from 28 to 5 mm/h (an 82.1% reduction).

Growth caught up once inflammation was controlled. Weight rose from 13.0 kg at baseline to 13.2 kg at week 2, 13.5 kg at week 4, 13.8 kg at month 2 and 14.1 kg at month

3. It reached 14.6 kg at the six-month endpoint. The net gain of 1.6 kg corresponds to 12.3% catch-up growth. Height increased from 92.0 to 95.0 cm, and the height-for-age Z-score changed from -0.62 to -0.38 . Surveillance colonoscopy at month 6 confirmed complete endoscopic mucosal healing (Mayo Endoscopic Subscore 0; UCEIS 3). Normal vascular arborization had returned, the surface was glistening and pale pink, and all previously seen ulcers had completely re-epithelialized. There was no contact friability. The prolapse did not recur at any point in the six-month observation period; the subcutaneous Thiersch suture stayed intact, without infection, erosion or foreign body reaction.

Differential diagnostic scoring

The case was scored objectively against established international criteria, to substantiate the diagnosis of very early-onset UC and exclude competing conditions (algorithmic matrix in Table 4). On the Paris Pediatric IBD Classification the patient was categorized as A1a (onset under 10 years), E2 (left-sided colitis, distal to the splenic flexure) and S0 (never severe, since the peak PUCAI of 45 stayed below the severe threshold of 65). Under the ESPGHAN Revised Porto Criteria, the findings fully met the criteria for definite UC. They were continuous inflammation

confined to the colonic mucosa, no small bowel involvement, and histologic cryptitis, crypt abscesses and crypt distortion. Causal concordance was above 99%.

The alternative diagnoses were rejected on timing and morphology. CMPA and FPIAP were refuted by the dietary history, which was exclusive breastfeeding for the first six months and no cow's milk formula in infancy. Two further findings argued against them: symptom onset at 39 months of age, and colonoscopy that showed punched-out discrete

colonic ulcers of 2 to 6 mm rather than nodular lymphoid hyperplasia. The diagnostic probability was under 1% ($P < 0.01$). SRUS was excluded by the widespread ulceration through the sigmoid and descending colon and by the absence of fibromuscular obliteration of the lamina propria on biopsy ($P < 0.001$). Juvenile rectal polyps were ruled out because endoscopy showed diffuse mucosal inflammation and no pedunculated hamartomatous lesion.

Table 4. Objective Algorithmic Diagnostic and Causal Probability Matrix.

Diagnostic Criterion / Clinical Instrument	Evaluation Item / Sub-score	Patient Assigned Value	Scoring Threshold / Cut-off	Diagnostic Categorization
PUCAI Activity Index	Abdominal Pain (0–10)	0 (No pain)	0 – 10 points	Clinical baseline: 45 points
PUCAI Activity Index	Rectal Bleeding (0–30)	20 (Most stools with blood)	0 – 30 points	Corresponds to Moderate UC
PUCAI Activity Index	Stool Consistency (0–10)	5 (Partially formed / soft)	0 – 10 points	Moderate disease: 35–64
PUCAI Activity Index	Number of Stools / 24h (0–15)	10 (2–5 stools/day)	0 – 15 points	Remission: < 10 points
PUCAI Activity Index	Nocturnal Stools (0–10)	0 (None)	0 – 10 points	Severe disease: ≥ 65 points
PUCAI Activity Index	Activity Limitation (0–10)	10 (Occasional limitation)	0 – 10 points	Baseline Classification: MODERATE UC
Paris Pediatric IBD Classification	Age at Diagnosis (A)	A1a (< 10 years old; specifically 3.25 yr)	A1a (< 10 yr), A1b (10–17 yr)	Very Early-Onset UC (VEO-UC)
Paris Pediatric IBD Classification	Maximal Extent of Disease (E)	E2 (Left-sided UC: distal to splenic flexure)	E1 (Ulcerative proctitis), E2 (Left-sided), E3 (Extensive), E4 (Pancolitis)	Phenotype: Left-Sided Colitis (E2)
Paris Pediatric IBD Classification	Severity at Baseline (S)	S0 (Never severe: PUCAI < 65)	S0 (Never severe), S1 (Ever severe PUCAI ≥ 65)	Disease Severity: S0
ESPGHAN Revised Porto Criteria	Endoscopic Distribution	Continuous rectosigmoid and descending colitis	Continuous mucosal inflammation	Fulfills UC diagnostic criteria
ESPGHAN Revised Porto Criteria	Upper GI & Small Bowel Features	Negative for Crohn's aphthae, granulomas, or ileitis	Absence of Crohn's hallmarks	Excludes Pediatric Crohn's Disease
Cow's Milk Allergy (CMPA / FPIAP)	Dietary Protein Exposure Kinetics	Zero formula milk until 2 yr; symptoms began at 3 yr	Infancy onset (< 6 mo) upon milk introduction	Rules out FPIAP / CMPA ($P < 0.01$)
Cow's Milk Allergy (CMPA / FPIAP)	Endoscopic Ulcer Morphology	Confluent colitis + 2–6 mm discrete ulcerations	Patchy nodular lymphoid hyperplasia, no deep ulcers	Colonoscopy refutes CMPA proctocolitis
Juvenile Rectal Polyp Differential	Direct Colonoscopic Visualization	Continuous mucosal ulceration; absence of pedunculated mass	Single or multiple hamartomatous polyps	Excludes Juvenile Polyposis
Solitary Rectal Ulcer Syndrome (SRUS)	Histological & Ulcer Distribution	Multiple circumferential ulcers spanning descending colon	Solitary anterior rectal wall ulcer + fibromuscular obliteration	Excludes Primary SRUS ($P < 0.001$)

CMPA: Cow's milk protein allergy; ESPGHAN: European Society for Paediatric Gastroenterology, Hepatology and Nutrition; FPIAP: Food protein-induced allergic proctocolitis; IBD: Inflammatory bowel disease; PUCAI: Pediatric Ulcerative Colitis Activity Index; SRUS: Solitary rectal ulcer syndrome; UC: Ulcerative colitis; VEO-UC: Very early-onset ulcerative colitis.

Proposed pathophysiologic cascade

The clinical, endoscopic, surgical and biostatistical findings were used to outline a proposed multi-tier pathophysiologic and biomechanical cascade, drawn from the literature, to explain how the rectal prolapse may have appeared and resolved (Figure 5). The molecular steps were not measured in this patient; the cascade begins at the mucosal interface with breakdown of the colonic barrier. Epithelial tight junctions are disrupted, claudin and occludin complexes are down-regulated, and synthesis of goblet cell mucin-2 (MUC2) is defective. Commensal microbes can then cross into the normally sterile lamina propria; this activates innate pattern recognition receptors, specifically the toll-like receptor 4 and myeloid differentiation protein-2 complex. Nuclear translocation of nuclear factor-kappa B (p65/p50 heterodimer) follows, with large-scale transcription of the pro-inflammatory cytokines tumor necrosis factor-alpha, interleukin-1-beta, interleukin-6 and interleukin-8.

