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Inflammatory Bowel Disease-An Updated Review From Pediatrics Aspects.

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Abstract:

Background: Inflammatory bowel disease (IBD) is a chronic, immune-mediated condition primarily targeting the gastrointestinal tract. It includes two main subtypes: Crohn's disease (CD) and ulcerative colitis (UC). Pediatric IBD (PIBD) incidence has risen significantly over the past decades, particularly in regions with historically low prevalence. These conditions involve complex interactions among genetic predisposition, gut microbiota, immune dysregulation, and environmental factors.

Aim: This review examines the latest advances in the diagnosis, treatment, and management of PIBD, emphasizing distinct challenges in pediatric cases compared to adult-onset IBD.

Methods: This updated review synthesizes evidence from recent studies and clinical guidelines on PIBD, focusing on diagnostic approaches, treatment modalities, and evolving therapeutic strategies. Particular emphasis is placed on biologic therapies, dietary interventions, and the differentiation of PIBD from other gastrointestinal disorders.

Results: Early diagnosis of PIBD remains critical to minimizing complications. While traditional therapies, such as corticosteroids and exclusive enteral nutrition (EEN), induce remission, biologics like anti-TNF agents and emerging therapies (e.g., anti-IL-12/IL-23 agents and fecal microbiota transplantation) demonstrate enhanced efficacy. Biologics are tailored based on disease severity and patient profiles, with therapeutic drug monitoring (TDM) optimizing outcomes. New diagnostic tools, such as fecal calprotectin, offer noninvasive methods for early detection. Emerging exclusion diets and microbiota-focused approaches hold promise for improved outcomes in PIBD management.

Conclusion: PIBD requires tailored management strategies distinct from adult-onset IBD due to its unique disease course, including growth impairment and prolonged inflammatory damage. Advances in biologic therapies, dietary interventions, and diagnostic tools have improved treatment efficacy and patient quality of life. Early intervention, personalized therapies, and ongoing research into emerging modalities are vital for enhancing long-term outcomes.

Keywords: Pediatric inflammatory bowel disease (PIBD), Crohn's disease, ulcerative colitis, biologic therapies, exclusive enteral nutrition (EEN), fecal calprotectin, therapeutic drug monitoring (TDM).

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Introduction:

The gastrointestinal (GI) tract is the primary target of inflammatory bowel diseases (IBDs), which are chronic illnesses characterized by immune-mediated processes. Cycles of flare-ups and remissions are characteristic of these illnesses. IBDs are multifactorial, complicated disorders that result from complex interactions between the immune system, gut microbiota, environmental factors, and genetic predisposition [1–5]. The prevalence of pediatric IBD (PIBD) has increased dramatically in recent decades, especially in areas where prevalence was previously low [6]. The prevalence of PIBD more than doubled from 33 per 100,000 people in 2007 to 77 per 100,000 in 2016, according to an analysis of two large U.S. claims datasets [7].

Crohn's disease (CD) and ulcerative colitis (UC) are the two main phenotypes that are included in IBDs [**Fig 1**]. Transmural inflammation, patchy disease activity, and the alternating of inflamed and normal segments (skipped lesions) are the hallmarks of Crohn's disease, which affects the whole GI tract, including the perianal region. Strictures and/or fistulas are further distinguishing characteristics; the most common manifestation is ileocolonic involvement. Granulomas, which are frequently missing, are what set CD apart from UC [8]. Proctitis, left-sided colitis, or pancolitis—the latter most commonly seen in juvenile cases—are the outcomes of UC, which is typically limited to the colon and presents as persistent rectal inflammation that advances proximally [9,10]. Although they are possible, backwash ileitis and upper gastrointestinal tract involvement are not prevalent in pediatric UC [12]. Notably, it might be difficult to distinguish between CD and UC because up to 10% of pediatric IBD patients have overlapping symptoms. Many of these IBD-unclassified ambiguous cases eventually develop into definite CD or UC [13]. Primary sclerosing cholangitis (PSC-IBD), which is frequently regarded as a separate phenotype because of its distinctive inflammation patterns, including proximal colon involvement, rectal sparing, and backwash ileitis, coexists with IBD in many children, especially those with UC. Increased risks of cholangiocarcinoma and colorectal cancer are linked to this phenotype [14,15]. In rare instances, a monogenic illness is much more likely to be identified as the underlying cause of IBD-like inflammation, especially in children with extremely early onset IBD (IBD diagnosed before age six). This probability varies from 13% to 41% among newborns with illness onset [16]. These monogenic origins encompass a wide range of illnesses, including intestinal epithelial cell abnormalities and primary immunodeficiencies, which frequently call for special treatment approaches [17]. In-depth analyses of these genetic foundations have already been published elsewhere [16,18].

