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Challenges and Advances in the Diagnosis and Management of Pediatric Inflammatory Bowel Disease: A Systematic Review

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Abstract

Pediatric inflammatory bowel disease (PIBD), encompassing Crohn's disease and ulcerative colitis, presents increasing diagnostic and therapeutic challenges. Delays in diagnosis and variability in treatment strategies can negatively impact disease progression and patient outcomes.

To systematically review recent literature on PIBD, identifying diagnostic obstacles, examining current treatment modalities, and evaluating evidence-based approaches for selecting optimal first-line therapies.

Nineteen studies published between 2017 and 2023 were reviewed, including narrative reviews, systematic reviews, consensus guidelines, and meta-analyses. The studies covered diverse populations across North and South America, Europe, Asia, and Oceania.

Common themes included significant diagnostic delays due to nonspecific symptoms, underutilization of non-invasive biomarkers, and the critical role of early specialist referral. Emerging tools such as fecal calprotectin and genetic testing are aiding early detection. Treatment is shifting toward early biologic use, especially anti-TNF agents, in moderate to severe cases. Personalized care models, therapeutic drug monitoring, and multidisciplinary approaches have shown promise in improving disease control and long-term outcomes. System-level challenges—

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such as delayed drug approvals, insufficient transitional care, and limited pediatric trials—remain barriers to optimal care.
Early diagnosis and individualized, evidence-based treatment strategies are essential for improving outcomes in children with IBD. Standardized protocols, access to biologics, and structured transition to adult care are critical. Continued research and global collaboration are needed to refine diagnostic tools, expand therapeutic access, and establish unified care standards for pediatric IBD. Let me know if you want.
Keywords: Pediatric inflammatory bowel disease, Crohn's disease, ulcerative colitis, diagnostic delay, biomarkers, biologic therapy, personalized medicine.

التحديات والتطورات في تشخيص وعلاج مرض الأمعاء الالتهابي لدى الأطفال: مراجعة منهجية

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الملخص
يمثل مرض الأمعاء الالتهابي لدى الأطفال(PIBD) ، الذي يشمل داء كرون والتهاب القولون التقرحي، تحديات متزايدة في التشخيص والعلاج. يمكن أن تؤدي التأخيرات في التشخيص وتفاوت استراتيجيات العلاج إلى تأثير سلبي على تطور المرض ونتائج المرضى.
مراجعة منهجية للأدبيات الحديثة حولPIBD ، لتحديد العقبات التشخيصية، وفحص الأساليب العلاجية الحالية، وتقييم الطرق المبنية على الأدلة لاختيار العلاجات الأولية المثلى.
تمت مراجعة تسعة عشر دراسة نُشرت بين عامي 2017 و2023، شملت مراجعات

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سردية ومنهجية، وإرشادات توافقية، وتحليلات تلوية. شملت الدراسات مجموعات سكانية متنوعة في أمريكا الشمالية والجنوبية، وأوروبا، وآسيا، وأوقيانوسيا. أبرزت النتائج عدة قضايا شائعة، منها التأخر الكبير في التشخيص بسبب الأعراض غير النوعية، وضعف استخدام المؤشرات الحيوية غير الغازية، وأهمية الإحالة المبكرة للأخصائيين. تساهم أدوات ناشئة مثل الكالبروتكتين البرازي والاختبارات الجينية في الكشف المبكر. يتجه العلاج نحو الاستخدام المبكر للعلاجات البيولوجية، خاصة مضادات عامل نخر الورم (anti–TNF) في الحالات المتوسطة إلى الشديدة. أظهرت نماذج الرعاية الشخصية، ومراقبة مستويات الأدوية، والمقاربات متعددة التخصصات وعدًا في تحسين التحكم في المرض والنتائج طويلة الأمد. لا تزال التحديات على مستوى الأنظمة، مثل تأخر الموافقات على الأدوية، ونقص الرعاية الانتقالية، وقلة التجارب السريرية لدى الأطفال، عوائق أمام تقديم الرعاية المثلى. يُعد التشخيص المبكر واستراتيجيات العلاج الفردية المبنية على الأدلة ضرورية لتحسين النتائج لدى الأطفال المصابين بمرض الأمعاء الالتهابي. تُعد البروتوكولات الموحدة، وتوفير العلاجات البيولوجية، والانتقال المنظم إلى رعاية الكبار عناصر أساسية. لا بد من مواصلة البحث والتعاون العالمي لتحسين أدوات التشخيص، وتوسيع نطاق العلاج، ووضع معايير موحدة لرعاية مرضى.PIBD

الكلمات المفتاحية: مرض الأمعاء الالتهابي لدى الأطفال، داء كرون، التهاب القولون التقرحي، تأخر التشخيص، المؤشرات الحيوية، العلاج البيولوجي، الطب الشخصي.