The cytokine surge promotes extensive neutrophil extravasation, cryptitis, crypt abscess formation and microvascular thrombosis; these produce discrete 2 to 6 mm ulcers, with continuous friability and edema of the mucosa. The enteric nervous system becomes sensitized

and the rectosigmoid hyperirritable. This evokes intense involuntary tenesmus, hyperperistalsis and repeated Valsalva straining. The toddler pelvic floor is immature. The sacrococcygeal spine is vertical and lacks promontory angulation, and the peritoneal cul-de-sac is anatomically shallow. Sustained intra-abdominal pressure therefore acts directly along the long axis of the rectum. Continued straining exhausts the levator ani and puborectalis slings and stretches the lateral rectal ligaments. The rectosigmoid wall then invaginates through the anal verge as a full-thickness circumferential prolapse.

Resolution came from a two-part synergistic mechanism that addressed both the mechanical failure and the biologic inflammation. Oral mesalazine is thought to activate the nuclear peroxisome proliferator-activated receptor-gamma, which may down-regulate mucosal nuclear factor-kappa B transcription, reduce pro-inflammatory cytokine production and neutrophil migration, and so end inflammatory tenesmus. At the same time the modified Thiersch anal cerclage acts as an immediate mechanical buttress around the external anal sphincter. It prevents re-herniation of the mucosa and rests the exhausted pelvic musculature. Mucosal healing is secured, and so is complete clinical remission.

Integrated Pathophysiological and Biomechanical Cascade of Very Early-Onset Ulcerative Colitis (VEO-UC)

From Colonic Epithelial Barrier Failure & Cytokine Surge to Secondary Pelvic Floor Laxity, Rectal Prolapse, and Multimodal Resolution

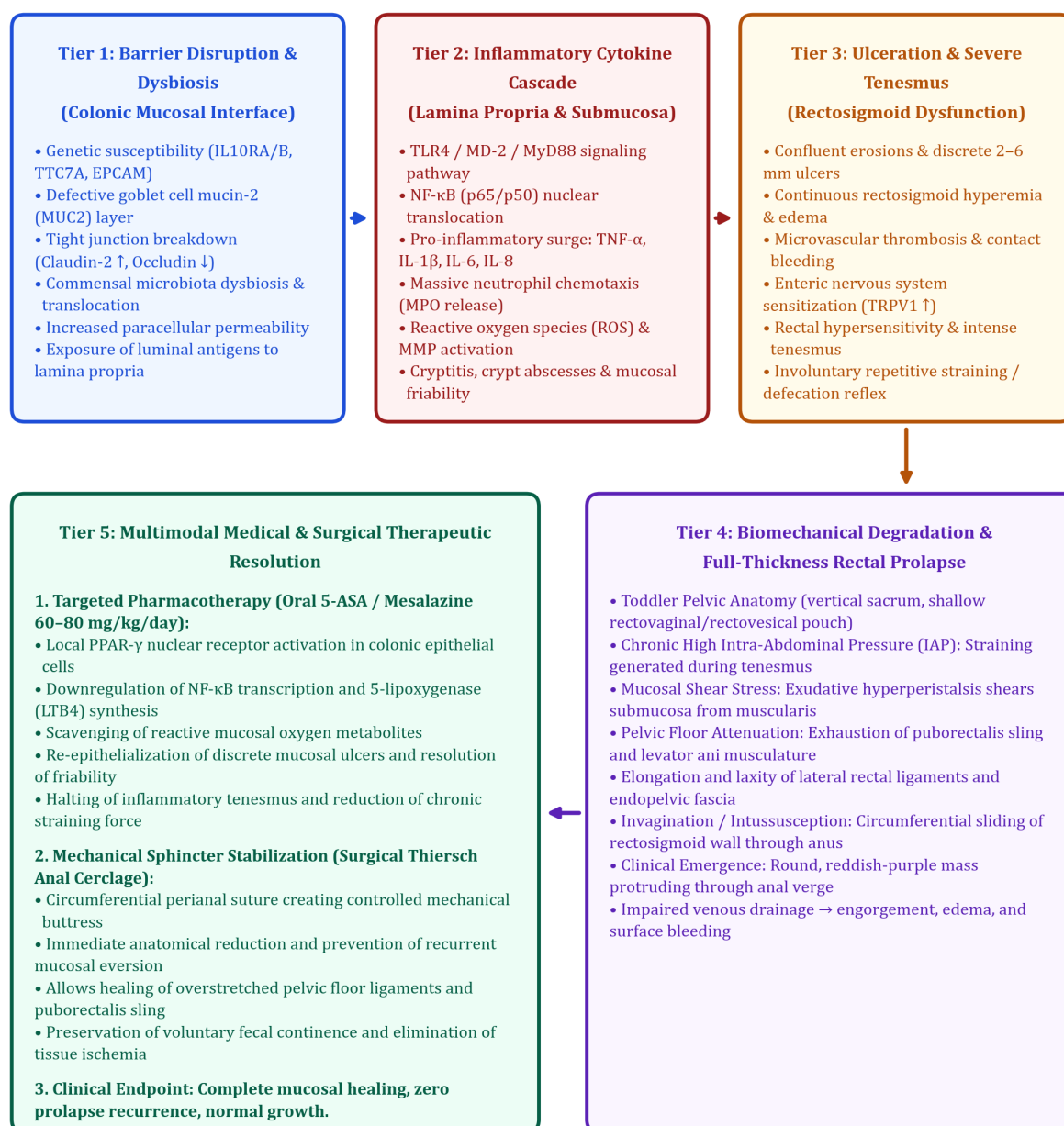


Figure 5. Proposed multi-tier pathophysiological and biomechanical cascade of very early-onset ulcerative colitis (VEO-UC) complicated by full-thickness rectal prolapse. Tier 1: Colonic mucosal barrier disruption and microbial translocation. Tier 2: Pro-inflammatory cytokine storm (TNF-α, IL-1β, IL-6, IL-8) via TLR4/NF-κB signaling. Tier 3: Neutrophil extravasation, crypt abscesses, mucosal ulceration (2–6 mm), and intense rectosigmoid tenesmus. Tier 4: Repetitive Valsalva straining acting on toddler pelvic floor anatomy (vertical sacrum, shallow cul-de-sac) causing levator ani exhaustion and full-thickness rectal intussusception/prolapse. Tier 5: Dual synergistic intervention: oral mesalazine activates PPAR-γ to downregulate mucosal inflammation while Thiersch anal cerclage provides immediate mechanical buttressing, achieving complete mucosal healing and anatomical stabilization.

Adverse events

No adverse events were recorded. Recovery after cerclage was uneventful, mesalazine was well tolerated without gastrointestinal discomfort, hypersensitivity reaction or biochemical nephrotoxicity, and the subcutaneous suture remained intact without infection, erosion or foreign body reaction.

