

Challenges in the Management of Inflammatory Bowel Disease in Children: A Narrative Review

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Abstract: There is a rising prevalence of pediatric inflammatory bowel disease (PIBD) worldwide. This article aims to explore the key issues in managing PIBD and attempts to propose evidence-based recommendations. We reviewed published literature on PIBD, including original research, systematic reviews, meta-analyses, consensus statements, and position papers. The databases searched were PubMed/MEDLINE, Cochrane Library, Web of Science, and Scopus, using terms related to inflammatory bowel disease, colitis, ulcerative colitis, Crohn's disease, children, adolescents, and pediatrics. The selected articles were critically appraised, summarised and incorporated into the review. PIBD presents multifaceted challenges. They include atypical presentations, very early onset cases, growth and nutritional challenges that affect linear development and pubertal progression, pharmacological management issues related to age-specific medication safety and efficacy and timing of surgical interventions. There are impacts on development; psychosocial burden challenges in education, social development, and family dynamics, all crucial in the future of the child. There are also limitations in access to PIBD services with personalised treatment approaches and challenges in transitional care. It is important to identify these unique challenges posed by PIBD and address them in a comprehensive manner in a multidisciplinary approach.

Keywords: adolescents, children, inflammatory bowel disease, IBD, colitis, ulcerative colitis, Crohn's disease

Introduction

Inflammatory bowel disease (IBD) is a chronic, relapsing inflammation affecting the gastrointestinal tract. It is primarily categorised into three types: Crohn's disease (CD), ulcerative colitis (UC), and IBD-unclassified (IBD-U).¹ Although the exact aetiology is far from clear, it is believed to arise from an inappropriate and uncontrolled inflammatory response to normal gut microbes triggered by dietary and environmental factors in genetically predisposed individuals.²

The rise of pediatric-onset IBD (PIBD) is a public health concern worldwide, with 10–20% of new cases under 18.^{3,4} PIBD is characterised by the manifestation of symptoms or diagnosis of any IBD subtype before the age of 17.^{1,5} In the Paris classification, IBD is classified by the age of diagnosis, location in the gastrointestinal tract, disease behaviour (eg, the presence of strictures and penetrations), and its effect on the child's growth (Table 1).¹ When the onset occurs before the age of 6 years, it is referred to as Very Early Onset IBD (VEO-IBD). This includes neonatal onset VEO IBD, which presents within the first month of life, and infantile onset VEO IBD, where the onset is before the age of 2 years.

Pediatric IBD tends to present more aggressively and extensively than in adults, often requiring intensive and prolonged immunosuppressive therapy. Due to its chronic nature and early onset, the disease imposes a greater long-term burden and higher morbidity on children compared to adults.^{6,7} Pediatric patients also face unique challenges, including growth failure, delayed puberty, and significant psychological comorbidities—factors that can have lasting repercussions into adulthood. Despite having the longest disease duration ahead of them, children with IBD are frequently left behind in accessing novel therapies. Regulatory approvals for pediatric use often lag years behind those for adults, delaying access to potentially more effective and targeted treatments.^{6,7}

Table 1 Classification of IBD by the Age of Onset According to the Paris Classification

Classification	Age
A1a	0 to <10 years
A1b	10 to <17 years
A2	17 to 40 years
A3	> 40 years

This narrative review aims to comprehensively address the current challenges in diagnosis, treatment approaches, monitoring strategies, psychosocial support, and transitional care for patients with PIBD.

We reviewed published literature on PIBD, including original research, systematic reviews, meta-analyses, consensus statements, and position papers. The databases searched were PubMed/MEDLINE, Cochrane Library, Web of Science, and Scopus. Search terms included: “inflammatory bowel disease”, “IBD”, “colitis”, “ulcerative colitis”, “Crohn’s disease”, “children”, “adolescents”, “pediatric”. The selected articles were critically appraised, summarised and incorporated into the review.

Increasing Prevalence: The Foundational Challenge

Summary of Global Epidemiology

The incidence and prevalence of childhood-onset IBD have risen rapidly to a level of a public health crisis.^{3,4,8} Approximately 10–20% of newly diagnosed IBD patients are under 18 years old.⁹ At the beginning, it was a disease of the Western countries, and later, the newly industrialised nations with more westernised societies also noted an increase in prevalence.^{6,9} During the last two decades, the prevalence of IBD has surged dramatically in newly industrialised regions across Asia, Africa, and South America. This epidemiological shift highlights a significant public health concern as these countries change their lifestyles and diets. It is alarming to note that the disease is not only emerging but is also entering an accelerated phase in many developing nations much earlier than the Western world indicating an early epidemic in PIBD in resource poor settings such as Asia and Africa posing a tremendous strain on their already overstretched healthcare expenses in terms of allocation of resources.¹⁰

Globally, the number of new pediatric IBD cases rose from an estimated 20,897 (95% CI: 16,747 to 25,988) in 1990 to 25,659 (20,744 to 31,574) in 2019, reflecting an increase of 22.8%.¹¹ At the regional level, the highest prevalence of cases was observed in East Asia and South Asia. The most notable rise in prevalence during 1990–2019 was reported from the Sub-Saharan nations (138–178%).¹¹ High incidence was also reported from the East Asian region, and the Australian sub-continent. The highest incidence rate in 2019 was found in high-income North America (7.62 (6.47 to 8.93) per 100,000) and high-income Asia Pacific (5.15 (4.14 to 6.38) per 100,000).¹¹ A rising prevalence was noted among children in most regions of the world, including many newly industrialized countries in Asia.^{4,12} Several studies from the Asian Pediatric Inflammatory Bowel Disease Study group involving children from Malaysia, the Philippines, Singapore, Sri Lanka, Taiwan and Thailand have shown increasing incidence during the last 5 years, a high proportion of very early onset IBD.^{13–15}

