Original Research

Exclusive enteral nutrition in Crohn's disease pediatric patients: from clinical remission to transmural healing

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Abstract

Background and Aims. Exclusive enteral nutrition (EEN) is a well-established first-line therapy for inducing remission in mild-to-moderate pediatric Crohn's disease (pCD). While clinical remission (CR) and mucosal healing (MH) are widely accepted therapeutic goals, the concept of transmural healing (TH) has gained increasing recognition. This study aimed to evaluate the effectiveness of EEN in pCD patients from Romania, focusing on nutritional status, remission outcomes, and the impact of various factors on treatment efficacy.

Methods. We conducted a retrospective observational study of pCD consecutive patients who received EEN for induction of remission between 2007 and 2017 at a referral center in Cluj-Napoca, Romania. CR was defined as a weighted Pediatric Crohn's Disease Activity Index (wPCDAI) <12.5, MH as a fecal calprotectin level <250 microg/g, and TH as the combination of MH and imagistic remission assessed by intestinal ultrasonography. Statistical analyses included descriptive and comparative approaches, including logistic regression, with $p < 0.05$ considered significant.

Results. Twenty patients with pCD, representing 45% of the cohort, were included. The median age at diagnosis was 14.2 years (9.9–18.4), and 65% were male. EEN was administered with a mean duration of 7.84±1.26 weeks. Body mass index Z-scores significantly improved following EEN ($p=0.02$). Hypoalbuminemia, detected in 55% of patients at diagnosis, resolved completely after EEN ($p=0.00015$). CR was achieved in 82% of patients with active clinical disease, MH in 26% of patients with microscopic activity, and TH in 20% of patients with imagistic activity. Age at diagnosis, disease behavior, location, activity, and anti-Saccharomyces cerevisiae antibody status were not significantly associated with CR or MH. Disease activity at initiation, measured by the wPCDAI, was inversely associated with TH ($p=0.004$).

Conclusions. This is the first study to report on EEN outcomes in pCD patients from Romania. EEN was effective in improving nutritional status and inducing CR, while MH was achieved in about one-quarter of patients. TH was also observed, though less frequently, and was negatively associated with higher baseline clinical disease activity. Regional factors may have influenced these outcomes.

Keywords: Crohn's disease, children, exclusive enteral nutrition, mucosal healing, transmural healing

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Background and aims

Crohn's disease (CD) is a chronic disorder that belongs to the group of inflammatory bowel diseases (IBD), characterized by transmural inflammation, which can involve any segment of the gastrointestinal tract, occasionally with extraintestinal manifestations. Although the precise pathogenesis of IBD remains elusive, it is widely recognized that genetic predisposition, epigenetic modifications, environmental factors, gut microbial alterations, and immune dysregulation play significant roles in the development and progression of this condition [1].

Approximately 10% of patients with CD are diagnosed before the age of 17 years [2]. Children with IBD, including CD, tend to exhibit a more aggressive disease phenotype with greater extents of bowel involvement and rapid early progression [3]. Also, they are prone to growth impairment, delayed puberty, bone structure and function damage, as well as psycho-social challenges [4-6]. Malnutrition and inflammatory response are factors that might contribute to the development of growth delay [7].

For the management of pediatric CD (pCD), the therapeutic targets include in the short-term - obtaining clinical response, in the intermediate term - clinical remission (CR), normalization of serum and fecal inflammatory biomarkers and promoting growth. Long-term goals are the induction of mucosal healing (MH), while also promoting good quality of life and absence of disability, with minimal steroid use [8]. These objectives aim to ensure optimal disease control and prevent long-term complications.

CR in pediatric pCD can be assessed using multi-item inflammatory disease activity scores, such as the Pediatric Crohn's Disease Activity Index (PCDAI) and the weighted Pediatric Crohn's Disease Activity Index (wPCDAI). The wPCDAI is formulated from three key domains: clinical symptoms, physical examination findings, and laboratory variables (including serum inflammatory markers), making it a more practical tool for evaluation compared to the PCDAI [9,10].