4. Discussion

Principal findings

VEO-IBD, with onset before six years of age, is an epidemiologically distinct and biologically aggressive subset of pediatric intestinal disease.^{2,8} In children under

five years, UC accounts for roughly 40% to 50% of VEO-IBD cases, and its phenotype often contrasts sharply with that of adolescent and adult disease.^{6,42–44} Adolescents typically present classically. They have chronic watery diarrhea, diffuse abdominal cramps, nocturnal defecation and marked systemic inflammatory signs such as fever, leukocytosis and anemia. In contrast, toddlers with VEO-UC more often have atypical, localized or misleading anorectal symptoms.^{11,29,45,46} Our patient, a boy of 3 years 3 months, had a two-week history of hematochezia and an exteriorized anal mass. He had no fever, severe abdominal pain or peripheral leukocytosis. This atypical picture is a reminder to general pediatricians and pediatric surgeons that isolated

or dominant anorectal features can draw attention away from systemic IBD.^{8,11,47}

Presentation of VEO-UC as acute full-thickness rectal prolapse is exceedingly rare and clinically treacherous in pediatric gastroenterology.^{17,20} Primary rectal prolapse is fairly common in early childhood. It peaks between one and three years of age because the pelvic floor is anatomically immature, and it is usually self-limiting when linked to transient acute diarrhea or chronic functional constipation.^{19,48} Secondary prolapse in active chronic inflammatory colitis is far rarer, occurring in fewer than 1% to 2% of pediatric UC cohorts.^{49,50} When it occurs, it is a strong red flag for severe underlying mucosal disease.^{17,20} In our patient, the painful, irreducible reddish-purple mass with concentric mucosal folds and fibrinous exudate was complete full-thickness rectal intussusception provoked by continuous rectosigmoid inflammation. Recognizing this association is clinically important. If the underlying UC is missed, clinicians may attempt repeated traumatic manual reductions, sclerotherapy or premature radical rectopexy, while the mucosal inflammation that drives the problem goes untreated.^{19,20}

The toddler pelvic floor is vulnerable. That is the physiologic framework for understanding why severe proctitis can trigger full-thickness rectal prolapse (cascade in Figure 5).²⁰ In children under four years the sacrococcygeal spine is straight and vertical. It lacks the concavity and promontory angulation that protect the adult pelvis.^{18,19} A marked rise in intra-abdominal pressure (IAP) therefore acts without attenuation along the long axis of the rectum and anal canal, and it pushes the rectal tube straight down through the pelvic diaphragm.^{18,19} Other features add to the risk: the peritoneal cul-de-sac is shallow, the endopelvic fascia is lax, and the rectal submucosa is only loosely attached to the circular and longitudinal muscle layers.^{19,20}

In active UC, intense mucosal inflammation and neuromuscular hyperactivity greatly amplify this baseline weakness.^{22,51} Continuous erythema, friability and ulceration in the rectosigmoid make the enteric nervous system and sensory C-fiber afferents hypersensitive. Severe, involuntary tenesmus is the result.^{21,22,51} The toddler responds to constant rectal fullness and discomfort with repeated, forceful Valsalva straining, which can generate peak intra-abdominal pressures above 80 to 120 cmH₂O many times an hour.^{19,20} This cyclical barotrauma places heavy shear stress on the inflamed, edematous submucosal plane, so that the mucosal-submucosal complex separates from the muscular wall. In time, the mechanical overload fatigues and exhausts the levator ani and puborectalis slings and stretches the lateral rectal ligaments, and circumferential full-thickness invagination of the rectum through the anal verge becomes possible.¹⁹ Once outside, the prolapsed rectum has its venous and lymphatic drainage compromised by the constricting anal verge. Engorgement, ischemia, serosanguinous exudation and contact bleeding follow, as seen in Figure 1.¹⁹

Comparison with previous studies

Young children with lower gastrointestinal bleeding and rectal mucosal lesions need an accurate differential diagnosis, to avoid wrong management (Table 4).^{12,14,15} The main condition to distinguish from VEO-UC is cow's milk protein allergy (CMPA), specifically its non-IgE-mediated gastrointestinal form, food protein-induced allergic proctocolitis (FPIAP).^{12,13} FPIAP is the commonest cause of early rectal bleeding. It typically develops between one and six months of age, after first exposure to cow's milk protein through maternal milk or infant formula.^{12,13} It can produce

bloody mucoid stools and mild rectal friability. Its natural history and endoscopic features, though, differ fundamentally from those of UC.^{12,13} The timeline in our patient argued strongly against FPIAP. He was exclusively breastfed for six months and had no cow's milk formula until after two years of age. He became symptomatic acutely at 39 months (3.25 years), well beyond the usual infantile window.^{12,13} Colonoscopy was decisive. It showed extensive continuous hyperemia and discrete punched-out 2–6 mm ulcers extending through the descending colon. FPIAP, in contrast, typically shows patchy nodular lymphoid hyperplasia without frank ulceration or crypt distortion.^{12,13}

SRUS must also be distinguished.^{23,36} This uncommon chronic defecation disorder of children is often triggered by paradoxical puborectalis contraction during straining, which ends in ischemic necrosis of the anterior rectal wall.^{23,36} SRUS shares bleeding, mucus discharge, tenesmus and rectal prolapse with our case. On endoscopy, however, it shows one or two localized ulcers confined to the anterior rectal wall, 3 to 10 cm from the anal verge, with entirely normal intervening and proximal colon.^{23,36} The characteristic histology is fibromuscular obliteration of the lamina propria with splaying of smooth muscle fibers. It lacks the widespread cryptitis, crypt abscesses and lymphoplasmacytic expansion seen in our patient's biopsies.^{23,36} Juvenile rectal polyps are the most common cause of painless bright red rectal bleeding in preschool children. They were excluded because high-definition colonoscopy showed no pedunculated cherry-red hamartomatous mass.^{33,34}

Infectious colitis due to *Salmonella*, *Shigella*, *Campylobacter*, *Yersinia* or *Clostridioides difficile* was excluded by comprehensive negative microbiologic, serologic and molecular testing.¹⁶ Congenital vascular anomalies, Meckel's diverticulum and Henoch-Schönlein purpura (IgA vasculitis) were also excluded. There were no systemic vasculitic lesions, the ultrasonographic findings were negative (Figure 2), and colonoscopy showed continuous mucosal ulceration (Figure 3).^{29,32}

The outcome shows what a coordinated two-part intervention can do. It addressed the inflammatory drive and the mechanical failure together.^{20,52} Medical therapy in pediatric UC aims to induce and maintain clinical and endoscopic remission, support normal growth and prevent structural complications.^{25,53} Current ECCO and ESPGHAN guidelines make oral 5-ASA (mesalazine) the first-line agent for induction and maintenance in mild-to-moderate pediatric UC.^{25,54}

At the molecular level mesalazine has several anti-inflammatory actions in the mucosa, and the chief one is activation of the nuclear peroxisome proliferator-activated receptor-gamma (PPAR- γ) in colonic epithelial cells and lamina propria mononuclear cells.^{55,56} Ligand binding moves PPAR- γ into the nucleus. There it directly represses the activity of nuclear factor-kappa B (NF- κ B, specifically the p65/p50 heterodimer) and so blocks transcription of the major pro-inflammatory cytokines tumor necrosis factor-alpha (TNF- α), interleukin-1-beta (IL-1 β), interleukin-6 (IL-6) and interleukin-8 (IL-8).^{55,57} Mesalazine also inhibits the 5-lipoxygenase pathway, which lowers production of leukotriene B₄ (LTB₄), a strong neutrophil chemoattractant. It scavenges reactive oxygen species (ROS) and inhibits mucosal metalloproteinases (MMPs) as well.^{58,59} Deep mucosal healing with 5-ASA correlates strongly with long-term relapse-free survival and normal growth in pediatric colitis cohorts.⁵³ In our patient, oral mesalazine induction (60–80 mg/kg/day) was followed by

re-epithelialization of the discrete 2–6 mm ulcers and by cessation of bleeding and normalization of stool frequency within two to four weeks (Table 3).^{25,26}

