

Review Article

Bacterial DNA in joint tissue and its role in osteoarthritis: a narrative review

Aavrati Rastogi, Roop B. Kalia*, Mukesh Bairwa

Department of Orthopedics, AIIMS, Rishikesh, Uttarakhand, India

Received: 17 April 2026

Revised: 14 July 2026

Accepted: 15 July 2026

*Correspondence:

Dr. Roop B. Kalia,

E-mail: roop.orth@aiimsrishikesh.edu.in

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Osteoarthritis (OA) is a complex condition that involves immunological, metabolic, and inflammatory processes, as well as mechanical deterioration. Even in the absence of overt infection, recent developments in molecular diagnostics have revealed that synovial fluid, synovial tissue, and articular cartilage from patients with OA contain bacterial DNA and other microbial components. These results cast doubt on the conventional theory of joint sterility and raise the possibility that the gut–joint axis plays a role in disease etiology. In accordance with the PRISMA-style methodology, this narrative review summarizes the most recent human data on microbial DNA detection in joint tissues, investigates mechanisms of innate immune activation and microbial translocation, and assesses their clinical implications. Microbial markers in OA joints differ from those in healthy controls. They are associated with inflammatory mediators such as lipopolysaccharide (LPS), according to observational, cross-sectional, and emerging interventional studies. Toll-like receptor (TLR)-mediated pathways may be activated by microbial components, leading to cartilage degradation and synovitis. Causality remains unknown despite encouraging results due to methodological flaws and potential contamination biases. Gaining insight into the role of microbes in OA could lead to the development of new biomarkers and treatments targeting the microbiome.

Keywords: Osteoarthritis, Joint microbiome, Synovial fluid, Cartilage, Bacterial DNA, Gut–joint axis, Inflammation

INTRODUCTION

The most common joint condition worldwide, OA, is a major contributor to pain, disability, and economic hardship.^{1,2} OA has since been recognized as a complex whole-joint disease involving synovial inflammation, subchondral bone remodeling, metabolic dysregulation, and immune activation. However, cartilage degeneration and biomechanical stress remain key characteristics.³ Systemic causes of OA, such as inflammation linked to obesity and metabolic endotoxemia, are receiving increasing attention.⁴

The idea that bacterial DNA and other microbial components can be found in joint tissues that are normally considered sterile is new and contentious.^{5,6}

Microbial DNA can now be detected in low-biomass tissues such as synovium and cartilage using sensitive molecular techniques, including next-generation sequencing (NGS) and 16S ribosomal RNA (rRNA) gene sequencing.^{7,8} These results provide significant queries about the source, biological significance, and pathogenic function of microbial markers in OA.

PURPOSE OF THE REVIEW

This study aims to comprehensively evaluate available data on presence and function of bacterial DNA in tissues of OA joints. In particular, it aims to summarize human studies that have found microbial DNA in synovial fluid, synovial tissue, and articular cartilage; investigate mechanisms underlying microbial translocation,

especially through gut-joint axis; assess innate immune activation pathways implicated in pathophysiology of

OA; and evaluate clinical implications and emerging therapeutic potential of microbiome-targeted approaches.

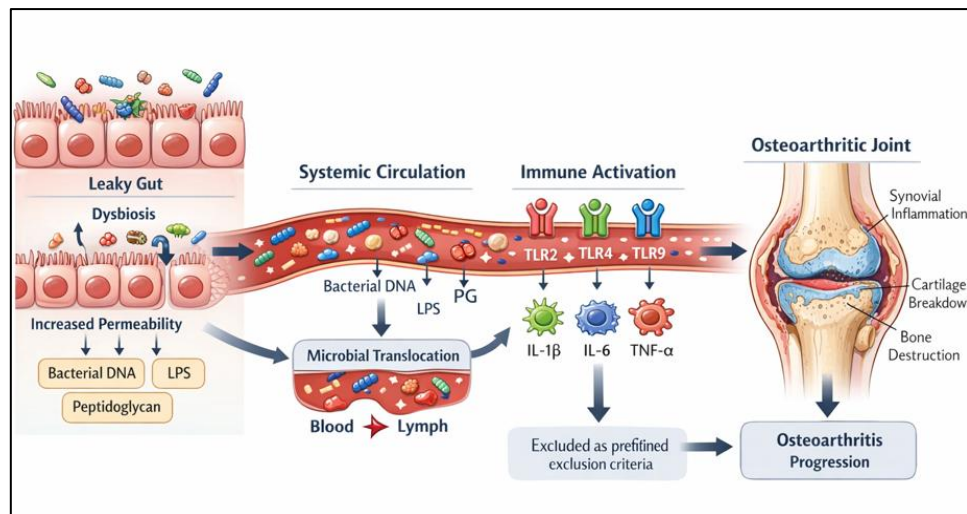


Figure 1: Gut-joint axis and OA.¹⁶

LITERATURE RESEARCH

To provide a clear and systematic synthesis of the existing literature on microbial involvement in OA, a PRISMA-aligned narrative methodology was used. Key elements of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework were adhered to improve methodological rigor and reproducibility. However, this study was not intended as a formal systematic review or meta-analysis.

