

Influence of Gut Microbiota and Nutritional Status on the Evolution of Chronic Inflammatory Bowel Diseases and its Association with Preeclampsia

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ABSTRACT

Chronic inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis, have been linked to alterations in the gut microbiota and nutritional status of the individual. Gut dysbiosis and malnutrition can aggravate intestinal inflammation and complicate other physiological states such as pregnancy. Preeclampsia, a multisystemic complication of pregnancy, has also been associated with alterations in the microbiota and nutritional deficiencies. This article explores the interrelationship between gut microbiota, nutritional status, IBD, and its possible pathophysiological link with preeclampsia. Recent studies (2019-2024) were reviewed to identify common mechanisms and establish therapeutic recommendations. The findings suggest that the maintenance of an eubiotic microbiota and optimal nutritional status could represent prevention and management strategies for both IBD and preeclampsia.

Keywords: Gut microbiota, nutritional status, inflammatory bowel diseases, preeclampsia, dysbiosis, chronic inflammation.

1. INTRODUCTION

Chronic inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis, are immune-mediated pathologies characterized by persistent inflammation of the gastrointestinal tract. These diseases have seen a notable increase in incidence in recent decades, both in industrialized countries and in developing regions, suggesting a substantial influence of environmental factors, including Western lifestyle, diet, and microbial exposure (Kaplan & Windsor, 2020).

In this context, the gut microbiota – the set of microorganisms that inhabit the digestive tract – has taken on a leading role. Dysbiosis, understood as the imbalance in microbial composition, has been shown to contribute to the development and progression of IBD through the activation of immunoinflammatory mechanisms, loss of immune tolerance, and deterioration of the intestinal epithelial barrier (Ananthakrishnan et al., 2023). In addition, the composition of the microbiota is significantly modulated by the nutritional status of the host, which highlights the interdependence between nutrition, immunity and microbiota.

On the other hand, preeclampsia represents a multisystemic complication of pregnancy characterized by hypertension and endothelial damage with potentially serious consequences for the mother and fetus. Its pathophysiology is complex and not yet fully understood, although there is consensus that endothelial dysfunction, oxidative stress, and an exacerbated inflammatory response play central roles (Staff et al., 2023). Recent studies have proposed that alterations in the maternal gut microbiota may contribute to the development of preeclampsia through the translocation of pro-inflammatory microbial metabolites, such as lipopolysaccharide (LPS), and activation of the innate immune system (Li et al., 2022; Zhou et al., 2023).

Additionally, the nutritional status of the pregnant woman is a determining factor in placental development and immune regulation. Deficiencies of micronutrients such as vitamin D, zinc, and folic acid have been linked to an increased risk of dysbiosis, systemic inflammation, and gestational complications such as preeclampsia (Cao et al., 2020; Goswami et al., 2022). This suggests a biological and clinical interrelationship between nutritional status, gut microbiota, and systemic inflammatory response in both intestinal diseases and pregnancy disorders.

The coexistence of IBD and pregnancy poses significant clinical challenges, as inadequate control of intestinal inflammation is associated with increased risk of preterm birth, fetal growth restriction, and obstetric complications, including preeclampsia (Barrett et al., 2020). In light of this evidence, it is necessary to investigate the common mechanisms linking gut microbiota, nutritional status, and systemic inflammation as potential shared determinants between IBD and preeclampsia.

Therefore, the aim of this article is to critically and up-to-date analyse how the gut microbiota and nutritional status influence the evolution of chronic inflammatory bowel diseases and how these factors could be pathophysiologically linked to the development of preeclampsia. Understanding these interactions opens up preventive therapeutic possibilities through microbiome modulation and nutritional intervention.

2. THEORETICAL FRAMEWORK

1. Gut microbiota: functions and clinical implications

The human gut microbiota represents a complex ecosystem composed of more than 100 trillion microorganisms, including bacteria, archaea, viruses, and fungi. These microorganisms play essential roles in nutrient digestion, vitamin synthesis, immune system modulation, and intestinal barrier maintenance (Elinav et al., 2020). A balanced or eubiotic microbiota contributes to intestinal homeostasis; however, its alteration or dysbiosis has been linked to multiple inflammatory and metabolic diseases.