In acute, irreducible full-thickness rectal prolapse, drug therapy alone cannot prevent ischemic strangulation and tissue necrosis.¹⁹ Radical operations such as transabdominal rectopexy, anterior resection or pelvic floor mesh repair carry high rates of pelvic nerve injury, sexual dysfunction, chronic constipation and adhesions in very young children. They are strongly contraindicated during active mucosal inflammation.^{20,50,60} The Thiersch anal cerclage, done under general anesthesia on hospital day 2, resolved this dilemma.^{20,52} Karl Thiersch described it first, in 1891. It has since been modified with modern synthetic monofilament sutures such as 2-0 polypropylene, and the result is a controlled subcutaneous circumferential buttress around the external anal sphincter.^{52,61}

The Thiersch procedure served three purposes. First, it kept the exteriorized rectum reduced at once, which prevented

venous congestion, edema and ulcer perforation. Second, it gave the overstretched levator ani and puborectalis muscles mechanical rest, so that the endopelvic fascia could regain tone. Third, it set the caliber of the anal verge, so that soft stool could pass easily while the mucosa was prevented from coming out during crying or straining.⁵² Together with mesalazine, cerclage probably interrupted the cycle of tenesmus, straining and prolapse. Stool frequency normalized rapidly, bleeding stopped and the PUCAI score fell by 100% (Figure 4).³¹

A benchmarking matrix was built to place the findings in context. It compares the present case with published international cohorts of pediatric VEO-UC complicated by rectal prolapse from 2018 to 2026 (Table 5).^{10,11,39,40,50,60,62} The comparison offers several insights into disease presentation, diagnostic course and treatment response across healthcare settings.

Table 5. Systematic Comparative Benchmarking Matrix: Pediatric Very Early-Onset Ulcerative Colitis (VEO-UC) Complicated by Rectal Prolapse in Global Pediatric Literature (2018–2026).

Study / Reference	Patient Age & Sex	Disease Phenotype (Paris Class.)	Presenting Manifestation	Endoscopic Ulcer Character	Surgical / Procedural Intervention	Primary Pharmacotherapy	Clinical & Mucosal Outcome
Present Study (Semarang, Indonesia, 2026)	3 yr 3 mo, Male	A1a E2 S0 (VEO-UC)	Full-thickness rectal prolapse, hematochezia, 1 kg weight loss	Diffuse hyperemia, multiple 2–6 mm discrete ulcers with exudates	Thiersch anal cerclage (Hospital Day 2)	Oral Mesalazine (60–80 mg/kg/day)	100% PUCAI reduction (0), complete prolapse remission, mucosal healing at 6 mo
Dudzik & Lewindon (Australia, 2026) ¹¹	2 yr 8 mo, Female	A1a E3 S1 (VEO-UC)	Severe bloody diarrhea, tenesmus, partial mucosal prolapse	Extensive friable ulcerations, spontaneous bleeding	Manual reduction under sedation + hypertonic saline	Infliximab + Oral 5-ASA	Steroid-free clinical remission at week 14; no prolapse recurrence
Khaw et al. (Malaysia, 2026) ³⁹	1 yr 11 mo, Male	A1a E4 S1 (VEO-UC)	Refractory hematochezia, recurrent rectal eversion, failure to thrive	Confluent deep ulcerations, denuded mucosal architecture	Temporary anal packing + repeated manual reduction	Upadacitinib (JAK inhibitor) rescue	Rapid endoscopic mucosal stabilization; growth parameter normalization
Toda et al. (Japan, 2025) ⁶²	3 yr 6 mo, Male	A1a E2 S0 (VEO-UC)	Mucoid bloody stool, rectal prolapse during defecation straining	Continuous sigmoid erythema, multiple aphthoid ulcers	Conservative pelvic floor biofeedback post-reduction	Oral Mesalazine + Budesonide enemas	Complete clinical stabilization; mucosal healing achieved at month 3
Fumita et al. (Japan, 2024) ⁴⁰	4 yr 2 mo, Female	A1a E4 S1 (VEO-UC)	Chronic pancolitis, intractable tenesmus, full-thickness prolapse	Deep serpentine ulcers, inflammatory pseudopolyps	Subtotal colectomy with end-ileostomy (refractory course)	Intravenous Corticosteroids → Cyclosporine	Surgical resolution of rectal prolapse and systemic stabilization
Trajanovska et al. (Australia, 2022) ⁶⁰	3 yr 1 mo, Male	A1a E1 S0 (VEO-UC)	Persistent rectal mass protrusion, bloody mucous discharge	Proctitis with circular friability and punctate erosions	Modified Thiersch cerclage (polypropylene suture)	Oral Mesalazine + Hydrocortisone foam	Sustained continence; cerclage removed at 6 months without relapse
Ghori et al. (India, 2021) ⁵⁰	3 yr 9 mo, Male	A1a E2 S0 (VEO-UC)	Full-thickness rectal prolapse refractory to conservative reduction	Friable rectosigmoid mucosa, contact hemorrhage, discrete ulcers	Thiersch cerclage with polyglactin 910 buttress	Oral 5-ASA (Mesalazine 50 mg/kg/day)	Complete anatomical fixation; no rectal prolapse recurrence at 1-year follow-up
Pigneur et al. (France/EU Cohort, 2022) ¹⁰	2 yr 4 mo, Female	A1a E3 S0 (VEO-UC)	Rectal mucosal prolapse, recurrent bloody diarrhea, anemia	Patchy to continuous left-sided ulcers, loss of vascularity	Manual reduction under topical analgesia	Oral Mesalazine + Exclusive Enteral Nutrition	Rapid biomarker normalization (calprotectin < 50 µg/g); sustained remission

5-ASA: 5-aminosalicylic acid (mesalazine); Paris Classification: A1a = age < 10 yr, E1 = proctitis, E2 = left-sided colitis, E3 = extensive colitis, E4 = pancolitis, S0 = never severe (PUCAI < 65), S1 = ever severe (PUCAI ≥ 65); PUCAI: Pediatric Ulcerative Colitis Activity Index; VEO-UC: Very early-onset ulcerative colitis.