MH refers to the restoration of the intestinal mucosal layer to a state free from visible damage and inflammation [8]. Achieving MH is associated with lower rates of hospitalization, fewer surgical interventions related to disease progression, sustained CR, and improved overall disease control [11,12]. MH is assessed using endoscopic methods (ileocolonoscopy, enteroscopy, video capsule endoscopy) and endoscopic activity scores, respectively (e.g., Simple Endoscopic Score for CD – SES-CD) [13]. Considering that endoscopic techniques are invasive, time-consuming, and expensive, non-invasive biomarkers have been proposed for the evaluation of MH, especially in pediatric IBD. Fecal calprotectin (FC) has shown a significant correlation with endoscopic activity scores in CD and is often employed as a non-invasive indicator of MH in clinical research. Although helpful for MH assessment, this biomarker should be integrated cautiously into IBD management strategies [14-16].

Transmural healing (TH) is a concept associated with CD and characterized by the resolution of inflammation across all layers of the intestinal wall. It is evaluated by cross-sectional imaging techniques including magnetic resonance enterography (MRE), computed tomography enterography, and intestinal ultrasound [8]. Studies revealed that TH is more frequently achieved in the colon and among patients who have not previously received biologic therapy [17]. Several factors were identified as negatively impacting TH, including lower anti-tumor necrosis factor (anti-TNF) drug levels, increased baseline bowel wall thickening, the presence of mesenteric fat proliferation, and the development of strictures [18,19]. Achieving TH is associated with favorable long-term outcomes, including sustained CR, reduced need of rescue therapy, medication dose escalation, and steroid use, fewer hospitalizations and a lower rate of surgery [12,20,21]. However, due to the limited capacity of current treatments to achieve TH, it is considered an adjunctive assessment rather than a primary treatment target [8,22].

While most treatment approaches for CD focus on managing the outcomes of the disease, such as inflammation, only a few strategies target the underlying etiopathogenesis of IBD.

Exclusive enteral nutrition (EEN) is a type of dietary therapy that involves providing all of the nutritional requirements through a special liquid formula (polymeric/semi-elemental/elemental), without the inclusion of any other food, which is administered orally or through a nasogastric tube, for a period of 6 to 8 weeks. Current guidelines recommend EEN as first line for induction of remission in children with active luminal CD, especially if growth delay is associated [23,24]. Studies have shown that EEN has the capacity of inducing CR, MH and TH. EEN offers better maintenance of remission rates with thiopurines after induction [25].

The exact mechanism of action for EEN remains unclear; however, several hypotheses have been proposed. It is suggested that EEN may exert its effects by modulating the gut microbiota [26] and by reducing dietary antigens [27] and specific factors in food [28], all of which could influence mucosal integrity and immune function. Additionally, EEN may modulate the gut cytokine profile, promoting epithelial restitution and wound healing [29,30]. Furthermore, EEN provides essential nutritional support, which helps sustain linear growth and maintain bone health.

The objective of our study was to evaluate the effectiveness of EEN in pCD patients from Romania, focusing on nutritional status and remission outcomes. By analyzing the influence of various factors on treatment outcomes, this research aims to identify patients most likely to benefit from EEN.

Methods

Study design

We conducted a retrospective observational study of the consecutive pCD cases treated with EEN between the years 2007 and 2017. This study was conducted in accordance with the principles of the Declaration of Helsinki. The use of medical information was permitted based on consent forms and was approved by the hospital's medical committee (7029/27.05.2025).

Patients

The study cohort was comprised of consecutive patients with active pCD from the 2nd Clinic of Pediatrics, Emergency Clinical Hospital for Children in Cluj-Napoca, Romania, which received EEN for induction of remission, between 2007 and 2017. The diagnosis of CD was established using the revised PORTO criteria of ESPGHAN [31]. We included cases with clinical disease activity or microscopic activity or imagistic activity. We excluded patients who received diet therapy plus other treatment which may induce remission (Mesalamine, corticosteroids) and those who were quickly changed to another form of therapy for reasons such as disease severity or patient refusal to consume the liquid formula. Administration of Azathioprine as maintenance therapy was not an exclusion criteria.

The choice of treatment type and duration was made by the treating physician, according to the existing guidelines [27,32]. The patient cohort also included cases followed before the publication of the 2014 ECCO-ESPGHAN pediatric guidelines on CD risk stratification [33] and prior to the optimization of biologic therapies. The polymeric casein-based liquid formula, enriched with transforming growth factor-b - Modulen IBD® from Nestlé Health Science - was used as the sole nutritional source, administered via oral route. The quantity and concentration of the formula were established based on the patients¢ energetic requirements.