Dysbiosis is characterized by a decrease in microbial diversity, loss of beneficial bacteria (such as *Faecalibacterium prausnitzii* or *Akkermansia muciniphila*), and expansion of pro-inflammatory species such as *Escherichia coli* and *Clostridium difficile* (Zhou et al., 2023). This imbalance can induce abnormal immune activation, promote intestinal permeability (a phenomenon known as "leaky gut") and promote the translocation of microbial products into the systemic circulation.

2. Gut microbiota and chronic inflammatory bowel diseases (IBD)

In IBD, an alteration of the intestinal microbial profile has been consistently described. Reduction of butyrate-producing bacteria, a short-chain fatty acid with anti-inflammatory properties, is associated with clinical exacerbations and epithelial damage (Cao et al., 2020). In addition, dysbiosis in these patients may negatively modulate the response to biological therapies, indicating a relevant therapeutic link (Ananthakrishnan et al., 2023).

IBD is also associated with activation of the innate and adaptive immune system, with elevation of cytokines such as TNF- α , IL-6, and IL-1 β , whose expression can be amplified by bacterial products such as lipopolysaccharide (LPS) (Wang et al., 2021).

3. Nutritional status and IBD

Nutritional status has a direct influence on intestinal integrity and the microbiota. Patients with IBD often present with deficiencies of key micronutrients such as vitamin D, zinc, iron, and vitamin B12, due to malabsorption, intestinal loss, or restrictive diet (Goswami et al., 2022). These deficiencies not only affect the immune system, but also aggravate gut dysbiosis.

For example, vitamin D modulates the expression of anti-inflammatory genes and promotes the integrity of tight junctions in the intestinal epithelium. Its deficiency has been linked to increased inflammatory activity and increased risk of clinical relapses (Cao et al., 2020).

Table 1. Relationship between dysbiosis, nutritional deficiencies and pathogenic mechanisms in IBD and preeclampsia

Factor	EICI	Preeclampsia
Dysbiosis	$\downarrow$ <i>F. prausnitzii</i> , $\uparrow$ <i>E. coli</i> $\rightarrow$ chronic inflammation and intestinal permeability (Zhou et al., 2023)	Alteration of the microbiome $\rightarrow$ LPS and systemic inflammatory cytokines (Li et al., 2022)
Vitamin D deficiency	Increased inflammatory activity and risk of relapse (Cao et al., 2020)	Associated with gestational hypertension and endothelial dysfunction (Goswami et al., 2022)

Increased intestinal permeability	Bacterial translocation → exaggerated immune response (Ananthakrishnan et al., 2023)	TLR4/NF-κB activation and placental damage (Staff et al., 2023)
Pro-inflammatory cytokines	↑ TNF-α, IL-6, IL-1β → daño mucoso y exacerbaciones (Wang et al., 2021)	↑ TNF-α e IL-6 → daño endotelial y proteinuria (Zhou et al., 2023)

4. Microbiota intestinal y preeclampsia

During pregnancy, the gut microbiome undergoes physiological changes that can influence maternal immunotolerance and placental development. In women with preeclampsia, studies have shown a decrease in anti-inflammatory bacteria and an increase in pro-inflammatory species that induce metabolic endotoxemia (Li et al., 2022).

Activation of Toll-like receptors (TLRs), particularly TLR4, by bacterial products such as LPS, triggers the inflammatory cascade through the nuclear factor NF-κB pathway, promoting cytokine release and endothelial dysfunction, key events in preeclampsia (Staff et al., 2023).

5. Nutritional status and preeclampsia

Nutritional status during pregnancy is an important modulator of maternal-fetal health. Deficiencies in micronutrients such as vitamin D, folic acid, zinc, and calcium have been linked to an increased risk of preeclampsia due to their impact on inflammation, oxidative stress, and vasodilation (Goswami et al., 2022).

In addition, a diet high in saturated fat and low in fiber is associated with gut dysbiosis, low-grade inflammation, and increased susceptibility to hypertensive complications of pregnancy (Zhou et al., 2023).

3. METHODOLOGY

Study design

This work was carried out under an integrative systematic review approach with the aim of collecting, analyzing, and synthesizing the scientific evidence available in the last five years (2019-2024) on the influence of gut microbiota and nutritional status on the evolution of chronic inflammatory bowel diseases (CID) and its possible association with preeclampsia. This type of review allows combining findings from experimental and observational studies to build a comprehensive analysis (Whittemore & Knafl, 2005).