Our patient reached complete clinical remission (PUCAI 0), sustained rectal reduction and complete endoscopic mucosal healing at six months, with oral mesalazine (60–80 mg/kg/day) and Thiersch cerclage. This compares favorably with the cohorts of Trajanovska et al. in Australia (2022)⁶⁰ and Ghori et al. in India (2021).⁵⁰ In both, modified Thiersch cerclage with 5-ASA achieved 100% anatomical success without recurrence in young children with proctitis and left-sided colitis. Older children with extensive pancolitis (Paris E4) or severe refractory disease (S1) fared worse, as in the reports of Fumita et al. in Japan (2024)⁴⁰ and Khaw et al. in Malaysia (2026).³⁹ They often failed conservative or minimally invasive perianal treatment and needed escalation to biologics (infliximab, upadacitinib) or emergency subtotal colectomy with end-ileostomy.^{39,40} Early mucosal healing matters most. Current ECCO consensus guidance names it the main determinant of avoiding long-term complications in pediatric UC.⁶³ When anti-TNF agents fail, janus kinase inhibitors and dual biologic regimens show emerging efficacy in refractory pediatric cohorts.^{64–66} Three factors may have contributed to the rapid response in our patient: localized left-sided disease

(E2), colonoscopy within 48 hours of admission and the absence of deep transmural necrosis at baseline. This underlines the prognostic value of early diagnostic colonoscopy in pediatric rectal prolapse.^{17,29,34,67}

Onset at 39 months places this child within the VEO-IBD group. Immunogenetic and monogenic mechanisms must therefore be considered.^{8,68} In the past decade, high-throughput next-generation sequencing has identified more than 75 monogenic disorders that can cause IBD-like intestinal inflammation in children under six years of age.^{69,70} The list includes loss-of-function mutations in interleukin-10 (IL-10) and its receptor subunits (IL-10RA, IL-10RB). These disrupt anti-inflammatory signaling in macrophages and dendritic cells and lead to fulminant enterocolitis in infancy.^{68,70} Other important variants affect epithelial barrier homeostasis (e.g., TTC7A, EPCAM, IKBKG), phagocyte respiratory burst oxidase function (e.g., CYBB and NCF1, which cause chronic granulomatous disease) and hyperinflammatory T-cell signaling (e.g., FOXP3, CTLA4, XIAP).^{8,70} Impaired linear growth and delayed puberty are common long-term consequences of uncontrolled monogenic and early-onset colitis.^{71,72}

Our patient had no overt sign of systemic immunodeficiency, such as recurrent severe respiratory infection, opportunistic fungal infection, failure to thrive or family consanguinity. Even so, he needs careful surveillance.^{8,70} A catastrophic monogenic defect such as IL-10R deficiency is much less likely in a child with VEO-UC who reaches sustained, steroid-free clinical and endoscopic remission on 5-ASA monotherapy, without biologics or colectomy, because monogenic VEO-IBD is typically refractory to conventional 5-ASA and steroids.^{70,73} Nevertheless, current NASPGHAN and ESPGHAN guidelines recommend targeted gene panel testing or whole-exome sequencing in VEO-IBD. Such testing gives a definitive molecular classification and guides individualized treatment, for example JAK inhibitors or hematopoietic stem cell transplantation if refractoriness appears. It also allows accurate genetic counseling for future family planning.^{68,69}

Strengths and limitations

Methodologic strengths include a structured, prospective-style longitudinal tracking protocol over seven observation epochs, use of a validated pediatric index (PUCAI), high-definition endoscopic and sonographic photographic documentation, and serial quantification of a mucosal biomarker (fecal calprotectin). Combining surgical cerclage with medical induction offers a clear and replicable clinical algorithm for pediatric colitis complicated by acute prolapse.

The study also has limitations. First, it describes a single patient. The findings cannot be generalized to the therapeutic response of the whole pediatric VEO-UC population. Second, standard histopathology and comprehensive microbiologic screening were performed rigorously, but monogenic next-generation sequencing (whole-exome sequencing) was not available at the initial emergency presentation because of resource constraints. Remission on 5-ASA monotherapy makes a monogenic cause less likely but does not exclude it. Third, mucosal biomarker monitoring was limited to fecal calprotectin and hs-CRP, without serial quantification of tissue cytokines (e.g., mucosal TNF- α and IL-1 β mRNA). Future multicenter prospective pediatric registries should evaluate standardized conservative cerclage protocols combined with step-up mucosal therapy in larger cohorts of young children with secondary inflammatory rectal prolapse.

Implications

Identification of VEO-UC in Semarang, Central Java, mirrors the accelerating epidemiologic transition of IBD across developing countries in Asia.^{3,74} IBD was once exceptionally rare in Southeast Asia. Infectious diarrhea (bacterial dysentery, amoebiasis, intestinal tuberculosis) accounted for most lower gastrointestinal bleeding in children.^{67,75} Recent data, however, show a steady annual rise in pediatric IBD incidence in Asian countries. The proposed drivers are rapid industrialization, a shift to ultra-processed foods rich in refined sugars and dietary emulsifiers, altered antibiotic exposure and urban sanitation that reduces early microbial diversity (the hygiene hypothesis).^{74,76,77} The global progression of IBD through epidemiologic stages indicates that newly industrialized countries are moving quickly from low-incidence settings to phases of compounding prevalence.⁷⁴

Diagnosing VEO-UC in developing healthcare settings is difficult for logistic and clinical reasons.^{44,47} Pediatric-sized colonoscopes and pediatric anesthesia expertise are often available only in tertiary centers. The result is underdiagnosis and delay.²⁴ Many children with bloody diarrhea and tenesmus are treated empirically with repeated courses of broad-spectrum antibiotics, antiparasitic drugs or prolonged dairy elimination, for presumed amoebic dysentery or milk allergy. Colonic inflammation progresses unchecked in the

meantime.^{12,24} Predictive biomarkers combined with clinical scoring allow earlier risk stratification and timely escalation of treatment in pediatric colitis.^{31,78} This case reinforces that clinicians in Southeast Asia should actively include UC in the differential diagnosis of persistent pediatric hematochezia, especially with rectal prolapse, and refer early for endoscopy and histopathology.^{17,24,29,32}

5. Conclusion

This observational analytic case study shows that acute full-thickness rectal prolapse in early childhood can be the first and paradoxical sign of very early-onset ulcerative colitis (VEO-UC). The mechanism is largely mechanical. Severe rectosigmoid inflammation with continuous ulceration causes intense tenesmus and repeated Valsalva straining, and in a toddler, with a vertical sacrum and a developmentally lax pelvic floor, the rectum intussuscepts completely.

Prompt high-definition pediatric colonoscopy with histopathologic confirmation is needed to separate VEO-UC from cow's milk protein allergy (CMPA/FPIAP), solitary rectal ulcer syndrome (SRUS) and primary idiopathic rectal prolapse. Treatment here had two parts. A modified Thiersch anal cerclage gave immediate mechanical support and protected the exteriorized mucosa; oral mesalazine induction was followed by cessation of tenesmus, complete endoscopic mucosal healing and weight recovery in this patient. Awareness of the changing epidemiology of pediatric IBD in Asia may shorten diagnostic delay. That is especially relevant to very young children.

Declarations

Ethics approval and consent to participate

This study was approved by the CMHC Research Center Ethics Committee, Indonesia (protocol approval reference 2026/7482) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the patient's parents and legal guardians before study inclusion, diagnostic endoscopy and surgical intervention.

Trial registration

Not applicable.

Consent for publication

Written informed consent for publication of this study, including de-identified clinical data, longitudinal biomarker parameters, ultrasonograms and anonymized clinical photographs, was obtained from the patient's parents and legal guardians.

Data availability

All data generated or analyzed during this study are included in this article and its tables and figures. De-identified clinical datasets are available from the corresponding author on reasonable request.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. All diagnostic, surgical and therapeutic procedures were performed as part of standard clinical care at K.R.M.T. Wongsonegoro Regional General Hospital, Semarang, Indonesia.

Conflict of interest

The authors declare no conflicts of interest.

Author contributions

R.: Conceptualization; Methodology; Data curation; Formal analysis; Investigation; Writing – original draft. N.S.: Investigation; Supervision; Resources; Writing – review &

editing. G.W.: Investigation; Resources; Visualization; Writing – review & editing. All authors approved the final version of the manuscript.