Data collection

Data were collected from the medical files and from the hospital's electronic database at diagnosis and at the first follow-up (end of the induction period). Demographic and medical information were obtained, including living setting, age at diagnosis, sex, symptoms at presentation, serum immunoglobulin type A, G and M levels, presence of anti-Saccharomyces cerevisiae antibodies (ASCA), p and c type antineutrophil cytoplasmic antibodies (p and cANCA) and anti-nucleotide antibodies (ANA), disease phenotype, duration of EEN; body mass index (BMI) Z-scores, albumin levels, disease activity score - wPCDAI, FC levels and intestinal ultrasound findings were evaluated at diagnosis and at the end of the EEN period. We established disease phenotype based on the Paris classification criteria [34]. According to international expert guidelines, underweight status was assessed using BMI Z-scores and categorized as follows: absent for a Z-score above -1 SD, mild for a Z-score between -1 and -2 SD, moderate for a Z-score between -2 and -3 SD, and severe for a Z-score below -3 SD [35]. Clinical disease activity was assessed using the wPCDAI score and classified as "mild", "moderate" or "severe" in case of wPCDAI between 12.5–40, >40-57.5 and >57.5, respectively. CR was considered when the wPCDAI was below 12.5 [36]. We used FC level >250 microg/g to define microscopic activity and MH was considered when FC level was below 250 microg/g [16]. For evaluating imagistic activity, a water enhanced intestinal ultrasonography was performed. The following criteria were used to define imagistic activity: bowel wall thickness >3 mm, blurred stratification with thickening of the submucosa or complete loss of stratification, presence of signal during color/power Doppler, peritoneal fluid collections, reaction of the mesenteric fat and enlargement of the lymph-nodes surrounding affected intestinal segment [37]. Imagistic remission was considered in the absence of these features. TH was assigned for the cases with MH and imagistic remission.

Statistical analysis

Median and interquartile range (IQR) were used to summarize non-normally distributed quantitative variables, while counts and percentages were used for qualitative variables. Associations between categorical variables were assessed using Chi-square or Fisher's exact tests, with odds ratios (OR) and 95% confidence intervals (95% CI) calculated from contingency tables. Paired sample t-test was used to compare the means of two related groups. Binary logistic regression was used to assess the relationship between the outcomes (CR and MH) and multiple variables, including age at diagnosis, presence of ASCA antibodies, disease location, behavior, and activity. A Firth logistic regression model was used to identify predictors of TH, including disease activity, behavior, and location, since our dataset included a small sample size and rare outcomes, which could lead to bias and unstable estimates with standard logistic regression. Significance was set at $p<0.05$. Statistical analyses were performed with Microsoft Excel (Microsoft Corporation, Redmond, WA) functions and R-Commander (Version 4.1.1).

Results

From the total of 44 consecutive pCD patients, EEN represented the induction treatment choice for 20 patients, which represent 45% of all cases. As for the living setting, 17/20 patients (85%) were from urban areas and 3/20 patients (15%) from rural areas. The median age at diagnosis was 14.2 years (IQR10.8-15.5), with a maximum of 18.1 years old and a minimum of 1 year old. Males represented 65% of cases, with a male:female ratio of 1.85:1. The most common clinical manifestations at presentation were abdominal pain, chronic diarrhea, reduced appetite and weight loss; the other symptoms are presented in figure 1.

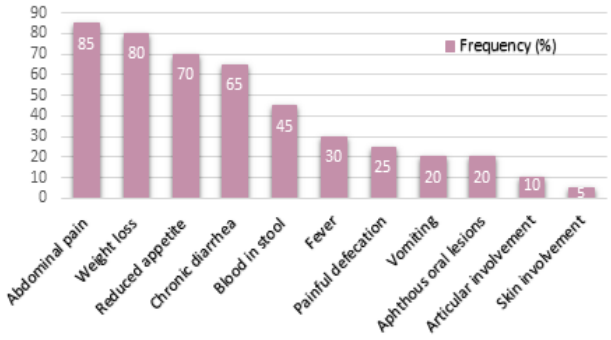

Figure 1. Symptoms/signs of pediatric Crohn's disease (pCD) patients at presentation.

