PBPC
ISSN 2674-9432
Qualis A3 CAPES 2021-2024
DOI - Crossref
Latindex
Indexado no Google Acadêmico

ORAL MICROBIOME AND THE PERIODONTITIS-CARDIOVASCULAR DISEASE AXIS: INFLAMMATORY, MICROBIAL, AND METABOLIC MECHANISMS

Jennifer Vera Santos Gumert[1], Aléxia Caroline Leandro da Conceição[2], José Augusto Pinheiro Sperandio[3], Christian Cesar Soares[4], Samara de Oliveira Ribeiro[5], Gabriela Azevedo Moraes de Brito[6], Ediliana Dias Chaves Campos de Amaral[7], Ana Caroline Justo Bellafronte Rique[8]

https://doi.org/10.36557/2674-9432.2026v5n2p267-277
Artigo recebido em 3 de Fevereiro e publicado em 3 de Abril de 2026

NARRATIVE REVIEW

ABSTRACT

Periodontitis is a chronic multifactorial inflammatory disease associated with oral biofilm dysbiosis and progressive destruction of tooth-supporting tissues. Increasing evidence suggests that its impact extends beyond the oral cavity and may contribute to systemic diseases, particularly cardiovascular diseases (CVD). In recent years, the oral microbiome has emerged as a biologically plausible mediator linking periodontal inflammation to atherosclerosis, endothelial dysfunction, systemic inflammation, and cardiometabolic disturbances. This study aimed to review recent literature on the oral microbiome–periodontitis–cardiovascular disease axis, focusing on inflammatory, microbial, and metabolic mechanisms. A narrative literature review was conducted using PubMed-indexed studies published between 2021 and 2026. The evidence indicates that oral dysbiosis and periodontitis may contribute to transient bacteremia, systemic cytokine release, endothelial activation, immune dysregulation, and microbial metabolite production with potential pro-atherogenic effects. Key pathogens such as *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, and *Tannerella forsythia* have been associated with vascular inflammation, oxidative stress, platelet activation, and lipid dysregulation. Furthermore, recent studies suggest that oral microbiome signatures may serve as non-invasive biomarkers for cardiovascular risk prediction. It is concluded that the oral microbiome–cardiovascular axis represents an emerging and clinically relevant field in contemporary periodontology, with promising translational implications for prevention, diagnosis, and integrated care.

Keywords: Periodontitis. Oral microbiome. Cardiovascular disease. Atherosclerosis. Systemic inflammation.

Instituição afiliada – [1] Centro Universitário UniDomBosco, Curitiba, Paraná, Brasil.
[2] Faculdade de Odontologia, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, Rio de Janeiro, Brasil.
[3] Clínica Integrada, Universidade Estadual de Londrina (UEL), Londrina, Paraná, Brasil.
[4] Cirurgião-dentista, Governador Valadares, Minas Gerais, Brasil.
[5] Faculdades Unidas do Norte de Minas (FUNORTE), Governador Valadares, Minas Gerais, Brasil.
[6] Centro Multidisciplinar de Odontologia Intensiva (CEMOI), Brasília, Distrito Federal, Brasil.
[7] Pontifícia Universidade Católica do Paraná (PUC-PR), Curitiba, Paraná, Brasil.
[8] Universidade do Grande Rio (UNIGRANRIO), Duque de Caxias, Rio de Janeiro, Brasil.

Autorcorrespondente*:* Jennifer Vera Santos Gumert **E-mail :** Jennifergumert@yahoo.com

1 INTRODUCTION

Periodontitis is a chronic inflammatory disease triggered by a dysbiotic microbial biofilm and characterized by progressive destruction of the periodontal ligament, alveolar bone, and connective tissue attachment. Once considered a localized oral condition, periodontitis is now increasingly recognized as a systemic inflammatory burden with potential effects on multiple organ systems, including the cardiovascular system (RAHIMI; AFSHARI, 2021; TONELLI; LUMNGWENA; NTUSI, 2023).