Acknowledgements

The authors thank the nursing staff, endoscopy technicians and surgical team at K.R.M.T. Wongsonegoro Regional General Hospital, Semarang, for their assistance in the care of the patient, and the patient and his family for their cooperation.

Use of artificial intelligence

No generative artificial intelligence tools were used in the preparation of this manuscript.

References

- Ungaro R, Mehandru S, Allen PB, et al. Ulcerative colitis. *Lancet*. 2017;389(10080):1756-1770. doi:10.1016/s0140-6736(16)32126-2
- Benchimol EI, Mack DR, Nguyen GC, et al. Incidence, Outcomes, and Health Services Burden of Very Early Onset Inflammatory Bowel Disease. *Gastroenterology*. 2014;147(4):803-813.e7. doi:10.1053/j.gastro.2014.06.023
- Ng SC, Shi HY, Hamidi N, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *Lancet*. 2017;390(10114):2769-2778. doi:10.1016/s0140-6736(17)32448-0
- Dhaliwal J, Tuna M, Shah BR, et al. Incidence of Inflammatory Bowel Disease in South Asian and Chinese People: A Population-Based Cohort Study from Ontario, Canada. *Clin Epidemiol*. 2021;Volume 13:1109-1118. doi:10.2147/clep.s336517
- Rucinski P, Akutko K, Pytrus T. Transitional care in pediatric inflammatory bowel disease: current strategies and future directions – a narrative review. *Gastroenterol Rev*. 2026;21(2):126-134. doi:10.5114/pg.2025.156726
- Van Limbergen J, Russell RK, Drummond HE, et al. Definition of Phenotypic Characteristics of Childhood-Onset Inflammatory Bowel Disease. *Gastroenterology*. 2008;135(4):1114-1122. doi:10.1053/j.gastro.2008.06.081
- Rosen MJ, Dhawan A, Saeed SA. Inflammatory Bowel Disease in Children and Adolescents. *JAMA Pediatr*. 2015;169(11):1053. doi:10.1001/jamapediatrics.2015.1982
- Kelsen JR, Sullivan KE, Rabizadeh S, et al. North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition Position Paper on the Evaluation and Management for Patients With Very Early-onset Inflammatory Bowel Disease. *J Pediatr Gastroenterol Nutr*. 2020;70(3):389-403. doi:10.1097/mpg.0000000000002567
- Ouahed J, Spencer E, Kotlarz D, et al. Very Early Onset Inflammatory Bowel Disease: A Clinical Approach With a Focus on the Role of Genetics and Underlying Immune Deficiencies. *Inflamm Bowel Dis*. 2020;26(6):820-842. doi:10.1093/ibd/izz259
- Pigneur B, Logrieco G, Cucinotta U, et al. P0285 Long-term outcome of children with very early-onset non-monogenic colitis: a single center retrospective study. *J Crohns Colitis*. 2025;19(Supplement_1):i729-i729. doi:10.1093/ecco-jcc/jjae190.0459
- Dudzik J, Lewindon P. Clinical phenotypes of very early onset inflammatory bowel disease in Australian children: A single-centre retrospective study. *J Pediatr Gastroenterol Nutr*. 2026;jpn3.70595. doi:10.1002/jpn3.70595
- Mennini M, Fiocchi AG, Cafarotti A, et al. Food protein-induced allergic proctocolitis in infants: Literature review and proposal of a management protocol. *World Allergy Organ J*. 2020;13(10):100471. doi:10.1016/j.waojou.2020.100471
- Coppola S, Carucci L, Anania C, et al. Diagnosis and Management of Food Protein-Induced Allergic Proctocolitis in the pediatric age: A position paper from the Italian Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the Italian Society for Pediatric Allergy and Immunology. *Pediatr Allergy Immunol*. 2025;36(12):e70264. doi:10.1111/pai.70264
- Vandenplas Y, Broekaert I, Domellöf M, et al. An ESPGHAN Position Paper on the Diagnosis, Management, and Prevention of Cow's Milk Allergy. *J Pediatr Gastroenterol Nutr*. 2024;78(2):386-413. doi:10.1097/mpg.0000000000003897
- Fiocchi A, Brozek J, Schünemann H, et al. World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) Guidelines. *World Allergy Organ J*. 2010;3(4):57-161. doi:10.1097/wox.0b013e3181defeb9
- Piccirillo M, Pucinischi V, Mennini M, et al. Gastrointestinal bleeding in children: diagnostic approach. *Ital J Pediatr*. 2024;50(1):13. doi:10.1186/s13052-024-01592-2
- Martini N, Kara Tahhan N, Aldarwish MS, et al. Rectal prolapse as a manifestation of inflammatory bowel disease with celiac disease in a 2-year-old male: a rare case report. *Ann Med Surg (Lond)*. 2023;85(4):1235-1239. doi:10.1097/ms9.0000000000000494
- Taouey SS, Bako ID, Laleye C, et al. Computed tomography morphometric comparison of the pelvis in children with and without rectal prolapse in Niger. *Transl Res Anat*. 2023;32:100253. doi:10.1016/j.tria.2023.100253
- Rentea R, St Peter S. Pediatric Rectal Prolapse. *Clin Colon Rectal Surg*. 2018;31(02):108-116. doi:10.1055/s-0037-1609025
- Kodia K, Huerta CT, Perez EA. Rectal prolapse in the pediatric population—a narrative review of medical and surgical management. *Transl Gastroenterol Hepatol*. 2024;9:47. doi:10.21037/tgh-23-128
- Krugliak Cleveland N, Rai V, El Jurdi K, et al. Ulcerative Colitis Patients Have Reduced Rectal Compliance Compared With Non-Inflammatory Bowel Disease Controls. *Gastroenterology*. 2022;162(1):331-333.e1. doi:10.1053/j.gastro.2021.09.052
- Limdi JK, Vasant DH. Anorectal Dysfunction in Distal Ulcerative Colitis: Challenges and Opportunities for Topical Therapy. *J Crohns Colitis*. 2016;10(4):503. doi:10.1093/ecco-jcc/jjv217
- Dehghani SM. Solitary rectal ulcer syndrome in children: A literature review. *World J Gastroenterol*. 2012;18(45):6541. doi:10.3748/wjg.v18.i45.6541
- Vernon-Roberts A, Aluzaita K, Khalilipour B, et al. Systematic Review of Diagnostic Delay for Children With Inflammatory Bowel Disease. *J Pediatr Gastroenterol Nutr*. 2023;76(3):304-312. doi:10.1097/mpg.0000000000003670
- Turner D, Ruemmele FM, Orlanski-Meyer E, et al. Management of Paediatric Ulcerative Colitis, Part 1. *J Pediatr Gastroenterol Nutr*. 2018;67(2):257-291. doi:10.1097/mpg.0000000000002035
- Turner D, Yerushalmi B, Kori M, et al. Once- Versus Twice-daily Mesalazine to Induce Remission in Paediatric Ulcerative Colitis: A Randomised Controlled Trial. *J Crohns Colitis*. 2016;jjw180. doi:10.1093/ecco-jcc/jjw180
- Winter HS, Krzeski P, Heyman MB, et al. High- and Low-Dose Oral Delayed-Release Mesalamine in Children With Mild-to-Moderately Active Ulcerative Colitis. *J Pediatr Gastroenterol Nutr*. 2014;59(6):767-772. doi:10.1097/mpg.0000000000000530
- Frieri G, Giacomelli R, Pimpo M, et al. Mucosal 5-aminosalicylic acid concentration inversely correlates with severity of colonic inflammation in patients with ulcerative colitis. *Gut*. 2000;47(3):410-414. doi:10.1136/gut.47.3.410
- Levine A, Koletzko S, Turner D, et al. ESPGHAN Revised Porto Criteria for the Diagnosis of Inflammatory Bowel Disease in Children and Adolescents. *J Pediatr Gastroenterol Nutr*. 2014;58(6):795-806. doi:10.1097/mpg.0000000000000239
- Levine A, Griffiths A, Markowitz J, et al. Pediatric modification of the Montreal classification for inflammatory bowel disease. *Inflamm Bowel Dis*. 2011;17(6):1314-1321. doi:10.1002/ibd.21493
- Turner D, Otley AR, Mack D, et al. Development, Validation, and Evaluation of a Pediatric Ulcerative Colitis Activity Index: A Prospective Multicenter Study. *Gastroenterology*. 2007;133(2):423-432. doi:10.1053/j.gastro.2007.05.029
- Thomson M, Tringali A, Dumonceau J, et al. Paediatric Gastrointestinal Endoscopy. *J Pediatr Gastroenterol Nutr*. 2017;64(1):133-153. doi:10.1097/mpg.0000000000001408
- Mahmud S, Parvez M, Baidya M, et al. Spectrum of Colonoscopy in Children: A Tertiary Centre Experience from Bangladesh. *Dhaka Shishu (Children) Hosp J*. 2023;38(1):8-16. doi:10.3329/dshj.v38i1.66996
- Bolia R, Thapar N, Withers GD, et al. Characterization of Colonoscopies in Preschool Children. *J Pediatr Gastroenterol*