Differential Diagnosis:

Given that delayed diagnosis is linked to a higher risk of complications, it is imperative that individuals suspected of having inflammatory bowel disease (IBD) be identified as soon as possible and referred for endoscopic evaluation. At the time of diagnosis, these consequences include internal fistulas, strictures, and decreased linear growth [19]. Regardless of the results of biomarkers, patients who come with overt rectal bleeding or perianal disease—which manifests as abscesses, ulcers, or fistulae (but not skin tags or fissures)—should have a colonoscopy [20]. On the other hand, distinguishing IBD from other organic or functional gastrointestinal illnesses may be more difficult in children who exhibit milder symptoms [20]. Less than 1% of this birth cohort had an IBD diagnosis during follow-up, despite the fact that more than 25% of children in a large population-based research in Sweden reported having recurrent functional stomach pain by the age of 16 [21]. A systematic, three-tiered diagnostic strategy that includes symptoms, hemoglobin, C-reactive protein (CRP), and fecal calprotectin offers a dependable, noninvasive way to assess probable IBD in instances without significant red flags, such as overt rectal bleeding or perianal illness [22]. Having a first-degree relative with confirmed IBD, unexplained weight loss, and extraintestinal symptoms like joint involvement (arthropathy and arthritis), skin conditions (erythema nodosum, pyoderma gangrenosum), ocular problems (uveitis, episcleritis), or hepatic disorders (primary sclerosing cholangitis, autoimmune hepatitis) are additional clinical indicators in children with chronic (≥4 weeks) abdominal pain, diarrhea, or both [22–25]. Additionally, although nonspecific, growth failure and delayed puberty may be the first signs of pediatric IBD, especially Crohn's disease [26, 27]. Anemia

increased inflammatory markers, thrombocytosis, and hypoalbuminemia are among the laboratory abnormalities frequently seen in IBD; nevertheless, normal blood test findings do not rule out the condition [26]. Intestinal inflammation is more strongly correlated with fecal inflammatory indicators, especially fecal calprotectin, than with blood-based markers. As intestinal inflammation worsens, feces include more calprotectin, a bacteriostatic cytosolic protein secreted by neutrophils [28]. IBD is firmly ruled out as a diagnosis when fecal calprotectin levels are normal (<50 μg/g) [29], while the probability of IBD increases as calprotectin levels rise. If infectious pathogens, such as Clostridium difficile, are ruled out, a referral for endoscopic assessment is highly advised when fecal calprotectin values surpass 250 μg/g [30–32]. Calprotectin can be substituted by lactoferrin, another fecal marker of neutrophil-driven inflammation. Its potential benefits are yet unknown, though, and its therapeutic value has not been well investigated [33].

Evidence-Based Treatment:

Before recently, biologics were only used to treat inflammatory bowel disease (IBD) when normal medications failed to produce clinical remission, which is the resolution of symptoms. This technique was known as the conventional step-up strategy. Historically, corticosteroids or exclusive enteral nutrition (EEN) were used to induce remission in Crohn's disease (CD), irrespective of the severity of the illness or prognostic factors for unfavorable outcomes [34]. EEN is thought to modify immune responses, reduce local inflammation, restore the integrity of the mucous and epithelial barriers, and change the gut microbiota. It consists of a full liquid formula-based diet that is given for 6 to 8 weeks [35]. Practical issues like long-term dietary restrictions and the unpalatable nature of liquid formulas have hindered EEN's adoption in the US, even though North American and European guidelines recommend it as first-line therapy for pediatric CD with purely inflammatory presentations [35]. Although corticosteroids are just as successful in producing remission, there is a considerable chance that they will cause systemic side effects, such as high blood pressure, high blood sugar, and weakened bones. Additionally, EEN has the benefit of treating nutritional deficits that are frequently identified at diagnosis [35, 36].
While thiopurines (azathioprine or 6-mercaptopurine), which were once widely used, are now prescribed selectively because of uncommon but severe long-term side effects, including lymphoma and nonmelanoma skin cancer, methotrexate is the recommended immunomodulator in North America for sustaining remission [37]. The primary use of these medications is for concurrent autoimmune liver disorders [37, 38]. On the other hand, thiopurines are currently used on an individual basis in Europe, where they have historically been preferred [39]. While maintenance therapy for pediatric ulcerative colitis (UC) mostly uses aminosalicylates, frequently in conjunction with thiopurines in Europe, remission is typically achieved with corticosteroids, aminosalicylates, or both. Interestingly, UC management does not use EEN [40].

