VOLUME - 15, ISSUE - 07, JULY - 2026 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Paediatrics

EXCLUSIVE ENTERAL NUTRITION VERSUS CROHN'S DISEASE EXCLUSION DIET WITH PARTIAL ENTERAL NUTRITION FOR INDUCTION OF REMISSION IN PEDIATRIC CROHN'S DISEASE: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Exclusive enteral nutrition (EEN) is an established induction therapy for pediatric Crohn's disease (CD), but adherence may be limited by its restrictive liquid-only regimen. Crohn's Disease Exclusion Diet combined with partial enteral nutrition (CDED + PEN) has emerged as a less restrictive alternative. Objective: To evaluate the available evidence comparing EEN with CDED + PEN or modified CDED + PEN for induction of remission in pediatric CD. **Methods:** A systematic PubMed/MEDLINE search was performed employing terms related to EEN, pediatric CD, dietary therapy, exclusion diet, PEN, corticosteroids, and nutrition. The primary outcome was clinical remission after induction therapy. Secondary outcomes included clinical response, sustained remission, biomarkers, endoscopic outcomes, adherence, tolerability, and safety. **Results:** Seventy-three records were identified, and 10 full-text articles were included in the qualitative synthesis. Two studies directly compared EEN with CDED + PEN or modified CDED + PEN. Both strategies showed comparable short-term clinical remission, while one randomized trial reported higher sustained remission with CDED + PEN. Supporting evidence reinforced EEN potency but highlighted adherence limitations. **Conclusion:** CDED + PEN appears to provide induction outcomes comparable to those of EEN in pediatric CD, with potential advantages in sustained remission and tolerability. However, direct comparative evidence remains limited, and larger pediatric randomized trials are needed.

KEYWORDS : Crohn's disease; exclusive enteral nutrition; Crohn's Disease Exclusion Diet; partial enteral nutrition; pediatric inflammatory bowel disease.

INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory bowel disease that may begin during childhood and adolescence. In pediatric patients, persistent intestinal inflammation may affect growth, nutritional status, pubertal development, and quality of life. Therefore, induction therapy should control symptoms, reduce inflammation, and avoid treatment-related harm [1,2].

Exclusive enteral nutrition (EEN) is an established induction therapy for pediatric CD. It replaces regular food with enteral formula for approximately 6–8 weeks and is widely used to avoid corticosteroid exposure while improving nutritional and inflammatory outcomes (1–3). However, its liquid-only regimen is difficult to maintain because of poor palatability, monotony, social limitations, and nasogastric tube discomfort, which may reduce adherence (4).

Crohn's Disease Exclusion Diet combined with partial enteral nutrition (CDED + PEN) has emerged as a less restrictive alternative. It allows selected whole foods while excluding dietary components potentially associated with dysbiosis, impaired intestinal barrier function, and inflammation(5,6). This systematic review aimed to compare EEN with CDED + PEN or modified CDED + PEN for induction of remission in pediatric CD.

MATERIALS AND METHODS

This systematic review with narrative synthesis evaluated EEN versus CDED + PEN or modified CDED + PEN for induction of remission in pediatric CD. The primary outcome was clinical remission after induction therapy. Secondary outcomes included clinical response, sustained remission, biomarkers, fecal calprotectin, endoscopic outcomes, mucosal healing, adherence, tolerability, and safety.

A systematic PubMed/MEDLINE search was performed using combinations of terms associated with EEN, pediatric CD, dietary therapy, exclusion diet, PEN, corticosteroids, and nutrition. Exploratory filters included the last 5 years, free full text, full text, meta-analysis, and randomized controlled trial when available. Key earlier studies identified through reference screening were also included when directly relevant (1–9).

Studies were eligible if they included pediatric CD and evaluated EEN, CDED + PEN, modified CDED + PEN, PEN, or relevant nutritional therapy outcomes. Adult-only studies without extractable pediatric data, ulcerative colitis-only cohorts, case reports, editorials, animal-only studies, and studies without relevant outcomes were excluded.

The PubMed/MEDLINE search identified 73 records across six search combinations. After title and abstract screening, 10 full-text articles were assessed and included in the qualitative synthesis. Two studies were included in the primary comparative synthesis, and eight were used as supporting evidence. The selection process is shown in Fig. 1. Because of limited direct comparative evidence and heterogeneity in protocols and outcome definitions, meta-analysis was not performed.

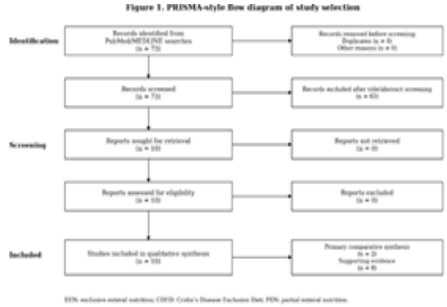

Figure 1. PRISMA-style flow diagram.

Seventy-three records were identified through PubMed/MEDLINE searches; 10 full-text articles were

included, including two primary comparative studies and eight supporting studies.