Unique Features of PIBD

PIBD has several unique characteristics in contrast to adult-onset IBD. Genetic susceptibility plays a substantial role in the aetiology of PIBD in children. Higher polygenic risk scores and multiple genetic variants are associated with a severe disease course in children and adolescents.^{16,17} PIBD is also associated with a higher risk of positive family history compared to adult- or elderly-onset IBD.¹⁸ Studies have reported that 11.1–13.7% of patients had a first-degree relative with IBD.^{19–21} Furthermore, children with VEO-IBD and CD present with more atypical features or extra-intestinal manifestations in nearly 22% of cases, which often results in delays in diagnosis (Table 2).^{5,22–27} Moreover, children and adolescents often present with more severe involvement of the intestine and a more aggressive disease course compared

Table 2 Atypical Features / Extra-Intestinal Features of PIBD

Extraintestinal System	Features
Dermatologic	Erythema nodosum Pyoderma gangrenosum
Musculoskeletal	Arthritis Osteopenia Osteoporosis Ankylosing spondylitis Growth failure/ weight loss
Hepatic	Primary sclerosing cholangitis Autoimmune hepatitis
Ocular	Episcleritis Uveitis Iridocyclitis
Renal	Nephrolithiasis
Pancreatic	Pancreatitis
Hematological	Anemia Venous thromboembolism
Others	Lethargy Anorexia

Notes: Adapted from Rosen MJ, Dhawan A, Saeed SA. Inflammatory Bowel Disease in Children and Adolescents. *JAMA Pediatr*. 169(11), 1053–1060 (2015).

Abbreviation: PIBD, pediatric inflammatory bowel disease.

to adults.²⁸ Pediatric IBD is mostly characterised by pan-enteric or colon-only CD, extensive UC, and variable disease location, and involvement of the upper gastrointestinal tract.^{29–32}

Impact of Early-Onset Disease on Long-Term Outcomes

Despite more aggressive medical management, including biological and immunomodulatory therapy, children with IBD have more periods of active disease.^{33,34} In contrast to adults, children with CD often experience chronic, disabling disease, necessitating intestinal resection.³⁵ Therefore, the primary goals of PIBD treatment are to induce and maintain mucosal healing, enhance quality of life, promote adequate weight gain and linear growth, and minimise irreversible bowel damage through aggressive treatment.^{36,37}

Furthermore, as these complications often occur early in life, specific issues including growth retardation, delayed in development of puberty, and nutritional impairment, which can impact bone health, require regular monitoring. Prolonged hospital admissions and frequent clinic visits have a significant impact on the education, which may challenge their earning capacity and achievements as adults. In addition, long-term psychological problems such as anxiety, depression, and hopelessness need special attention.³⁸

Diagnostic Uncertainty: A Critical Hurdle in Early Detection

Atypical Presentation and Consideration of Other Differential Diagnoses

PIBD is known to present with atypical features, leading to diagnostic delays contributing to worse disease progression and treatment outcomes.³⁹ Isolated ileal disease and onset below five years are two risk factors associated with delayed diagnosis.⁴⁰ The clinical presentation is often vague, leading to initial misdiagnosis as infectious colitis, allergic gastroenteritis or irritable bowel syndrome and other pain-predominant disorders of gut-brain interactions, with a prevalence of 10–20% in the paediatric population.⁴¹ Sometimes, the diagnostic delay could be more than 12 months, with a higher frequency in CD (27.1%) compared to UC (13.9%).⁴²

UC typically presents with blood and mucous diarrhoea, while Crohn's disease has a more varied and often misleading symptom profile (Table 2). Only 25% of children with CD have the triad of abdominal pain, weight loss and diarrhoea at presentation.²⁵ The variable patterns of presentation and heterogeneity of extraintestinal symptoms may lead to delays in referral to specialist services.⁴³

Patients with PIBD present with extra intestinal manifestations (EIMs) before the onset of bowel symptoms pose a unique challenge. Among children with PIBD, 22% present with growth failure, anaemia, perianal disease, or other EIMs as the only predominant initial feature.²⁵ It had been reported that at least one-third of patients who do not have EIM at diagnosis will eventually develop at least one EIM during the long-term follow-up.⁴³

Appropriate Diagnostic Workup and Biomarkers

The absence of simple diagnostic blood and stool tests further challenges the initial diagnosis of PIBD. The usually requested blood tests include a complete blood count to check for high white cell and platelet counts, and low haemoglobin, and raised erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels. However, ESR, CRP, serum albumin, haemoglobin, platelets, packed cell volume, white cell count, and alanine transferase (ALT), which showed normal results in 10% of patients with new-onset IBD.⁴² Faecal calprotectin remains an invaluable tool in screening children for IBD and deciding on endoscopic evaluation. Faecal calprotectin has high sensitivity (98%) and low specificity of 68% in children with suspected IBD.¹ There are a few drawbacks to using calprotectin as a diagnostic marker for PIBD (Figure 1).⁴⁴⁻⁴⁷ In addition, quantifying faecal calprotectin is relatively expensive, limiting its application in resource-poor settings.