From the beginning to March 2025, a thorough literature search was carried out using the PubMed/MEDLINE, Scopus, and Web of Science databases. Medical Subject Headings (MeSH) and free-text terms, such as "osteoarthritis," "synovial microbiome," "bacterial DNA joint," "gut-joint axis," and "lipopolysaccharide OA," were used in the search method. To ensure the best possible sensitivity and specificity, the search technique was refined using Boolean operators. The methodology for database searching and study identification was consistent with established techniques used in earlier evaluations of the microbiome and OA.

Studies that examined the presence of microbial DNA, microbiome composition, or microbial-derived components in OA in human populations were deemed eligible. Randomized controlled trials, observational studies, cross-sectional analyses, and systematic reviews were among the study designs that qualified. Excluded were studies that only addressed septic arthritis, animal models, or non-peer-reviewed sources. These standards were established to ensure clinical applicability and alignment with prior evidence summaries in the field.

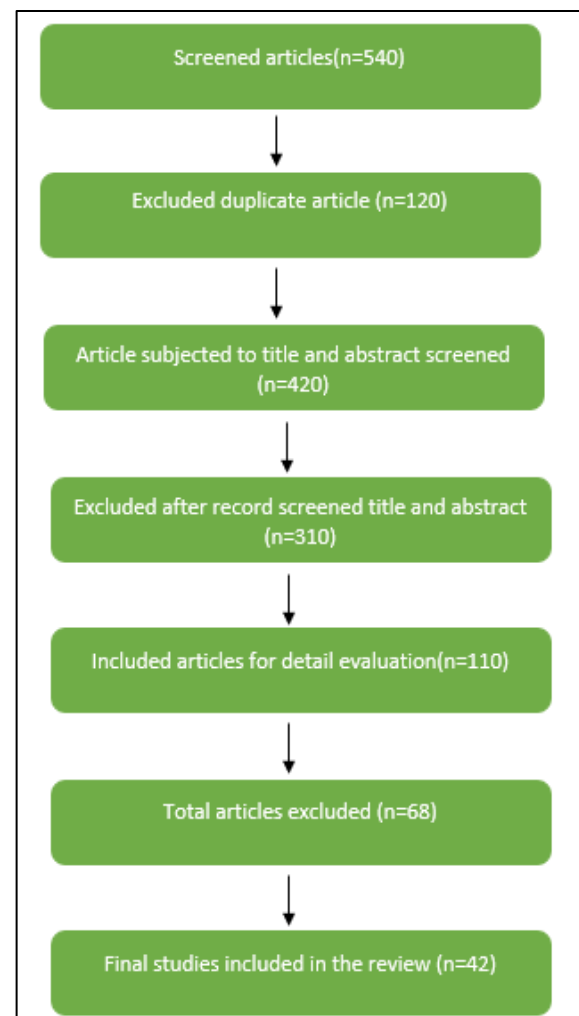


Figure 2: Screening of articles for review.

The methodical PRISMA-style procedure was used in the study selection phase. Initially, database searches turned up 540 results. 420 studies underwent title and abstract screening after duplicates were removed and the initial screening. Based on their applicability to review's goals, 110 of these articles were chosen for full-text evaluation. In end, 42 papers were included in synthesis because they met inclusion criteria. According to PRISMA reporting guidelines, research selection procedure is depicted in PRISMA flow diagram (Figure 2).

The author, year of publication, study design, sample type (e.g., synovial fluid, cartilage, or gut microbiome),

analytical techniques (e.g., 16S rRNA or next-generation sequencing), and key findings regarding microbial involvement in OA were carefully considered when extracting data. A quantitative meta-analysis was not possible due to the variation in study designs, demographics, and methodology.

Consequently, a qualitative narrative approach was used to synthesize the results, focusing on mechanistic insights, evidence consistency, and clinical significance. This method aligns with other narrative reviews that examined the gut-joint axis and microbiome-related processes in OA.

Table 1: Representative human studies included in the PRISMA-based qualitative synthesis on microbial involvement in OA.