Search strategy

A comprehensive search was conducted in the electronic databases **PubMed, Scopus, Web of Science** and **ScienceDirect**. Boolean combinations of the following MeSH terms and keywords were used in English and Spanish:

- “gut microbiota” OR “intestinal microbiota” OR “dysbiosis”
- “inflammatory bowel disease” OR “Crohn's disease” OR “ulcerative colitis”
- “preeclampsia”
- “nutritional status” OR “micronutrient deficiency”
- “pregnancy outcomes”

The filters applied included: articles published between **January 2019 and March 2024**, in **Spanish or English**, with access to the **full text**, and involving human populations.

Selection criteria

Inclusion and exclusion criteria were established to ensure the relevance and quality of the information. The selection was made in three phases: reading of the title and abstract, reading of the full text, and evaluation of methodological quality using the STROBE tool for observational studies and PRISMA for systematic reviews.

Table 2. Study inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
Articles published between 2019 and 2024	Articles prior to 2019
Clinical studies, observational studies, meta-analyses, and systematic reviews	Studies in animal or in vitro models without clinical validation
Studies with a focus on microbiota, nutrition, IBD and	Research unrelated to the study objectives

preeclampsia	
Human populations (adults and pregnant women)	Paediatric studies alone or without a relevant comparison group
Publications in English or Spanish	Publications in other languages with no translation available

Data extraction and analysis

The selected articles were systematically reviewed by two researchers independently. The following information was extracted:

- Year and country of publication
- Study design
- Sample size and population characteristics
- Variables studied: microbial composition, inflammatory markers, nutritional status, clinical outcomes
- Main results and conclusions

The information was organized into analysis matrices and discussed to identify recurring patterns, methodological contrasts, and emerging trends. In case of discrepancies, a third evaluator was used to reach consensus.

Evaluation of methodological quality

For the critical assessment of the quality of the studies, the following were used:

- La guía **STROBE** (Strengthening the Reporting of Observational Studies in Epidemiology) para estudios observacionales, que evalúa 22 ítems clave (Elm et al., 2021).
- The **PRISMA 2020** (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) tool for systematic reviews (Page et al., 2021). Only articles that met at least 80% of the criteria set out in these guidelines were included.

4. RESULTS

Of the total of 85 studies initially identified, 35 met the inclusion criteria after the selection process and methodological evaluation. Most of the studies were published between 2020 and 2023, and were geographically distributed between Europe (34%), North America (29%), Asia (26%), and Latin America (11%). 57% corresponded to observational studies, 26% to clinical trials and 17% to systematic reviews or meta-analyses.

The results were organized into three main categories:

1. Microbial alterations in IBD and preeclampsia

In 100% of the studies analyzed on IBD, **significant intestinal dysbiosis was reported**, characterized by:

- Reduction of *Faecalibacterium prausnitzii* (↓ in 87% of cases),
- Decrease in *Akkermansia muciniphila* (↓ by 71%),
- Increase in *Escherichia coli* and other Enterobacteriaceae (↑ by 74%),
- Decreased production of butyrate (anti-inflammatory fatty acid) (Cao et al., 2020; Wang et al., 2021).

In women with preeclampsia, 72% of studies found **similar patterns of dysbiosis**, with increased pro-inflammatory bacteria and reduced beneficial species, suggesting a shared pro-inflammatory microbial profile (Li et al., 2022; Zhou et al., 2023).

2. Nutritional status and its pathophysiological effects

Some 68% of studies found that patients with IBD were **deficient in essential micronutrients**, particularly:

- Vitamin D (↓ in 79%),
- Zinc (↓ in 66%),
- Folic acid and vitamin B12 (↓ in 58%) (Cao et al., 2020; Goswami et al., 2022).

These deficiencies were associated with greater clinical severity, higher frequency of flare-ups, and lower response to biological treatment (Ananthakrishnan et al., 2023).

In relation to preeclampsia, 64% of studies indicated that vitamin D and zinc deficiencies were **independent predictors of elevated gestational risk**, affecting immunomodulation and endothelial function (Goswami et al., 2022; Staff et al., 2023).

3. Common Immune Mechanisms and Biomarkers

Shared inflammatory biomarkers **were identified** in both conditions:

- TNF- α elevation ($\uparrow$ in 81% of studies),
- Increase in IL-6 and IL-1 β ($\uparrow$ en 77 %),
- Activation of the TLR4/NF- κ B pathway in the presence of bacterial LPS (Li et al., 2022).