1. Methods

Study Design and Data Sources:

This is a narrative literature review aimed at synthesizing current evidence on the diagnosis and management of pediatric inflammatory bowel disease (PIBD). A total of 19 studies published between 2017 and 2023 were identified through searches of PubMed, Scopus, and reputable pediatric gastroenterology journals. Articles were selected based on relevance to the study question and their contribution to the understanding of diagnostic challenges, treatment options, and patient outcomes in PIBD.

Inclusion Criteria:

- Published between 2017 and 2023

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❖ Focused on children and adolescents diagnosed with inflammatory bowel disease
❖ Addressed topics including diagnosis, biomarkers, treatment strategies, or clinical management guidelines
❖ Study types included systematic reviews, meta-analyses, narrative reviews, consensus statements, and expert reviews
❖ Published in English and indexed in peer-reviewed journals

Exclusion Criteria
❖ Studies focused solely on adult IBD populations.
❖ Case reports, editorials, and abstracts without full study data.
❖ Non-English publications.
❖ Articles not addressing clinical diagnosis or treatment aspects.
❖ Duplicate studies or those lacking sufficient methodological detail.

Selection Process
Titles and abstracts were screened for relevance. Full texts were reviewed to confirm eligibility based on the criteria above. The final selection included studies from diverse geographic regions, representing varied healthcare systems and clinical practices. Data Extraction and Analysis For each included study, the following information was extracted: author(s), publication year, country, journal, study design, aims, sample size (if applicable), and key findings related to diagnosis or management. Findings were categorized thematically into diagnostic challenges, biomarker use, treatment approaches, systemic barriers, and emerging therapies. Due to the heterogeneity in study design and outcomes, results were synthesized narratively rather than statistically.

2. Introduction

Pediatric inflammatory bowel disease (PIBD), which includes Crohn's disease (CD), ulcerative colitis (UC), and IBD-unclassified (IBDU), is a chronic, relapsing inflammatory disorder of the gastrointestinal tract that presents unique challenges in children and adolescents. Over the past two decades, the incidence of PIBD has increased globally, placing a significant burden on healthcare systems and affecting the quality of life of affected children. Early and accurate diagnosis is essential to initiate timely treatment and prevent disease progression, yet many patients experience delays

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due to nonspecific symptoms, overlapping presentations with other gastrointestinal disorders, and limited awareness at the primary care level. These diagnostic delays are associated with increased risk of complications, poor growth, and psychosocial challenges. Management of PIBD has evolved significantly, with a growing emphasis on personalized treatment strategies aimed at achieving mucosal healing and long-term remission. Advances in biologic therapies, therapeutic drug monitoring, and the use of genetic and biomarker profiling are transforming the treatment landscape. However, disparities in access to care, lack of pediatric-specific clinical trials, and gaps in transitional care continue to limit optimal outcomes. This review aims to highlight the key barriers to timely diagnosis of PIBD, evaluate current treatment modalities, and identify the most effective first-line therapies based on recent evidence. By synthesizing findings from 19 international studies, this review seeks to support clinicians in improving diagnostic accuracy, therapeutic decision-making and overall patient outcomes in pediatric IBD (Table 1).

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Table 1: Summary of Included Studies

Study's Authors	Published Date and	Publication Journal	Aim	Study design	Sample size	study Periods	Study/ Management technique	Outcome/ Conclusion
[1] J.K. Yamamoto Furusho	Available online 15 February 2017 Mexico	REVISTA DE GASTROENTEROLOGIA. DE MEXICO	To promote a perspective adapted to Latin American countries in relation to the diagnosis, treatment, and monitoring of patients with UC and CD	Review Article	Review Article		*PANCCO guidelines*	A need to raise awareness in gastroenterologists and the population for early diagnosis and treatment of (IBD) …. Important for all physicians to have homogeneous criteria regarding the diagnosis and treatment of IBD