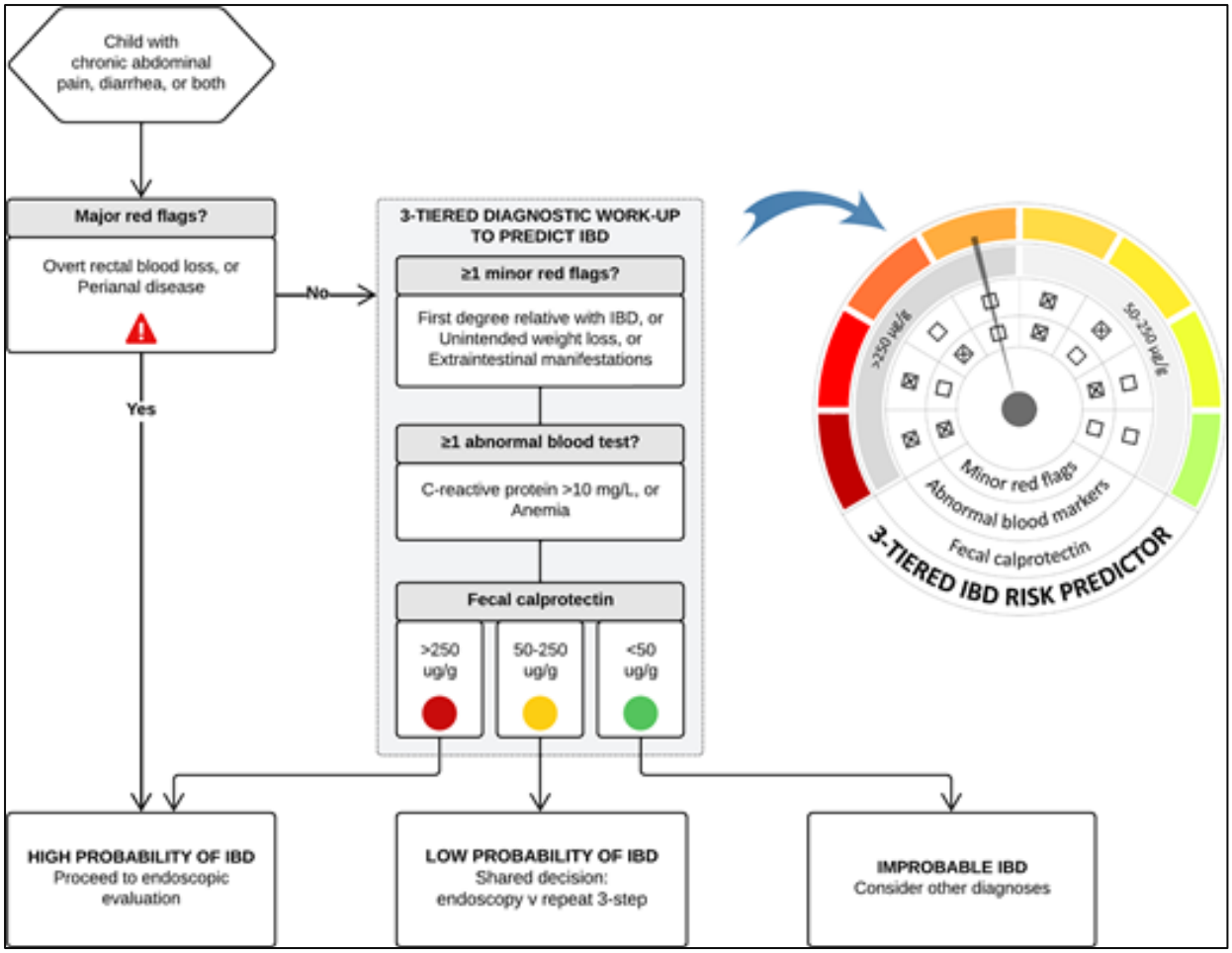

Figure 1: Decision Tree for Inflammatory Bowel Disease.

The majority of IBD patients show clinical improvement in 2–4 weeks after induction therapy [41]. The alleviation of symptoms does not, however, ensure that the underlying intestinal inflammation will stop, which could lead to long-term problems and increasing bowel damage [42]. As a result, more complete results are now the top priority in modern IBD management. While clinical remission and the return of fecal calprotectin and C-reactive protein levels to baseline are considered medium-term goals, symptom alleviation is considered a short-term goal. Endoscopic and transmural healing, growth normalization, quality-of-life restoration, and the lack of functional handicap are long-term goals. Histological or molecular remission are examples of advanced endpoints that are still debatable and difficult to attain [41–45]. To expedite treatment goals, upfront biological therapy—possibly in conjunction with surgical intervention—is advised for CD patients who present with high-risk indicators, such as stricturing/penetrating disease, perianal fistulas, deep colonic ulcers, or panenteric disease [39, 46, 47]. In cases of significant growth limitation, anti-tumor necrosis factor (anti-TNF) therapy should also be taken into consideration. All patients who do not achieve short- and medium-term treatment goals within 12 weeks of starting induction therapy are recommended to be promptly escalated to anti-TNF medication [39]. This step-up strategy is more common in North America, where thiopurines are used less frequently [48]. In order to identify CD patients who are at high risk for problems and might benefit from early anti-TNF treatments, Kugathasan et al. have created and validated a prediction model that uses clinical, serological, and genetic variables [49]. Early biological therapy may also be promising for UC, according to new data from adult studies [50]. The validated Pediatric Ulcerative Colitis Activity Index, which is based on important historical and clinical criteria, is an effective tool for evaluating the severity of pediatric illness [51–53]. By improving long-term efficacy, minimizing side effects, and facilitating customized dose modification, therapeutic drug monitoring (TDM) has completely transformed the use of biologics. In order to adjust

dosage and administration intervals based on pharmacokinetics, TDM measures trough drug levels, or serum concentrations just before further intravenous or subcutaneous doses. Target trough levels for anti-TNF drugs are well established, but research is currently ongoing to determine comparable benchmarks for more recent biologics such ustekinumab and vedolizumab [39].

