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Crohn's disease: a narrative review

Enfermedad de Khron: una revisión narrativa

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ABSTRACT

Objective: to conduct a literature review of Crohn's disease based on its causes, risks, and treatments.
Method: a literature review based on narrative and systematic synthesis. *Data sources*: Scopus, ScienceDirect, PubMed. *Data selection*: Documents were selected and analyzed using a critical literature review, taking into account inclusion and exclusion criteria.
Results: a corpus of 26 articles was analyzed, of which 14 were systematic reviews, 4 narrative reviews, 2 literature reviews, 1 prospective studies, 1 bibliographic review, 1 multicenter study, and 3 cross-sectional study. The study population consisted of only one category: 19 articles focused on women. The studies were conducted in various countries: USA, UK, Netherlands, China, Spain, Qatar, Australia, and Brazil, each contributing a unique perspective to the research. The diagnoses were characterized by eight articles that highlighted the relationship between intestinal dysbiosis, chronic inflammation, and specific microbial variations, emphasizing the usefulness of the microbiome and inflammatory markers in identifying Crohn's disease. The associated factors were characterized by ten articles that mentioned the influence of smoking, genetics, inadequate diet, obesity, and stress as elements that promote disease progression and relapse. Clinical manifestations were described in six articles that evidenced persistent inflammation, the presence of fistulas, weight loss, mental alterations associated with the gut-brain axis, and decreased bacterial diversity, underscoring the importance of a comprehensive and personalized approach. Seven articles were identified as studies conducted in high-income countries, where advanced biological treatments and access to precision therapies predominate. Five articles came from middle-income countries, with mixed approaches combining conventional and complementary medicine. Finally, three articles did not specify the socioeconomic level of the studied population, although they mentioned limitations in access to specialized treatments and variability in available health resources.
Conclusion: Crohn's disease (CD) is characterized by a complex interplay between gut dysbiosis (exacerbated by factors such as smoking, genetics, and stress), chronic inflammation, and the need for a comprehensive therapeutic approach. The results highlight that future management should be individualized, focusing on microbiota modulation (TMF) and targeted therapies (anti-TNF/HBOT), with the need to ensure equitable access to precision therapies across all socioeconomic levels.

Keywords: Crohn's Disease; Gut Microbiota; Inflammatory Bowel Diseases; Risk Factors;

Intestinal Dysbiosis.

RESUMEN

Objetivo: realizar una revisión bibliográfica de la enfermedad de Crohn basado en su causa, riesgos y tratamientos.
Método: revisión de la literatura basado en una síntesis narrativa y sistemática. *Fuentes de datos*: Scopus, Science direct, Pubmed. Selección de datos: Los documentos fueron seleccionados y analizados bajo una revisión crítica de literatura tomando en cuenta los criterios de inclusión y de exclusión.
Resultados: se analizó un corpus de 26 artículos, de los cuales 14 corresponden revisión sistemática, 4 a revisión narrativa, 2 a revisión bibliográfica, 1 a prospectivo, 1 a revisión bibliográfica, 1 a estudio multicéntrico y 3 a revisión transversal. La población estudiada solo contiene una categoría: 19 artículos se centraron en mujeres. Los estudios se realizaron en diversos países: EE. UU, Reino Unido, Países Bajos, China, España, Catar, Australia, Brasil, cada uno aportó una perspectiva única a la investigación. Los diagnósticos se caracterizaron por 8 artículos que destacaron la relación entre disbiosis intestinal, inflamación crónica y variaciones microbianas específicas, resaltando la utilidad de la microbioma y los marcadores inflamatorios para identificar la enfermedad de Crohn. El factor asociado fue caracterizado por 10 artículos que mencionaron la influencia del tabaquismo, la genética, la dieta inadecuada, la obesidad y el estrés como elementos que favorecen la progresión y recaída de la enfermedad. Las manifestaciones clínicas se describieron en 6 artículos que evidenciaron la inflamación persistente, presencia de fístulas, pérdida de peso, alteraciones mentales asociadas al eje intestino-cerebro y disminución de la diversidad bacteriana, subrayando la importancia de un abordaje integral y personalizado. Respecto al nivel socioeconómico, se identificó que 7 artículos correspondían a estudios realizados en países de altos ingresos, donde predominan tratamientos biológicos avanzados y acceso a terapias de precisión. 5 artículos provenían de países de ingresos medios, con enfoques mixtos entre medicina convencional y complementaria. Finalmente, 3 artículos no especificaron el nivel socioeconómico de la población estudiada, aunque mencionaron limitaciones en el acceso a tratamientos especializados y variabilidad en los recursos de salud disponibles.
Conclusión: la enfermedad de Crohn (EC) se caracteriza por una interacción compleja entre disbiosis intestinal (agravada por factores como el tabaquismo, la genética y el estrés), inflamación crónica y la necesidad de un enfoque terapéutico integral. Los resultados destacan que el manejo futuro debe ser individualizado, enfocándose en la modulación de la microbiota (TMF) y en terapias ajustadas (anti-TNF/TOHB), con la necesidad de garantizar el acceso equitativo a terapias de precisión en todos los niveles socioeconómicos.

