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THERAPEUTIC APPROACHES AND EPIDEMIOLOGY OF CROHN'S DISEASE IN BRAZIL: A SCOPING REVIEW

ABORDAGENS TERAPÊUTICAS E EPIDEMIOLOGIA DA DOENÇA DE CROHN NO BRASIL: UMA REVISÃO DE ESCOPO

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ABSTRACT: This paper addresses the therapeutic strategies and epidemiology of Crohn's Disease (CD) in the Brazilian context, covering the period from January 2019 to May 2024. A scoping review was conducted using databases such as PubMed, Scopus, SciELO, Cochrane Library, Web of Science, and the Virtual Health Library (VHL). In addition, incidence and prevalence rates of CD in Brazil were examined using data from the Unified Health System (SUS). This study highlighted that CD represents a challenge for the Brazilian healthcare system, with a substantial number of patients requiring frequent therapeutic interventions. This approach focuses on biological medications, such as anti-TNF-α agents. The epidemiological analysis also emphasized the importance of closely monitoring CD incidence and prevalence rates in Brazil, especially considering the growing number of diagnosed cases.

KEYWORDS: Crohn's disease. Epidemiology. Scoping review. Therapeutic approaches.

RESUMO: O presente trabalho aborda as estratégias terapêuticas e a epidemiologia da Doença de Crohn (DC) no contexto brasileiro durante o período de janeiro de 2019 a maio de 2024. Para tanto, foi realizada uma revisão de escopo em bases de dados como PubMed, Scopus, SciELO, Cochrane Library, Web of Science e Biblioteca Virtual em Saúde (BVS). Ademais, foram exploradas as taxas de incidência e prevalência da DC no Brasil, com base em dados do Sistema Único de Saúde. Este estudo evidenciou que a DC representa um desafio para o sistema de saúde brasileiro, com um número substancial de pacientes que necessitam de intervenções terapêuticas frequentes. Esta abordagem tem como foco os medicamentos biológicos, como os anti-TNF-α. A análise epidemiológica também destacou a importância do das taxas de incidência e prevalência da DC no Brasil, especialmente ao considerar o crescente número de casos diagnosticados.

PALAVRAS-CHAVE: Doença de Crohn. Epidemiologia. Revisão de escopo. Abordagens terapêuticas.

INTRODUCTION

Crohn's Disease (CD) is a chronic inflammatory condition that primarily affects the gastrointestinal tract, potentially appearing in any part of the digestive system, from the mouth to the anus. Its characteristics include flare-ups, gastrointestinal complications, weight loss, and, in more severe cases, manifestations such as strictures, fistulas, and abscesses. Although the exact cause remains unknown, it is believed that the disease results from a complex interaction of genetic, environmental, microbial, and immunological factors. Treatment generally involves a combination of medications, lifestyle modifications, and, occasionally, surgical interventions to control symptoms and reduce inflammation[1–5].

International literature has documented a continuous increase in the incidence and prevalence rates of inflammatory bowel diseases (IBD), especially in Western Europe, North America, and Oceania, where prevalence rates may exceed 0.5%[6–7]. In developed countries such as Canada and several European nations, rates range from 319 to 322 cases per 100,000 person/year[1,2].

While highly industrialized nations are seeing a stabilization in incidence, emerging regions such as Asia, the Middle East, and Latin America are experiencing accelerated growth in cases, suggesting an epidemiological transition similar to that seen in Western countries decades ago[8]. This rise may be associated with factors such as westernization of the diet, lifestyle changes, environmental exposures, and improvements in diagnostic methods[8]. However, obtaining robust epidemiological data in these regions faces significant challenges, due to underreporting, limited access to diagnosis, and the absence of comprehensive national registries on CD[8–9]. Studies conducted in China and India show that, although incidence rates have historically been lower, the growth curve is exponential and may result in challenges similar to those faced by Western countries[10–11].

In the therapeutic field, CD management has significantly evolved in recent decades, driven by the advent of biological therapies and small molecules that target specific inflammatory pathways[12]. Therapeutic models implemented in Europe and North America have shown reductions in hospitalization rates and the need for surgery due to the early introduction of biological agents, such as TNF-alpha inhibitors and immune response modulators[12–13]. However, in low and middle-income countries, the high cost and restricted access to these medications often limit their use, leading to disease progression before adequate treatment can be initiated[14–15].