Biologics in Pediatric IBD Management

The biological agents employed in pediatric IBD treatment demonstrate distinct mechanisms and applications:

1. **Anti-TNF Agents**:

- **Infliximab (IV)**: Utilized upfront in high-risk CD cases or severe growth delays, or as a step-up for nonresponders to conventional therapies (EEN, steroids, or methotrexate). For UC, infliximab addresses steroid dependency and cases refractory to aminosalicylate-based maintenance therapy [38, 64].
- **Adalimumab (SC)**: Employed similarly to infliximab for CD, and for UC patients intolerant to or losing response to infliximab [38, 64].
- **Golimumab (SC)**: Specifically indicated for UC refractory to conventional maintenance therapies [64].

2. **Anti-integrin (Vedolizumab, IV)**: Recommended for both CD and UC after anti-TNF failure [38, 64].
3. **Anti-IL-12/IL-23 (Ustekinumab)**: Administered via a single IV loading dose followed by subcutaneous maintenance, it is reserved for CD patients unresponsive to anti-TNF therapy [38].

Emerging Therapies

Two novel approaches warrant mention despite not yet being standard in pediatric IBD care. First, exclusion diets devoid of processed foods, such as the Crohn's Disease Exclusion Diet and the CD Treatment-with-Eating Diet, are under investigation for their potential to replicate EEN efficacy while addressing palatability challenges [55–58]. Second, fecal microbiota transplantation (FMT) aims to restore a dysbiotic microbiome and has shown efficacy in adult UC patients, with pediatric trials for UC and CD currently underway. Preliminary reports indicate that FMT from screened donors is generally well-received by children and their families [59–63].

Child-Onset IBD and Adult-Onset IBD:

Studies have repeatedly shown that children with inflammatory bowel disease (IBD) are more likely to experience intestinal problems and a more aggressive course of the disease than people with IBD that develops in adulthood [65–67]. The longer lifetime risk linked to earlier onset, which permits the accumulation of more inflammatory damage, is partially responsible for this phenomena. Childhood onset, however, also probably indicates those who are more susceptible to IBD, with underlying variables playing a role in the disease's early initiation as well as its widespread course [65,67]. In addition, IBD that develops in childhood is linked to a threefold higher risk of all-cause death than the general population, and this risk continues throughout adulthood [14]. Although the absolute risk is still modest, this heightened risk is partially associated with a higher chance of cancer, especially gastrointestinal cancers [68]. Furthermore, although joint involvement is less common in this population, children with IBD are more likely to exhibit extraintestinal symptoms at diagnosis [69]. Reduced weight gain or impaired linear growth are two common symptoms of pediatric IBD (PIBD), which frequently interferes with normal growth and development [70]. Males with IBD had a slightly lower mean adult height than matched controls, but the difference was less than an inch, according to a retrospective research that included 436 PIBD patients [71]. Catch-up growth frequently happens in early adulthood, and adolescents with IBD may have prolonged growth periods [72]. Females with Crohn's disease (CD) are especially prone to pubertal delay, which emphasizes the significance of early endocrinologist referral for prompt care [27,73].

Adolescents with IBD face unique challenges as they move from pediatric to adult care. Significant personal, social, emotional, neuroanatomical, and developmental changes characterize this process, which

takes place throughout "emerging adulthood," and is frequently accompanied by a decrease in parental involvement [74]. Parents usually play an important role in the family context, helping with disease monitoring, medication adherence, and advocating for their children in medical and educational contexts. However, IBD patients frequently experience a delayed transition to adulthood, which is associated with higher healthcare costs, difficulties, decreased treatment adherence, and increased disease progression [75]. Programs for structured transitional care have proven effective in reducing these difficulties. During the first two years after transition, these programs dramatically decreased hospital admissions and surgery rates, according to a meta-analysis of adolescents with chronic inflammatory disorders [76]. Lastly, compared to adult care, the therapeutic options for juvenile IBD are noticeably more constrained. Prior to being made available to young patients, the majority of innovative treatments undergo extensive testing and approval processes for adults. Newer drugs like vedolizumab and ustekinumab are still not approved for usage in children, whereas infliximab was approved for pediatric Crohn's disease eight years after it was first approved for adults [77–79]. As a result, many kids are given off-label medications, frequently without solid pediatric-specific safety and dosage information. The PIBD Network has released consensus statements to close this gap and optimize pediatric clinical trial design in order to improve treatment results and shorten regulatory delays [80].