Palabras clave: Enfermedad de Crohn's; Microbioma Intestinal; Enfermedades Inflamatorias Intestinales; Factores De Riesgo; Disbiosis Intestinal.

INTRODUCTION

Inflammatory bowel disease (IBD), which encompasses both ulcerative colitis and Crohn's disease, is now recognized as a complex disorder whose origin has not yet been fully clarified, thus remaining of uncertain cause, which complicates any attempt at prevention and means that available treatments focus more on controlling symptoms than on resolving the underlying problem (Pascal et al., 2017). Adding to this picture is the fact that more people worldwide are developing inflammatory bowel disease (IBD) and that cases are appearing at earlier stages of

life (Pittayanon et al., 2020), making it a public health challenge that still faces difficulties in accurate diagnosis (Lin et al., 2025). Among the possible factors involved, a relationship with intestinal dysbiosis has been noted (Wang et al., 2021). However, it is not yet clear whether the alteration of the microbiota is a trigger or simply a consequence of the disease. However, these changes in the intestinal ecosystem aggravate the clinical picture and, in combination with intestinal barrier dysfunction, promote the chronic inflammation characteristic of these disorders (Hsu et al., 2023). Clinically, IBD behaves irregularly, alternating between flare-ups of inflammation and periods of apparent remission, which makes it difficult to predict and monitor each patient. Its most common symptoms—diarrhea, gastrointestinal bleeding, abdominal pain, fever, and malnutrition—significantly impair quality of life (Wang et al., 2021). Added to this is a strong psychological impact, with a greater tendency toward depression, anxiety, or obsessive disorders (Zhuang et al., 2020). Beyond these complications, a high incidence of different types of gastrointestinal cancer has been observed (Wang et al., 2021), including pancreatic cancer, which is problematic due to its late detection, difficulty in curing it, and high recurrence rate after surgery (Wang et al., 2021). Finally, conventional therapeutic methods such as chemotherapy and radiotherapy have significant limitations, including effects on the normal microbiome (Wang et al., 2021).

In some studies on Crohn's disease (CD), the fundamental challenge in clinical practice and research remains the same: despite 90 years of advances, there are still no drugs available that promote generalized, sustained remission (Hutfless et al., 2023). However, studies have confirmed the high efficacy of specific therapies, highlighting that ustekinumab (UST) promotes mucosal healing and fistula closure with lower immunogenicity (Janssen et al., 2023). In the surgical field, the importance of multimodal prehabilitation to manage modifiable risk factors before major surgery and thus reduce postoperative complications is recognized; however, there is currently a lack of specific studies evaluating its effect in patients with CD (Nieva et al., 2020). This lack of evidence extends to long-term outcomes, as the main limitation in research is the absence of conclusive evidence on sustained remission without corticosteroids (CS), since none of the studies maintained remission in all reported treatment objectives (Janssen et al., 2023). Despite this methodological limitation (Kabbert et al., 2020), therapies continue to be compared: the biosimilar CT-P13 demonstrated superior efficacy in steroid-free remission and maintenance compared to other biological agents and JAK1 inhibitors, unlike the dietary approach, which is emerging as an effective adjunct, given that a high-fiber diet improved CD remission rates in patients with or without routine treatment, suggesting its usefulness in preventing acute flare-ups (Magro et al., 2019).

Inflammatory bowel disease (IBD) is a chronic condition whose treatment seeks to improve quality of life through biological therapies and personalized approaches. Recent research indicates that intestinal dysbiosis is not only a consequence but also a key driver of disease progression (Wang et al., 2021a). This microbial imbalance enables the identification of biomarkers and new therapeutic targets, especially in active Crohn's disease (Tharu et al., 2024), which represents greater vulnerability; restoring its integrity and balancing the microbiota is essential for treatment. In this context, the microbiome is emerging as a therapeutic target, and integrative therapies such as traditional Chinese medicine (TCM) are proving promising alternatives.

Therefore, the objective of this study was to analyze Crohn's disease considering its causes, risks, and treatments.

METHOD

A comprehensive narrative review of Crohn's disease was conducted to explore the current scientific literature, consulting the Scopus, PubMed, ScienceDirect, and SciELO databases. To refine the search, the following terms were used: "Crohn's disease," "intestinal microbiota," "treatment," and "inflammatory bowel disease." In addition, the operators AND and OR were used to refine and broaden the search scope. The search period ranged from January 2008 to October 2025, encompassing original articles, narrative reviews, systematic reviews, and quantitative research, all written in English and Spanish. Case reports, theses, research, books, and letters to the editor were excluded due to their less empirical nature or specific focus. Within the databases, a total of 184,850 articles were initially identified using the designed search string. Of these, 15,407 corresponded to the Scielo database, 61,700 to Google Scholar, 1,594 to Scopus, 6,149 to PubMed, and 100,000 to Science Direct. Next, 1,876 duplicate articles were removed. Subsequently, 163,451 articles that did not align with the study objective and another 87,338 that did not meet the established inclusion criteria were excluded. As a result of this filtering and selection process, a final corpus of 24 articles relevant to the review was obtained.