Role of Endoscopy, Imaging, and Genetic Testing

IBD is a clinicopathological diagnosis that requires integrating macroscopic and microscopic appearances and small bowel imaging. The Porto group recommends that upper and lower gastrointestinal endoscopy is essential for the diagnosis.¹ Due to

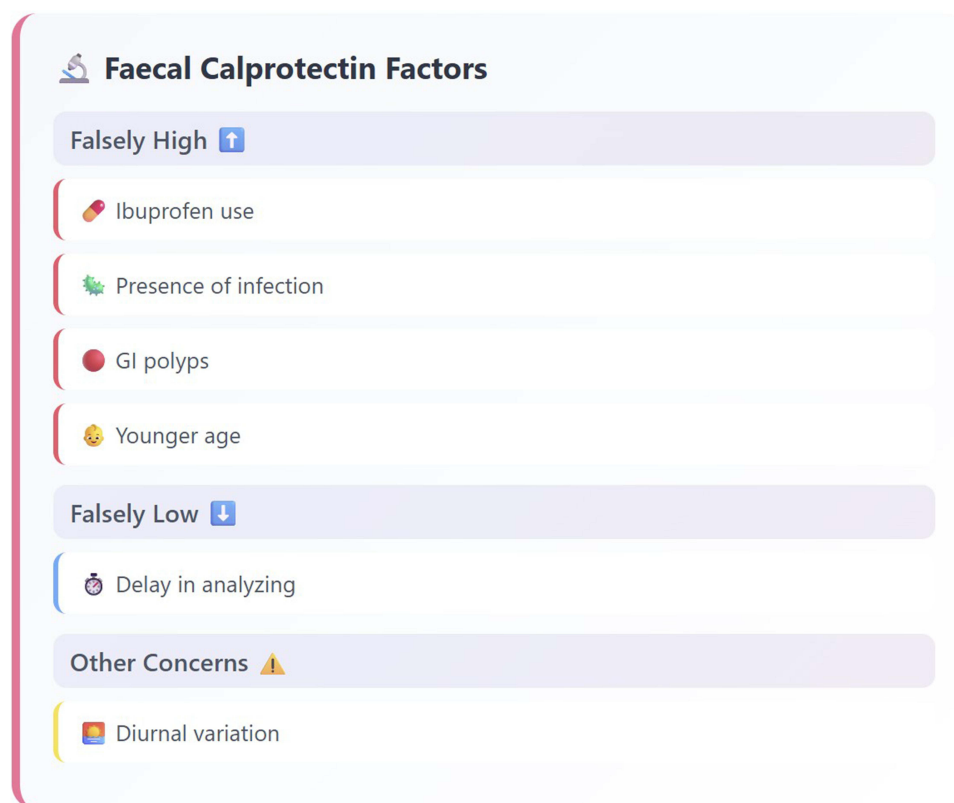


Figure 1 Factors affecting faecal calprotectin assay.

its invasiveness, several imaging modalities such as ultrasound, magnetic resonance imaging (MRI), and direct visualisation through capsule endoscopy have been researched to monitor intestinal inflammation.⁴⁸ In addition, imaging of the small bowel is mandatory for all children with a suspected IBD unless the ileocolonoscopy and histological features are strongly suggestive of UC. Magnetic resonance enterography (MRE) is routinely utilised to screen the small bowel and is known to have limited sensitivity to detect subtle mucosal changes compared to the capsule endoscopy.⁴⁹ As a result, video capsule endoscopy (VCE) is increasingly used for direct visualisation of the small bowel. It offers superior detection of superficial inflammation of the small bowel mucosa compared to MRE, while both modalities demonstrate similar accuracy in localising inflammation.⁵⁰ VCE has shown superior sensitivity in detecting small bowel involvement in CD over small bowel radiography, computed tomography (CT), colonoscopy and ileoscopy with minimal discomfort.⁵¹

Despite the promising advantages, the use of VCE in children with IBD is challenging. Obstacles include the need for proper bowel preparation and endoscopic placement of the capsule when swallowing is difficult. Capsule retention is a notable risk (about 5%), particularly in those with a body mass index below the 5th percentile (43%).⁵¹ VCE may sometimes be misleading as it detects nonspecific or incidental findings that mimic IBD.⁴⁹

Screening for monogenic causes of IBD has become standard practice in selected children diagnosed before the age of 2, and in those aged 2–6 years with specific clinical features suggestive of a monogenic aetiology.⁵² Genetic factors, such as polymorphisms in genes like nucleotide-binding oligomerization domain-containing protein 2 (NOD2) and toll-like receptors (TLRs), have been linked to IBD susceptibility. These genetic mutations may affect the composition and function of the gut microbiome, leading to dysbiosis, which could compromise the intestinal mucosal barrier, triggering abnormal immune responses that contribute to the development of IBD.²

Genome-wide association studies (GWAS) have unequivocally identified numerous genomic regions containing IBD-risk factors, revealing several features of the genetic architecture of CD and UC.⁵³ However, due to the numerous challenges, little effort has been dedicated to identifying IBD genes exclusively in the PIBD.⁵⁴ A family history of IBD is the most significant risk factor for disease at all ages.⁵³ IBD patients with a family history of disease are more likely to present at a younger age, are more likely to experience extra-intestinal manifestations, have perforating disease, and require longer follow-up.^{55–57} Therefore, identification of the underlying genetic architecture is useful in planning therapeutic strategies and prognostication. However, high costs, limited availability, and the fact that it can often be negative are considered challenges in day-to-day clinical practice.

Very Early Onset IBD (VEO-IBD): Special Considerations

Genetic susceptibility plays a more significant role in VEO-IBD. So far, over 100 monogenic defects for IBD have been reported.^{57,58} The Porto IBD Group has developed a diagnostic gene panel comprising 75 monogenic defects for the evaluation of PIBD.¹⁷ These mutations are associated with primary immune deficiencies or disorders of intestinal epithelial barrier dysfunction.^{59–61} Therefore, genetic screening has become an essential diagnostic tool in understanding the aetiology and behaviour of PIBD and is extremely helpful in tailoring treatments.^{57,62} Several studies have shown the effectiveness of haematopoietic stem cell transplantation in children with VEO-IBD with underlying PIDS.^{63,64} This treatment modality is not well established in developing countries where the demand is on the rise, with an increasing number of children being detected.