Cardiovascular diseases remain the leading cause of morbidity and mortality worldwide and include atherosclerotic cardiovascular disease, coronary artery disease, stroke, and heart failure. Among the proposed nontraditional contributors to cardiovascular risk, oral health has gained considerable attention, especially in the context of chronic periodontal inflammation and microbial dysbiosis (KIM et al., 2024; CARRA et al., 2023).

The oral microbiome, composed of highly structured bacterial, fungal, and viral communities, plays a fundamental role in maintaining oral and systemic homeostasis. However, ecological disruption of this microbiome may favor the emergence of pathogenic communities capable of promoting both local tissue destruction and systemic inflammatory consequences. This has led to growing interest in the "oral–cardiovascular axis," a conceptual framework describing how oral microbial dysbiosis may contribute to vascular disease through inflammatory, microbial, and metabolic pathways (WANG et al., 2024; TONELLI; LUMNGWENA; NTUSI, 2023).

Recent literature has moved beyond merely asking whether periodontitis is associated with cardiovascular disease and now increasingly focuses on the underlying mechanisms that may explain this relationship. These include bacteremia and endotoxemia, endothelial dysfunction, immuno-inflammatory activation, oxidative stress, and microbiome-derived metabolites involved in vascular pathology and atherogenesis (LU et al., 2024; QIN; ZHANG; WANG, 2026).

Therefore, this review aimed to synthesize recent evidence on the oral microbiome and the periodontitis–cardiovascular disease axis, with emphasis on inflammatory, microbial, and metabolic mechanisms.

2 METHODOLOGY

This study consists of a **narrative literature review** conducted using the **PubMed** database. Articles published between **2021 and 2026** were considered. The search strategy included combinations of the following terms: *oral microbiome*, *oral microbiota*, *periodontitis*, *cardiovascular disease*, *atherosclerosis*, *endothelial dysfunction*, *microbial metabolites*, and *systemic inflammation*.

Eligible studies included:

- narrative reviews,
- systematic reviews,

- meta-analyses,
- observational studies,
- and mechanistic articles directly related to the association between oral microbiome dysbiosis, periodontal disease, and cardiovascular outcomes.

Studies unrelated to cardiovascular mechanisms or not directly addressing oral microbiome-related pathways were excluded. The selected studies were analyzed qualitatively and grouped into the following thematic categories:

1. oral microbiome dysbiosis and periodontal disease;
2. inflammatory pathways;
3. microbial translocation and vascular effects;
4. microbial metabolites and immunometabolism;
5. clinical and translational implications.

3 RESULTS AND DISCUSSION

3.1 Oral microbiome homeostasis and periodontal dysbiosis

The oral cavity harbors one of the most diverse microbial ecosystems in the human body. Under healthy conditions, the oral microbiome exists in a balanced symbiotic state, contributing to local defense, epithelial integrity, and immune regulation. However, ecological disruption of this environment can lead to microbial dysbiosis, characterized by increased abundance of pathogenic anaerobic species and a pro-inflammatory host response (SEDGHI et al., 2021; RAJASEKARAN et al., 2024).

In periodontitis, dysbiosis is not merely defined by the presence of isolated pathogens but by a shift in the ecological structure and functional activity of the microbial community. Keystone pathogens such as *Porphyromonas gingivalis*, *Tannerella forsythia*, *Treponema denticola*, and *Fusobacterium nucleatum* play central roles in modulating host immunity, disrupting tissue homeostasis, and sustaining chronic periodontal inflammation.

This ecological perspective has changed the way periodontal disease is understood: rather than a simple infection caused by specific bacteria, periodontitis is now viewed as a complex host–microbiome inflammatory disorder with systemic implications.

3.2 Inflammatory pathways linking periodontitis to cardiovascular disease

One of the most biologically plausible links between periodontitis and cardiovascular disease is chronic low-grade systemic inflammation. Periodontal tissues affected by dysbiosis release large amounts of inflammatory mediators, including **C-reactive protein (CRP)**, **interleukin-6 (IL-6)**, **tumor necrosis factor-alpha (TNF-α)**, and

interleukin-1 beta (IL-1β), which may spill over into the systemic circulation and contribute to vascular injury (KIM et al., 2024; WANG et al., 2024).