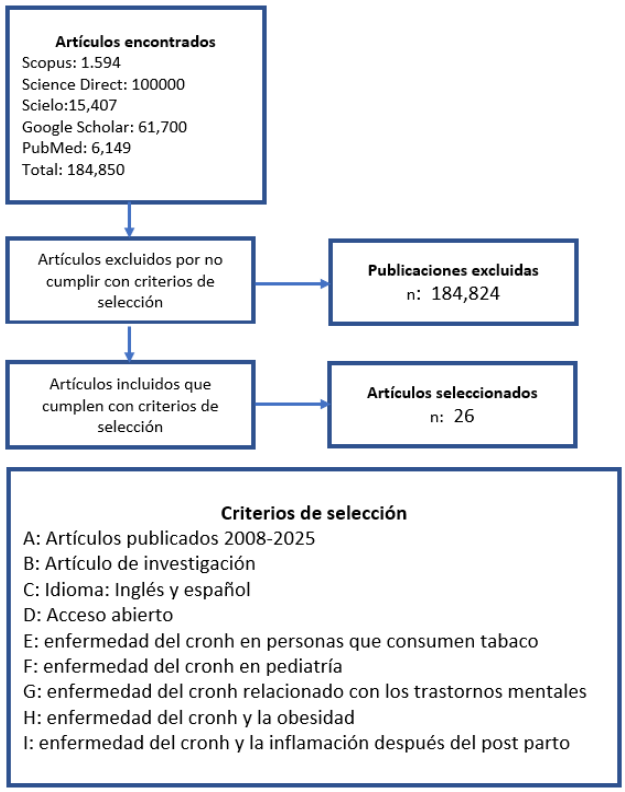

Figure 1. Flow diagram

RESULTS

A corpus of 26 articles was analyzed, of which 14 were systematic reviews, 4 were narrative reviews, 2 were bibliographic reviews, 1 was a prospective study, 1 was a bibliographic review, 1 was a multicenter study, and 3 were cross-sectional reviews. The study population included adults (women and men). The studies were conducted in various countries, such as the US,

the UK, the Netherlands, China, Spain, Qatar, Australia, and Brazil. Participants entered the studies with certain conditions, including intestinal microbiota dysbiosis, mucin alterations, intestinal inflammation, abdominal pain (colicky/continuous), abdominal distension, fever, diarrhea, intestinal reactivity, and severe manifestations such as fistulas. Patients with weight loss, nutritional deterioration, fatigue, and general malaise were also included. A subgroup of patients was characterized by needing surgery or having a history of intestinal resection, in addition to presenting comorbidities such as obesity, smoking, and mental disorders.

Table 1. Results table

Study title	Methodology	Objective/Sample	Main results
Crohn's disease in endoscopic remission, obesity, and cases of high genetic risk demonstrate overlapping shifts in the colonic mucosal-luminal interface microbiome. Jacobs et al., 2022	Observational study	Objective: To use wash samples to characterize the microbiome of the mucosal-luminal interface. Sample: Samples were taken from 110 controls without CD and 88 patients with CD in remission.	Crohn's disease and obesity are associated with reduced bacterial diversity and altered composition in the mucosal-luminal interface microbiome.
Review article: impact of cigarette smoking on intestinal inflammation—direct and indirect mechanisms Papoutsopoulou et al., 2020	Literature review.	Objective: To evaluate the current epidemiological, experimental, and clinical evidence that may explain how smoking impacts the pathogenesis of inflammatory bowel disease.	Smoking promotes intestinal inflammation by affecting the function and interactions between the intestinal epithelium, the immune system, and the microbiota.
High microbiota reactivity of adult human intestinal IgA requires somatic mutations Kabbert et al., 2020	Systematic review and meta-analysis	Objective: "We evaluated the efficacy and safety of six commonly used biologics using a Bayesian method."	Infliximab combined with azathioprine is more effective in inducing initial clinical response
A Systematic Review on Long-Term Efficacy Outcome Measures in Crohn's Disease Patients Janssen et al., 2023	Systematic review	Objective: To determine the outcome measures used to assess long-term efficacy in clinical trials of Crohn's disease.	It is estimated that a quarter of patients with inflammatory bowel disease (IBD) worldwide could develop non-alcoholic fatty liver disease (NAFLD), with an upward trend.
Systematic Review of Crohn's Disease Case Definitions in Administrative or Claims Databases Hutfless et al., 2023	Systematic review	Objective: To review case definitions of Crohn's disease using diagnostic codes and claims in administrative databases.	The variable nature of CD (relapse-remission) makes point-in-time assessments problematic, as they do not reflect the patient's ongoing health.
Microbial and metabolic features associated with outcome of infliximab therapy in pediatric Crohn's disease Wang et al., 2021	Study methodology	Objective: The objective of our study was to characterize the structure of the gut microbiome and metabolic activities in pediatric patients with CD with different clinical outcomes after infliximab (IFX) therapy. Sample: Fecal samples were collected from 20 healthy children and 29 newly diagnosed pediatric patients with CD.	Gut microbiota dysbiosis in pediatric CD contributes to inflammation and mucosal damage by altering gut metabolism.