Familial cases with very early onset of CD and UC are on the rise.^{65,66} Hence, genetic screening is becoming exceedingly important in the understanding of IBD.⁶⁷ The distinct and more severe disease phenotypes seen in VEO cases pose a challenge in classifying the disease. The incidence of unclassified IBD (IBD-U) is higher in young children (34% in children under 2 years and 21% in children under 7 years) compared to just 6% in adults.⁶⁸

Nutritional Deficits and Growth Failure

Impact of IBD on Linear Growth and Pubertal Development

Monitoring of age-specific complications, such as growth retardation, pubertal delay, developmental delay, decreased bone age and nutritional impairment is one of the key challenges in PIBD. Many factors contribute to the development of growth failure (Figure 2).

Causes of Growth Failure in Inflammatory Bowel Disease

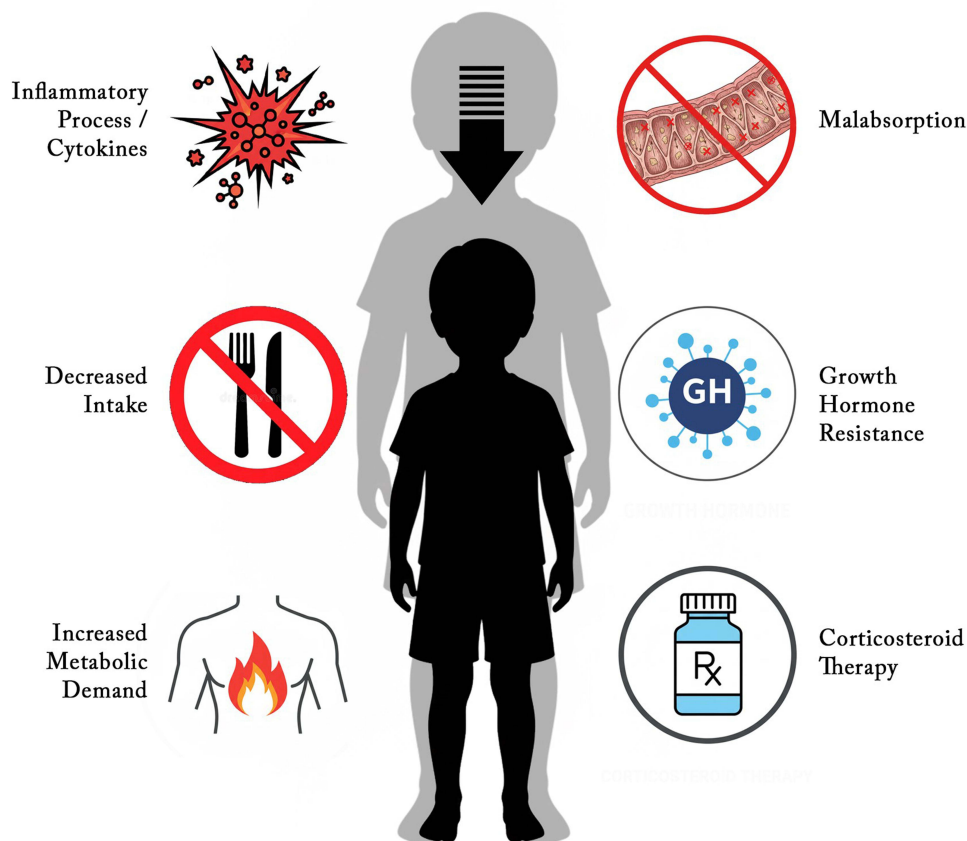


Figure 2 Causes of growth failure in PIBD.

Growth failure affects approximately 40% of children with CD and 10% of those with UC.⁶⁹ Only a minority (19%) of children with CD achieve a final adult height which is still 8 cm shorter than expected.⁷⁰ A cohort study confirmed a long-term height deficit that persists into adulthood. Patients with PIBD are also underweight, with reported mean weight SDS values ranging from -0.65 to -1.0 .^{71,72} Consequently, careful monitoring of linear growth is crucial, with treatment aimed at supporting and restoring normal growth.

Monitoring Nutritional Deficiencies, Pubertal Staging and Growth Parameters

Children with IBD are at a high risk of various micronutrient deficiencies due to disease factors such as chronic blood loss, intestinal malabsorption, decreased oral intake, and ongoing inflammation. For example, Vitamin D deficiency occurs in 35% of children with IBD, and 60% exhibit suboptimal levels (25-hydroxyvitamin D level, <30 ng/mL).⁷³ Children with low vitamin D levels are at increased risk of disease recurrence. Maintaining serum vitamin D levels above 30 ng/mL significantly enhances the likelihood of sustaining clinical remission.⁷⁴ Therefore, a daily intake of 1000 to 1600 mg of elemental calcium and 800 to 1000 IU of vitamin D is recommended for children with IBD.⁷³ Likewise, deficiencies in micronutrients such as iron, B₁₂, and zinc can adversely affect growth and puberty (Figure 3).^{75,76}

Exclusive Enteral Nutrition as Primary Therapy

Exclusive enteral nutrition (EEN) is as effective as corticosteroid therapy for inducing clinical remission in children with CD.⁷⁷ The Porto group currently recommends EEN as the first-line therapy for inducing remission in active, luminal, mild-to