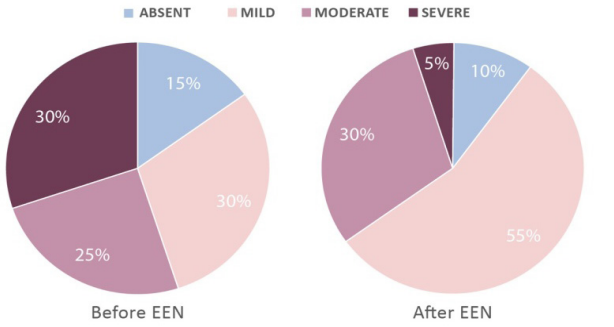

Figure 2. Underweight in pCD patients according to Body Mass Index Z-scores before and after exclusive enteral nutrition (EEN).

We evaluated BMI Z-scores at presentation: 3/20 patients had normal weight for length, 6/20 patients were mildly underweight, 5/20 patients moderately underweight and 6/20 patients severely underweight. After the induction treatment, 2/20 patients had normal weight for length, 11/20 patients were mildly underweight, 6/20 patients moderately underweight and only 1/20 patients severely underweight. There was a statistically significant improvement in BMI Z-scores following EEN, with a p-value of 0.02 ($p<0.05$), a mean difference of 0.62 and a 95% CI of 0.08 to 1.17. Figure 2 illustrates the distribution of underweight severity among patients before and after EEN.

More than half of patients (55%) had hypoalbuminemia at diagnosis and the percentage was reduced to 0% after induction treatment; this change in the pre-induction and post-induction albumin level was significant ($p=0.00015<0.05$).

Serum immunoglobulin type A, M, G, and antibody profiles are summarized in table II. Notably, 6/20 patients (30%) had elevated IgA levels, and all had normal IgM levels. ASCA antibodies were positive in 12/20 patients (60%), while pANCA were negative in all. The presence of ASCA antibodies was not associated with the likelihood of achieving any type of remission ($p=1$ for CR, $p=0.6$ for MH, and $p=0.62$ for TH).

Concerning phenotypic characteristics, the majority belonged to the A1b age group (12/20 patients - 60%). Ileocolonic disease (L3) was the most prevalent, affecting 10/20 patients (50%). Esophagogastroduodenal involvement (L4a) was present in 5% of children (1 case out of 20); no patients had L4b association or isolated L4 disease. The most common disease behavior was inflammatory (B1), seen in 15/20 cases (75%). Perianal disease occurred in 1/20 patients (5%). The phenotypic classification of pCD cases is detailed in table I.

Table I. Distribution of pCD cases according to disease characteristics.

Patients	Age at diagnosis			Location				Behavior				Perianal disease presence
	A1a	A1b	A2	L1	L2	L3	L4a	B1	B2	B3	B2B3	
Number	5	12	3	6	4	10	1	15	1	1	3	1
Frequency	25%	60%	15%	30%	20%	50%	5%	75%	5%	5%	15%	5%

Patients	IgA			IgM			IgG			ASCA positivity	ANA positivity	cANCA positivity	pANCA positivity
	L	N	H	L	N	H	L	N	H				
Number	2	12	6	0	20	0	2	16	2	12	3	1	0
Frequency	10%	60%	30%	0%	100%	0%	10%	80%	10%	60%	15%	5%	0%

Patients	Clinical disease activity			
	Absent	Mild	Moderate	Severe
Number	3	3	10	4
Frequency	15%	15%	50%	20%

(A1a: < 10 years, A1b: 10 - <17 years, A2: 17 - 40 years; L1: distal 1/3 ileum/limited cecal disease, L2: colonic, L3: ileocolonic, L4a: upper gastrointestinal disease, proximal to the Treitz ligament; B1: nonstricturing nonpenetrating, B2: stricturing, B3: penetrating; B2B3: both penetrating and stricturing disease; IgA: immunoglobulin type A, IgM: immunoglobulin type M, IgG: immunoglobulin type G, L: low, N: normal, H: high, ASCA: anti-Saccharomyces cerevisiae antibodies, ANA: anti-nucleotide antibodies, cANCA: c type antineutrophil cytoplasmic antibodies, pANCA: p type antineutrophil cytoplasmic antibodies).

Clinical disease activity was assessed prior to EEN initiation using the wPCDAI score and 85% of patients had clinical activity; the severity distribution is presented in table II. Three patients out of 20 (15%) were in CR, but had either both microscopic and imagistic activity (2 cases - 10%) or only imagistic activity (1 case - 5%).