A microbial signature for Crohn's disease Pascal et al., 2017	Study methodology	Objective: To compare the fecal microbiome of CD patients with UC patients and subjects without IBD in a longitudinal study. Sample: 34 patients with Crohn's disease (CD). 33 patients with ulcerative colitis (UC). 36 and 35 healthy relatives of patients with CD and UC, respectively.	Low microbial diversity in Crohn's disease confirms that CD and UC are distinct subtypes, and reduced Faecalibacterium could be a differential marker.
Gut microbiota dysfunction in Crohn's disease Buffet-Bataillon et al., 2025	Systematic literature review	Objective: To identify microbial biomarkers and develop a predictive model to differentiate Crohn's disease and ulcerative colitis, as well as associate them with disease activity. Sample: 482 samples (50 healthy controls, 173 Crohn's patients, 259 ulcerative colitis patients).	In IBD, there are alterations in oxidative stress, metabolism, and dysbiosis associated with the severity of Crohn's disease.
Diagnosis of Crohn's disease and ulcerative colitis using the microbiome Kang et al., 2023	Systematic literature review	Objective: to differentiate and diagnose these two diseases using the microbiome and identify specific biomarkers associated with disease activity.	CD and UC differ in microbial composition, with more Actinobacteria and Escherichia in Crohn's disease.
Remission in Crohn's disease is accompanied by alterations in the gut microbiota and mucin production. Magro et al., 2019	Cross-sectional analysis	Objective: Investigated dysbiosis and mucin production in patients with CD during remission. Sample: 18 patients with CD and 18 healthy controls (HC) residing at the same address.	In Crohn's remission, a microbial imbalance with excess mucins persists.
Impact of terminal ileal microbiota dysbiosis and tryptophan metabolism alterations on mental disorders in patients with Crohn's disease Lin et al., 2025	Cross-sectional review	Objective: To analyze the relationship between gut microbiota, tryptophan metabolism, and mental health in patients with Crohn's disease Sample: 52 cases and 11 controls with colorectal cancer; of these, the microbiota was evaluated in 37 patients and tryptophan catabolites in 28.	Crohn's disease in patients with mental disorders is associated with less microbial diversity and tryptophan alterations associated with depression and anxiety.
Contribution of the Gut Microbiome to the Perpetuation of Inflammation in Crohn's Disease: A Systematic Review Paidimarri et al., 2024	Systematic review.	Objective: To analyze the pathways of the gut microbiome and its metabolites that prolong inflammation in Crohn's disease. Sample: 11 articles published between 2020 and 2024 were reviewed, including human and animal studies.	Crohn's disease progresses due to dysbiosis and external factors such as diet, antibiotics, and genetics.

Safety and Efficacy of Fecal Microbiota Transplantation in Treatment of Inflammatory Bowel Disease in the Pediatric Population Hsu et al., 2023	Systematic review	Objective: To evaluate the safety and efficacy of fecal microbiota transplantation (FMT) in pediatric patients with inflammatory bowel disease (IBD) through a systematic review and meta-analysis, comparing results with adults. Sample: 11 studies with 352 patients (under 21 years of age), 34 evaluated 1 month post-FMT, with protocols	FMT (fecal microbiota transplantation) is an option for children with IBD, with a 12,5-point decrease in the pediatric Crohn's disease activity index.
Nutritional therapy in pediatric Crohn's disease Day et al., 2008	Systematic review	Objective: to evaluate the efficacy of exclusive enteral nutrition (EEN) in pediatric Crohn's disease (CD), focusing on remission, inflammation control, growth, and avoidance of medication, exploring its mechanisms Sample: data from children with CD (25 % of cases before age 20), with a high incidence of weight loss (up to 85 %) and growth retardation, extracted from pediatric series and trials comparing EEN with other therapies.	SNE (exclusive enteral nutrition) is effective and safe in pediatric Crohn's disease, but requires further long-term studies.
Targeting gut microbiota dysbiosis in inflammatory bowel disease Farah et al., 2025	Systematic review	Objective: To analyze the efficacy of probiotics, prebiotics, synbiotics, and fecal transplantation in IBD, based on 71 clinical trials with patients with Crohn's disease and ulcerative colitis.	The therapies showed benefits, with fecal transplantation being the most notable.
The Impact of Dietary Interventions on the Microbiota in Inflammatory Bowel Disease Nieva et al., 2024	Systematic review	The efficacy of microbiota-based therapies in patients with Crohn's disease and ulcerative colitis was evaluated in 71 trials.	The therapies were beneficial, with fecal transplantation being the most notable.
Evaluation of changes in intestinal microbiota in Crohn's disease patients after anti-TNF alpha treatment. Sanchis-Artero et al., 2021	Multicenter study	Objectives: To evaluate changes in the intestinal microbiota in patients with Crohn's disease (CD) before and after six months of anti-TNF treatment. Sample: 43 subjects. These were divided into: 27 patients with (CD), who started anti-TNF treatment. 16 healthy individuals who served as the control group	Anti-TNF treatment partially improved the gut microbiota in Crohn's disease, increasing beneficial bacteria and promoting the recovery of AGCC-producing Clostridia. (anti-tumor necrosis factor)