Despite these global trends, significant gaps remain in understanding the epidemiology and management of CD in different regions, particularly in Latin America. In Brazil, data on incidence and prevalence are still fragmented, and the heterogeneity in access to diagnosis and treatment represents an additional challenge for evaluating the disease's impact on the population[15–16]. Furthermore, there are few comparative studies on the different therapeutic approaches available in the country, making it difficult to formulate effective health policies to improve patients' quality of life.

In this context, this article aims to review the therapeutic approaches and epidemiology of CD in Brazil, during the period from January 2019 to May 2024, highlighting the complexity of the disease, the importance of personalized treatment strategies, and the potential for improved outcomes through new therapeutic approaches and monitoring techniques.

METHODOLOGY

A scoping review approach was used to synthesize the available knowledge on Crohn's Disease in Brazil. A systematic search was conducted in databases such as PubMed (National Library of Medicine),

Scopus (Elsevier), SciELO (Scientific Electronic Library Online), Cochrane Library, Web of Science, and the Virtual Health Library (VHL), using relevant search terms for Crohn's Disease: ("Crohn's disease" AND "increases" AND "Brazil"); ("Crohn's disease" AND "Brazil"); ("Crohn's disease" AND "pathology"); ("Crohn's disease" AND "biological"); ("Crohn's disease" AND "treatment"); ("Crohn's disease" AND "epidemiology"), covering the period from 2019 to 2024. Studies of various types were included, along with clinical trials, meta-analyses, and systematic reviews that discussed therapeutic approaches and the epidemiology of Crohn's Disease in Brazil. To obtain data on the Brazilian population, the DataSUS platform, provided by the Ministry of Health, was used. The following descriptors were selected: mortality → by region of the federation → hospital morbidity of SUS (SIH/SUS) → by place of hospitalization, for ICD codes K50–K51, accessed through institutional login from the Hospital das Clínicas at Universidade Federal de Minas Gerais (UFMG).

RESULTS

The initial scoping review identified a total of 239 articles from the PubMed, Scopus, SciELO, Cochrane Library, Web of Science, and VHL databases. Fifteen duplicate articles were manually removed. Additional exclusions were made due to access restrictions, for not specifically addressing Crohn's Disease, or for being outside the scope and objectives of the present study. At the end of the process, 8 articles were selected for inclusion in the analysis, as presented in Table 1. The entire screening process is illustrated in Figure 1.

Table 1. Characteristics of the studies included in the review (n = 8). Belo Horizonte, Minas Gerais, Brazil, 2024.

Authors	Objective(s)	Methodology	Main features
Martins, et al. (2021)[21]	Analyze the epidemiological aspects of inflammatory bowel diseases (IBD) in the western region of Minas Gerais	Retrospective observational study based on data from medical records of patients diagnosed with IBD between 2015 and 2020.	It identified an increase in the incidence of IBD in the region, a higher prevalence in women and a predominance of colitis ulcerative disease on Chron's disease.
Ng, et al. (2017)[7]	Evaluate the global incidence and prevalence of IBDs in the 21st century, with an emphasis on regional trends.	Systematic review of population studies on IBDs published between 1990 and 2016.	He observed a stabilization of incidence in Western countries, but accelerated growth in developing countries, suggesting the impact of industrialization.
Quaresma, Kaplan e Kotze (2019)[23]	Discuss the globalization of IBDs and their epidemiological, clinical, and social impacts.	Narrative review with analysis of global epidemiological data on IBDs.	It identified distinct partners of prevalence, suggesting that environmental factors are key determinants in the development of DIIS.
Renuzza, et al. (2022)[24]	Determine the incidence, prevalence and epidemiological profile of IBDs in Paraná.	Retrospective study analyzing hospital data and medical records of patients diagnoses between 2010 and 2020.	It showed an increase in the incidence of IBDs in the state, especially in young adults, as well as regional disparities in access to treatment.
Costa, et al. (2022)[18]	Analyz the epidemiological profile of patients with Chron's disease and Retocolitis Ulcerative disease in the last 6 years.	Retrospective study analyzing clinical and epidemiological data from patients treated at hospitals	It identified a progressive increase in cases, a higher prevalence un women and a relation with environmental and dietary factors.
Buie, et al. (2022)[6]	Evaluating trends of hospitalization for Chron's	Systematic review with temporal analysis of studies on IBD-related	Demonstrated reductions in hospitalization rates in developed countries due to the advance of