Nutritional Deficiencies in Inflammatory Bowel Disease

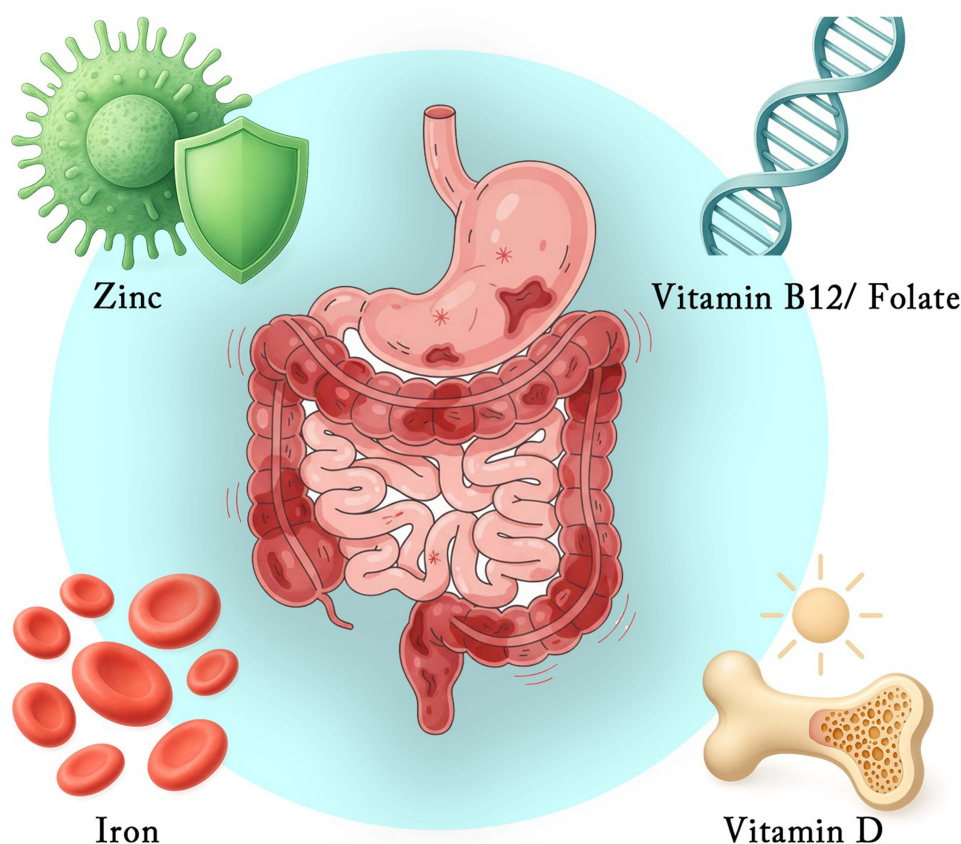


Figure 3 Nutritional deficiencies of children with IBD.

-moderate CD, regardless of disease location.⁷⁸ It is crucial to note that EEN does not negatively affect bone mineral density, weight gain, or linear growth, as with corticosteroids.^{79–81} A Southeast Asian study demonstrated that after 8 weeks of EEN, 91% of children with CD achieved remission, with significant improvements in weight, pediatric Crohn's disease activity index (PCDAI) scores, and inflammatory markers.⁸² In addition, higher rates of mucosal healing have been observed, accompanied by the correction of nutritional deficiencies, and improvements in lean body mass, and quality of life, all with the benefit of sparing steroids.^{83–85} However, these benefits are limited to patients with luminal CD, and there is insufficient data to support its use for extraintestinal and perianal involvement, or in UC.⁸⁶ Although EEN has a vital role in CD, consuming only a liquid diet for 8 weeks is challenging.⁸⁷ Parents may also struggle with EEN due to its impact on social situations and associated costs.⁸⁸ Poor compliance is the commonest reason for inadequate response to EEN.^{89,90} Predictors of poor adherence include colonic involvement, faecal calprotectin level greater than 600 µg/g at diagnosis, older age and increased clinical and biochemical disease activity at the beginning of EEN.^{85,87,89}

Medication Challenges: Balancing Innovation and Affordability

The Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) of the International Organisation for the Study of Inflammatory Bowel Disease (IOIBD) provides evidence- and consensus-based recommendations for treat-to-target strategies divided into immediate, intermediate and long-term targets.³⁶

Corticosteroids (CS) are helpful in remission induction in moderately severe CD and UC. Although the reported short-term remission rates ranged from 50 to 64%,^{91–93} a substantial proportion (14–49%) of children become steroid-dependent by one year.⁹⁴ Prolonged use of CS adversely affects height velocity, and bone health.⁹²

Thiopurines (azathioprine, 6-mercaptopurine), calcineurin inhibitors (tacrolimus), and methotrexate (MTX) are used as immunomodulators to maintain remission, as well as steroid-sparing agents in PIBD. However, several challenges exist in day-to-day clinical practice with these therapeutic agents. Azathioprine (AZA) leads to severe bone marrow suppression in patients with low thiopurine-S-methyltransferase (TPMT) enzyme activity.⁹⁵ In addition, the Nudix Hydrolase 15 (NUDT15) polymorphism-related thiopurine-induced leukopenia is more common in certain Asian populations and is associated with a more rapid onset of leukopenia and hair loss.⁹⁵ Therefore, testing TPMT enzyme activity, NUDT 15 polymorphism, and thiopurine metabolite levels helps to titrate the azathioprine dose. However, these tests are not accessible in many centres, and regular monitoring of the patient's blood count and liver and pancreatic enzymes is being used in day-to-day clinical practice.