Gut Microbiota in Different Treatment Response Types of Crohn's Disease Patients Treated with Biologics over a Long Disease Course Zhao et al., 2025	Literature review	Objectives: To explore differences in gut microbiota among CD patients who have divergent long-term responses to biologic therapy, focusing on a prolonged disease course Sample: 16 patients with CD	The R2A group (remission to active) has depleted microbiota, while R (long-term remission) and mA (mild active) show more diverse and stable microbiota.
Metagenomic Profiling of Fecal-Derived Bacterial Membrane Vesicles in Crohn's Disease Patients Kameli et al., 2021	Cross-sectional study.	Objectives: to characterize the composition of bacterial outer membrane vesicles (OMVs) and their relationship with the gut microbiota in patients with active Crohn's disease and in remission Sample: 64 patients, with 32 with active disease and 32 in remission.	In Crohn's disease, dysbiosis and alterations in OMVs (bacterial outer membrane vesicles) were observed, linked to severity and possible biomarkers.
Hyperbaric oxygen therapy ameliorates intestinal and systematic inflammation by modulating dysbiosis of the gut microbiota in Crohn's disease. Li et al., 2024	Prospective open-label	Objective: To investigate the efficacy and safety of hyperbaric oxygen therapy (HBOT) in patients with Crohn's disease. Sample: 20 patients with active Crohn's disease. They were divided into two groups of 10 patients each: a HBOT group and a control group	HBOT (Hyperbaric Oxygen Therapy) improves inflammation and microbiota, reduces CRP (C-reactive protein) and CDAI (Crohn's Disease Activity Index), and is a safe therapeutic option for Crohn's disease.
Nutritional Therapy Strategies in Pediatric Crohn's Disease Verburgt et al., 2021	Literature review	Objectives: to provide an overview of existing nutritional therapies in pediatric CD and to compile the most relevant advances in research in the field of therapy	Exclusive Enteral Nutrition (EEN) induces remission and heals the intestine, Partial Enteral Nutrition (PEN) helps maintain it, and the Crohn's Disease Exclusion Diet (CDED) + PEN achieves high remission with better tolerance.
Contribution of the Gut Microbiome to the Perpetuation of Inflammation in Crohn's Disease: A Systematic Review Paidimarri et al., 2024	Systematic review	Objective: to understand the role of dysbiosis in the pathogenesis of CD	Inflammation in CD causes dysbiosis, reducing Faecalibacterium and increasing Escherichia, which exacerbates intestinal inflammation.
Gut Microbiota Profiles and Microbial-Based Therapies in Post-operative Crohn's Disease: A Systematic Review Zhuang et al., 2021	Systematic review	Objective: to investigate the profiles of the gut microbiota in patients with CD before and after surgery and to evaluate microbial therapies to prevent postoperative recurrence	In postoperative CD, recurrence is associated with recolonization with proinflammatory bacteria and lower production of short-chain fatty acids.
Probiotics in Crohn's disease remission: a systematic review, Azevedo et al., 2022	Systematic review	The study aimed to conduct a systematic review, through clinical trials, on the use of probiotics in humans with Crohn's disease	In Crohn's disease, studies showed clinical benefits and improved intestinal permeability after surgery.

A systematic review of the patient burden of Crohn's disease-related rectovaginal and anovaginal fistulas Iglay et al., 2022	Systematic review	To assess the burden of rectovaginal fistulas (RVFs) and anovaginal fistulas (AVFs) associated with Crohn's disease (CD).	The high burden of disease and treatment, demonstrating high prevalence of RVF (rectovaginal fistulas) in women with Crohn's disease.
Crohn's disease: is minimally invasive surgery the gold standard? A narrative review Luglio et al., 2023	Narrative review	Description of the forms of minimally invasive surgery (MIS) currently used for the surgical treatment of Crohn's disease (CD).	MIS (Minimally Invasive Surgery) has shown better perioperative results in the surgical treatment of CD.