Authors	Objective(s)	Methodology	Main features
	disease and Ulcerative colitis in the 21st century.	hospitalizations in different countries.	biological therapies while developing countries show an increase on fees.
Kotze, et al (2020)[19]	Assessing the progression of IBDs in Latin America and the Caribbean.	Systematic review of epidemiological studies on IBDs in the region.	It identified an increase in the incidence and prevalence of IBDs, with challenges in early diagnosis and unequal access to treatment.
Martins, Volpato e Zago-Gomes (2018)[20]	Investigate the prevalence and phenotype of IBDs in Brazil	Cross-sectional study based on the analysis of medical records of patients diagnosed with IBDs in specialized centers.	It demonstrated heterogeneity in the distribution of IBDs in Brazil, with regional differences in clinical presentation and access to treatment.

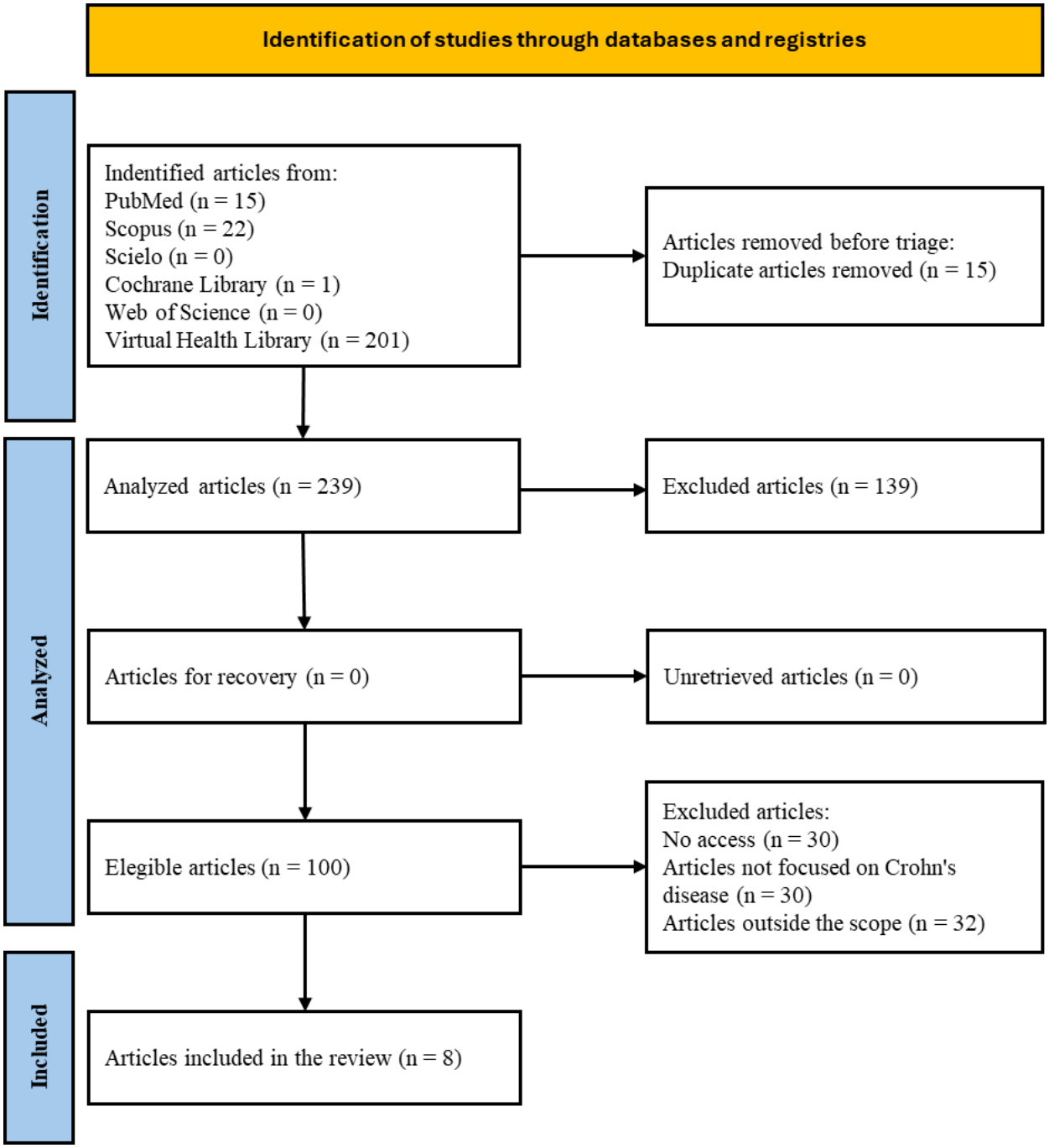

Figure 1. Flowchart for selecting studies according to the *Preferred reporting Items for Systematic Reviews and Meta Analysis for Scoping Review (PRISMA-ScR) Checklist*. Belo Horizonte, Minas Gerais, Brazil, 2024. Source: Adapted from Page MJ, et al.[17] BMJ 2021;372:n71.

DISCUSSION

PATHOPHYSIOLOGY

The production of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-12 (IL-12), by intestinal immune cells plays a crucial role in chronic inflammation of the gastrointestinal tract. These cytokines promote the recruitment of other immune cells and the activation of the immune response[1–4].

The integrity of the intestinal epithelial barrier is essential for regulating the passage of substances from the intestinal lumen to the underlying tissues. Alterations in the mucosal layer and tight junction proteins, such as claudins and occluding, can increase intestinal permeability, allowing the translocation of luminal antigens and triggering an inflammatory response, as seen in Crohn's Disease (CD)[1-4].

Although the mechanisms underlying innate immune dysfunction in CD are not yet fully understood, evidence points to a complex interaction between genetic, environmental, and microbial factors[2]. Genetic studies have identified over 240 variants associated with the disease, involving genes related to bacterial recognition, autophagy, epithelial barrier regulation, and immune response. In addition to genetic factors, environmental aspects play a significant role in the development of CD. Smoking, intestinal dysbiosis, certain dietary patterns, the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics, as well as psychological stress and emotional factors, have all been associated with an increased risk of developing the disease. Geographical factors such as urbanization and industrialization may also influence its incidence[1–4].

DIAGNOSIS