EEN was administered for a mean period of 7.84 (±1.26) weeks, with treatment durations ranging from 6 to 11 weeks. All patients accepted oral intake of Modulen IBD®, as per the inclusion criteria. Figure 3 illustrates the distribution of pCD patients according to the achievement of various types of remission following EEN. CR was obtained in 14/17 patients (82%) with active clinical disease, after a mean time frame of 2 weeks (range: 1 to 6.7 weeks). MH was achieved in 5/19 patients (26%), after an average period of 7.7 weeks, (range: 5.1 to 16.5 weeks). Imagistic remission and TH were observed in 4/20 patients (20%), with a mean time frame of 9.3 weeks (range: 6.2 to 16.5 weeks).

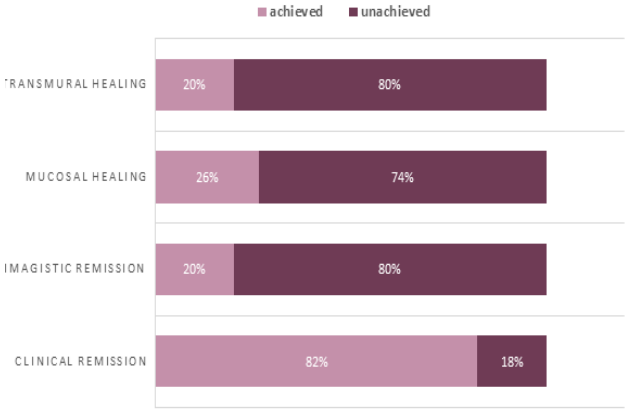

Figure 3. Representation of the percentage of pCD patients in whom different types of remission were achieved after EEN.

In the multivariable logistic regression model, CR was not independently associated with disease behavior (p=0.83), presence of ASCA antibodies (p=0.77) or age at diagnosis (p=0.33). Although not statistically significant, clinical disease activity showed a trend toward decreased odds of CR (OR=0.06, p=0.31). While the association between disease location and CR did not reach statistical significance (OR=4.25, p=0.45), remission rates varied across location types, with the lowest observed in patients with L2 (colonic) disease.

Age at diagnosis, ASCA serology, disease behavior, location, and activity were evaluated as predictors of MH. Although none of the variables reached statistical significance, clinical disease activity (OR=0.04, p=0.10) and ASCA positivity (OR=0.11, p=0.26) were associated with reduced odds of MH. Disease location demonstrated a potential positive effect for MH (OR=5.93, p=0.20), while age at diagnosis showed a trend toward lower odds of MH (OR=0.67, p=0.09). Disease behavior had no effect on MH (OR=1.00, p=0.98).

Clinical disease activity was significantly associated with TH (OR≈0.12, p=0.004), indicating lower odds of healing in patients with more severe disease. Disease behavior and location were not significantly associated with TH (p=0.41 and p=0.19, respectively).

Discussion

This is the first study to provide insights into the clinical presentation and early treatment outcomes of pCD patients in Romania. EEN was used as the induction therapy of choice in 45% of cases with active CD. CR was achieved in 82% of cases, after a mean duration of 2 weeks. MH was observed in 26% of cases and TH in 20% of cases, both requiring longer to attain than CR. EEN significantly improved BMI, with a marked reduction in the proportion of cases with severe underweight. Hypoalbuminemia, present in 55% of patients before EEN, resolved completely after treatment. Our findings indicate that patients with more severe disease were less likely to achieve TH. However, no strong associations were identified between disease activity, disease location, disease behavior, presence of ASCA antibodies, or age at diagnosis and the likelihood of achieving CR and MH.

Serum albumin serves as a valuable biomarker in CD, reflecting both disease activity and nutritional status. It is included as a parameter in disease activity indices such as the wPCDAI and the PCDAI [10]. Hypoalbuminemia can be observed in active CD due to chronic inflammation, protein-losing enteropathy, and malabsorption and is associated with greater disease severity, higher hospitalization rates, and worse postoperative outcomes [38-42]. Previous studies have demonstrated that EEN is effective in restoring serum albumin levels and is superior to corticosteroids in this regard [43,44]. Findings from our study further support this assertion, demonstrating a significant improvement in albumin levels following EEN.

Evidence regarding the effects of EEN on anthropometric parameters remains inconsistent across studies. While several reports show important weight gain and BMI improvements following EEN [45-48], others found no significant differences when comparing pre- and post-treatment data [43,49,50]. In our study, significant BMI improvement was observed at the end of EEN therapy, with the proportion of severely underweight patients decreasing from 30% to 5%, and those classified as mildly underweight increasing from 30% to 55%, reflecting positive nutritional recovery. Our findings suggest that EEN is effective in short-term nutritional recovery.