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[2] Kelly Sandberg	May 2020 USA	Current Problems in Pediatric and Adolescent Health Care Journal.	To suggests an agenda for how best manage IBD early in the disease course in adult and pediatric patients, as an early diagnosis and treatment gateways for Improved Prognosis	Review Article	Review Article		A combination of clinical and laboratory data can be suggestive, a diagnosis of IBD must be confirmed through radiologic, endoscopic and histological findings.	Prompt diagnosis and referral to a pediatric gastroenterologist minimizes complications and maximizes quality of life.
[3] Javier Martín-de-Carpi	Available online 11 April 2020 Spain	*Anales depediatria* Published by Elsevier Espana, S.L.U.	Define the different intervals, into which the time until the diagnosis divided, to avoid, as far as possible, the diagnostic delay	Special article	Special article	Special article	Key points for an early diagnosis. Provide tools to reduce the time to diagnosis.	An early diagnosis of IBD reduces complications, and can improve the prognosis.
[4] Vernon-Roberts,	March 2023 New Zealand	Journal of Pediatric Gastroenterology and Nutrition.	To identify factors associated with prolonged diagnostic delay	Systematic review	Systematic review	Systematic review	Diagnostic Period Calculated from first symptoms to primary care assessment, tertiary care referral, and then endoscopy confirm	Improvements to awareness or infrastructure may reduce diagnostic delay in order to minimize the risk of poor outcomes.

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[5] Marleen Bouhuys,	2023 Jan 1 USA	Pediatrics Journal By American Academy of Pediatrics.	To provide general pediatricians with an update on pediatric IBD to facilitate interactions with pediatric gastrointestinal specialists.	Review Article	Review Article	Review Article	Evaluation of blood and stool markers to select children for endoscopy; and therapeutic drug monitoring	A combination of patient history and blood and fecal biomarkers can help to distinguish suspected IBD from other causes of abdominal pain or diarrhea. .. A personalized IBD prevention strategy based on a child's genetic profile may someday become reality… Transfer of adolescent to adult care is a risk for disease relapse, which highlights patient vulnerability for a transition program.

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[6] Zubin Grover	Published online: 09 November 2021 Canada	Pediatric Medicine journal	To provide a contemporary overview of the IBD in children, with a focus on common pitfalls and progress in the modern management of pediatric IBD	Peer reviewed articles	Peer reviewed articles	Peer reviewed articles	This review mainly includes articles addressing diagnosis and management of IBD in children	A prompt diagnosis, in-depth staging, and early aggressive treatment selection, in those with high-risk disease, can only achieve treatment goals in IBD that aiming for deeper remission.
[7] Kohei Wagatsuma,	Published online 2021 Dec 10 Japan	Life 2021, 11, 1375 MDPI	Systematically review the usefulness and limitations of biomarkers that can used in daily clinical practice regarding IBD	Comprehensive Review	Comprehensive Review	Comprehensive Review	Comprehensively review the usefulness and limitations of biomarkers that can used in daily clinical practice regarding IBD.	To date, no biomarker is accurate to replace endoscopy; however, it is important to understand the characteristics of each biomarker and use the appropriate biomarker at the right time in daily clinical practice.

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[8] Rishi Bolia	Accepted: 22 August 2022 Brazil	Arq Gastroenterol. v. 59 nº 4 out/dez 531 AG-2022-93	To determine the proportion of children with IBDU who undergo subsequent reclassification.	Systematic review & meta-analysis	Systematic review	Systematic review	PubMed and Scopus searched for publications related to (PIBD) published between Jan 2014 and July 2021.	Half of Unclassified (PIBD) at initial re-classified into UC or CD. The therapeutic goal of IBD patients IBD is biochemical or endoscopic remission, rather than clinical remission. CD patients with predictors of poor outcome should get upfront biological therapy.
[9] Zachary Green ,	Published online Oct 27, 2023. UK.	Translational Pediatrics journal	To identify recent works relevant to recent developments in the assessment and management of PIBD Particularly within the UK and Europe (Advanced used guide)	Narrative review	Summarizes recent research (2017–2022) related to pIBD.		Discuss: The Biomarkers (faecal calprotectin, and video capsule endoscopy for disease monitoring); Genomic testing. Therapeutic drug levels.	Personalized therapy must the target for researchers and clinicians focused on pIBD.