The diagnosis of CD is a complex process that involves multiple procedures. Clinical evaluation reveals a wide range of symptoms, including gastrointestinal manifestations, weight loss, fatigue, and abdominal tenderness. Laboratory tests aim to detect inflammatory markers, anemia, and nutritional deficiencies, while stool tests assess the presence of mucus, blood, and fecal calprotectin. Imaging exams are essential for detailed visualization of the intestinal wall and for identifying possible complications, such as strictures and fistulas. Histological findings, such as the presence of granulomas, transmural inflammation, and tissue lesions, help assess the severity and extent of inflammation, complementing the diagnosis. Other tests, such as ultrasound and X-rays, may also be used[1,2,8,25].

Classification of CD is essential for therapeutic planning and risk stratification of complications. The most commonly used systems are the Montreal Classification, which considers disease location, behavior, and age at diagnosis, and the Paris Classification, which also includes the temporal evolution of the disease, contributing to more precise patient categorization[12].

EPIDEMIOLOGY

The incidence of Crohn's Disease (CD) in Brazil has increased over recent decades, following trends observed in other developing countries. This growth may be attributed to changes in dietary patterns, urbanization, exposure to environmental agents, and alterations in the intestinal microbiome.

Kotze et al.[19] analyzed the progression of Inflammatory Bowel Diseases (IBD) in Latin America and the Caribbean, with particular focus on Brazil. They reported an incidence rate of 0.08 cases per 100,000 person/year in 1988, which increased to 0.68 between 1991–1995, reaching 3.50 between 2001–2005,

and peaking at 5.48 in 2015. The ratio between ulcerative colitis (UC) and CD varied across Brazilian states, revealing the complexity of IBD distribution in the country. The overall UC:CD ratio was 1.081, with regional differences: 0.481 in Alagoas, 0.679 in Rio de Janeiro, and 0.596 in Mato Grosso do Sul. Diagnosis age (17 to 40 years), disease extension, and inflammatory behavior are frequent phenotypic characteristics, with the incidence of perianal complications varying considerably[20].

Other studies[10,20,21], such as Martins et al.[26], analyzed IBD prevalence in Minas Gerais, revealing high values [30.29 per 100,000 inhabitants — UC: 15.06; CD: 15.23]. The estimated incidence was 2.98 per 100,000 inhabitants per year. Most patients were middle-aged, female, married, and of caucasian ethnicity. In Campinas (São Paulo), Fucilini et al.[27] found an overall prevalence of 15.59 per 100,000 inhabitants, with CD accounting for 10.38 per 100,000, and they also described the clinical distribution by sex and disease type.