- Nutr. 2023;77(3):396-400. doi:10.1097/mpg.0000000000003826
35. Travis SPL, Schnell D, Krzeski P, et al. Developing an instrument to assess the endoscopic severity of ulcerative colitis: the Ulcerative Colitis Endoscopic Index of Severity (UCEIS). *Gut*. 2012;61(4):535-542. doi:10.1136/gutjnl-2011-300486
 36. Thirumal P, Sumathi B, Nirmala D. A Clinical Entity Often Missed—Solitary Rectal Ulcer Syndrome in Children. *Front Pediatr*. 2020;8:396. doi:10.3389/fped.2020.00396
 37. Shentova R, Baycheva M, Hadjiiski P, et al. Role of faecal calprotectin as a predictor of endoscopic activity in paediatric patients with ulcerative colitis. *Gastroenterol Hepatol*. 2020;43(1):57-61. doi:10.1016/j.gastrohep.2019.08.011
 38. Ho SSC, Ross M, Keenan JI, et al. Fecal Calprotectin in Combination With Standard Blood Tests in the Diagnosis of Inflammatory Bowel Disease in Children. *Front Pediatr*. 2021;8:609279. doi:10.3389/fped.2020.609279
 39. Khaw EZX, Chew KS, Mohd Ranai N, et al. Efficacy and Safety of Upadacitinib in Refractory Very-Early-Onset Ulcerative Colitis: A Case Report. *J Paediatr Child Health*. 2026;62(10):2067-2069. doi:10.1111/jpc.70544
 40. Fumita T, Terui K, Shibata R, et al. Surgical outcomes of very-early-onset ulcerative colitis: retrospective comparative study with older pediatric patients. *Pediatr Surg Int*. 2024;40(1):73. doi:10.1007/s00383-024-05662-8
 41. Levine AE, Zheng HB, Suskind DL. Linking Genetic Diagnosis to Therapeutic Approach in Very Early Onset Inflammatory Bowel Disease: Pharmacologic Considerations. *Paediatr Drugs*. 2022;24(3):207-216. doi:10.1007/s40272-022-00503-4
 42. Oliva-Hemker M, Hutfless S, Al Kazzi ES, et al. Clinical Presentation and Five-Year Therapeutic Management of Very Early-Onset Inflammatory Bowel Disease in a Large North American Cohort. *J Pediatr*. 2015;167(3):527-532.e3. doi:10.1016/j.jpeds.2015.04.045
 43. Kerur B, Benchimol EI, Fiedler K, et al. Natural History of Very Early Onset Inflammatory Bowel Disease in North America: A Retrospective Cohort Study. *Inflamm Bowel Dis*. 2021;27(3):295-302. doi:10.1093/ibd/izaa080
 44. Lee WS, Chew KS, Huang JG, et al. Disease phenotypic and outcome of very-early onset inflammatory bowel disease in Asian children: an understudied population. *Front Pediatr*. 2025;13:1487253. doi:10.3389/fped.2025.1487253
 45. Levine A, de Bie CI, Turner D, et al. Atypical Disease Phenotypes in Pediatric Ulcerative Colitis. *Inflamm Bowel Dis*. 2013;19(2):370-377. doi:10.1002/ibd.23013
 46. Glickman JN, Bousvaros A, Farraye FA, et al. Pediatric Patients With Untreated Ulcerative Colitis May Present Initially With Unusual Morphologic Findings. *Am J Surg Pathol*. 2004;28(2):190-197. doi:10.1097/00000478-200402000-00006
 47. Huma Arshad Cheema, Nadia Waheed, Anjum Saeed, et al. Very early onset inflammatory bowel disease (VEO-IBD): spectrum of clinical presentation, diagnostic tools and outcome in children. *J Pak Med Assoc*. 2021;71(10):2350-2354. doi:10.47391/jpma.05-725
 48. Moon JK, Stratigis JD, Lipskar AM. Rectal Prolapse in the Pediatric Population. *Curr Gastroenterol Rep*. 2025;27(1):6. doi:10.1007/s11894-024-00953-5
 49. Abdalfatah A, Hageen AW, Albader D, et al. Efficacy and safety of split-dose ultra-low-volume polyethylene glycol with ascorbic acid versus sodium picosulfate with magnesium citrate for bowel preparation: a systematic review and meta-analysis. *Eur J Gastroenterol Hepatol*. 2026;38(10):1121-1129. doi:10.1097/MEG.0000000000003163
 50. Mahdavi Mortazavi SM, Immanieh MH, Honar N, et al. Adding Senna alkaloid to laxative agents in bowel preparation for pediatric colonoscopy: a clinical trial study. *Arab J Gastroenterol*. 2026;27(2):260-262. doi:10.1016/j.ajg.2026.01.003
 51. Rao SSC, Read NW, Davison PA, et al. Anorectal sensitivity and responses to rectal distention in patients with ulcerative colitis. *Gastroenterology*. 1987;93(6):1270-1275. doi:10.1016/0016-5085(87)90255-1
 52. Flum AS, Golladay ES, Teitelbaum DH. Recurrent rectal prolapse following primary surgical treatment. *Pediatr Surg Int*. 2010;26(4):427-431. doi:10.1007/s00383-010-2565-x
 53. Turner D, Ricciuto A, Lewis A, et al. STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treatment-Target strategies in IBD. *Gastroenterology*. 2021;160(5):1570-1583. doi:10.1053/j.gastro.2020.12.031
 54. Wine E, Aloï M, Van Biervliet S, et al. Management of paediatric ulcerative colitis, part 1: Ambulatory care—An updated evidence-based consensus guideline from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition and the European Crohn's and Colitis Organisation. *J Pediatr Gastroenterol Nutr*. 2025;81(3):765-815. doi:10.1002/jpn3.70097
 55. Rousseaux C, Lefebvre B, Dubuquoy L, et al. Intestinal antiinflammatory effect of 5-aminosalicylic acid is dependent on peroxisome proliferator-activated receptor- γ . *J Exp Med*. 2005;201(8):1205-1215. doi:10.1084/jem.20041948
 56. Cevallos SA, Lee JY, Velazquez EM, et al. 5-Aminosalicylic Acid Ameliorates Colitis and Checks Dysbiotic *Escherichia coli* Expansion by Activating PPAR- γ Signaling in the Intestinal Epithelium. *mBio*. 2021;12(1):e03227-20. doi:10.1128/mbio.03227-20
 57. Kaiser GC, Yan F, Polk DB. Mesalamine blocks tumor necrosis factor growth inhibition and nuclear factor κ B activation in mouse colonocytes. *Gastroenterology*. 1999;116(3):602-609. doi:10.1016/s0016-5085(99)70182-4
 58. Beiranvand M. A review of the biological and pharmacological activities of mesalazine or 5-aminosalicylic acid (5-ASA): an anti-ulcer and anti-oxidant drug. *Inflammopharmacology*. 2021;29(5):1279-1290. doi:10.1007/s10787-021-00856-1
 59. Ireland A, Jewell DP. Mechanism of action of 5-aminosalicylic acid and its derivatives. *Clin Sci (Lond)*. 1990;78(2):119-125. doi:10.1042/cs0780119
 60. Diffrancia E, Corsello A, Genduso M, et al. Bowel preparation for colonoscopy in children: a survey of the Italian society of pediatric gastroenterology, hepatology and nutrition. *Ital J Pediatr*. 2026;52(1):67. doi:10.1186/s13052-026-02227-4
 61. Abd El-Mabood ES, Ali H, Elwan T. Modified Gant-Miwa approach versus modified Thiersch's stitch for the management of rectal mucosal prolapse in children: how to decrease recurrence?. *Egypt J Surg*. 2014;33(3):154. doi:10.4103/1110-1121.141900
 62. Toda M, Jimbo K, Suzuki M, et al. The Role of Human Leukocyte Antigen Alleles and Maternal Microchimerism in Very-Early-Onset Ulcerative Colitis in Japanese Children. *Inflamm Bowel Dis*. 2025;31(9):2451-2457. doi:10.1093/ibd/izaf048
 63. Peyrin-Biroulet L, Ferrante M, Magro F, et al. Results from the 2nd Scientific Workshop of the ECCO (I): Impact of mucosal healing on the course of inflammatory bowel disease. *J Crohns Colitis*. 2011;5(5):477-483. doi:10.1016/j.crohns.2011.06.009
 64. Ledder O, Dolinger M, Dubinsky MC, et al. Tofacitinib in Pediatric Ulcerative Colitis: A Retrospective Multicenter Experience. *Inflamm Bowel Dis*. 2025;31(2):425-431. doi:10.1093/ibd/izae112
 65. Yerushalmy-Feler A, Spencer EA, Dolinger MT, et al. Upadacitinib for Induction of Remission in Pediatric Ulcerative Colitis: An International Multicenter Study. *J Crohns Colitis*. 2025;19(5):jjae182. doi:10.1093/ecco-jcc/jjae182
 66. Yerushalmy-Feler A, Olbjorn C, Kolho KL, et al. Dual Biologic or Small Molecule Therapy in Refractory Pediatric Inflammatory Bowel Disease (DOUBLE-PIBD): A Multicenter Study from the Pediatric IBD Porto Group of ESPGHAN. *Inflamm Bowel Dis*. 2024;30(2):159-166. doi:10.1093/ibd/izad064
 67. Romano C, Oliva S, Martellosi S, et al. Pediatric gastrointestinal bleeding: Perspectives from the Italian Society of Pediatric Gastroenterology. *World J Gastroenterol*. 2017;23(8):1328. doi:10.3748/wjg.v23.i8.1328
 68. Uhlig HH, Schwerdt T, Koletzko S, et al. The Diagnostic Approach to Monogenic Very Early Onset Inflammatory Bowel Disease. *Gastroenterology*. 2014;147(5):990-1007.e3. doi:10.1053/j.gastro.2014.07.023
 69. Uhlig HH, Charbit-Henrion F, Kotlarz D, et al. Clinical Genomics for the Diagnosis of Monogenic Forms of Inflammatory Bowel Disease. *J Pediatr Gastroenterol Nutr*. 2021;72(3):456-473. doi:10.1097/mpg.0000000000003017