IBD and Familial Risk:

The most important risk factor for acquiring inflammatory bowel disease (IBD) is still having a first-degree family who has the illness [81]. Determining whether people with a higher familial risk would benefit from preventive measures is a difficult problem with no easy answers. More than 200 genetic loci linked to an elevated risk of Crohn's disease (CD), ulcerative colitis (UC), or both have been found through genome-wide association studies (GWAS), which have thoroughly examined IBD among complicated disorders using data from over 25,000 people [1,82,83]. Numerous cellular functions, including the innate immunological response to bacterial compounds, the function of the epithelial barrier, and the cellular stress response, are mediated by the genes associated with these loci [84]. These results imply that the pathophysiology of IBD can result from malfunctions in interrelated molecular pathways that are essential for preserving intestinal tract immunological homeostasis [85]. Future customized preventative techniques based on individual genetic susceptibilities may become possible since different cellular pathways differ in their sensitivity to environmental stressors. However, population-level retrospective analyses, which are prone to recall bias and reverse causality, provide the majority of the current evidence on environmental risk factors [2]. Smoking, urban living, cesarean delivery, tonsillectomy, appendectomy, use of antibiotics or oral contraceptives, lactose intolerance, and vitamin D insufficiency are all environmental factors linked to IBD and raise the incidence of CD. On the other hand, UC risk is also associated with vitamin D deficiency, urban living, and the use of oral contraceptives [2]. High vitamin D levels, bed sharing, breastfeeding, and being close to pets or farm animals are all protective factors. Notably, appendectomy and smoking are protective for UC but risk factors for CD [2].

Dietary practices are one of the environmental factors that may be changed the most and have a direct bearing on preventing IBD. While diets heavy in fruits, vegetables, and fiber are beneficial, diets high in meat, sweets, and ultraprocessed foods are linked to an elevated risk of IBD [2,86,87]. Food additives such artificial emulsifiers and sweeteners may alter the composition and function of the gut microbiota, according to research in animal models and a small number of human studies [88]. There are also ongoing prospective trials looking into dietary changes to prevent IBD in people who are at risk [89,90]. Although making significant dietary changes might be difficult, a child's diagnosis of IBD should start a conversation about changing to a better diet, which could help the whole family, even siblings who are not afflicted. IBD-focused dietitians can be a great resource for highlighting this strategy. Changes in the intestinal microbiota influence several dietary and environmental factors that impact the risk of IBD. A key mechanism behind these interactions is increasingly understood to be dysbiosis [91,92]. Restoring a healthy microbiota has drawn interest as a possible therapeutic strategy. The sustainability and consistency of the effects of fecal microbiota transplantation (FMT) are yet unknown, despite the fact that it appears to have greater potential for UC than CD [91,92,94]. The routine use of prebiotics or probiotics to treat IBD in adults or children is

not supported by current research [95,96]. Currently, the only way to prevent IBD in high-risk children through microbiome-targeting therapies is through research.

Primary Care of IBD:

A highly coordinated and multidisciplinary healthcare approach is necessary when caring for children with inflammatory bowel disease (IBD). Primary care physicians, pediatric gastroenterologists, dietitians, physiotherapists, and psychological support groups are all included in this [97]. Primary care physicians may experience extraintestinal symptoms, which might be caused by independent inflammatory events with common genetic predispositions or by immune responses that have been translocated from the colon [98]. While some symptoms, like erythema nodosum, oral aphthous ulcers, and episcleritis, may go away with good intestinal inflammation control, other symptoms, including primary sclerosing cholangitis, anterior uveitis, and ankylosing spondylitis, frequently develop on their own [99].

Even when the disease is in remission, fatigue, a chronic and incapacitating symptom in many pediatric IBD (PIBD) patients, frequently compromises quality of life [100]. Numerous factors, such as disease activity, medication, hematologic deficiencies, family dynamics, psychological well-being, and physical activity levels, all have an impact on this symptom. A multifaceted strategy is required for optimal care, which includes physical training regimens, iron and other vitamin supplements, and more intensive treatment for deeper remission [101]. In order to treat fatigue, it is essential to screen for behaviors like excessive use of electronic media, which interferes with sleep [102]. Although only a small percentage of PIBD patients fit the diagnostic criteria for mental illnesses, psychological variables such as anxiety and sadness are common in about one-third of these patients [103]. In these situations, cognitive behavioral treatment has proven to be effective. In the treatment of PIBD, procedural anxiety is a major problem, particularly for children who need frequent biologic infusions. Topical anesthetics are good at controlling pain, but they don't help with procedural dread, which can cause PTSD and anticipatory anxiety. To reduce medical trauma, distraction strategies including play therapy, virtual reality, and guided imagery are advised [104]. Patients with PIBD are also at risk for adverse medication reactions, with infections being the most frequent side effect. According to a Swedish cohort research, patients with PIBD had a roughly tenfold higher risk of hospitalization due to severe infections than the general population [107]. Sometimes stopping immunosuppressants is required to speed up recovery [106]. It is crucial to proactively maximize immunization status before starting immunosuppressive treatment. Although yearly influenza vaccination is generally advised, live vaccinations are contraindicated while receiving high-dose corticosteroids, thiopurines, methotrexate, or biologics [108].