The Southern region shows a higher prevalence of these diseases over the years considered. Epidemiological data from Paraná revealed a significant incidence of CD of 3.34 per 100,000 inhabitants in 2019, particularly in certain age groups (11–30 years), highlighting the importance of the regional context in the manifestation of IBDs[28]. An analysis of hospitalizations related to these diseases reveals a higher occurrence in the Southeast region between January 2014 and December 2019, with 26,851 hospital admissions recorded in the SUS, reflecting both population density and access to healthcare services[29].

In the DATASUS/SIH morbidity list, both CD and UC (Ulcerative Colitis) are grouped under the same code (ICD K50–K51). This approach may not provide accurate epidemiological profiles when the two diseases are analyzed separately. Although there is no breakdown by sex or age, the data made available by DATASUS/SIH — through research using the descriptors “mortality by region of the federation/hospital morbidity of SUS (SIH/SUS) by place of hospitalization” for ICD K50–K51 — reveal the following statistics (Table 2).

Table 2. Morbidity and Mortality in Brazil for ICD: K50/K51. Belo Horizonte, Minas Gerais, Brazil, 2024.

Year	2020	2021	2022	2023	2024
Morbidity (hospital admissions)	4.424	4.637	5.126	6.650	1.817 (until March)
Mortality (0-76 years old)	230	223	254	No data	No data

Regarding morbidity (hospital admissions), a progressive increase is observed over the years. Mortality shows a pattern similar to that of morbidity, with a slight decrease in the year 2021. Analyzing mortality by Brazilian region for ICD K50, it is noted that between 2020 and 2022, the Southeast region had the highest mortality rate, followed by the Northeast and South regions, as shown in **Table 3**.

Table 3. Mortality by Brazilian region for ICD K50. Belo Horizonte, Minas Gerais, Brazil, 2024.

Region	2020	2021	2022
North	5	9	7
Northeast	46	30	47
Southeast	121	136	129
South	35	35	53
Midwest	23	13	18

These patterns remained consistent through March 2024, with the first three months of the year accounting for 27.32% of the hospital admissions recorded in 2023, reflecting a continued gradual increase[28].

Finally, data compiled by CONITEC indicate a significant rise in the incidence of CD in the city of São Paulo over a 10-year period, increasing from 3.1 per 100,000 in 2014 to 5.8 per 100,000 in 2024, representing a 60% increase[29].

In countries where the prevalence is rising, hospitalization rates have predominantly stabilized, suggesting advancements in the management and care of IBDs, especially due to the introduction of biological therapies. On the other hand, newly industrialized countries in Asia and Latin America consistently report increasing hospitalization rates, characterized by a rapid rise in incidence but low prevalence[10].

Several factors may explain this increase in hospitalization rates in these countries, with the rapid growth in annual IBD diagnoses being the most likely explanation. Previous studies cited by Renuzza et al.[24] have correlated the rising incidence—and consequently, hospitalizations—of IBD with social and economic factors. In part, economic development improves access to healthcare systems, electronic surveillance, specialists, and diagnostics[24].

The analysis of the epidemiological profile of IBDs reveals a marked prevalence among women, especially in the age group of 20 to 29 years, and predominantly among individuals of white ethnicity. This scenario demands targeted prevention policies for this group, aiming to mitigate the impact of these diseases. These findings are supported by recent studies, such as those by Costa et al.[18], which highlight the importance of understanding and directing efforts toward this specific epidemiological profile.

However, comprehensive understanding of IBD in Latin America and the Caribbean remains limited, as pointed out in the systematic review conducted by Kotze et al[19]. The heterogeneity among countries in the region is notable and may be influenced by a variety of factors, ranging from historical and cultural aspects to genetic characteristics and lifestyle. In light of this, there is an urgent need to develop large-scale population-based registries that can provide more accurate perspectives on the epidemiology and natural course of IBDs in the region.

In the Brazilian context, the difficulties in obtaining accurate data on IBD epidemiology are evident, as highlighted by Quaresma, Kaplan, and Kotze[23]. The absence of mandatory reporting for these diseases contributes to the complexity and inaccuracy of the available data. Furthermore, factors such as a possible lack of professional qualification among physicians, especially in remote regions, and challenges in accessing diagnostic methods can lead to underreporting and misdiagnosis. Delayed diagnosis—due to the insidious progression of IBDs and the lack of identification of the disease as a cause of death—also contributes to the gaps in understanding the epidemiology of these conditions in Brazil.

