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RHEUMATOLOGIC INVOLVEMENT IN INFLAMMATORY BOWEL DISEASE: UPDATED EVIDENCE ON SPONDYLOARTHRITIS AND THE CASE FOR INTEGRATED CARE

COMPROMETIMENTO REUMATOLÓGICO NAS DOENÇAS INFLAMATÓRIAS INTESTINAIS: EVIDÊNCIAS ATUALIZADAS SOBRE ESPONDILOARTRITES E O CASO PARA CUIDADO INTEGRADO

RHEUMATOLOGICAL INVOLVEMENT IN INFLAMMATORY BOWEL DISEASE: UPDATED EVIDENCE ON SPONDYLOARTHRITIS AND THE CASE FOR INTEGRATED CARE

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ABSTRACT

Introduction: Crohn's disease (CD) and Ulcerative Colitis (UC) are part of the group of Inflammatory Bowel Diseases (IBD), autoimmune and chronic conditions that primarily affect the gastrointestinal tract. However, extraintestinal manifestations may also be present, especially spondyloarthritis (SpA).

Purpose: This study aimed to highlight the prevalence of extraintestinal manifestations, focusing on SpA, in association with IBD, emphasizing the importance of early awareness for appropriate follow-up with specialists.

Methods: This narrative literature review was based on a clinical and epidemiological search for information on patients with CD or UC concomitant with SpA. The period covered was 2011–2025, using the databases SciELO and PubMed, with descriptors such as 'Crohn Disease,' 'Colitis, Ulcerative,' 'Inflammatory Bowel Diseases,' 'Spondyloarthritis,' 'Sacroiliitis,' 'Arthritis,' 'Prevalence,' 'Epidemiology,' and 'Frequency'.

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Revista ARACÊ
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Results and Discussion: The results reveal a significant prevalence of musculoskeletal involvement in association with IBD, with particular emphasis on the higher prevalence of axial SpA associated with CD.

Final Considerations: When present, extraintestinal manifestation associated with IBD should be diagnosed early in order to enable an integrated therapeutic management, addressing both comorbidities, with the aim of reducing morbidity and mortality in these patients, preventing disease progression, and providing quality of life through appropriate case management and follow-up by gastroenterology and rheumatology specialists.

Keywords: Inflammatory Bowel Disease. Extraintestinal Manifestations. Axial and Peripheral Spondyloarthritis.

RESUMO

Introdução: A Doença de Crohn (DC) e a Retocolite Ulcerativa (RCU) fazem parte do grupo das Doenças Inflamatórias Intestinais (DII), condições autoimunes e crônicas que afetam primariamente o trato gastrointestinal, em contrapartida, manifestações extraintestinais podem estar presentes, principalmente as espondiloartrites (EpA).

Objetivo: Este estudo objetivou mencionar a prevalência das manifestações extraintestinais, com foco nas EpA, em associação à DII mediante a importância do conhecimento precoce para o adequado seguimento com especialistas.

Métodos: Essa revisão bibliográfica narrativa se baseou em uma procura clínica e epidemiológica de informações dos pacientes com DC ou RCU concomitante às EpA. Período foi de 2011-2025 nas bases de dados scielo e pubmed com descritores como "Crohn Disease", "Colitis, Ulcerative", "Inflammatory Bowel Diseases", “Spondyloarthritis”, “Sacroiliitis", “Arthritis”, “Prevalence", “Epidemiology”, “Frequency".

Resultados e discussão: Os resultados revelam uma prevalência do acometimento musculoesquelético junto à DII, o destaque foi a maior prevalência da EpA axial associada à DC.

Considerações finais: A manifestação extraintestinal quando presente associada à DII deve ser diagnosticada precocemente com o intuito de permitir um manejo terapêutico integrado, abordando ambas as comorbidades, a fim de diminuir a morbimortalidade desses pacientes, impedir progressão de doença e ofertar qualidade de vida mediante adequada condução do quadro e acompanhamento de especialistas gastroenterologistas e reumatologistas.

Palavras-chave: Doença Inflamatória Intestinal. Manifestações Extraintestinais. Espondiloartrites Axial e Periférica.

RESUMEN

Introducción: La enfermedad de Crohn (EC) y la colitis ulcerosa (CU) son enfermedades inflamatorias intestinales (EII), afecciones autoinmunes crónicas que afectan principalmente al tracto gastrointestinal. Sin embargo, también pueden presentarse manifestaciones extraintestinales, en particular la espondiloartritis (EspA).

Revista ARACÊ
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Objetivo: Este estudio tuvo como objetivo evaluar la prevalencia de manifestaciones extraintestinales, con especial atención a la EspA, asociadas con la EII, destacando la importancia de la detección temprana para un seguimiento adecuado con especialistas.