Malnutrition, severe active disease, and high-dose corticosteroid treatment increase the likelihood of catastrophic consequences, yet the majority of PIBD patients have minor symptoms when it comes to COVID-19. Since immunization has been seen to produce high antibody responses, even in individuals with weakened responses to natural infection, vaccination against SARS-CoV-2 is strongly recommended [110,111]. One important factor in the therapy of PIBD is the possibility of cancers linked to medication. While European practice individualizes the use of methotrexate or thiopurines, many pediatricians in North America avoid this class of medications due to the link between thiopurine use and lymphoma [37, 39]. In a prospective cohort study with more than 24,000 patient-years, 15 patients had malignancies, and five of those patients had lymphoma; four of these patients were on thiopurines at the time of diagnosis. Interestingly, the increased risk goes away after stopping thiopurines for a year or more [112]. A systematic analysis in children reported no significant increase in lymphoma risk with anti-TNF medication [114], despite adult research suggesting a possible link between anti-TNF therapy and lymphoma risk [113]. These results highlight how crucial customized risk-benefit analyses are when developing a treatment plan for juvenile IBD [114].

Future Directions in IBD Treatment and Mangement in Children:

The treatment and management of pediatric inflammatory bowel disease (IBD) continue to evolve with advancements in research, technology, and clinical practices. IBD, encompassing Crohn's disease and

ulcerative colitis, presents unique challenges in children due to its chronic nature, multifaceted pathophysiology, and potential for long-term complications. Future directions aim to enhance therapeutic efficacy, improve quality of life, and address unmet needs in pediatric populations through innovations in personalized medicine, biologics, dietary management, digital health, and multidisciplinary care.

Advancements in Precision and Personalized Medicine

A significant focus of future IBD treatment lies in precision medicine, which tailors therapies based on genetic, molecular, and environmental factors unique to each patient. Advances in genomic and proteomic research are uncovering genetic variants and biomarkers associated with disease susceptibility, progression, and treatment response. These insights are paving the way for targeted interventions. For instance, pharmacogenomics can optimize medication selection, minimizing adverse effects while maximizing therapeutic outcomes. Emerging techniques, such as transcriptomic profiling and microbiome analysis, offer further potential to refine treatment strategies and predict disease trajectories. Additionally, machine learning and artificial intelligence (AI) are being integrated into clinical practice to analyze large datasets and predict individual responses to therapy. Predictive algorithms can guide clinicians in selecting optimal therapeutic pathways, thereby enhancing the precision of disease management.

Expansion of Biologic and Small Molecule Therapies

The development of biologic therapies has transformed the management of pediatric IBD, offering targeted approaches that modulate the immune response. Anti-tumor necrosis factor (TNF) agents, such as infliximab and adalimumab, remain foundational treatments, but newer biologics are expanding therapeutic options. Interleukin inhibitors (e.g., ustekinumab) and integrin inhibitors (e.g., vedolizumab) demonstrate efficacy in cases resistant to traditional biologics. Small molecule therapies, such as Janus kinase (JAK) inhibitors, represent another promising avenue. These oral agents provide an alternative to injectable biologics, with potential advantages in terms of patient compliance and accessibility. Future research aims to evaluate the long-term safety and efficacy of these therapies in pediatric populations, particularly given their limited use in children to date. Combination therapies, which integrate biologics with small molecules or other immunomodulators, are also under investigation. These strategies seek to enhance remission rates, reduce treatment failure, and prevent complications by targeting multiple pathways simultaneously.

Microbiome-Based Therapies

The gut microbiome is increasingly recognized as a critical factor in the pathogenesis and progression of IBD. Dysbiosis, or an imbalance in gut microbial communities, contributes to chronic inflammation and disease flares. Emerging therapies aim to restore microbial homeostasis through interventions such as fecal microbiota transplantation (FMT), probiotics, and prebiotics. FMT has shown promise in inducing remission in adult IBD patients, and ongoing trials are exploring its safety and efficacy in children. Similarly, next-generation probiotics, comprising specific strains with anti-inflammatory properties, are being developed as adjunctive treatments. These microbiome-based approaches highlight the potential for non-pharmacologic strategies to complement conventional therapies.