RESULTS

Ten articles were included in the qualitative synthesis. Two studies directly compared EEN with CDED + PEN or modified CDED + PEN, providing the primary comparative evidence (5,8). The remaining studies provided supporting evidence for EEN efficacy, PEN, exclusion diets, tolerability, and mechanisms of action (1–4,6,7,9).

Levine et al. reported that CDED + PEN and EEN achieved similar clinical response and remission at Week 6 in children with mild-to-moderate CD. However, sustained remission at Week 12 favored CDED + PEN, suggesting a possible advantage beyond the initial induction period (5).

Urlep et al. compared PEN combined with modified CDED versus EEN in children with active CD. Clinical remission at Week 6 was similar between groups, and endoscopic response, endoscopic remission, and mucosal healing were also comparable. Although limited by sample size, this study supports the potential equivalence between modified CDED + PEN and EEN during induction therapy (8).

Supporting evidence reinforces EEN as an effective pediatric induction strategy and suggests that PEN may be more useful when combined with exclusion diets than when used alone(1,2). Recent network meta-analytic evidence also ranked EEN and CDED + PEN favorably among induction strategies, while tolerance data highlight the pragmatic limitations of EEN adherence(3,4).

Tolerance and adherence studies highlighted important practical limitations of EEN, including poor palatability, dietary monotony, social restrictions, and reduced long-term acceptability. In contrast, CDED + PEN may improve treatment adherence by allowing selected whole foods while preserving the anti-inflammatory benefits of nutritional therapy.(3,4).

Mechanistic studies further demonstrated that both EEN and exclusion-based dietary interventions modulate intestinal microbiota composition, epithelial barrier integrity, and inflammatory signaling pathways, supporting the biological plausibility of their clinical effectiveness. (5,6)

DISCUSSION

This review suggests that CDED + PEN may achieve induction outcomes comparable to those of EEN in pediatric CD, with possible advantages in sustained remission and acceptability. However, direct comparative evidence remains limited to two pediatric studies; therefore, conclusions should be interpreted with caution (5,8).

Table 1. Summary of key evidence

Study	Design	Focus	Main finding
Levine 2019 (5)	RCT	CDED+PEN vs EEN	Similar W6; higher W12 remission
Cohen-Dolev 2018 (6)	Cohort	EEN vs steroids	Favorable remission/growth
Urlep 2023 (8)	Cohort	mCDED+PEN vs EEN	Similar clinical/endoscopic
Narula 2018 (1)	Cochrane	Enteral nutrition	Supports pediatric EEN
Jatkowska 2025 (2)	SR/MA	PEN	More useful with exclusion diets
Chen 2026 (3)	NMA	EN strategies	EEN/CDED+PEN ranked high
Sandrine 2025 (4)	Tolerance	EEN acceptability	Taste/monotony/social limits
Geesala 2024 (7)	Review	Mechanisms	Microbiome/barrier/inflammation

EEN remains an important first-line nutritional therapy because it avoids corticosteroids and may improve inflammatory and nutritional outcomes (1,3). Nevertheless, adherence remains a major limitation, particularly among adolescents. CDED + PEN may address this drawback by allowing selected foods while continuing partial formula supplementation (4–7).

Adherence and tolerability are critical determinants of treatment success in pediatric Crohn's disease. Although EEN demonstrates excellent efficacy, its restrictive liquid-only regimen frequently limits long-term compliance. Studies evaluating treatment acceptance have reported challenges related to palatability, dietary monotony, and social restrictions. By allowing selected whole foods, CDED + PEN may improve patient adherence while maintaining therapeutic efficacy, representing a potentially more sustainable nutritional strategy for children and adolescents (4,5).

The biological rationale for both approaches involves modulation of the gut microbiome, microbial metabolites, epithelial barrier function, and inflammatory pathways (7,9). CDED + PEN may also reduce exposure to dietary components associated with dysbiosis or intestinal permeability, including processed foods, emulsifiers, maltodextrin, and selected additives (7).

Recent advances in microbiome research provide additional support for dietary-based therapies in pediatric Crohn's disease. Häcker et al. demonstrated that EEN induces individualized protective microbiome signatures associated with remission induction, while mechanistic evidence summarized by Geesala et al. suggests that nutritional therapies reduce pro-inflammatory microbial pathways, improve epithelial barrier function, and modulate immune responses. These findings may explain why both EEN and CDED + PEN achieve comparable short-term clinical outcomes despite differing dietary compositions (7,9).

The main limitation of this review is the small number of direct comparative pediatric studies. In addition, included studies varied in design, dietary protocols, remission definitions, follow-up duration, and reporting of endoscopic or biomarker outcomes. Therefore, larger randomized trials are needed applying standardized clinical, biochemical, endoscopic, adherence, and quality-of-life outcomes.

CONCLUSIONS

CDED + PEN appears to achieve induction remission outcomes comparable to those of EEN in pediatric CD, with possible advantages in sustained remission and tolerability. EEN remains an established induction therapy, while CDED + PEN represents an attractive alternative for selected patients. Further pediatric randomized trials are needed before superiority or equivalence can be confirmed.

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