Métodos: Esta revisión narrativa de la literatura se basó en una búsqueda clínica y epidemiológica de información sobre pacientes con EC o CU concomitante con EspA. El período fue de 2011 a 2025 en las bases de datos Scielo y PubMed con descriptores como "Enfermedad de Crohn", "Colitis Ulcerosa", "Enfermedades Inflamatorias Intestinales", "Espondiloartritis", "Sacroileítis", "Artritis", "Prevalencia", "Epidemiología" y "Frecuencia".

Resultados y discusión: Los resultados revelan una prevalencia de afectación musculoesquelética en la EII, con un aumento notable en la prevalencia de EspA axial asociada a EC.

Consideraciones finales: Las manifestaciones extraintestinales, cuando se presentan asociadas a la EII, deben diagnosticarse precozmente para permitir un manejo terapéutico integral, abordando ambas comorbilidades. Esto reduce la morbilidad y la mortalidad en estos pacientes, previene la progresión de la enfermedad y mejora la calidad de vida mediante un manejo y seguimiento adecuados por parte de gastroenterólogos y reumatólogos.

Palabras clave: Enfermedad Inflamatoria Intestinal. Manifestaciones Extraintestinales. Espondiloartritis Axial y Periférica.

Revista ARACÊ
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1 INTRODUCTION

Inflammatory Bowel Disease (IBD) includes Crohn's Disease (CD) and Ulcerative Colitis (UC). Both are immune-mediated pathologies that primarily affect the intestine, however, extraintestinal manifestations are frequent in these patients, one of which is spondyloarthritis (SpA), which may present with axial or peripheral involvement (PETTERSSON et al., 2025). SpA is the most common extraintestinal manifestation in IBD, the proportion varies according to the cohort and the assessment method (GIONCHETTI, CALABRESE, RIZZELO, 2015).

Such manifestations increase morbidity, functional disability, and reduce the quality of life of affected individuals. In pathophysiology, there is an extension and translocation of immune complexes from the intestine to other organs. This is influenced by genetic predisposition, intestinal dysbiosis, environmental conditions, and isolated inflammatory events (NARDONE et al., 2025).

The decision regarding therapeutic management becomes more complex, considering the treatment target (NARDONE et al., 2025), since the presence of IBD is related to the diagnosis of axial spondyloarthropathy. SpA is classified into type I peripheral arthritis, also called pauciarticular, and type II, which is polyarticular (GIONCHETTI, CALABRESE, RIZZELO, 2015). Axial SpA encompasses isolated sacroiliitis, low back pain, and ankylosing spondylitis, which is present in 62% of patients with UC (HAMMOUDEH et al., 2018).

From an immunological perspective, joint and intestinal diseases share the same inflammatory pathways mediated by pro-inflammatory cytokines as part of their pathogenesis, namely Tumor Necrosis Factor (TNF), interleukin-23 (IL-23), and interleukin-17 (IL-17). SpA is characterized as seronegative, meaning there is no presence of typical autoantibodies, which differs from rheumatoid arthritis, for example, which has also been reported in association with IBD (FELICE et al., 2023).

In terms of pathophysiology, there is an interaction between the gut–joint axis in the inflammatory process that begins in the gastrointestinal tract through dysbiosis, which increases intestinal permeability and, consequently, triggers immune activation. Therefore, genetic, environmental, and immunological factors play a fundamental role in the pathogenesis of IBD, leading to dysbiosis, which in turn emerges as a triggering factor for intestinal immune-mediated diseases (FELICE et al., 2023).

Regarding the diagnosis of IBD, clinical investigation should follow a detailed medical history, identifying chronic diarrhea, recurrent abdominal pain, hematochezia, fatigue, and

Revista ARACÊ
ISSN: 2358-2472

already considering the possibility of extraintestinal manifestations (ALVARADO-JULIO et al., 2022). Low back pain lasting more than 3 months, arthritis, and uveitis should be evaluated as potential SpA associated with IBD; increased inflammatory markers, HLA-B27 positivity, and the presence of sacroiliitis on imaging support this association (FRAGOULIS et al., 2019).

The importance of early treatment initiation lies in achieving disease remission from a clinical and endoscopic perspective, thus improving quality of life and reducing complications such as surgical interventions and hospitalizations (FELICE et al., 2023). The intention behind choosing biologic therapies is to simultaneously treat the intestinal pathology and the rheumatologic disease, aiming to reduce gastrointestinal inflammation and alleviate the articular manifestations (NAG et al., 2023).

2 JUSTIFICATION

The importance of collaborative work between gastroenterologists and rheumatologists in ensuring proper treatment management is essential. Referral to rheumatology services and the lack of studies addressing this unique prevalence of spondyloarthritis in patients with IBD remain an issue, as few investigations focus specifically on the prevalence of spondyloarthritis.