In this sense, data collection accurate and the implementation of effective epidemiological surveillance strategies are essential to improve the understanding and coping with these diseases in Brazil.

HEALTH PROMOTION

Health promotion plays a fundamental role in the comprehensive care of Crohn's Disease (CD), aiming to improve quality of life, prevent complications, and reduce the socioeconomic burden of the disease. A patient-centered approach that considers physical, emotional, and social aspects is essential for the success of interventions[30].

Health education is a key strategy, fostering self-care and adherence to treatment. Well-informed patients are more likely to recognize early signs of disease progression, thereby reducing the need for hospitalizations and invasive interventions. Educational programs should cover everything from basic aspects of pathophysiology to symptom management and the importance of regular medical follow-up[30].

The work of multidisciplinary teams is indispensable. Physicians, nurses, nutritionists, psychologists, and social workers must collaborate to develop individualized therapeutic plans. Psychological support, for instance, is crucial due to the chronic and sometimes debilitating nature of the disease, helping to alleviate anxiety and depression often associated with CD[30,31].

Proper nutrition is an integral part of health promotion in these patients. A balanced diet, tailored to individual needs and the stage of the disease, is recommended — avoiding ultra-processed foods, those high in fat, or potentially irritating to the intestinal mucosa. During active phases of the disease, specific supplementation may be necessary to correct common nutritional deficiencies such as iron, vitamin B12, and folic acid[31].

In addition, smoking cessation is important, as tobacco use is associated with worse clinical outcomes in CD. Anti-smoking campaigns and public policies that restrict tobacco use indirectly contribute to disease control. Encouraging regular physical activity, within the patient's limits, also provides metabolic, immunological, and psychological benefits[31].

Another relevant aspect is ensuring equitable access to healthcare services. Regional and social inequalities hinder early diagnosis and proper follow-up. Public policies aimed at expanding primary care, training healthcare professionals, and decentralizing specialized services are priorities to promote equality in health care[31].

Lastly, health promotion in the context of CD goes beyond clinical control. It encompasses comprehensive care, considering individual, family, and community factors, and requires coordination between educational, care-related, and policy actions.

PHARMACOLOGICAL TREATMENT

The most recent Brazilian Clinical Protocol and Therapeutic Guidelines (PCDT) for Crohn's Disease, published in November 2017, establishes specific criteria for patient inclusion. To be eligible under the protocol, patients must present a confirmed diagnosis of Crohn's disease, supported by a medical report and at least one of the following: endoscopic findings, small bowel radiological transit study, enteral computed tomography, or enteral magnetic resonance imaging. Additionally, patients must be classified under the International Statistical Classification of Diseases and Related Health Problems (ICD-10) with the codes K50.0, K50.1, or K50.8[32].

Medications approved by the National Committee for Health Technology Incorporation in the Brazilian Unified Health System (CONITEC/SUS) are incorporated into PCDT after extensive evaluation of evidence regarding efficacy and available therapeutic alternatives and are made available to patients through the Specialized Component of Pharmaceutical Assistance (CEAF).

Table 4 presents a compilation of chemical synthesis drugs approved for the treatment of Crohn's disease[32].

Table 4. Chemically synthesized drugs used in the treatment of Crohn's disease. Belo Horizonte, Minas Gerais, Brazil.

Medicines	Action mechanism	Indication
Sulfasalazine	Inhibits the synthesis of cytokines, prostaglandins and leukotrienes; inhibits the clonal expansion of pathogenic B and T lymphocytes. Reduces leukocyte adhesion.	Mild to moderate colonic or ileocolonic disease.
Mesalazine	It acts locally by inhibiting the cyclooxygenase responsible for the release of prostaglandins by the colon mucosa.	Modest effect in mild to moderate colonic or ileocolonic

