Research Article

Academia Journal of Medicine
Vol. 9, No. 2, July–December 2026

Periodontitis and Systemic Diseases: Exploring the Bidirectional Link and Its Clinical Implications

Shilpi Gupta[1*], **Sanjay Janardan Gawali**[2], **Arushi Gupta**[3], **Sumit Bhatt**[4], **Sai Sagar**[5] and **Bhuvan Nagpal**[6]

[1]*Postgraduate Student, Department of Periodontology, Santosh Dental College, Ghaziabad, Uttar Pradesh.*
[2]*Associate Professor, Department of Periodontology, Guru Gobind Singh College of Dental Sciences and Research centre, Burhanpur, Madhya Pradesh.*
[3]*Consultant Periodontist, Laxmi Devi Memorial Hospital, Maunath Bhanjan Uttar Pradesh- 275101*
[4]*PhD Scholar, Assistant Professor, Department of Oral and Maxillofacial Surgery, Rajasthan Dental College & Hospital, Nirwan University, Jaipur, Rajasthan.*
[5]*Senior House Surgeon, Govt Hospital Neyattinkara, Trivandrum, Kerala.*
[6]*Department of Pathology & Laboratory Medicine, Tohana Manglam Diagnostics and Centre for Oral Pathology and Maxillofacial Diagnostics, Hisar, Haryana.*

***** Corresponding author. E-mail: Docshilpigupta@gmail.com

https://doi.org/10.48165/ajm.2026.9.02.18

ARTICLE INFO

Article history:
Published: 2026

Keywords:
Periodontitis
Systemic diseases
Systemic conditions

ABSTRACT

Periodontitis is a chronic inflammatory disease characterized by dysbiotic microbial communities and a dysregulated host immune response, resulting in progressive destruction of the periodontal supporting tissues. Increasing evidence suggests that its effects extend beyond the oral cavity, establishing important associations with systemic diseases such as diabetes mellitus, cardiovascular disease, adverse pregnancy outcomes, respiratory disorders, rheumatoid arthritis, and chronic kidney disease. The relationship is considered bidirectional, as systemic conditions can modify periodontal susceptibility and disease progression, while periodontal inflammation may contribute to systemic inflammatory and metabolic disturbances. Proposed mechanisms include bacteremia, systemic dissemination of microbial products, cytokine release, oxidative stress, immune dysregulation, and endothelial dysfunction. Understanding these interactions highlights the importance of integrating periodontal assessment with overall medical care. This review discusses the biological mechanisms underlying the periodontitis–systemic disease relationship, summarizes current evidence regarding major systemic associations, and explores their clinical implications for prevention, diagnosis, and multidisciplinary management.

INTRODUCTION

Periodontitis is one of the most prevalent chronic inflammatory diseases worldwide and represents a major cause of tooth loss in adults. It is initiated by a dysbiotic microbial biofilm that triggers an exaggerated or dysregulated host immune-inflammatory response, leading to destruction of the periodontal ligament and alveolar bone.[1] Although traditionally regarded as a localized oral disease, contemporary evidence increasingly recognizes periodontitis as a condition capable of influencing systemic inflammatory homeostasis.[2]

The oral cavity represents an important interface between the external environment and the systemic circulation. Periodontal tissues affected by inflammation may facilitate transient bacteremia and the systemic dissemination of microbial components, inflammatory mediators, and

tissue-degradation products.[3] Consequently, persistent periodontal inflammation may contribute to an increased systemic inflammatory burden and influence distant organs and physiological pathways. Conversely, systemic diseases and their associated metabolic, vascular, and immune alterations may modify periodontal susceptibility, severity, and response to treatment, supporting the concept of a bidirectional relationship.[4]

Among the systemic conditions most frequently investigated in relation to periodontitis are diabetes mellitus and cardiovascular disease. Associations have also been reported with adverse pregnancy outcomes, respiratory diseases, rheumatoid arthritis, chronic kidney disease, metabolic disorders, neurodegenerative conditions, and certain malignancies. Several mechanisms have been proposed to explain these relationships, including systemic dissemination of periodontal pathogens, cytokine-mediated inflammation, oxidative stress, endothelial dysfunction, immune dysregulation, and alterations in microbial communities.