3 PURPOSE

This study aims to review the recent literature on the association between IBD and spondyloarthritis, emphasizing prevalence, clinical manifestations, shared pathophysiology, and therapeutic implications.

4 METHODS

This is a narrative literature review study in which searches were conducted in scientific databases such as PubMed and SciELO. The search period considered was from 2011 to 2025. Furthermore, the languages included were English and Portuguese, with the following search terms and descriptors: "Crohn Disease", "Colitis, Ulcerative", "Inflammatory Bowel Diseases", "Spondyloarthritis", "Sacroiliitis", "Arthritis", "Prevalence", "Epidemiology", "Frequency".

Inclusion and exclusion criteria were applied with the purpose of refining the selection of studies for a critical synthesis of the works retrieved from the databases. Relevant topics

Revista ARACÊ
ISSN: 2358-2472

for inclusion: articles pertinent to the proposed theme, available in full text, with relevant contribution to the subject of the study, written in Portuguese, English, or Spanish, with priority given to observational studies and narrative reviews. As for the exclusion criteria: publications in languages other than those mentioned, lack of full text availability, subjects unrelated to the proposed scope of this review, and studies prior to 2011.

5 RESULTS AND DISCUSSION

Clinic and Epidemiology of IBD

The present narrative review demonstrates that rheumatologic manifestations are common in patients with IBD, particularly in the form of SpA, as they are the most frequent to date. CD has shown a stronger association with SpA when compared to UC (GIONCHETTI, CALABRESE, RIZZELO, 2015). Peripheral spondyloarthritis is more prevalent in women, whereas in men axial involvement is more common (HUBER et al., 2025).

Studies show that the prevalence of axial spondyloarthritis was 5%, while peripheral involvement accounted for 16% in patients with IBD (PETTERSSON et al., 2025). Approximately 36.8% of the population living with CD develop associated spondyloarthritis within 8 years after the diagnosis of IBD, whereas in UC cases this percentage is 25.5% (FATICA et al., 2024). The literature indicates that individuals with CD involving the colon have an increased risk for the development of synovitis (HAMMOUDEH et al., 2018).

Pathophysiology of Musculoskeletal Manifestations

The most recent definition of the pathogenesis of SpA is based on the possibility that the initial immune dysfunction occurs at the level of the intestinal mucosa (ZIOGA et al., 2022). The hypothesis of a gut–skin–joint axis has been suggested by researchers in the context of inflammatory bowel diseases, aiming to relate extraintestinal manifestations to the gastrointestinal microbiota (SUN, LI, ZHANG, 2022). The theory that environmental and behavioral conditions favor the pathogenesis of IBD is supported by the finding that SpA was also more frequently diagnosed in partners of individuals with IBD. As an example, smoking has been shown to be a shared risk factor for both comorbidities, specifically CD and SpA. However, this association has not been demonstrated in UC (SHRESTHA et al., 2024). The proposed association between smoking and SpA in patients with IBD is stronger in axial SpA, whereas no such association has been observed in peripheral SpA (PETTERSSON et al., 2025).

Revista ARACÊ
ISSN: 2358-2472

It has been recognized that patients with SpA present a specific intestinal microbiome profile, and the perpetuation of certain cytokine activations contributes to the establishment of an immune dysregulation environment directly linked to pro-inflammatory pathways, leading to tissue damage. HLA-B27 plays a key role in the heritability of ankylosing spondylitis but is less prevalent in axial SpA associated with IBD. Furthermore, the major histocompatibility complex is implicated in susceptibility to psoriatic arthritis and peripheral arthritis, along with the production of certain cytokines also related to IBD, such as the IL-17/IL-23 axis, NF-κB pathways, and type 2 helper T cells (FELICE et al., 2023).

A study has raised the hypothesis that bacterial antigens and reactive T-cell clones may lodge in the joint after being initially activated in the intestine. However, the precise immunological mechanism explaining the link between intestinal and articular inflammation remains unknown. Evidence suggests that macrophages originating from the intestines of IBD patients may adhere to endothelial cells in synovial tissue, thereby promoting an increase in T-cell infiltration (FRAGOULIS et al., 2019). Another hypothesis under investigation is the recirculation theory, which suggests that immune system cells are activated and subsequently migrate to extraintestinal sites, contributing to extraintestinal manifestations (ROHEKA et al., 2024).