Authors	Year	Study title	Study design	Purpose	Key findings	Conclusion
Scanzello et al ³	2012	Role of synovitis in OA	Review (Human-based evidence)	Evaluate inflammatory mechanisms	Synovial inflammation contributes to OA	Inflammation is central to OA ³
Huang et al ⁹	2016	LPS-mediated inflammation in OA	Review	Assess the role of endotoxins	LPS linked with OA inflammation	Microbial products influence OA ⁹
Zhao et al ⁵	2018	Bacterial DNA in synovial fluid	Cross-sectional	Detect microbial DNA	Bacterial DNA is present in OA synovial fluid	Suggests non-sterile joint ⁵
Collins et al ⁶	2018	Gut microbiome and OA	Observational	Link the microbiome with OA	Dysbiosis correlates with OA severity	Supports gut-joint axis ⁶
Berthelot et al ⁷	2019	Gut microbiome in OA	Systematic review	Summarize Microbiome's role	Strong gut–OA association	The microbiome contributes to OA ⁷
Dunn et al ⁸	2020	Cartilage microbial DNA signatures	Cross-sectional	Analyze cartilage microbiome	Altered microbial DNA in OA cartilage	Cartilage is not sterile ⁸
Boer et al ¹⁰	2022	Microbiome composition in OA	Observational	Study gut microbiota	Specific taxa linked to OA	Microbiome influences OA risk ¹⁰
Song et al ¹¹	2011	Plasma carboxypeptidase B downregulates inflammatory responses in autoimmune arthritis	Experimental	To investigate the anti-inflammatory role of plasma CPB in autoimmune arthritis and its effects on complement-mediated inflammation.	CPB deficiency worsened experimental arthritis, while CPB-mediated cleavage of C5a reduced its inflammatory activity.	CPB may limit autoimmune joint inflammation by regulating complement activation and inflammatory-cell
Favazzo et al ¹²	2023	A systems view of risk factors for knee osteoarthritis reveals insights into the pathogenesis of the disease	Review	Explore systemic mechanisms	The microbiome drives inflammation	Strong gut-joint link ¹²
Andriacch	2015	Microbiome-	Narrative	To develop a	OA risk was	Knee OA is a

Continued.

Authors	Year	Study title	Study design	Purpose	Key findings	Conclusion
et al ¹³		metabolome axis	review	unified framework explaining how aging, obesity and joint trauma interact with mechanical, biological and structural factors to initiate and progress knee OA.	associated with interactions among gait mechanics, cartilage structure and biology. Changes in walking mechanics may alter cartilage.	multifactorial disease rather than simply wear and tear.
Wang et al ¹⁴	2011	Identification of a central role for complement in osteoarthritis	Experimental study	To determine whether the complement system contributes to OA pathogenesis and whether complement activation influences joint tissue damage.	Complement activation was implicated in OA-related cartilage damage and synovial inflammation.	An important contributor to OA pathogenesis and a potential therapeutic target for limiting joint inflammation and tissue damage.
Sharif et al ¹⁵	2009	Thrombin-activatable carboxypeptidase B cleavage of osteopontin regulates neutrophil survival and synoviocyte binding in rheumatoid arthritis.	Experimental study	Thrombin-cleaved osteopontin and its subsequent processing by carboxypeptidase B (CPB) affect neutrophil survival and synoviocyte	Synovial fluid showed elevated levels of cleaved osteopontin forms (OPN-R and OPN-L), which correlated with inflammatory cytokines, including TNF- α and IL-6. OPN-R enhanced binding	CPB-mediated processing of osteopontin may help regulate inflammation by limiting synoviocyte

DISCUSSION

A paradigm shift in understanding OA is highlighted by the findings presented in this review, which emphasize the potential significance of microbial components in disease etiology.^{9,10} The biological plausibility of the gut-joint axis is supported by the presence of bacterial DNA in joint tissues and by data linking changes in the gut microbiota to OA severity.^{11,12}

But there are still important uncertainties about etiology. It's unclear whether microbial DNA is a secondary effect of joint deterioration or main cause of inflammation.^{13,14} Low biomass in the joint tissues also presents methodological difficulties, such as the risk of contamination, which need to be properly addressed in subsequent research.^{15,16}

Despite these limitations, there is strong evidence for the functional significance of microbial components in OA,

as they are consistently correlated with inflammatory mediators, including LPS.