However, an association between periodontitis and a systemic disease does not necessarily establish causality. Differences in study design, periodontal definitions, disease severity, shared risk factors, and potential confounding variables continue to influence the interpretation of available evidence. Therefore, a critical understanding of the biological plausibility and strength of evidence is essential before translating these associations into clinical recommendations.[3,5]

This review explores the relationship between periodontitis and systemic diseases, focusing on the underlying biological mechanisms, evidence supporting major systemic associations, the bidirectional nature of these interactions, and their implications for contemporary clinical practice.

PERIODONTITIS

Pathogenesis and Inflammatory Basis

Periodontitis is a chronic, multifactorial inflammatory disease initiated by a dysbiotic microbial biofilm and characterized by progressive destruction of the periodontal supporting tissues. The disease develops through a complex interaction between periodontal microorganisms and the host immune response rather than through the direct action of bacteria alone. Accumulation of pathogenic microorganisms within the subgingival environment alters the local microbial ecosystem and stimulates innate and adaptive immune responses. Individuals with susceptible host responses may develop persistent inflammation, resulting in degradation of periodontal connective tissue and alveolar bone.

The transition from periodontal health to disease involves changes in the composition and activity of the subgingival microbiota. Microorganisms such as *Porphyromonas gingivalis*, *Tannerella forsythia*, *Treponema denticola*, and other anaerobic species can contribute to dysbiosis and sustain inflammatory signaling. Microbial-associated molecular patterns are recognized by host pattern-recognition receptors, including Toll-like receptors, on epithelial and immune cells. This interaction activates intracellular signaling pathways and promotes the release of pro-inflammatory mediators such as interleukin-1β (IL-1β), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and prostaglandin E_2.

Persistent inflammation subsequently promotes recruitment and activation of neutrophils, macrophages, lymphocytes, and other immune cells. Matrix metalloproteinases and other proteolytic enzymes contribute to extracellular matrix degradation, while receptor activator of nuclear factor kappa-B ligand (RANKL)-mediated osteoclast activation promotes alveolar bone resorption. The balance between inflammatory tissue destruction and endogenous repair mechanisms therefore becomes disturbed, leading to progressive periodontal attachment loss.

An important characteristic of periodontitis is that the host inflammatory response itself becomes a major contributor to tissue destruction. Oxidative stress generated by activated immune cells can further damage periodontal tissues and amplify inflammatory signaling. In addition, inflammatory mediators produced locally may enter the systemic circulation, potentially contributing to a state of low-grade systemic inflammation. Thus, periodontitis should be considered not merely as a localized microbial infection but as a chronic inflammatory condition with potential systemic consequences.[6,7]

Biological Mechanisms Linking Periodontitis to Systemic Diseases

The association between periodontitis and systemic diseases is mediated by several interconnected biological pathways. Periodontal inflammation can facilitate bacteremia and dissemination of microbial products, allowing periodontal pathogens and their components to enter the systemic circulation. This may trigger the release of pro-inflammatory mediators such as IL-1β, IL-6, TNF-α, and C-reactive protein, contributing to systemic inflammation.

In addition, periodontitis is associated with increased oxidative stress, endothelial dysfunction, and immune dysregulation, which may influence cardiovascular and metabolic health. Periodontal inflammation may also affect insulin resistance and glucose metabolism, while systemic

conditions such as diabetes can impair host defense and enhance periodontal inflammation. Alterations in the oral and gut microbiome may further contribute to systemic immune and metabolic disturbances. Collectively, these mechanisms support a potentially bidirectional relationship, in which periodontitis may influence systemic health while systemic diseases can modify periodontal susceptibility and progression.[8,9]