Anti-TNF therapy, primarily infliximab and adalimumab, has become the mainstay of treatment for PIBD both in remission induction and maintenance.⁹⁰ Increasingly, data are pointing towards the early introduction of therapy with these agents—a “top-down approach”—as being highly beneficial in moderate to severe CD, fistulating CD, perianal disease, and small intestinal disease.^{37,96} Similarly, in UC, with acute severe colitis, the primary induction consists of infliximab, alongside corticosteroids.³⁷ The challenge in clinical practice is to perform therapeutic drug monitoring to identify the optimal drug concentration for a specific patient and anti-TNF anti-drug antibody levels. In addition, insights into the genomic drivers of response or loss of response are also emerging, which may result in personalised pharmacogenomic profiling, allowing the correct drug to be selected for the molecular phenotype, preventing immunogenicity or toxicity, and enabling stratified clinical trials.⁹⁷

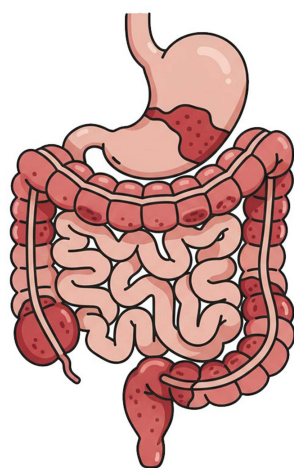
Primary non-response rates remain significant, affecting up to 30%, while an additional 25–50% subsequently lose response in anti-TNF therapy.^{98,99} Therefore, newer monoclonal therapies are being developed for primary non-responders or for others who develop resistance. The main classes include the anti- $\alpha 4\beta 7$ integrin (Vedolizumab), anti-IL-23 therapies, such as joint anti-IL-12/23 drugs (Ustekinumab) and targeted anti-IL-23 antibodies (Risankizumab). However, remission rates appear to vary between 44% and 76%, depending on patient characteristics and the specific drug used.^{100,101} Evidence supporting therapeutic monitoring for vedolizumab and Ustekinumab in the pediatric population remains limited; however, adult studies have demonstrated improved mucosal healing with higher trough levels.¹⁰² The affordability and accessibility of anti-TNF drugs and their newer variants remain significant challenges for clinicians in resource-limited settings. Compounding this issue is the limited availability of therapeutic drug monitoring, which is crucial for optimising treatment efficacy and safety. As a result, children in developing countries often face substantial barriers to receiving effective and timely care for conditions that require these biologic therapies.

Surgical Interventions: Type, Timing and Outcome

The behaviour of CD is heterogeneous and evolves throughout childhood and adulthood, to stricturing disease (B2) in up to 50%, fistulating disease (B3) in 5–35%, or occasionally both in 5%.^{103–105} However, complication rates, hospitalisations and other morbidities remain stable over the last 30 years.¹⁰⁶ Intestinal resection rates of CD (right hemicolectomy) are decreasing, from 8.9% in 1997 to 1.5% in 2017.¹⁰⁷ In contrast, the need for surgery in UC remains stubbornly high, although it continues to be lower than that of CD.¹⁰⁸ Among children with CD, 14% require intra-abdominal surgery within 5 years of diagnosis.¹⁰⁹ Figure 4 shows the indications for surgical interventions for children with IBD.

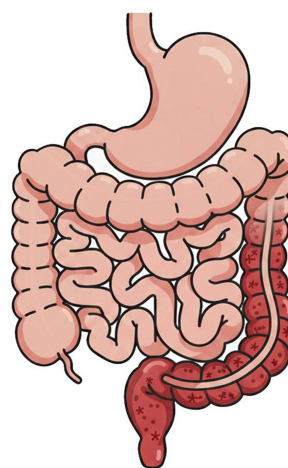
Growth impairment is frequently associated with CD than UC, affecting 15–40% of patients and often resulting in short stature in adulthood.¹¹⁰ Multiple retrospective studies have suggested that surgery promotes catch-up growth, improved BMI and normalize nutrition.^{111–114} Based on this evidence, it is recommended that surgery be performed in children with localised refractory disease coupled with growth failure despite optimal medical interventions.¹¹⁵ Laparoscopic-assisted hemicolectomy is the commonest surgery for CD, while colectomy with an ileoanal pouch is usually performed for UC.^{114,116}

Surgical Indications in Inflammatory Bowel Disease



Crohn's Disease

- Fistulating disease
- Intraabdominal abscesses
- Bowel strictures
- Medically refractory localized disease



Ulcerative Colitis

- Medically refractory disease

Figure 4 Indications for surgical interventions for IBD in children.

Anastomotic leak, small bowel obstruction, wound healing complications, fistula formation, venous thromboembolism, and pouchitis are postoperative complications. In contrast, bowel obstruction due to adhesions and anastomotic strictures, vitamin B12 deficiency, and bile acid malabsorption were noted in surgeries performed for Crohn's disease.¹¹⁴

Challenges on Quality of Life and Psychological Impact

IBD is a chronic disease with a relapsing and remitting nature with protracted symptoms such as abdominal pain, altered bowel habits, an array of extraintestinal symptoms and several therapeutic adverse effects, all of which can negatively affect the quality of life (QoL). Symptoms of IBD, including abdominal pain, fatigue and diarrhoea, harm overall QoL and especially on social functioning.^{117,118} In addition, PIBD leads to chronic fatigue and school absenteeism, both of which have negative ramifications on QoL.¹¹⁹ Fatigue, difficulty in keeping up with peers, and the burden of living with a chronic disease from a young age can have a significant emotional impact on children.^{120–122} Moreover, they have a higher prevalence of sleep disturbance, even during remission, which could negatively impact QoL.¹²³ It is therefore imperative that gastroenterologists, primary care pediatricians, together with schoolteachers social workers and educational psychologists join hands to support children with IBD to improve their symptoms, minimize negative social and psychological impact, and unconditionally support their education through a, formal plan including unfettered access to restrooms and extended time to complete assignments.¹²¹