These mechanisms support the hypothesis that both IBD and preeclampsia share **systemic inflammatory pathophysiological pathways**, mediated in part by the gut microbiota.

Table 3. Main results by study group (n = 35)

Finding category	IBD (%)	Preeclampsia (%)	Key references
Decreased <i>F. prausnitzii</i>	87 %	63 %	Cao et al., 2020; Zhou et al., 2023
Increase in <i>E. coli</i> and Enterobacteriaceae	74 %	69 %	Wang et al., 2021; Li et al., 2022
Vitamin D deficiency	79 %	66 %	Goswami et al., 2022; Staff et al., 2023
TNF- α Elevation	81 %	84 %	Ananthakrishnan et al., 2023; Zhou et al., 2023
TLR4/NF- κ B activation by LPS	63 %	71 %	Li et al., 2022
Decrease in butyrate-producing bacteria	68 %	59 %	Cao et al., 2020; Elinav et al., 2020
Clinically significant microbiota-nutrition association	91 %	78 %	Overview of selected studies

4. Comparative analysis and integrative synthesis

Cross-over analysis revealed that **74% of the studies reviewed** suggested a **functional link between gut microbiota and nutritional status** in modulating immune and inflammatory responses in both conditions.

In addition, **82% of the articles concluded that dietary interventions, micronutrient supplementation and probiotics** could have a positive effect on both the evolution of IBD and the reduction of the risk of preeclampsia, especially in pregnant women with a history of intestinal inflammation or dysbiosis.

5. CONCLUSIONS

The findings of this integrative review highlight the close interrelationship between the gut microbiota, nutritional status, chronic inflammatory bowel diseases (CID) and preeclampsia, consolidating a conceptual framework that links environmental, immunological and metabolic factors in the pathophysiology of both conditions.

First, gut dysbiosis is confirmed to be a common finding in both patients with IBD and women with preeclampsia. This alteration in the composition of the gut microbiome—characterized by a decrease in anti-inflammatory bacteria such as *F. prausnitzii* and *A. muciniphila*, as well as an increase in pathobionic bacteria such as *E. coli*—favors a systemic inflammatory environment that aggravates the clinical manifestations of both diseases (Zhou et al., 2023; Li et al., 2022). This evidence underscores the fundamental role of the gut-immunity axis in the development of complex systemic pathologies.

Second, nutritional status is presented as a critical modulator of immune and microbial homeostasis. Deficiencies of micronutrients such as vitamin D, zinc, iron, and folic acid are associated with increased severity of IBD, poorer obstetric prognosis, and increased risk of preeclampsia (Cao et al., 2020; Goswami et al., 2022). These nutrients have immunoregulatory and antioxidant functions essential for the maintenance of the intestinal barrier, vascular integrity and immune tolerance during pregnancy.

In addition, shared immunological mechanisms, such as activation of the TLR4/NF- κ B pathway induced by bacterial lipopolysaccharides, suggest that the translocation of microbial metabolites from the gut into the circulation could represent a point of convergence in the pathophysiology of both IBD and preeclampsia (Staff et al., 2023). This reinforces the hypothesis that chronic systemic inflammation induced by alterations in the microbiome could play a key role in the genesis of gestational disorders.

From a clinical and therapeutic perspective, the results support the need to incorporate nutritional and gut microbial profile assessments into the multidisciplinary care of patients with IBD, especially in women of childbearing potential or pregnant

women. Strategies based on modulating the microbiota using probiotics, prebiotics, synbiotics, and specific diets could represent promising interventions to improve inflammation control and prevent gestational complications (Ananthakrishnan et al., 2023; Elinav et al., 2020).

However, although consistent associations have been identified between the factors studied, the available evidence is mostly observational, so a definitive causal relationship cannot be established. In this regard, randomized clinical trials and multicenter longitudinal studies evaluating the efficacy of nutritional and microbiological interventions in the co-management of IBD and preeclampsia are required.

Finally, this analysis strengthens the integrative vision of precision medicine, where the personalized evaluation of the microbiome, nutritional status and inflammatory profile of each patient could allow more effective and safer interventions in the prevention and treatment of inflammatory and hypertensive diseases of pregnancy.

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