CR rates in pCD following EEN range from 58% to 100%, as represented in table II [26,44,45,47,48,51-53]. A prospective randomized induction trial reported that all patients treated with EEN achieved CR [26]; however, remission was defined using the Harvey Bradshaw Index

(HBI) <2, whereas most studies used the PCDAI <10. Unlike HBI, which relies solely on clinical parameters, PCDAI and wPCDAI incorporate additional biomarkers such as erythrocyte sedimentation rate (ESR) and albumin, potentially influencing reported remission rates. In our cohort, where wPCDAI score was used for clinical disease activity, EEN led to CR in 82% of patients, aligning with outcomes reported in the literature.

Rates of MH in pCD after treatment with EEN vary widely across studies, ranging from 14.7% to 89% [26,45,47,48,52,53], depending probably on study design, patient population, and duration of therapy, as shown in table II. Also, the variability in reported MH outcomes across studies may be influenced by differences in MH definitions, which range from FC reduction (e.g., FC <200 microg/g) to endoscopic healing based on endoscopic scores (e.g., SES-CD, CD Endoscopic Index of Severity). *Matuszczyk et al* conducted a prospective trial and evaluated the impact of a 6-week course of EEN with a polymeric formula (Modulen IBD®) in children with mild and moderate active CD. A notable decline in FC levels was observed and MH, defined as FC level <200 microg/g, was identified in 25% of cases [45]. A randomized controlled trial evaluating the effectiveness of two dietary interventions in patients with mild to moderate active pCD reported a marked reduction in FC levels at 6 weeks, followed by a non-significant increase between weeks 6 and 12; however, despite this decline, MH (defined as FC <200 microg/g) was achieved in only a small subset of patients (5 cases – 14.7%) [47]. The MH rate from our study (26%) is comparable to previously reported findings, though it falls at the lower end of the documented range. However, we applied a slightly higher FC threshold (250 microg/g) and included patients with severe disease (20%). Standardizing MH assessment across studies and clinical settings is essential to ensure comparability and facilitate the integration of MH as a widely adopted treatment goal in pCD management. While endoscopic assessment remains the gold standard for evaluating MH in research settings, its invasiveness and the need for sedation in children present significant challenges. Therefore, the development and validation of non-invasive biomarkers, such as FC and serum inflammatory markers, is important for routine clinical practice.

Disease phenotype does not appear to influence CR or endoscopic response, following the completion of an EEN course [48, 54]. The impact of disease location on EEN outcomes in CD has been variable across different studies. While some research suggested that patients with ileal involvement may respond more favorably to EEN compared to those with colonic disease, other studies failed to identify a significant association between disease location and treatment outcomes [54-56]. A recent Italian multicenter study showed that CD patients over 15 years of age and those presenting with severe disease (PCDAI >50) were less likely to achieve CR following EEN [57]. In contrast, Grover et al. reported that the following disease activity indicators - PCDAI score, C-reactive protein (CRP) levels, or SES-CD score-, did not serve as reliable predictors of early endoscopic response [48]. Furthermore, findings from the recent Spanish PRESENCE study demonstrated that patients with mild to moderate disease (wPCDAI <57.5), FC levels below 500 microg/g, ileal involvement, and elevated CRP (>15 mg/L) were more likely to achieve a favorable clinical response after EEN [58]. In our study, neither disease behavior, disease location, nor baseline disease activity were significantly associated with CR or MH. However, trends suggested that higher clinical disease activity may decrease the likelihood of achieving these outcomes.

A recent systematic review reported variable rates of TH in both adult and pCD patients, ranging from 14.0% to 42.4% [59]. Notably, TH has not been widely evaluated in pediatric studies. The first study to specifically assess TH following EEN was conducted by Grover et al., who reported a TH rate of 21% at eight weeks. They also observed significant improvements in MRE-based scores after the EEN course, even among patients who did not achieve TH [48]. In their study on long-term EEN in pCD patients, Chen et al. reported that at the time of achieving MH, 17% of cases also demonstrated TH, while 44.8% continued to exhibit mesenteric fibrofatty proliferation [49]. Our findings are consistent with these results, with TH observed in 20% of patients within an average time frame of 9.3 weeks.

Table II. Clinical remission and mucosal healing rates for pCD patients treated with EEN reported in different studies.