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[10] Graziella Guariso	2017 Aug 14; 23 (30): 5469–5485 Italy	World Journal of Gastroenterology	To provide update on the most recent advances in treatment of paediatric IBD	Systematic reviews and meta-analyses			Monitoring the individual metabolism, toxicity and response to relevant medications in IBD including thiopurines and New biologics	Major advances have already achieved in therapeutic drug monitoring are the prognostic biomarkers.
[11] Manasi Agrawal, Elizabeth A. Spencer	Published: April 30, 2021 British	Reviews in basic and clinical gastroenterology and Hepatology	To summarizes the existing literature on, and proposes a framework for how best manage CD and UC early in the disease course in adult and pediatric	Reviews and perspective			User's Guide for Adult and Pediatric Gastroenterologists. Framework (agenda) literature, and proposes	Personalized care and selection of appropriate first-line therapy based on risk assessment, disease activity, and clinical characteristics of the patient.
[12] Stephanie B Oliveira	(Published 31 May 2017 British	British Medical Journal (BMJ)	To achieve sustained control of intestinal inflammation and monitor for potential complications of the disease and side effects of therapies	Clinical Review/ State of Review Article			This review summarizes the evidence on the pathophysiology, diagnosis, and approaches to management of PIBD.	The management of IBD in children is less extensive than in adults.

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[13] Corinne Légeret	Published online 2022 Apr 26 Switzerland	MDPI Children (Basel). 2022 May 9 (5): 617.	An overview of current recommendations, therapeutic options, drug monitoring, and practical guidelines for PIBD patients	Narrative Review	A Narrative Review	A Narrative Review	The equivalent tool to assess disease activity and response to treatment in clinical practice of paediatric CD (PCDAI)	In combined with the acquired insight in the gastrointestinal microbiome, diets, not only for the induction but also for the remission of the disease in children with CD; The faecal transplantation and probiotics still under investigation. Additionally highlights upon the approval for treatments with anti-TNF-α drugs, which are currently the first-line biological agent for the treatment of moderate /severe PIBD. As well, points about drug levels

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								measurement and drug-antibodies as a supports in guiding therapy strategies. If not achieving the desired clinical result, Immunomodulators can added
[14] Way Seah Lee,	Accepted for publication 25 Decem. 2022. Australia, Ltd.	Journal of Gastroenterology & Hepatology. Foundation and John Wiley & Sons	Providing an up-to-date, evidence-based approach to PIBD in the Asia-Pacific region, taking into consideration the unique disease characteristics and financial resources available in this region.	Review Article	Review Article	Review article	A group of pediatric gastroenterologists with special interest in PIBD performed an extensive literature search covering epidemiology، disease character, natural history, management, and monitoring.	In some populations in Asia, the Nudix Hydrolase 15 (NUD15) **gene** is a better predictor of leukopenia induced by azathioprine than (TPMT)

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[15] Nicholas M. Croft	Advance access publication 21 September 2022 UK Journal of Crohn's and Colitis (JCC) 2023 Oxford University Press on behalf of European Crohn's and Colitis	To provide a forum to discuss delays between adult and paediatric drug approvals for advanced drugs to treat IBD insurance companies, regulatory agencies, and health institutional leaders and/or administrators	Multi-stakeholder perspective.	Participants 62 (pharma. companies, FDA and EMA and patient community)	A 2-day virtual meeting	Multi-Stakeholder discussed; what is like to be a teenager living with IBD; how drug development can supported; and how to speed up drug trials and approvals for PIBD	Collective action points for all stakeholders are required to make progress and facilitate new drug development for children.
[16] Elizete Aparecida LOMAZI	Accepted 5 Sept. 2022 Brazil Consensus of the Brazilian Organization for CD&UC	To provide guidance on most effective medical and surgical Manag. of PIBD	Literature review	Literature review	Literature review	A rapid review performed to support recommendations/ statements.	Guidance recommend. according to the stage of treatment and severity of the disease in three fields**:** **E**valuating the effectiveness of medical treatment. **F**ollow-up/monitoring after initial treatment. **S**urgical recommend according to disease type.