DISCUSSION

The purpose of developing these findings is to analyze Crohn's disease by examining its causes, risks, and treatments, and to compare them with other research.

Cause

It is estimated that a quarter of patients with Inflammatory Bowel Disease (IBD) could develop Non-Alcoholic Fatty Liver Disease (NAFLD). This high burden of hepatic comorbidity supports the view that low microbial diversity in Crohn's disease (CD) distinguishes CD from ulcerative colitis (UC), with Faecalibacterium as a differential marker (Pascal et al., 2017). Smoking promotes intestinal inflammation by affecting the function and interactions between the intestinal epithelium, the immune system, and the microbiota. This is related to Crohn's disease (CD) and obesity, as lower bacterial diversity at the mucosal-luminal interface has been observed (Xie et al., 2025). Specifically, CD and ulcerative colitis (UC) differ in their microbial composition, with more Actinobacteria and Escherichia (Kang et al., 2023), which contributes to mucosal damage by altering intestinal metabolism (Wang et al., 2024), generating a vicious cycle where inflammation in CD causes dysbiosis and reduces Faecalibacterium and increases Escherichia, which aggravates inflammation, including changes such as oxidative stress and metabolism. At the same time, dysbiosis is associated with the severity of Crohn's disease (Buffet-Bataillon et al., 2025) and is prognostic: active remission (R2A) shows depleted microbiota, while long-term remission (R) presents a more diverse and stable microbiota (Zhao et al., 2025). This imbalance represents a clinical challenge even after surgery, as recurrence in postoperative CD is associated with recolonization with proinflammatory bacteria (Zhuang et al., 2021).

Non-alcoholic fatty liver disease (NAFLD)

It is estimated that up to a quarter of patients with inflammatory bowel disease (IBD) may develop non-alcoholic fatty liver disease (NAFLD). This liver disease is very common worldwide (Shil et al., 2023) and affects a large proportion of adults (Barton Duell et al., 2022). Its pathogenesis is related to intestinal dysbiosis, which causes inflammation by damaging the barrier and allowing toxins to pass through (Ortiz-López et al., 2024); for this reason, it is also linked to obesity/diabetes (Martín Domínguez et al., 2013). In fact, it constitutes a key cardiovascular risk; therefore, its management focuses on controlling metabolic comorbidities and weight loss (IMSS 2014). The pediatric population requires screening and is treated with weight loss/lifestyle changes due to the limited pharmacology available (Aller et al., 2018).

Smoking

Smoking promotes intestinal inflammation by altering the function and interaction of the epithelium, the immune system, and the microbiota, with its highest prevalence in Crohn's disease (CD) compared to ulcerative colitis (UC) (Alhalabi et al., 2025); it is also an independent predictor that increases complications and prolongs hospitalization after CD surgery (Shaham

et al., 2025). In terms of effects, active smoking increases hospitalization for CD, while, in contrast, it decreases the severity of ulcerative colitis (UC) (Attauabi et al., 2025). However, previous smoking does not have a negative impact, it is important to note that former smokers who started smoking at an early age have a higher risk of developing UC (Chen et al., 2025); This habit, combined with perceived stress, is linked to lower optimal adherence to treatment in patients with inflammatory bowel disease (IBD) (Horovitz, 2025).

Oxidative stress

These changes include oxidative stress and altered metabolism. At the same time, dysbiosis is associated with the severity of Crohn's disease (Buffet-Bataillon et al., 2025), leading to oxidative stress due to excess ROS (Reactive Oxygen Species) that overwhelm antioxidant defenses (Moret et al., 2014). Despite this, the balance of oxidative stress is vital in IBD, as excess exogenous antioxidants can be harmful (Chen et al., 2025). In addition, infections and cytokines increase ROS, so future therapies should focus on controlling it (Sahoo et al., 2023). Finally, oxidative stress biomarkers (which reflect the ROS/antioxidant imbalance) can be used to assess current disease activity (Chen et al., 2025) and are promising indicators for distinguishing between activity and remission in Crohn's disease (Buffet-Bataillon et al., 2025).

Postoperative CD

The management of postoperative Crohn's disease (CD) is guided by risk and surveillance. The main risk factors for recurrence have been confirmed as smoking and a fistulizing pattern (Dragoni et al., 2023). In addition, immediate postoperative complications significantly increase the long-term risk (Seoane Vigoa et al., 2011). For diagnosis and classification of recurrence, the endoscopic Rutgeerts Index classification is key, despite its potential for interpretation variability (Alonso Lázaro et al., 2020). Complementarily, MR enterography is an effective imaging method for detecting recurrence (Ripollés et al., 2011). Based on this, the guidelines recommend performing a colonoscopy at 6-12 months and initiating individualized preventive therapy (Doménech et al., 2017), given that pharmacological treatments (biological/ immunosuppressants) are essential to prevent CD recurrence (Doherty et al., 2021).