Author	Year	CR Rate	Evaluation method CR	MH Rate	Evaluation method MH
Grover et al. [48]	2014	84%	PCDAI	42%	SES-CD
Hojsak et al. [51]	2014	84.2%	PCDAI	-	-
Connors et al. [44]	2017	86.6%	PCDAI	-	-
Levine et al. [47]	2019	58.8%	PCDAI	14.7%	FC
Pigneur et al. [26]	2019	100%	HBI	89%	CDEIS
Matuszczyk et al. [45]	2021	65%	PCDAI	25%	FC
Lv et al. [52]	2022	88.6%	PCDAI	80.8%	CDEIS
Urlep et al. [53]	2023	81.3%	PCDAI	43.8	SES-CD

(CR: clinical remission; MH: mucosal healing; PCDAI: pediatric Crohn's disease activity index; HBI: Harvey Bradshaw index; FC: fecal calprotectin; SES-CD: simple endoscopic score for Crohn's disease; CDEIS: Crohn's Disease Endoscopic Index of Severity).

In our study, we observed that baseline disease activity, as measured by the wPCDAI, was inversely correlated with the achievement of TH, with patients experiencing more severe disease being less likely to achieve TH. This finding aligns with existing evidence that supports the relationship between inflammatory burden and healing outcomes in CD. Previous research has demonstrated that serum TNF-α concentrations could serve as a biomarker for predicting deep remission, with cut-off values of 9.40 pg/mL. This suggests that patients with lower inflammatory activity, as reflected by reduced TNF-α levels, are more likely to achieve deep remission, including both MH and TH [60]. Integrating both clinical (wPCDAI score) and biochemical (e.g., TNF-α levels) markers may enhance the ability to predict and monitor TH in CD patients, supporting a more tailored, precision-based therapeutic approach.

Observations from the RISK pCD cohort study showed that the likelihood of achieving TH was lower among patients with baseline ileal involvement, luminal narrowing, low albumin levels, and elevated ASCA IgG antibodies [61]. However, in our study, we did not observe any association between ASCA antibody positivity and any type of outcome, including CR, MH and TH, in both univariate and multivariate analyses. These findings suggest that while certain baseline characteristics may predict TH, the role of ASCA antibodies in predicting outcomes may vary depending on the specific context.

The utilization of EEN for inducing remission in pCD varies significantly across clinical settings, likely influenced by differences in physician recommendations. Data from the German and Austrian pediatric IBD registry indicate that EEN was recommended in 88.5% of patients, with 71.8% accepting it as their treatment choice [62]. Over time, international studies reported a broader range of EEN implementation, ranging from 9% to 89% [63-65]. These discrepancies are probably driven by physician experience, familiarity with EEN, costs, as well as concerns regarding patient adherence.

Our study has several limitations that should be acknowledged. As a retrospective observational analysis, it may be susceptible to selection bias, and the design may limit the ability to establish definitive causal relationships. The relatively small sample size may have reduced the statistical power, making it more challenging to identify significant associations for certain predictors of remission. Although it was conducted at a single center - 2nd Clinic of Pediatrics, Emergency Clinical Hospital for Children in Cluj-Napoca, Romania - this institution serves as a regional referral center, receiving pediatric patients from across Romania. This broader patient base may enhance the representativeness of the cohort, though the generalizability of our findings to other healthcare settings remains a consideration. The study period encompassed years before and after the publication of the 2014 ESPGHAN guidelines on CD risk stratification and biologic therapy optimization, which may have influenced treatment decisions. However, this extended timeframe also provided an opportunity to include more complicated cases (those with severe disease activity and structuring and/or penetrating disease), offering a broader perspective on EEN outcomes. Finally, the absence of a control group receiving alternative induction therapies (such as corticosteroids or biologics) means that the relative efficacy of EEN could not be directly compared.

Conclusions

This study is the first to report on the outcomes of EEN in pCD patients from Romania. EEN proved to be an effective induction therapy, achieving high rates of CR, with modest rates of MH. Importantly, our study offers valuable insights into the potential of EEN to induce TH, although baseline clinical disease activity appears to be a negative predictive factor for TH. Furthermore, EEN had a positive and significant impact on both BMI and serum albumin, supporting its role in improving nutritional status.

Conflict of interest

Daniela Elena Serban received financial support from Nestlé Health Science to attend the ESPGHAN Congress.

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