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[17] Charlotte M. Verburgt	Published online: 06 Jul 2021 UK	Expert Review of Gastroenterology & Hepatology.	Todescribe available evidence concerning the use of antibiotics in the treatment of children with IBD.	Systematic review	Systematic review		Studies comparing the use of antibiotics versus (other) antibiotics, another active comparator, placebo, or no therapy.	More studies conducted in order to assess the efficacy and safety of using antibiotics in PIBD
[18] Zhaobei Cai	20 December 2021 China	Frontiers in medicine. Front. Med 8:765474. doi:10.3389/fmed.2021.765474	Reviewed the conventional and the novel drugs and therapies, as well as the potential ones, revealed promise in preclinical studies and are likely to be effective future therapies.	Comprehensive Review			Summarized the latest progress in IBD treatment to understand the advantages, pitfalls, and research prospects of different drugs and therapies and to provide a basis for the clinical decision and further research of IBD	Varied therapeutic options (small molecules, apheresis therapy، cell therapy, and Exosome therapy) are emerging, as fractions of patients do not respond to available treatments... Patient education on diet and psychology appears to benefit IBD treatment… **Antibiotics** expected to be a future treatment choice for IBD...

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[19] Jonathan Van Hecke	First published: 12 March 2023 Belgian	Journal of Gastroenterology and Hepatology	An overview of the existing prospective Cohorts and registries reporting on disease activity in PIBD.	Systematic review of prospective studies	systematic review	systematic review	Induce clinical remission, scored by the (PCDAI) or (PUCAI) or the (PGA) The standard of care agreed on in the guidelines of (ECCO) and (ESPGHAN).	Proportions of disease activity did not differ between 1- and 5-year follow-up in the Belgian Crohn's disease cohort, suggesting stable disease activity.

Abbreviations

CD : Crohn's disease
C4c's : Collaborative network for European Clinical Trials for Children
CQ : Clinical Question
DD. : Diagnostic delay
D.P. : Diagnostic Period (Calculated from first symptoms to primary care assessment, tertiary care referral, and then endoscopy confirm).
EMA : European Medicines Agency
ESPGHAN : European Society for Pediatric Gastroenterology Hepatology and Nutrition
ECCO
FDA : Food and Drug Administration
GI : Gastrointestinal
ITB : Intestinal tuberculosis.
IBD : Inflammatory Bowel Disease
MDPI : Multidisciplinary Digital Publishing Institute
PGA : Physician's Global Assessment
PANCCO : Pan American Crohn's and Colitis Organization.
PCDAI : Pediatric Crohn's disease Activity Index
PIBDU : Pediatric Inflammatory Bowel Disease (the term used when an individual has chronic colitis but cannot subtyped into

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UC or CD based on the clinical, endoscopic, imaging and histopathological features)
PUCAI : Pediatric Ulcerative colitis Activity Index
TPMT : Thiopurine-S-methyltransferase
UC : Ulcerative colitis.

The timely and accurate diagnosis of pediatric inflammatory bowel disease (PIBD) remains a major challenge across healthcare systems. Multiple studies have consistently reported delays in diagnosis due to nonspecific symptoms and the overlap with other gastrointestinal disorders, which can lead to poorer clinical outcomes if not promptly addressed [1, 3, 4, 5].
Tools like fecal calprotectin, stool biomarkers, and genetic profiling are emerging as valuable adjuncts in narrowing the differential diagnosis and guiding referral to pediatric gastroenterologists [5, 7, 9].
There is a clear consensus on the importance of early specialist involvement. Several authors advocate for prompt endoscopic confirmation of suspected IBD once clinical suspicion is established, as this has been associated with reduced complication rates and improved prognosis [2, 6, 8]. Comprehensive diagnostic frameworks and guidelines tailored to regional contexts, such as the PANCCO and ECCO/ESPGHAN consensus statements, reinforce the need for standardized diagnostic protocols [1, 13, 19]. Recent studies emphasize the growing utility of non-invasive biomarkers such as fecal calprotectin, CRP, ESR, and stool Lactoferrin in early disease identification and monitoring. While endoscopy remains the gold standard, these markers help differentiate IBD from functional disorders and prioritize referrals [5, 7, 9]. Despite their usefulness, current biomarkers lack the specificity to fully replace invasive diagnostics, though their role in day-to-day clinical decision-making continues to expand [7, 9]. Treatment paradigms have shifted toward early and aggressive management, particularly in patients at high risk for complications. The goal has moved beyond symptom control to achieving mucosal healing and sustained biochemical remission [6, 8, 10].
Biologic therapies, especially anti-TNF agents, are increasingly favored as first-line options in moderate to severe cases due to their efficacy and safety profile [13, 14, 15]. However, accessibility and cost remain barriers, particularly in low- and middle-income countries, where tailored regional strategies are essential [1, 14].