Medicines	Action mechanism	Indication
Metronidazole	It penetrates the bacterial cell wall, breaks DNA and inhibits DNA synthesis in some microorganisms.	In the case of infections or abscesses that have not yet been surgically treated.
Azathioprine	Inhibits nucleic acid biosynthesis pathways. Purine antagonist. Prevents cell proliferation of cells involved in the immune response.	Effective in colonic disease, in remission and maintenance. Can be combined with allopurinol for dose reduction to reduce adverse effects.
Methotrexate	Antimetabolite that inhibits the formation of tetrahydrofolate, decreasing the production of Purine.	Induction and maintenance of remission in patient's refractory to corticosteroids.
Cyclosporine	It participates in the inhibition of cytokines, especially IL-2, which stimulates lymphocyte populations.	It is associated with cases of premature birth and low birth weight, and breastfeeding is contraindicated during use.
Corticosteroids	Blocking the arachidonic acid cascade by inducing lipocortin, which inhibits phospholipase A2 and COXs.	Effective in the acute phase and in moderate to severe disease.
Allopurinol	Xanthine oxidase inhibitor capable of diverting the metabolism of azathioprine to the production of 6-thioguanine, leading to a significant reduction in disease activity, without increasing liver toxicity	It is not used as monotherapy, only in combination with azathioprine in mild to moderate disease for induction and maintenance of remission

When patients do not show a satisfactory clinical response to conventional therapies after six weeks of treatment, the use of biological medications is considered an option for disease remission. Within the context of the Brazilian Unified Health System (SUS), there are currently four biological drugs available, as established by the PCDT for Crohn's disease. **Table 5** summarizes the biological medications approved for the treatment of the disease.

Table 5. Biological drugs used in the treatment of Crohn's disease. Belo Horizonte, Minas Gerais, Brazil, 2024.

Medicines	Action mechanism	Indication
Adalimumab	Recombinant monoclonal antibody that binds to tumor necrosis factor alpha (TNF-alpha), interfering with binding sites on the TNF-alpha receptor and subsequent inflammatory processes caused by cytokines.	Induction of remission and maintenance of moderate to severe disease, can be associated with azathioprine.
Infliximab	It binds with high affinity to soluble and transmembrane forms of TNF-α, but not to lymphotoxin alpha (TNF-β). As it forms stable complexes with TNF-α, its bioactivity progressively decreases.	Induction of remission and maintenance of moderate to severe disease, can be associated with azathioprine.
Certolizumab pegol	It is made up of a humanized Fab fragment of an anti-TNF-α monoclonal antibody bound to chemically with two molecules of polyethylene glycol (PEG). There is an increased affinity for TNF-α, but it does not bind to TNF-β.	Indução da remissão e manutenção da doença moderada a grave.
Ustekinumab	Human monoclonal antibody that binds to and interferes with the pro-inflammatory cytokines interleukin (IL)-12 and IL-23, decreasing the activation of NK cells (natural killers) and the activation of CD4+ T cells.	Induction of remission and maintenance of moderate to severe disease.

According to the Brazilian Association for Ulcerative Colitis and Crohn's Disease (ABCD), around 20% of Crohn's disease (CD) patients have experienced more than 10 flare-ups in the past two years, while 25% have undergone at least one surgery in the past three years. The Brazilian Society of Coloproctology (SBCP), based on data from the Informatics Department of the Brazilian Unified Health System (DataSUS), analyzed the incidence and prevalence rates of inflammatory bowel diseases in Brazil between 2012 and 2020, covering 140,705 CD patients of both sexes[33]. Of these individuals, 75% are assisted by the SUS and have access to anti-TNF-α therapy. Studies indicate that between 20% and 50% of patients treated with anti-TNF-α will eventually experience treatment failure, highlighting the need to expand the range of biological therapies offered by SUS. In December 2023, Conitec[34] issued a favorable report recommending the incorporation of Ustekinumab, a human monoclonal antibody that binds to interleukins (IL)-12 and IL-23. Thus far, there is no Brazilian data on treatment failure involving other classes of biologics besides anti-TNF-α.

Since 2010, the Brazilian Organization for Crohn's and Colitis (GEDIIB)[35] has been publishing guidelines and updates on the diagnosis and treatment of Crohn's disease. The latest update was published in 2022 and aims to guide specialists and patients in promoting early diagnosis and accelerating both induction and maintenance of disease remission. The evidence that contributes to pharmacotherapy available in PCDT for CD (standardized by SUS) is presented in **Table 6**.

Table 6. Medicines incorporated into the SUS used in the off-label CD clinic. Belo Horizonte, Minas Gerais, Brazil, 2024.