Periodontitis and Cardiovascular Diseases

Periodontitis has been associated with several cardiovascular conditions, including atherosclerosis, coronary artery disease, myocardial infarction, stroke, and hypertension. Chronic periodontal inflammation may contribute to cardiovascular pathology through bacteremia, systemic release of inflammatory mediators, oxidative stress, and endothelial dysfunction. Periodontal pathogens and their products may promote vascular inflammation and atherosclerotic processes. Although observational studies generally support an association, evidence for a direct causal relationship remains limited. Periodontal treatment may reduce systemic inflammatory markers and potentially improve cardiovascular risk profiles, but definitive cardiovascular outcome benefits require further evidence. Clinically, cardiovascular risk assessment and optimal periodontal management should be considered complementary components of overall health care.[2,10]

Periodontitis and Diabetes Mellitus

The relationship between diabetes mellitus and periodontitis is strongly considered bidirectional. Hyperglycemia promotes periodontal inflammation through advanced glycation end products, oxidative stress, impaired neutrophil function, and altered immune responses. Conversely, persistent periodontal inflammation may increase systemic inflammatory burden and contribute to insulin resistance and poorer glycemic control. Evidence suggests that periodontal therapy can produce modest improvements in glycemic parameters, particularly HbA1c, although the magnitude of benefit varies among studies. Regular periodontal assessment, effective plaque control, metabolic management, and collaboration between dental and medical professionals are therefore important in patients with diabetes.[10]

Periodontitis and Adverse Pregnancy Outcomes

Periodontal inflammation has been investigated in relation to preterm birth, low birth weight, pre-eclampsia, and gestational diabetes. Proposed mechanisms include systemic maternal inflammation, bacteremia, translocation of periodontal pathogens or their products, and inflammatory effects on placental tissues. However, the evidence remains heterogeneous, and associations do not consistently demonstrate causality. While maintaining periodontal health during pregnancy is important, current evidence should be interpreted cautiously when considering periodontal disease as an independent risk factor for adverse pregnancy outcomes.[5]

Periodontitis and Respiratory Diseases

The oral cavity can act as a reservoir for microorganisms that may be aspirated into the lower respiratory tract, particularly in vulnerable individuals. Periodontal pathogens have therefore been implicated in respiratory infections, including pneumonia, aspiration pneumonia, and chronic obstructive pulmonary disease (COPD). Chronic periodontal inflammation may additionally contribute to respiratory disease through systemic inflammatory pathways. Evidence regarding asthma is less consistent. Maintaining good oral hygiene and periodontal health may be particularly important in individuals at increased risk of aspiration and respiratory infections.[11]

Periodontitis and Rheumatoid Arthritis

Periodontitis and rheumatoid arthritis share several inflammatory and immunological pathways. *Porphyromonas gingivalis* has attracted particular interest because of its potential ability to promote protein citrullination, which may contribute to the development of anti-citrullinated protein antibodies (ACPAs) in susceptible individuals. Genetic susceptibility, smoking, dysbiosis, and chronic inflammation may further contribute to both conditions. The relationship appears potentially bidirectional, with rheumatoid arthritis affecting periodontal health and periodontal inflammation potentially influencing disease activity. Preliminary evidence suggests that periodontal treatment may reduce inflammatory burden, although its effect on rheumatoid arthritis activity remains under investigation.[12]

Periodontitis and Chronic Kidney Disease

Chronic kidney disease (CKD) and periodontitis are both associated with persistent systemic inflammation, oxidative stress, endothelial dysfunction, and altered immune responses. Uremia can impair host defense and increase susceptibility to periodontal inflammation, while periodontal inflammation may contribute to the systemic inflammatory burden in patients with CKD. Observational studies have reported associations between periodontitis and CKD progression and mortality. However, whether periodontal treatment can significantly modify renal outcomes remains uncertain and requires further longitudinal and interventional research.[13]

Periodontitis and Metabolic Syndrome

Periodontitis has been associated with metabolic syndrome, which encompasses obesity, insulin resistance,

dyslipidemia, and hypertension. Both conditions share chronic low-grade inflammation, oxidative stress, and altered metabolic signaling. Adipose tissue-derived inflammatory mediators may enhance periodontal inflammation, while periodontal inflammation may further contribute to metabolic dysfunction. This interaction highlights the importance of considering periodontal health as part of comprehensive metabolic risk management.[3]