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Personalized care—based on disease phenotype, genetic predisposition (e.g., NUD15 or TPMT mutations), and therapeutic drug monitoring—has become a central theme in optimizing outcomes [5, 11, 14]. Drug level monitoring and immunogenicity assessment are now integral to guiding therapy adjustments and improving long-term disease control.[13 ،10]
Several studies underscore the systemic issues hindering optimal PIBD management, such as the lack of pediatric-specific clinical trials, delays in drug approval compared to adults, and inconsistent transition programs for adolescents [5, 12, 15]. Multistakeholder efforts are underway to address these delays and promote equitable access to newer therapies [15, 16]. The transition from pediatric to adult care also poses a risk of disease flare-ups, highlighting the need for structured programs to support young patients through this vulnerable period [5]. The field continues to evolve with promising developments in small molecules, Exosome therapy, apheresis, microbiota-based interventions, and even fecal transplantation ،13] [18
Antibiotics, while still under investigation, may play a future role in targeted therapy [17, 18]. The importance of incorporating dietary guidance and psychosocial support into treatment plans has also been highlighted as a means to improve quality of life and treatment adherence [18]

3. Analysis and Comparison of Studies on the Diagnosis and Management of Pediatric Inflammatory Bowel Disease (IBD)

A total of 19 studies from multiple continents, including North and South America, Europe, Asia, and Oceania, were analyzed in this research. The studies utilized various methodologies such as systematic reviews, narrative reviews, meta-analyses, and consensus guidelines. The studies highlighted recurring themes and new trends regarding early diagnosis, treatment strategies, and future perspectives.

a) Diagnosis

Delayed diagnosis was a recurring theme across multiple studies, emphasizing the need for early disease identification using clinical acumen and appropriate diagnostic tools. Studies stressed the importance of fecal biomarkers and blood tests as initial screening tools to guide endoscopic confirmation [1, 3, 4, 5, 7, 9]. This points

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to the evolution of using accurate and fast diagnostic techniques, such as biomarkers, which are critical to reducing diagnostic delays and improving response time to the disease (Table 2).

Table 2: Diagnosis

Study	Total Participants	Topic	Key Findings	Highlight
Yamamoto-Furusho JK (2017)	Unspecified, Latin America	Diagnosis and Treatment of IBD in Latin America	Early diagnosis using modern tools such as biomarkers and blood tests had a significant impact in early disease identification.	Importance of early diagnosis using blood tests and biomarkers.
Vernon-Roberts A (2023)	Analytical review of several studies	Factors causing diagnostic delay in pediatric IBD	Diagnostic delays led to significant complications, emphasizing the need for biomarker and laboratory tests to accelerate diagnosis.	Diagnostic delay as a key contributor to complications, emphasizing the need for faster diagnosis using accurate tools.

b) Management Strategies:

A notable shift toward early and aggressive treatment, especially in moderate to severe cases of pediatric IBD, was observed. Biologic therapies, particularly anti-TNF agents, were widely recommended as the first-line therapy in appropriate clinical settings [13, 14]. Personalized treatment approaches, including genetic testing, disease phenotype classification, and drug monitoring, were increasingly promoted to maximize treatment response and reduce toxicity [5, 11, 14]. These findings align with those of researchers like Grover (2021) and Bouhuys (2023), who emphasized the importance of proactive treatment and the use of modern therapies such as biologic drugs [6, 5]. (Table 3).

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Table 3: Disease Management and Treatment

Study	Total Participants	Topic	Key Findings	Highlight
Grover Z (2021)	500 children across multiple global medical centers	Pediatric IBD management strategies	Biologic therapy was the first-line treatment in moderate to severe cases. Anti-TNF medications were highlighted as first therapeutic options.	Use of biologic therapy (Anti-TNF medications) as the first-line treatment.
Cai Z (2021)	250 patients	Emerging therapies under investigation like small molecule inhibitors and exosome therapy	The study focused on research related to small molecule inhibitors and emerging therapies such as exosome treatment. Promising results but needing further research.	Emerging therapies like small molecule inhibitors and exosome therapy.

c) Systemic Challenges:

The studies identified various systemic barriers affecting the management of pediatric IBD, such as healthcare infrastructure limitations, delays in drug approval for pediatric populations, and insufficient support for transitioning patients from pediatric to adult care [5, 12, 15]. Multi-stakeholder initiatives have emerged to address these gaps and enhance pediatric-specific research and expand therapeutic access [15, 16]. These challenges present significant obstacles to implementing optimal treatment strategies and providing sustainable care for children with IBD. (Table 4).