More importantly, several studies show decreased QoL and increased risk of depression and anxiety disorders among children with IBD.^{34,124} Increased disease activity, low family stability, and familial psychiatric disorders are identified as risk factors.^{117,121} It is natural for parents of children with IBD to have challenges both in their QoL and psychological problems. Caregivers of children with IBD also experience disruptions in multiple aspects of their lives, including

emotional stress, reduced productivity, and difficulties in balancing work and caregiver responsibilities.¹¹⁸ Intervention programs including elements of a healthy diet and physical activity could reverse some of these issues.¹²⁵

Bridging the Gap: Transitional Care to Adult Services

There are several fundamental differences in paediatric and adult care in IBD. Firstly, paediatric care usually takes a more family-oriented and multidisciplinary approach, requiring parental involvement, while adult care often emphasises patient independence. Furthermore, the primary therapeutic target in children is more closely tied to growth and puberty, while adult care focuses mainly on fertility, psychological well-being, and cancer surveillance.¹²⁶ A smooth transition would ensure clear adherence to treatment, which has a positive long-term impact. Thus, there is a critical need to organise a deliberate process for children with IBD during their transition to adult care, identifying a transition as a period in which care could be implemented.¹²⁶ The timing of the transition from pediatric to adult care is determined by country-specific regulations, but it is ideally initiated in early adolescence. To ensure a smooth process, joint consultations involving both pediatric and adult care providers are recommended in their respective settings. The actual transition to adult care is preferably made during a stable remission to minimise disruption and optimise outcome.¹²⁷

Patient readiness plays a critical role in the successful transition to adult care. For a smooth transition, adolescents must acquire key competencies, including solid understanding about their disease, effective self-management skills, and ability make informed decisions *cc.*^{126,127} The most important factors for a successful transition were decision-making regarding IBD, followed by independent communication from the patient and patient satisfaction.¹²⁸ The Transition Readiness Assessment Questionnaire (TRAQ) is a useful tool to identify the readiness for transition.¹²⁹ However, despite all these efforts, smooth transitioning is still a challenge for many reasons, including lack of coordination, increased patient load in adult care, less time for clinic encounters, overwhelmed healthcare staff, and insufficient infrastructure, leading to the collapse of years of achievement by pediatric gastroenterologists.

The Role of Emerging Therapies

As poor palatability and tolerance of EEN stand out as the primary disadvantage, Crohn's disease treatment with eating diet (CD-TREAT) was developed to replicate the nutritional composition of EEN, whilst incorporating some whole foods to overcome issues with palatability, with the exclusion of some components such as gluten, lactose and alcohol had been proposed.^{130,131} However, more clinical studies are needed before recommending CD-TREAT to children. Other dietary interventions such as low fermentable oligo- di- mono- saccharides and polyols (FODMAP diet) have not been very effective in clinical practice.^{85,86} In growing children, dietary restriction could adversely affect the nutritional status. In addition, children on exclusion diets have a significant predilection to develop eating disorders, avoidance/restriction food intake disorders, and orthorexia nervosa, all of which may have unintentional consequences.¹³²

In addition to biologics, oral small-molecule drugs represent a promising emerging class of therapies under consideration for pediatric use.⁴² These include Janus kinase (JAK) inhibitors, such as tofacitinib and upadacitinib, as well as sphingosine-1-phosphate receptor agonists, like ozanimod. Nonetheless, these drugs are not yet approved for use in pediatric practice. However, the trial data from adult populations demonstrate promising efficacy in UC with clinical response rates reaching up to 60% during the maintenance phase.^{133–135} In addition, for patients who do not respond to individual advanced treatments, dual-targeted therapy, which involves combining two advanced treatments, is another potential option.¹³⁶

The main goal in PIBD care is to achieve more tailored treatment. Personalised medicine in PIBD involves using biomarkers and genomic testing to individualise care and identify potential therapeutic targets.⁴² The inherent heterogeneity of IBD makes it challenging to predict individual patient treatment responses and disease courses.⁶² Therefore, effective treatment at an early stage is crucial for preventing the development of disease complications. Given the limited treatment options available for PIBD, optimising existing treatments to enhance their durability is essential.

Health System Gaps and Resource Limitations

To ensure high-quality care for children with IBD, it is essential to address challenges within the healthcare system and ensure adequate resource availability. These issues encompass access to expertise, models of care delivery, technological applications, and primarily, economic considerations.

Access to specialist care is a significant factor influencing the timely diagnosis of PIBD.¹³⁷ Studies highlight considerable variability in how IBD is diagnosed and services are accessed, with no common referral pathways established in some regions.⁴² Delays before seeing a specialist are a factor that can impede timely diagnosis and adversely affect the long-term outcome.¹³⁷

The management of IBD is multifaceted and requires input from a multidisciplinary team. Challenges faced by families, such as the child's or parent's work-related absenteeism, may be best addressed in centres offering multidisciplinary care that include support from professionals like psychologists, social workers, dietitians, and specialised nurses.¹³⁸ It is recommended that very young children with IBD be treated by paediatricians with expertise in multidisciplinary IBD care.¹³⁸ While the sources emphasise the need for and potential benefits of multidisciplinary care in addressing various aspects of PIBD, they do not explicitly detail challenges specific to implementing or sustaining these care models within the health system. However, the call for specialised centres implies a resource or system challenge in making such comprehensive care widely available.