Risk factors

Crohn's disease progresses due to dysbiosis and external factors such as diet, antibiotics, and genetics, leading to the loss of beneficial bacteria. In contrast, in ulcerative colitis, E. coli levels increase. Dysbiosis causes alterations in OMVs (bacterial external membrane vesicles), which are linked to severity and may serve as potential biomarkers (Jang et al., 2021). However, the variable nature of CD makes point-in-time l assessments problematic, as they do not reflect the patient's ongoing health, and even in remission, a microbial imbalance with excess mucins persists (Magro et al., 2019). This high disease burden demonstrates a high prevalence of rectovaginal fistulas (RVFs) in women with CD (Iglay et al., 2022). In patients with mental disorders, less microbial diversity and tryptophan alterations associated with depression and anxiety are observed (Lin et al., 2025).

E. coli

Adherent-invasive E. coli (AIEC) is closely associated with Crohn's disease due to its ability to invade and survive in intestinal cells (Kabbert et al., 2020), with a prevalence of 28 % in patients compared to 9 % in controls (Kameli et al., 2021). Its virulence depends on chitinase A (Fargeas et al., 2024), and studies such as PACIFIC show that Hong Kong strains exhibit greater antibiotic resistance. However, they are sensitive to the EcoActive™ phage cocktail (Pittayanon et al., 2020). In addition, probiotics such as L. helveticus and H. A. platensis inhibit its pathogenicity

and modulate inflammation, highlighting its complementary therapeutic potential (Day et al., 2008).

Bacterial external membrane vesicles

Dysbiosis alters OMVs (bacterial outer membrane vesicles), which are linked to severity and may serve as potential biomarkers (Kameli et al., 2021). This is relevant because inflammation in CD itself drives this dysbiosis (more Escherichia/Proteus), thereby deteriorating the intestinal barrier (Paidimarri et al., 2024). Therefore, BMVs are emerging as a potential therapy for IBD (Zeng et al., 2024), demonstrating improvement in colitis and representing a new therapeutic target (Wang et al., 2021), as some BMVs are anti-inflammatory and protective (Azevedo et al., 2022). However, other pathogen MVOs, such as AIEC, contribute to inflammation and damage the barrier (Jang et al., 2021), which is why the immunological impact of fecal VMBs in Crohn's patients is being investigated.

Rectovaginal Fistulas

This high disease burden demonstrates a high prevalence of rectovaginal fistulas (Iglay et al., 2022), which are rare but serious and therefore difficult to treat. Because of this, treatment combines biological drugs and surgery, although most patients require several surgeries. Smoking and the use of sedatives reduce the chances of success. In cases of persistent vulvovaginal discomfort in girls, genital Crohn's disease should be suspected as an initial manifestation (Otero-Piñeiro et al., 2023); (Meyer et al., 2022)

Mental disorders

Patients with mental disorders show less microbial diversity and tryptophan alterations associated with depression and anxiety (Lin et al., 2025), requiring comprehensive care and appropriate assessments to improve their health (Massironi et al., 2025), with effective treatment being crucial to improving their prognosis (Fiest et al., 2016). However, social determinants of health represent the most modifiable route for prevention (Fiest et al., 2016). At the therapeutic level, combined treatment (psychotherapy + pharmacotherapy) is superior to pharmacotherapy alone (Brioso et al., 2023), where the central mechanism against anxiety is the extinction of fear through new learning of inhibition (Nassiri et al., 2025). Furthermore, evidence highlights the importance of the gut-brain axis, as imbalances in the microbiota and tryptophan metabolism are linked to an increased risk of mental disorders (Sugie et al., 2025).

Treatment

Various treatments have proven effective in Crohn's disease, with FMT (fecal microbiota transplantation) standing out for restoring the microbiota, especially in children with IBD (Farah et al., 2025; Hsu et al., 2023). Anti-TNF (anti-tumor necrosis factor) therapies and HBOT (hyperbaric oxygen therapy) reduce inflammation and promote the growth of beneficial bacteria (Sanchis-Artero et al., 2021). In the field of nutrition, exclusive enteral nutrition (EEN), partial enteral nutrition (PEN), and the Crohn's disease exclusion diet (CDED) promote remission and good tolerance (Day et al., 2008). (Verburgt et al., 2021), Infliximab with azathioprine enhances the initial clinical response (Kabbert et al., 2020), and MIS (minimally invasive surgery) offers better surgical results with less risk (Luglio et al., 2023).