Periodontitis and Liver Diseases

Emerging evidence suggests an association between periodontitis and liver disorders, particularly non-alcoholic fatty liver disease (NAFLD), now commonly termed metabolic dysfunction-associated steatotic liver disease (MASLD). Periodontal pathogens and inflammatory mediators may reach the liver through systemic and portal circulation and contribute to hepatic inflammation. Alterations in the oral microbiome and the oral–gut–liver axis may further influence hepatic metabolism and immune responses. Associations have also been investigated in cirrhosis, although causal relationships remain unclear.[3]

Periodontitis and Neurodegenerative Diseases

Growing research has explored potential links between periodontitis and neurodegenerative disorders, particularly Alzheimer's disease and cognitive decline. Proposed mechanisms include chronic systemic inflammation, microbial dissemination, neuroinflammation, oxidative stress, and disruption of the blood–brain barrier. Periodontal pathogens and their virulence factors have been detected or investigated in relation to neurological tissues and inflammatory pathways. Associations with Parkinson's disease have also been reported, although evidence remains emerging and does not currently establish a causal relationship.[14-16]

Periodontitis and Cancer

Chronic periodontal inflammation has been investigated as a potential risk factor for several malignancies, including oral and head-and-neck, colorectal, pancreatic, lung, and breast cancers. Possible mechanisms include persistent inflammation, microbial dysbiosis, immune modulation, oxidative stress, and DNA damage. Certain periodontal pathogens may influence cellular signaling and the local tissue environment in ways that could support carcinogenesis. However, most available evidence is observational, and the influence of common risk factors such as smoking, alcohol consumption, obesity, and socioeconomic status must be carefully considered.[14-16]

Periodontitis and Other Systemic Conditions

Beyond the conditions discussed above, periodontitis has been investigated in relation to osteoporosis, inflammatory bowel disease, psoriasis, anemia, and erectile dysfunction. These associations may involve overlapping inflammatory, immune, metabolic, and vascular pathways. However, the strength of evidence varies considerably between conditions. Further well-designed longitudinal and interventional studies are needed to determine whether periodontal disease is an independent risk factor, a marker of shared susceptibility, or a modifiable contributor to these systemic disorders.[14-16]

Bidirectional Nature of the Periodontitis–Systemic Disease Relationship

The relationship between periodontitis and systemic diseases is increasingly recognized as bidirectional, with each condition potentially influencing the onset, progression, and severity of the other. Systemic diseases such as diabetes mellitus, cardiovascular disorders, and autoimmune conditions can alter immune function, vascular health, tissue repair, and metabolic homeostasis, thereby increasing susceptibility to periodontal inflammation. Conversely, persistent periodontal inflammation can contribute to systemic inflammatory burden through bacteremia, microbial products, cytokine release, oxidative stress, and immune activation.

Several shared risk factors, including smoking, obesity, poor diet, socioeconomic factors, and inadequate oral hygiene, may contribute to both periodontal and systemic diseases. Common inflammatory pathways involving IL-1β, IL-6, TNF-α, oxidative stress, and NF-κB signaling provide biological plausibility for these associations. Genetic susceptibility and environmental exposures may further determine individual differences in disease development and progression.

The oral–systemic axis can therefore be conceptualized as a dynamic interaction in which periodontal dysbiosis and inflammation influence systemic immune and metabolic processes, while systemic conditions modify the periodontal microenvironment and host response. This model emphasizes that oral health should be considered an integral component of overall health rather than an isolated clinical entity. However, the strength and direction of these relationships differ among diseases, and biological plausibility should not be interpreted as definitive evidence of causality.