Diagnosis of Spondyloarthritis in IBD

The gastroenterologist should begin to investigate the presence of SpA concomitant with IBD, particularly when there is chronic low back pain lasting more than three months, a history of dactylitis or tenosynovitis, peripheral joint swelling, or signs of enthesitis (GIONCHETTI, CALABRESE, RIZZELO, 2015). Plasma calprotectin is closely linked to inflammatory markers, and the measurement of fecal and plasma calprotectin has been identified as a tool for detecting gastrointestinal inflammation in patients with SpA who have not yet exhibited clinical symptoms. Moreover, a relationship has been observed between calprotectin levels and inflammation, in which patients with high fecal calprotectin values showed greater inflammatory activity in the sacroiliac joints, while those with lower values demonstrated less articular inflammation (FRAGOULIS et al., 2019).

One barrier for specialists dealing with this comorbidity is the fact that protocols aimed at screening for EIMs still lack standardization in clinical trials. A limitation worth mentioning is the underdiagnosis reported in studies: analyses have shown that, in the diagnosis of axial SpA as a manifestation of IBD, up to 26% of the patients included in the study already exhibited sacroiliitis on imaging (HUBER et al., 2024).

Revista ARACÊ
ISSN: 2358-2472

Treatment of Spondyloarthritis in IBD

The emergence of EIMs is an important factor in the treatment follow-up of patients with IBD, with biologics targeting TNF-α and the JAK/STAT pathway being among the most widely used. Combined therapies have also been shown to provide significant improvement in individuals with complex manifestations (NARDONE et al., 2025).

When facing IBD associated with SpA, treatment presents a challenge, since for this rheumatologic manifestation the prescription of anti-inflammatory drugs is common. However, in IBD such a class is generally avoided to prevent disease flares, with COX-1 inhibitors being more likely to trigger flares compared to COX-2 inhibitors (NAG et al., 2023). Study results also address the feasibility of methotrexate in treatment management, with evidence supporting its use in CD but not in UC, and with limited data regarding SpA. Therefore, the literature recommends reserving methotrexate for cases of intolerance to the aforementioned therapies (ZIOGA et al., 2022).

The main drugs currently used for the management of this association are immunobiologics. Much has been discussed regarding infliximab, whose efficacy is well established in the literature to date for both ulcerative colitis and Crohn's disease. Reinforcing the effectiveness of this class, many studies are underway, and drugs such as vedolizumab, ustekinumab, and natalizumab have shown potential results for therapeutic management. It is worth emphasizing that the choice of biologic therapy must be individualized, with several factors to be carefully considered by the specialist. The treatment goal is to halt the progression of the natural history of the disease and prevent its complications (NAG et al., 2023).

When discussing mortality in patients with IBD, infection and sepsis represent potential factors, often related to the use of biologics given their mechanism of action on the immune system. Anti-TNF therapy is frequently associated with upper respiratory and urinary tract infections. A relevant point in this discussion is the concern regarding the prescription of the anti-TNF class due to the possible risk of developing non-Hodgkin's lymphoma during therapy with infliximab and immunomodulators (NAG et al., 2023).

Several hypotheses about dual therapy combining biologics with distinct agents have been reported in the literature, aiming to strengthen the management of both comorbidities in the same individual. However, further evidence is necessary for the implementation of dual-target therapy (FELICE et al., 2023). Another resource routinely used today is ultrasound for

Revista ARACÊ
ISSN: 2358-2472

the detection of inflammatory arthritis; nonetheless, many reports addressing the association of IBD with peripheral SpA have relied on this tool (WANG, TSAI, 2023).

In light of the above, multidisciplinary follow-up between gastroenterologists and rheumatologists is essential for the clinical management of these patients, given the complexity of the pathologies (NAG et al., 2023). Evidence showing that patients referred to rheumatology services already present with advanced disease underscores the delay in recognizing the signs of SpA concomitant with IBD (PETTERSSON et al., 2025). Autoimmune diseases, such as IBD, may represent a public health issue, and some institutions within the SUS have specialized outpatient centers dedicated to patients with these pathologies. However, the scarcity of demographic data on prevalence remains a challenge (TORRES et al., 2011).

6 CONCLUSION

Inflammatory bowel diseases, notably CD and UC, present a significant systemic inflammatory impact that extends beyond the gastrointestinal tract, with spondyloarthritis being their most frequent and clinically challenging extraintestinal manifestation. This narrative review highlighted the prevalence, clinical features, and therapeutic implications of these manifestations, both in their axial and peripheral forms. Given their morbidity potential, the possibility of underdiagnosis, and the therapeutic complexity involved, the implementation of early screening strategies becomes essential, particularly in primary care services, where patient contact often first occurs. Continuing medical education directed at SUS professionals is crucial for the timely recognition of these manifestations, ensuring prompt referral to specialized services and promoting integrated and individualized management. Investments in population-based research adapted to the Brazilian context are equally necessary to support public health policies and improve clinical guidelines addressing IBD and its extraintestinal manifestations.

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