The rising incidence of pediatric-onset IBD particularly contributes to a high economic burden due to the need for longer healthcare utilisation and more intensive treatment regimens compared to adults.^{139,140} The use of biologics and the presence of psychiatric comorbidities had been identified as a significant contributor to the higher healthcare costs in PIBD.^{141,142} In regions like Asia, the high cost is a primary consideration for the use of biologics, alongside difficulties in access and concerns about infectious risks. The high cost of biologics and small molecules is highlighted as a significant consideration in resource-limited settings.¹⁴³

Additionally, there is a substantial indirect economic burden on families, which includes work absenteeism for parents and out-of-pocket expenses.¹³⁸ Out-of-pocket costs are reported to be highest for families experiencing frequent relapses and active disease. For parents with marginal income, this might lead to serious financial repercussions due to out-of-pocket expenses related to IBD.¹³⁸

Conclusion

Management of PIBD is complex clinical work and benefits from an integrated, multidisciplinary approach. Combining different outcome measures and therapeutic targets can improve patient outcomes. Individualised treatment plans are essential because IBD is heterogeneous. Therefore, therapy needs to be tailored based on the patient's life stage. Biomarkers, multi-omics research, and genomic testing are important for understanding heterogeneity, predicting outcomes, and enabling personalised care. Further, personalised pharmacogenomic profiling may help select the right drug at the right time, potentially avoiding complications and shared decision-making with patients is crucial. Guided transition to adult care is vital for maintaining the quality of care and adherence.

Areas requiring further investigation include identifying effective interventions to address barriers that contribute to diagnostic delays. More research is needed on causality in fields such as the microbiome and metabolomics (implied by a multi-omics research focus), as well as the long-term benefits of achieving extended endpoints like histological remission. The development and validation of improved Patient Reported Outcomes (PROs) and Quality of Life (QoL) tools for routine clinical practice are also recognised gaps. Further collaborative work is necessary to determine optimal medical management.

Expert Opinion

The landscape of pediatric inflammatory bowel disease presents a complex tapestry of challenges that demand innovative solutions and strategic research priorities. While significant advances have been made in understanding PIBD pathophysiology, substantial knowledge gaps persist that require urgent attention from the global pediatric gastroenterology community.

The heterogeneity of PIBD phenotypes necessitates a paradigm shift toward precision medicine approaches. Current treatment algorithms, largely extrapolated from adult studies, may not adequately address the unique inflammatory cascades and disease trajectories observed in developing children. Future research must prioritise the development of pediatric-specific therapeutic algorithms that account for the distinct immunological milieu of growing individuals, particularly considering the interplay between inflammation, growth hormone pathways, and pubertal development.

In our review of the existing literature, we observed a significant paucity of paediatric-specific data concerning the economic impact of PIBD. The majority of available information originates from hospital-based studies, with many national reports providing aggregated data that combine adult and paediatric populations. While some paediatric-specific per-patient cost estimates are available, these are limited in scope, often derived from single-centre studies or payer-specific cohorts focusing primarily on adult IBD cases.^{144,145} This gap highlights the need for more comprehensive, multi-centre research to accurately assess the economic burden of IBD in the paediatric population, which is essential for informing targeted healthcare policies and resource allocation.

The economic sustainability of PIBD care represents an increasingly critical concern, particularly as the global incidence continues to rise in resource-limited settings. The current reliance on expensive biologic therapies, while clinically effective, creates an unsustainable economic burden for healthcare systems worldwide. Innovative approaches to drug development, including biosimilar adoption strategies and novel oral small-molecule therapies, must be prioritised to ensure equitable access to effective treatments across diverse socioeconomic contexts.

Digital health technologies offer unprecedented opportunities to revolutionise PIBD management through enhanced monitoring capabilities and patient engagement strategies. The integration of wearable devices, smartphone applications, and telemedicine platforms could facilitate real-time disease monitoring, early detection of flares, and improved medication adherence. However, the implementation of these technologies must be carefully evaluated through rigorous clinical trials to ensure they genuinely improve patient outcomes rather than merely adding technological complexity to care.

The psychosocial dimensions of PIBD remain inadequately addressed in current care models. The profound impact of chronic illness on neurocognitive development, social functioning, and family dynamics requires comprehensive research into evidence-based interventions. Future studies should explore the effectiveness of family-centred therapy approaches, peer support networks, and school-based intervention programs in mitigating the psychological burden of PIBD.

Training and workforce development represent critical bottlenecks in optimising PIBD care globally. The shortage of pediatric gastroenterologists with specialised IBD expertise limits access to appropriate care, particularly in emerging economies where disease incidence is rapidly increasing. Innovative educational models, including simulation-based training, virtual reality learning platforms, and international mentorship programs, could help address these workforce shortages while maintaining high standards of care.

The integration of artificial intelligence and machine learning technologies holds promise for advancing PIBD research and clinical practice. These tools could potentially identify novel biomarkers, predict treatment responses, and optimise therapeutic dosing regimens. However, the development of AI-driven solutions must prioritise interpretability and clinical utility while addressing concerns about algorithmic bias and data privacy.

International collaboration remains essential for advancing PIBD research, given the relatively small patient populations in individual centres. The establishment of global pediatric IBD registries, standardised outcome measures, and collaborative research networks will be crucial for conducting adequately powered studies and generating robust evidence to guide clinical practice. Such collaborations must also address the unique challenges faced by different geographic regions, ensuring that research findings are applicable across diverse populations and healthcare systems.

The ultimate goal of PIBD research should be the development of curative therapies that can halt disease progression and restore normal intestinal function. This ambitious objective will require sustained investment in translational research, innovative clinical trial designs, and partnerships between academic institutions, pharmaceutical companies, and patient advocacy organisations.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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