Role of Periodontal Therapy in Systemic Health

Periodontal therapy primarily aims to control local infection and inflammation, but its potential systemic benefits have gained increasing attention. Scaling and root planing, supported by effective oral hygiene practices, reduces periodontal microbial load and inflammation. Antimicrobial agents may be used selectively as adjuncts,

while surgical periodontal therapy may be indicated for persistent or advanced disease. Successful periodontal treatment has been associated with reductions in systemic inflammatory markers such as C-reactive protein and improvements in glycemic control, particularly in patients with diabetes. However, evidence regarding its ability to prevent cardiovascular events or other major systemic outcomes remains insufficient. Differences in study design, treatment protocols, follow-up duration, and patient characteristics limit definitive conclusions regarding the systemic benefits of periodontal therapy.[17,18]

Clinical Implications

Recognition of the oral–systemic relationship highlights the need for a comprehensive approach to periodontal care. A detailed medical history should identify systemic diseases, medications, lifestyle factors, and relevant risk factors. Patients with diabetes, cardiovascular disease, or other chronic inflammatory conditions should receive appropriate periodontal assessment and risk-based follow-up. Effective communication between dentists, physicians, and other healthcare professionals can facilitate early identification and management of shared risk factors. Patient education regarding oral hygiene, smoking cessation, diet, physical activity, and regular dental visits is essential. Ultimately, periodontal management should be individualized according to disease severity, systemic health, risk profile, and patient needs.[19,20]

Emerging Concepts and Future Directions

The increasing understanding of oral–systemic interactions are driving the development of precision periodontology, in which treatment and prevention are tailored according to individual microbial, genetic, inflammatory, and systemic risk profiles. Biomarkers may potentially help identify patients at increased risk of systemic complications. Advances in microbiome research may provide opportunities for microbiome-based diagnostic and therapeutic approaches, while artificial intelligence may facilitate integrated risk prediction using clinical, microbiological, and systemic health data. Host-modulation therapies and personalized preventive strategies also represent promising areas of research. Future studies should prioritize well-designed longitudinal studies and randomized controlled trials to establish causal relationships and determine whether periodontal treatment can influence meaningful systemic clinical outcomes.

Limitations of Current Evidence

Despite substantial evidence linking periodontitis with systemic diseases, several limitations remain. Much of the available literature is based on observational studies, which are susceptible to residual confounding and cannot reliably establish causality. Variations in periodontal disease definitions, diagnostic criteria, disease severity, treatment protocols, and systemic outcome measures contribute to substantial heterogeneity between studies. Shared risk factors such as smoking, obesity, age, and socioeconomic status may partially explain observed associations. Publication bias and differences in study populations further limit generalizability. Therefore, biological plausibility and statistical association should be carefully distinguished from evidence of a causal relationship.

CONCLUSION

Periodontitis is increasingly recognized as an important component of the oral–systemic health interface, with evidence linking it to several chronic systemic conditions. Chronic periodontal inflammation may contribute to systemic inflammatory, metabolic, vascular, and immune disturbances, while systemic diseases can simultaneously influence periodontal susceptibility and disease progression. Although the strength of evidence varies across individual conditions, the bidirectional relationship highlights the importance of maintaining periodontal health as part of comprehensive healthcare. Multidisciplinary collaboration, early risk assessment, individualized periodontal management, and patient-centered preventive strategies are essential. Future research should focus on establishing causality, identifying clinically useful biomarkers, and determining whether effective periodontal treatment can reduce the incidence or severity of systemic disease.

REFERENCES

Martínez-García, M., & Hernández-Lemus, E. (2021). Periodontal inflammation and systemic diseases: An overview. *Frontiers in Physiology, 12*, 709438.

Aarabi, G., Zeller, T., Seedorf, H., Reissmann, D. R., Heydecke, G., Schaefer, A. S., & Seedorf, U. (2017). Genetic susceptibility contributing to periodontal and cardiovascular disease. *Journal of Dental Research, 96*(6), 610–617.

Harrandah, A. M. (2025). The oral-gut-systemic axis: Emerging insights into periodontitis, microbiota dysbiosis, and systemic disease interplay. *Diagnostics, 15*(21), 2784.

Radaic, A., & Kapila, Y. L. (2021). The oralome and its dysbiosis: New insights into oral microbiome-host interactions. *Computational and Structural Biotechnology Journal, 19*, 1335–1360.

Parihar, A. S., Katoch, V., Rajguru, S. A., Rajpoot, N., Singh, P., & Wakhle, S. (2015). Periodontal disease: A possible risk-factor for adverse pregnancy outcome. *Journal of International Oral Health, 7*(7), 137–142.