FMT (Fecal microbiota transplantation)

Various treatments have shown efficacy in Crohn's disease, with FMT (fecal microbiota transplantation) standing out for restoring the microbiota, especially in children with IBD (Porcari et al., 2023); (Hsu et al., 2023), which underscores the role in the efficacy of transplantation

(Arora et al., 2024), as it improves remission and clinical response (Luciane de Fatima Caldeira et al., 2020), making it a safe and effective option with good results and few adverse effects (Ko et al., 2024); (Hsu et al., 2023). In fact, oral FMT combined with partial enteral nutrition (PEN) could be effective in children with active Crohn's disease (Zou et al., 2025), being a safe and highly effective treatment for Clostridioides difficile infection in patients with ulcerative colitis, achieving high cure rates (Porcari et al., 2023).

ANTI-TNF (Anti-tumor necrosis factor)

Anti-TNF (anti-tumor necrosis factor) therapies and HBOT (hyperbaric oxygen therapy) reduce inflammation and promote beneficial bacteria (Sanchis-Artero et al., 2021), as TNF is a key mediator of inflammation in IBD, and its inhibition is an essential advance (Jang et al., 2021). Anti-TNF therapy revolutionized the treatment of Crohn's disease by improving remission rates, making it the most effective, safe, and accessible option for IBD (Zeng et al., 2024). However, a lack of primary response to this treatment has been observed to predict lower efficacy with second-line biologics (Casteelea et al., 2018).

Infliximab with azathioprine

Infliximab with azathioprine enhances the initial clinical response (Love et al., 2011), being more effective than drugs alone, achieving greater remission and lower steroid use (LÉmann et al., 2006); (Frédéric Colombel et al., 2010); (Lyu et al., 2025). These benefits are crucial in children with severe CD, where initial treatment is associated with better sustained remission and greater growth (Jongsma et al., 2022). However, combination therapy, although it enhances remission, carries a higher risk of adverse effects (Love et al., 2011). Therefore, treatment must be tailored to each patient: it is useful in young people, but significantly increases the risks of lymphoma and infections in older adults (Scott et al., 2015).

HBOT (Hyperbaric Oxygen Therapy)

HBOT reduces inflammation and promotes beneficial bacteria, making it a safe and effective option with few side effects (McCurdy et al., 2022). Its key mechanism is to reduce inflammation and promote tissue repair (Wu et al., 2021), making it valuable in complex Crohn's disease, improving recovery and reducing the need for surgery (Li et al., 2024; Krstulović et al., 2025). It optimizes the microbiota and is more effective in combination with ustekinumab (Li et al., 2024). In refractory perianal Crohn's disease, relief is only temporary, underscoring the need for further long-term research (Hajjar et al., 2025).

CONCLUSION

Non-alcoholic fatty liver disease (NAFLD) is developed by IBD affecting adults through intestinal dysbiosis associated with obesity and diabetes, conditions that generate cardiovascular risk. These metabolic comorbidities must be controlled through weight loss. Smoking alters the microbiota and immunity, promoting intestinal inflammation; this habit aggravates Crohn's disease (CD), although it reduces its severity in ulcerative colitis, and its early onset or combination with stress worsens treatment adherence. Intestinal dysbiosis exacerbates Crohn's disease by increasing reactive oxygen species (ROS), so balancing oxidative stress is essential. Controlling ROS and using oxidative biomarkers are useful for assessing Crohn's disease activity. Postoperative management of CD seeks to prevent recurrence, which is influenced by smoking, fistulizing pattern, and surgical complications. Such recurrence is detected with the Rutgeerts Index or entero-MRI and justifies the recommendation of colonoscopy and preventive therapy.

Additionally, Escherichia coli Adherence and Invasion (ECAI) contributes to the pathogenesis

of Crohn's disease through invasion and antimicrobial resistance, which can be controlled with probiotics and bacteriophages. Likewise, bacterial vesicles are emerging as potential markers and treatments to reduce inflammation in Crohn's disease. Finally, rectovaginal fistulas in this disease are a rare but severe complication whose management requires a combination of biological therapy and surgical approach. At the same time, imbalances in the microbiota and tryptophan metabolism influence mental disorders, so their management must integrate psychological support with medical treatment for a comprehensive recovery.

In this therapeutic context, Fecal Microbiota Transplantation (FMT) is presented as an option that restores the microbiota and improves remission in Crohn's disease, especially in children. It is safe and effective, and its benefits are enhanced when combined with partial enteral nutrition, as well as being very effective against Clostridioides difficile in ulcerative colitis. Anti-TNF therapies and Hyperbaric Oxygen Therapy (HBOT) also reduce inflammation and benefit the microbiota; although inhibiting TNF improves remission, the lack of initial response limits subsequent treatments. The combination of infliximab and azathioprine improves remission and reduces steroid use, especially in children with severe Crohn's disease; however, its high risk of lymphoma and infections in older adults requires individualized adjustment. As for HBOT, it reduces inflammation, improves the microbiota, and promotes tissue repair, making it a safe and useful therapy in complicated Crohn's disease. However, its effect in refractory perianal Crohn's disease is temporary and requires further research.

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