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THE IMPACT OF GUT MICROBIOTA IN RHEUMATOID ARTHRITIS: A SCOPING REVIEW

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Background. Rheumatoid arthritis (RA) is one of the most common autoimmune chronic inflammatory rheumatic diseases, leading to progressive joint destruction and disability. Gut dysbiosis contributes to the disruption of the integrity of the intestinal barrier and immune dysfunction. The impact of alterations in gut bacterial composition in individuals with preclinical and established RA remains controversial. Understanding the role of the gut microbiota in the incidence and outcomes of RA will improve prevention and optimize treatment approaches for this high-burden disease.

Objectives. Our aim was to outline the literature describing the impact of gut microbiota on disease incidence and outcomes in patients with RA.

Methods. A search of MEDLINE database via Pubmed and Cochrane Library was performed for publications studying the impact of gut microbiota in rheumatoid arthritis. Articles published from inception to December 2024 written in English were included. Titles and abstracts were screened by two independent reviewers (AM and AS), who then assessed full-text articles for inclusion.

Results. After deduplication, 420 titles and abstracts were screened. 10 articles were included in the review. Dysbiosis affects regulatory T-cells, inflammatory mediators, cytokines and disease activity in RA. Clinical RA has been associated with reduced *Lactobacillus* and *Bacteroides* in many studies. It has been shown that some bacteria (*Porphyromonas gingivalis* and *Prevotella copri*) can mediate protein citrullination to induce an immune response that leads to the generation of autoantibodies.

P. gingivalis, a periodontal pathogen implicated in the etiology of RA, upregulates the expression of proinflammatory genes in the gut and contributes to the onset and progression of RA. *P. copri* has been considered a potential disease trigger in RA. A Spanish observational cross-sectional study found that the genus *Collinsella* plays an important role in the cumulative inflammatory burden within established RA. *Oxalobacteraceae* abundance has a protective effect on RA.

Antibiotic use was associated with a higher chance of RA, with bactericidal antibiotics carrying a higher risk than bacteriostatic antibiotics (45% vs. 31%). There is mixed evidence regarding the use of probiotics for the prevention and treatment of RA. There is evidence to suggest that probiotic supplements with *Lactobacillus casei* and *Lactobacillus acidophilus*, which have anti-inflammatory, antimicrobial, and antioxidant properties, act symbiotically in the gut, and promote gut wall integrity and prevent intestinal permeability (“leaky gut”). Regular use of proton pump inhibitors

(PPI) leads to gut dysbiosis, which contributes to the development of RA. Moreover, a higher risk of RA has been observed in individuals with longer duration of PPI using.

Therapeutic fasting, a high-fiber plant-based diet, and a ketogenic diet help normalize the gut microbiome, increase the mucus layer in the gastrointestinal tract, and prevent the migration of intestinal commensals to secondary lymphoid organs. Disease-modifying antirheumatic medications, including methotrexate, has a positive effect on the gut microbiota according to most studies. Among the possible reasons for the ineffectiveness of methotrexate is considered that its metabolism is associated with the gut microbiota.

Conclusion. There is sparse literature published on the role of gut microbiota in RA. Pharmacological and non- pharmacological interventions aimed at restoring the gut microbiota show promise in preventing and slowing RA progression. However, the complex interplay between the gut microbiota and autoimmune pathways in RA requires further investigation.

Key words: microbiota, Lactobacillus, dysbiosis, prevention, arthritis, antibiotic, metabolism.