Hajishengallis, G., Chavakis, T., & Lambris, J. D. (2020). Current understanding of periodontal disease pathogenesis and targets for host-modulation therapy. *Periodontology 2000,*

84(1), 14–34.

Armitage, G. C. (2004). Periodontal diagnoses and classification of periodontal diseases. *Periodontology 2000, 34*, 9–21.

Yamazaki, K. (2023). Oral-gut axis as a novel biological mechanism linking periodontal disease and systemic diseases: A review. *Japanese Dental Science Review, 59*, 273–280.

Arigbede, A. O., Babatope, B. O., & Bamidele, M. K. (2012). Periodontitis and systemic diseases: A literature review. *Journal of Indian Society of Periodontology, 16*(4), 487–491.

Țica, O., Romanul, I., Ciavoi, G., Pantea, V. A., Scrobota, I., Șipoș, L., Daina, C. M., & Țica, O. (2025). A clinical review of the connections between diabetes mellitus, periodontal disease, and cardiovascular pathologies. *Biomedicines, 13*(9), 2309.

Saini, R., Saini, S., & Sharma, S. (2010). Periodontitis: A risk factor to respiratory diseases. *Lung India, 27*(3), 189.

Inchingolo, F., Inchingolo, A. M., Avantario, P., Settanni, V., Fatone, M. C., Piras, F., et al. (2023). The effects of periodontal treatment on rheumatoid arthritis and of anti-rheumatic drugs on periodontitis: A systematic review. *International Journal of Molecular Sciences, 24*(24), 17228.

Baciu, S. F., Mesaroș, A. Ș., & Kacso, I. M. (2023). Chronic kidney disease and periodontitis interplay: A narrative review. *International Journal of Environmental Research and Public Health, 20*(2), 1298.

Wu, Z., Zhang, Y., Wang, L., Yi, Y., Dai, B., Chen, H., & Yang, F. (2026). Periodontitis and systemic diseases: Insights into the correlation, mechanisms, and clinical implications. *Frontiers in Immunology, 17*, 1777955.

Najafimakhsoos, N., Pashollari, E., Malavolta, N., Zangari, F., & Cesari, C. (2026). Periodontitis and rheumatoid arthritis: Shared pathophysiology, bidirectional association, and therapeutic implications—A narrative review. *Healthcare, 14*(10), 1411.

Abdulkareem, A. A., Al-Taweel, F. B., Al-Sharqi, A. J. B., Gul, S. S., Sha, A., & Chapple, I. L. C. (2023). Current concepts in the pathogenesis of periodontitis: From symbiosis to dysbiosis. *Journal of Oral Microbiology, 15*, 2197779.

Foroughi, M., Torabinejad, M., Angelov, N., Ojcius, D. M., Parang, K., Ravnan, M., & Lam, J. (2025). Bridging oral and systemic health: Exploring pathogenesis, biomarkers, and diagnostic innovations in periodontal disease. *Infection, 53*, 2277–2302. https://doi.org/10.1007/s15010-025-02568-y

Huang, D., Wang, Y. Y., Li, B. H., Wu, L., Xie, W. Z., Zhou, X., & Ma, B. (2024). Association between periodontal disease and systemic diseases: A cross-sectional analysis of current evidence. *Military Medical Research, 11*(1), 74.

Varoni, E. M., & Rimondini, L. (2022). Oral microbiome, oral health and systemic health: A multidirectional link. *Biomedicines, 10*(1), 186.

Foroughi, M., Torabinejad, M., Angelov, N., Ojcius, D. M., Parang, K., Ravnan, M., & Lam, J. (2025). Bridging oral and systemic health: Exploring pathogenesis, biomarkers, and diagnostic innovations in periodontal disease. *Infection, 53*(6), 2277–2302. https://doi.org/10.1007/s15010-025-02568-y

How to Cite this Article: Gupta S., Gawali S.J., Gupta A., Bhatt S., Sagar S., Nagpal B.. (2026). Periodontitis and Systemic Diseases: Exploring the Bidirectional Link and Its Clinical Implications. *AJM*, ***9***(2), 97-102. https://doi.org/10.48165/ajm.2026.9.02.18