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Table 4: Systemic Challenges and Infrastructure Issues

Study	Total Participants	Topic	Key Findings	Highlight
Grover Z (2021)	500 children across multiple global medical centers	Challenges in providing integrated care for children	Systemic challenges such as delays in drug approvals for pediatric patients and inadequate support for transitioning from pediatric to adult care were significant barriers.	Highlighting the challenges children face in receiving comprehensive care.
Bolia R (2022)	600 children	Reclassification of pediatric IBDU	The study emphasized the importance of more accurate classification of IBD, which helps improve treatment strategies.	Importance of reclassifying the disease for better treatment planning.

d) Emerging Therapies:

The studies reviewed emerging therapies such as small molecule inhibitors, exosome therapy, and gut microbiota modulation through diet or fecal transplants [13, 18]. Antibiotics also remain an area of potential interest, though further evidence is needed to confirm their effectiveness [17, 18]. These emerging treatments hold promise for improving disease management but require additional research and analysis before widespread application in clinical practices.

e) Comparison between Studies:

Studies by Vernon-Roberts (2023) and Martín-de-Carpi (2020) point to the necessity of improving the understanding of symptoms and factors causing diagnostic delay in children [4, 3]. Other studies, like Wagatsuma (2021), align with these findings, highlighting the importance of biomarkers in speeding up diagnosis [7]. On the other hand, Guariso (2017) made advancements in drug monitoring to

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increase treatment effectiveness and reduce side effects [10], which aligns with modern trends in biologic drug use [13].

These studies demonstrate the need for improving diagnostic and treatment methods through multi-faceted strategies, incorporating biomarkers, biologic treatments, and personalized therapy based on genetic and clinical test results [5, 11, 14].

f) Perspective:

Through the comparison of the various studies analyzed in this research, it can be concluded that the study by Grover Z (2021) is the most comprehensive and realistic in addressing the topic of managing pediatric Inflammatory Bowel Disease (IBD), especially regarding effective treatment strategies and health system challenges.

❖ **Sample Size and Practical Results**: Grover Z's study stands out for including a large sample of 500 pediatric patients across multiple global medical centers, making its results applicable across various medical contexts. The study provides practical statistics on biologic medications, such as anti-TNF agents, which have shown significant effectiveness in treating moderate to severe cases of IBD. This represents an important step toward achieving more targeted and less toxic treatment for children suffering from this chronic disease.

❖ **Biologic Therapy as the Primary Approach**: The study emphasizes that biologic therapy should be the first-line treatment for moderate to severe pediatric IBD cases, particularly those that do not respond to conventional treatments. Biologic drugs directly target the inflammatory factors, reducing symptoms and preventing long-term complications that could occur in the future. This indicates a crucial shift in treatment strategies, toward more precise and well-planned treatments based on the specific characteristics of each case.

❖ **Systemic Challenges Identified**: In addition to providing treatment solutions, the study also highlighted the importance of systemic challenges that could impact the provision of care to children, such as delays in drug approvals for new medications, and the lack of adequate support for transitioning patients from pediatric to adult care. These factors were some of the key obstacles affecting sustainable care for

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children with IBD. Addressing these challenges requires a collaborative effort from all stakeholders to improve health policies and provide the necessary resources for continuous treatment and better transition methods between age groups.

❖ **Practical Applications in Medical Practice**: On a practical level, Grover Z's study serves as a valuable reference for healthcare providers, particularly in situations requiring early biologic intervention. It also offers recommendations for early disease diagnosis using biological tools and laboratory tests, which is a crucial step in improving the quality of life for children with IBD through early diagnosis and rapid intervention.

❖ **Importance of Integrated Treatment Strategies**: The study also highlights the significance of integrated treatment strategies, which combine biologic therapy, close monitoring, and the use of genetic tests to determine the most suitable treatment for each patient. These strategies not only improve treatment effectiveness but also contribute to reducing long-term medical costs by minimizing the need for repeated treatments and health complications.

Grover Z's study (2021) is one of the most prominent studies that provides a comprehensive and integrated model for managing pediatric Inflammatory Bowel Disease. Its focus on biologic therapy as a primary treatment option for moderate and severe cases, along with its attention to systemic challenges affecting healthcare delivery, makes it a vital reference in this field. This study represents a significant advancement in developing treatment, diagnostic methods, and management of IBD in children, contributing to improving the quality of life for pediatric patients worldwide.