Dietary Interventions and Nutritional Support

Dietary management is a cornerstone of pediatric IBD care, particularly in mitigating disease activity and improving nutritional status. Exclusive enteral nutrition (EEN) is an established treatment for inducing remission in Crohn's disease, and its mechanisms continue to be elucidated. Future research seeks to refine dietary protocols and explore the role of specific nutrients, such as omega-3 fatty acids and fiber, in modulating inflammation. Personalized nutrition plans based on an individual's microbiome, genetics, and disease phenotype are a promising frontier. By tailoring dietary recommendations, clinicians can address specific deficiencies, promote gut healing, and reduce reliance on medications. Novel approaches, such as the Crohn's Disease Exclusion Diet (CDED), are gaining attention for their potential to sustain remission in pediatric populations.

Integration of Digital Health and Remote Monitoring

Digital health technologies are revolutionizing IBD management, enabling real-time monitoring and patient-centered care. Wearable devices and smartphone applications now facilitate the tracking of symptoms, medication adherence, and lifestyle factors. Remote monitoring systems allow clinicians to identify disease flares early, adjust treatment plans proactively, and reduce the need for hospital visits. Telemedicine has become an essential tool for delivering care, particularly in underserved or remote areas. Advances in digital platforms aim to enhance the accessibility and continuity of multidisciplinary care, ensuring that pediatric patients receive comprehensive support. Additionally, AI-driven chatbots and decision-support systems are being developed to assist patients and caregivers in managing daily challenges associated with IBD. These tools provide education, reminders, and emotional support, fostering self-management and empowerment.

Psychosocial Interventions and Mental Health Support

Psychological and emotional well-being are integral components of pediatric IBD management. High rates of anxiety, depression, and stress are reported among children with IBD, often exacerbated by the chronic nature of the disease and its impact on daily life. Future strategies prioritize early identification of mental health concerns and integration of psychosocial interventions into routine care. Cognitive behavioral therapy (CBT) and mindfulness-based stress reduction (MBSR) are evidence-based approaches that can improve coping skills, reduce stress, and enhance quality of life. The incorporation of virtual reality (VR) tools and digital mental health platforms offers innovative methods for delivering these therapies, particularly for children who may benefit from interactive and engaging formats.

Prevention of Long-Term Complications

Preventing complications such as growth failure, osteoporosis, and treatment-related malignancies remains a priority in pediatric IBD management. Early and aggressive control of inflammation is critical to mitigating these risks. Future research aims to identify optimal timing and intensity of interventions to achieve sustained remission while minimizing side effects. Vaccination strategies are another essential aspect of preventive care. As immunosuppressive therapies increase susceptibility to infections, ensuring that patients are adequately vaccinated is imperative. Research into novel vaccine formulations and schedules tailored to immunocompromised children could further improve outcomes.

Emphasis on Multidisciplinary and Holistic Care

The management of pediatric IBD requires a holistic approach that addresses physical, emotional, and social dimensions of health. Multidisciplinary teams, including gastroenterologists, dietitians, physiotherapists, psychologists, and social workers, are essential in delivering comprehensive care. Future models of care emphasize seamless collaboration and integration of services to optimize patient outcomes. Patient and caregiver education is another critical focus. Empowering families with knowledge about disease management, treatment options, and lifestyle modifications fosters shared decision-making and enhances adherence to therapeutic plans. The future of pediatric IBD treatment and management is marked by innovation and a shift toward personalized, patient-centered care. Advances in precision medicine, biologic and small molecule therapies, microbiome-based interventions, digital health, and psychosocial support offer new hope for improving outcomes and quality of life for children with IBD. By addressing the physical, emotional, and social challenges associated with the disease, these strategies aim to transform the landscape of pediatric IBD care, ensuring that each child receives optimal and individualized treatment. Continued research, collaboration, and investment in these areas are essential to achieving these goals and paving the way for a brighter future for children affected by IBD.

Conclusion:

Pediatric inflammatory bowel disease (PIBD) presents distinct challenges compared to adult-onset IBD, necessitating age-specific diagnostic and therapeutic approaches. Early diagnosis is critical, as delayed intervention increases the risk of complications, including growth failure, strictures, fistulas, and reduced