70. Nambu R, Warner N, Mulder DJ, et al. A Systematic Review of Monogenic Inflammatory Bowel Disease. *Clin Gastroenterol Hepatol.* 2022;20(4):e653-e663. doi:10.1016/j.cgh.2021.03.021
71. Sarbagili-Shabat C, Timmer F, Morogianni K, et al. Nutritional Status, Body Composition and Growth in Paediatric-Onset Ulcerative Colitis: A Systematic Review. *Nutrients.* 2026;18(1):169. doi:10.3390/nu18010169
72. Jin HY, Lim JS, Lee Y, et al. Growth, puberty, and bone health in children and adolescents with inflammatory bowel disease. *BMC Pediatr.* 2021;21(1):35. doi:10.1186/s12887-021-02496-4
73. Parente P, Pastore M, Grillo F, et al. Very Early Onset-IBD: evidence for the need of a multidisciplinary approach. *Pathologica.* 2022;114(1):3-11. doi:10.32074/1591-951X-336
74. Kaplan GG, Windsor JW. The four epidemiological stages in the global evolution of inflammatory bowel disease. *Nat Rev Gastroenterol Hepatol.* 2021;18(1):56-66. doi:10.1038/s41575-020-00360-x
75. Talib MA, Aziz MT, Suleman H, et al. Etiologies and outcome of lower gastrointestinal bleeding in patients presenting to a tertiary care Children's Hospital. *Pak J Med Sci.* 2021;37(2). doi:10.12669/pjms.37.2.2676
76. Chhibba T, Gros B, King JA, et al. Environmental risk factors of inflammatory bowel disease: toward a strategy of preventative health. *J Crohns Colitis.* 2025;19(4):jjaf042. doi:10.1093/ecco-jcc/jjaf042
77. Ananthakrishnan AN, Bernstein CN, Iliopoulos D, et al. Environmental triggers in IBD: a review of progress and evidence. *Nat Rev Gastroenterol Hepatol.* 2018;15(1):39-49. doi:10.1038/nrgastro.2017.136
78. Hyams JS, Davis Thomas S, Gotman N, et al. Clinical and biological predictors of response to standardised paediatric colitis therapy (PROTECT): a multicentre inception cohort study. *Lancet.* 2019;393(10182):1708-1720. doi:10.1016/s0140-6736(18)32592-3