4. The Importance of Retrospective Cohort Studies in Low-Resource Settings

It is important to emphasize that scientific research is not limited to a single study design, but rather encompasses a range of methodologies and tools tailored to the research objective and available resources. Randomized Controlled Trials (RCTs) are considered one of the highest levels of scientific evidence due to their rigorous design, which minimizes bias and enhances result reliability. However, RCTs often require significant resources, long-term planning, and strict ethical approvals, which can pose substantial challenges, especially in resource-limited settings.

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Alternatively, other types of studies—such as Retrospective Cohort Studies—offer a simpler and more feasible approach while remaining scientifically valid and internationally recognized. These studies involve collecting data from patients previously seen in clinics or admitted to hospitals and analyzing this information using sound methodological and statistical tools. They help identify disease patterns, diagnostic practices, treatment responses, and success rates in real-world clinical settings. Their strength lies in the ability to generate valuable insights from routine medical records, particularly in local contexts like Libya.

Specifically in the Libyan context, retrospective cohort studies can play a critical role in shedding light on the epidemiological features of pediatric inflammatory bowel disease (PIBD), understanding the challenges in diagnosis and treatment, and improving the quality of care based on real-world data. Relying on flexible research designs such as retrospective cohorts provides a practical and effective alternative, aligning with global scientific standards and supporting the generation of evidence-based medical knowledge tailored to the needs of the national healthcare system.

5. Strengths and Limitations

a) Strengths

The studies reviewed offer several strengths, including a broad global scope with diverse study locations and large sample sizes, which enhance the generalizability and reliability of the findings. They employed comprehensive methodologies, such as systematic reviews, narrative reviews, meta-analyses, and consensus guidelines, providing a well-rounded view of pediatric IBD management. Notably, the exploration of emerging therapies like small molecule inhibitors and exosome therapy highlights ongoing innovations in treatment. Additionally, the emphasis on personalized medicine, integrating genetic testing and disease phenotype, represents a progressive approach to treatment. The studies also addressed systemic challenges, such as delays in drug approval and insufficient transition support, shedding light on healthcare system improvements.

b) Limitations

However, there are limitations, including variations in study methodologies that make direct comparisons challenging. Many studies lacked long-term follow-up data, crucial for understanding

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the sustainability of treatments. Geographical and demographic variability may also impact the generalizability of results, as regional healthcare systems and disease prevalence differ. Furthermore, while emerging therapies show promise, they require more validation through larger, randomized trials. Lastly, the studies focused predominantly on moderate to severe cases of IBD, leaving a gap in the understanding and treatment of milder cases.

6. Conclusion and Future Research

This review analyzed 19 recent studies on pediatric inflammatory bowel disease (PIBD), shedding light on the current challenges in both diagnosis and management of this chronic condition. One of the most pressing issues remains delayed diagnosis, often caused by nonspecific symptoms and limited awareness among primary care providers. The use of non-invasive biomarkers, such as fecal calprotectin, and early referral to pediatric gastroenterologists have emerged as essential strategies to improve early detection and enable faster intervention. Therapeutically, the field is increasingly adopting early and personalized treatment approaches. Biologic therapies, particularly anti-TNF agents, have proven effective as first-line treatments for moderate to severe cases, while personalized treatment strategies—such as genetic testing, drug level monitoring, and disease phenotype classification—have shown promise in enhancing patient outcomes and optimizing care.

Despite these advancements, systemic barriers persist, including healthcare infrastructure limitations and delays in drug approval for pediatric populations. These barriers must be addressed to ensure that children with IBD receive timely and appropriate treatment. Moreover, while emerging therapies, such as small molecule inhibitors and exosome therapy, present promising new avenues, further research is required to establish their long-term efficacy and safety. The studies reviewed provide a comprehensive understanding of pediatric IBD management, emphasizing the importance of personalized, early, and aggressive treatment strategies. However, gaps remain in understanding and treating milder cases, as well as in long-term outcomes. Future research should focus on addressing these gaps, with particular attention to developing strategies for the management of less severe cases and evaluating the long-term effects of treatments. Additionally, more emphasis is needed on overcoming the systemic challenges within

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healthcare systems to ensure equitable, sustainable care for children with IBD globally. Implementing standardized guidelines and fostering international collaboration will be critical for improving long-term outcomes and the quality of life for these children.

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