Strengths and limitations

The incorporation of several human study designs, adherence to a PRISMA-aligned methodology, and integration of mechanistic and clinical evidence strengthen this review. But there are a few restrictions to be aware of. Causal inference is limited because most of the included research is observational or cross-sectional. The possibility of contamination in low-biomass samples and the variation in microbiome analysis methods remain major obstacles. The scarcity of large-scale randomized controlled studies further constrains the application of recent discoveries to clinical practice.

Clinical implications

The identification of microbial DNA in joint tissues offers the potential to develop new biomarkers for

diagnosing and tracking OA. Additionally, probiotics, prebiotics, and dietary modifications are treatments that target the gut microbiota and may offer novel approaches to illness management. Another promising strategy for reducing inflammation and delaying disease progression is to modulate innate immune signaling pathways.

CONCLUSION

The conventional understanding of OA as a solely degenerative condition is called into question by the discovery of bacterial DNA in synovial fluid, synovial tissue, and articular cartilage. There is mounting evidence that microbial components-possibly from the mouth or gut microbiome-may contribute to joint deterioration and inflammation. In the end, a better understanding of the gut-joint axis and the joint microbiome may reframe the pathophysiology of OA and aid in the development of innovative diagnostic and therapeutic approaches.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

- Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet*. 2019;393(10182):1745-59.
- Berenbaum F. Osteoarthritis as an inflammatory disease. *Nat Rev Rheumatol*. 2013;9(11):684-92.
- Scanzello CR, Goldring SR. The role of synovitis in osteoarthritis pathogenesis. *Bone*. 2012;51(2):249-57.
- Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: a disease of the joint as an organ. *Arthritis and rheumatism*. 2012;64(6):1697.
- Lepus CM, Song JJ, Wang Q, Wagner CA, Lindstrom TM, Chu CR, Sokolove J, Leung LL, Robinson WH. Brief report: carboxypeptidase B serves as a protective mediator in osteoarthritis. *Arthritis & Rheumatology*. 2014;66(1):101-6.
- Collins KH, Paul HA, Reimer RA, Seerattan RA, Hart DA, Herzog W. Relationship between inflammation, the gut microbiota, and metabolic osteoarthritis. *J Orthop Res*. 2018;36(1):176-86.
- Berthelot JM, Le Goff B, Maugars Y. The role of the gut microbiome in osteoarthritis: a systematic review. *Joint Bone Spine*. 2019;86(6):685-91.
- Dunn CM, Velasco C, Rivas A, Madison A, Cassandra G, Paul BJ, et al. Identification of cartilage microbial DNA signatures in osteoarthritis. *Arthritis Rheumatol*. 2020;72(7):1111-22.
- Huang Z, Kraus VB. Does lipopolysaccharide-mediated inflammation have a role in osteoarthritis? *Arthritis Res Ther*. 2016;18:167.
- Boer CG, Radjabzadeh D, Medina-Gomez C, Sanzhima G, Dieuwke S, Pascal A, et al. Intestinal microbiome composition and its relation to osteoarthritis. *Ann Rheum Dis*. 2022;81:154-61.
- Song JJ, Hwang I, Cho KH, Garcia MA, Kim AJ, Wang TH, et al. Plasma carboxypeptidase B downregulates inflammatory responses in autoimmune arthritis. *The Journal of Clinical Investigation*. 2011;121(9).
- Favazzo LJ, Hendesi H, Villani DA, Sarah S, Qurratul-Ain D, Eric MS, et al. The gut microbiome-joint connection: implications for osteoarthritis. *Curr Opin Rheumatol*. 2020;32(1):92-101.
- Andriacchi TP, Favre J, Erhart-Hledik JC, Chu CR. A systems view of risk factors for knee osteoarthritis reveals insights into the pathogenesis of the disease. *Annals of biomedical engineering*. 2015;43(2):376-87.
- Wang Q, Rozelle AL, Lepus CM, Scanzello CR, Song JJ, Larsen DM, et al. Identification of a central role for complement in osteoarthritis. *Nature medicine*. 2011;17(12):1674-9.
- Sharif SA, Du X, Myles T, Song JJ, Price E, Lee DM, et al. Thrombin-activatable carboxypeptidase B cleavage of osteopontin regulates neutrophil survival and synoviocyte binding in rheumatoid arthritis. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*. 2009 Oct;60(10):2902-12.
- Chisari E, Wouthuyzen-Bakker M, Friedrich AW, Parvizi J. The relation between the gut microbiome and osteoarthritis: A systematic review of literature. *PloS one*. 2021;16(12):e0261353.

Cite this article as: Rastogi A, Kalia RB, Bairwa M. Bacterial DNA in joint tissue and its role in osteoarthritis: a narrative review. *Int J Clin Trials* 2026;13(4):482-6.