Medicines	Dosage	Maintenance dose
Budesonide (mild involvement of the ileum and/or right colon)	Induction: 9 mg/day for 2-3 months	There is no maintenance dose
6-mercaptopurine	Induction: 1-1.5 mg/kg/day	Maintenance dose= induction dose
Vedolizumab (monoclonal antibody to integrin ÿ4ÿ7)	Induction: 300 mg/unit: 300 mg IV in weeks 0.2 and 6	Maintenance: 300 mg/unit: 300 mg IV every 8 weeks or 108 mg SC every 2 weeks starting after the second or third intravenous induction dose
Risanquizumab (IgG1 monoclonal antibody that selectively binds to the unique p19 subunit of human IL-23)	Induction: 600 mg/unit: 600 mg IV in weeks 0.4 and 8	Maintenance: 360 mg/2.4 mL (syringe): 360 mg SC at week 12 and every 8 weeks thereafter

BIOSIMILAR INDUSTRY AND PERSPECTIVES

Biosimilars have been increasingly adopted by physicians, health authorities, and patients as a viable alternative for the treatment of various diseases, although their acceptance in the United States remains limited due to a lack of accumulated experience and confidence in using these drugs[40]. Nevertheless, these biopharmaceuticals face significant challenges, such as high costs and the complexity involved in their development and regulation. Despite these hurdles, the provision of these medications by the Brazilian Unified Health System (SUS) has expanded access to treatment, although it also represents an increase in public health expenditures.

Biologic drugs enable the maintenance of remission in individuals with Crohn's Disease (CD), which directly impacts the reduction of costs related to hospitalizations, surgical procedures, and inpatient medications. However, there is a shortage of studies comparing the financial costs of treating

patients who remain in remission with those who develop complications such as fistulas, abscesses, and infection - situations that demand a broader technological arsenal for clinical recovery.

According to a meta-analysis by Ungaro et al.[40], early biological treatment is associated with better clinical outcomes — including clinical remission, steroid-free remission, mucosal healing, and lower rates of relapse, hospitalizations, complications, and surgeries. The evidence suggests that the early use of biologics may reduce the utilization of hospital resources and is considered cost-effective in some studies.

One of the limitations identified in the development of this study is the difficulty in obtaining specific data on CD from public SUS databases, since both Crohn's Disease and Ulcerative Colitis (UC) are grouped under the same International Classification of Diseases (ICD) code.

PRACTICAL IMPLICATIONS

The findings of this scoping review highlight the importance of a multidisciplinary and evidence-based approach to the management of Crohn's Disease (CD) in Brazil. Characterizing the epidemiology of the disease in the country enables more efficient resource allocation, promoting access to effective therapies and specialized care. The analyzed data also underscores the relevance of early diagnosis, and the implementation of strategies aimed at reducing disease progression, with the goal of minimizing complications and hospital admissions.

These findings point to the need for well-structured clinical protocols and updated guidelines that ensure more effective and accessible treatment for patients. In the context of clinical practice and public policy formulation, the study reveals gaps in care and potential areas for improvement. Among the suggested strategies are the expansion of access to biological therapies, the continuous training of healthcare professionals, and the strengthening of primary care as fundamental pillars for enhancing CD management.

In addition, the development of programs aimed at promoting intestinal health and providing comprehensive support to chronic patients should be considered. Based on the results obtained, the reinforcement of healthcare networks and the encouragement of further research to deepen knowledge about the specific characteristics of CD in the Brazilian context are recommended.

CONCLUSION

This scoping review provides a comprehensive overview of therapeutic approaches and the epidemiology of Crohn's Disease (CD) in Brazil. It was found that CD poses a significant challenge to healthcare systems, with a considerable number of patients experiencing recurrent flare-ups and requiring frequent therapeutic interventions. The analysis of treatment approaches revealed a substantial reliance on biological medications, such as anti-TNF-α agents.

The epidemiological analysis also underscored the importance of monitoring incidence and prevalence rates, especially in light of the growing number of diagnosed cases. It is essential that future research focuses on identifying risk factors and social determinants that may influence the onset and progression of CD.

The national production of biopharmaceuticals, including biosimilars, is a strategic element for reducing costs and decreasing dependence on imports, bringing benefits to both the Brazilian Unified Health System (SUS) and patients. Initiatives such as the Productive Development Partnerships (PDPs)

are fundamental in this process, promoting collaboration between public and private sectors in the production of medications considered strategic for the health system.

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