quality of life. Current diagnostic advancements, such as fecal calprotectin and comprehensive endoscopic evaluations, have significantly improved early detection. Noninvasive biomarkers are particularly valuable in differentiating PIBD from other gastrointestinal conditions in children with subtle or nonspecific symptoms. Traditional treatment options, including corticosteroids and exclusive enteral nutrition (EEN), remain pivotal in managing PIBD, particularly for inducing remission. However, corticosteroid-related side effects highlight the need for alternative options. Biologic therapies, particularly anti-TNF agents like infliximab and adalimumab, have emerged as transformative in PIBD treatment, enabling improved control of inflammation and disease progression. Advanced strategies, such as therapeutic drug monitoring (TDM), ensure optimized dosing, minimizing side effects and enhancing long-term remission rates. Emerging therapies offer additional promise. Exclusion diets designed to replicate the anti-inflammatory effects of EEN address practical barriers, improving compliance and patient satisfaction. Fecal microbiota transplantation (FMT), while still in the experimental phase, has demonstrated encouraging results in restoring gut microbiota balance, particularly for ulcerative colitis. These approaches reflect a growing trend toward personalized medicine in PIBD management. The distinction between child-onset and adult-onset IBD underscores the importance of tailored strategies. Children often experience more severe disease progression, with higher lifetime risks of complications and mortality. Effective early interventions, alongside evolving biologic and dietary strategies are critical for reducing the cumulative burden of inflammation and improving outcomes. Future research must focus on understanding the underlying mechanisms of PIBD, identifying predictive biomarkers for treatment response, and developing novel therapies. Collaboration across specialties, including gastroenterology, immunology, and nutrition, will further enhance care. Ultimately, a comprehensive, patient-centered approach combining early diagnosis, targeted treatment, and proactive management will optimize outcomes and improve the quality of life for children with PIBD.

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114 Bouhuys, M., Lexmond, W. S., & van Rheenen, P. F. (2023). Pediatric inflammatory bowel disease. *Pediatrics*, *151*(1). **رض الأمعاء الالتهابي – مراجعة محدثة من جوانب طب الأطفال**.

الملخص:

الخلفية :مرض الأمعاء الالتهابي (IBD) هو حالة مزمنة مناعية، تستهدف أساسًا الجهاز الهضمي. ويشمل نوعين رئيسيين: مرض كرون (CD) والتهاب القولون التقرحي (UC).وقد ارتفعت نسبة حدوث مرض الأمعاء الالتهابي لدى الأطفال (PIBD) بشكل كبير في العقود الأخيرة، لا سيما في المناطق التي كانت تتمتع بنسبة انتشار منخفضة تاريخيًا. هذه الحالات تشمل تفاعلات معقدة بين الاستعداد الوراثي، والميكروبيوم المعوي، والخلل المناعي، والعوامل البيئية.

الهدف :تهدف هذه المراجعة إلى استعراض أحدث التطورات في تشخيص وعلاج وإدارة مرض الأمعاء الالتهابي لدى الأطفال(PIBD) ، مع التركيز على التحديات المميزة في الحالات الأطفال مقارنةً بالـ IBD الذي يبدأ في مرحلة البلوغ.

الطرق :تجمع هذه المراجعة المحدثة الأدلة من الدراسات الحديثة والإرشادات السريرية المتعلقة بـPIBD ، مع التركيز على الأساليب التشخيصية، وطرق العلاج، والاستراتيجيات العلاجية المتطورة. كما يتم التركيز بشكل خاص على العلاجات البيولوجية، والتدخلات الغذائية، والتمييز بين PIBD وأمراض الجهاز الهضمي الأخرى.

النتائج :يظل التشخيص المبكر لـ PIBD أمرًا بالغ الأهمية لتقليل المضاعفات. بينما تساعد العلاجات التقليدية، مثل الكورتيكوستيرويدات والتغذية المعوية الحصرية (EEN)في تحقيق التRemission، فإن العلاجات البيولوجية مثل العوامل المضادة لـ TNF والعلاجات الناشئة) مثل العوامل المضادة لـ IL-12/IL-23 وزرع الميكروبيوتا البرازية (تظهر فاعلية معززة. يتم تخصيص العلاجات البيولوجية بناءً على شدة المرض وملفات المرضى، مع تحسين النتائج باستخدام مراقبة الأدوية العلاجية .(TDM) توفر الأدوات التشخيصية الجديدة، مثل الكالبروتكتين البرازي، طرقًا غير جراحية للكشف المبكر. كما أن الأنظمة الغذائية الاستبعادية الناشئة والتركيز على الميكروبيوتا تحمل وعدًا لتحسين النتائج في إدارة.PIBD

الاستنتاج :يتطلب مرض الأمعاء الالتهابي لدى الأطفال استراتيجيات إدارة مخصصة تختلف عن تلك الخاصة بالـ IBD الذي يبدأ في مرحلة البلوغ بسبب مسار المرض الفريد، بما في ذلك ضعف النمو والأضرار الالتهابية المطولة. لقد حسنت التطورات في العلاجات البيولوجية، والتدخلات الغذائية، والأدوات التشخيصية من فعالية العلاج وجودة حياة المرضى. إن التدخل المبكر، والعلاجات الشخصية، والبحث المستمر في الأساليب الناشئة أمر بالغ الأهمية لتحسين النتائج على المدى الطويل.

الكلمات المفتاحية :مرض الأمعاء الالتهابي لدى الأطفال(PIBD) ، مرض كرون، التهاب القولون التقرحي، العلاجات البيولوجية، التغذية المعوية الحصرية(EEN) ، الكالبروتكتين البرازي، مراقبة الأدوية العلاجية.(TDM)