These inflammatory mediators are known to promote endothelial activation, increase expression of vascular adhesion molecules, enhance monocyte recruitment, and stimulate the formation of foam cells within arterial walls. This cascade contributes to atherosclerotic plaque development and instability. In addition, persistent periodontal inflammation has been associated with oxidative stress and reduced nitric oxide bioavailability, both of which impair endothelial function and favor arterial stiffness and thrombogenicity.

The inflammatory burden associated with periodontitis may be especially relevant in individuals with preexisting cardiometabolic risk factors such as obesity, insulin resistance, metabolic syndrome, and hypertension. In such cases, periodontal inflammation may act as an additive or amplifying factor in the progression of vascular disease (LU et al., 2024).

3.3 Microbial pathways: bacteremia, endotoxemia, and vascular colonization

In addition to inflammation, the oral microbiome may influence cardiovascular health through direct microbial mechanisms. In patients with active periodontal disease, routine activities such as tooth brushing, chewing, or dental procedures can induce episodes of **transient bacteremia**, allowing oral microorganisms and their virulence factors to enter the bloodstream (TONELLI; LUMNGWENA; NTUSI, 2023).

Among periodontal pathogens, *Porphyromonas gingivalis* has received particular attention due to its ability to invade epithelial cells, endothelial cells, macrophages, and vascular tissues. Its virulence factors—especially **gingipains**, lipopolysaccharides, fimbriae, and outer membrane vesicles—can alter endothelial permeability, trigger pro-inflammatory signaling, and modulate immune evasion. These properties make *P. gingivalis* a biologically plausible contributor to vascular inflammation and atherogenesis.

Moreover, DNA and microbial remnants from oral pathogens have been identified in atherosclerotic plaques in previous studies, supporting the possibility that oral microorganisms may participate directly in vascular lesions. Although such findings do not establish causality on their own, they reinforce the mechanistic plausibility of a direct oral–vascular microbial connection.

Recent research has also begun to investigate whether oral microbial profiles may function as **non-invasive biomarkers** of cardiovascular disease risk. In 2026, microbiome-based predictive models suggested that oral microbial signatures may help identify individuals at higher risk for atherosclerotic cardiovascular disease (QIN; ZHANG; WANG, 2026).

3.4 Metabolic pathways and microbial-derived cardiovascular effects

One of the most current and promising areas of investigation involves the role of **microbial metabolites** produced by the oral microbiome. Oral microbial communities are metabolically active and capable of generating biologically relevant compounds that influence host immunity, vascular biology, and systemic metabolism (WANG et al., 2024).

Potential mechanisms include:

- alterations in the **nitrate–nitrite–nitric oxide pathway**, which is relevant for blood pressure regulation;
- production of inflammatory lipids and endotoxins;
- interactions with amino acid metabolism;
- and cross-talk with the **oral–gut axis**, which may further amplify systemic inflammation and metabolic dysfunction.

The oral microbiome may therefore contribute to cardiovascular disease not only through local inflammation or direct microbial dissemination, but also through **metabolic signaling**. This is especially important in the emerging field of **immunometabolism**, which explores how microbial and inflammatory pathways influence host metabolic regulation, immune cell phenotypes, and chronic vascular inflammation.

This metabolic perspective broadens the understanding of how periodontal disease may affect cardiovascular health and highlights the oral microbiome as an active participant in systemic disease biology rather than a passive bystander.

3.5 Clinical implications and cardiovascular biomarkers

Clinically, several recent studies have shown that periodontitis is associated with elevated levels of cardiovascular risk biomarkers, including **high-sensitivity CRP**, **IL-6**, **TNF-α**, **fibrinogen**, endothelial dysfunction markers, and oxidative stress indicators. These findings support the concept that periodontal inflammation contributes to a pro-atherogenic systemic environment.

Furthermore, evidence suggests that periodontal therapy—especially **non-surgical periodontal treatment**—may reduce certain inflammatory biomarkers and improve systemic inflammatory status, although the degree and consistency of these effects vary across studies. While current evidence does not yet conclusively demonstrate that periodontal treatment alone prevents hard cardiovascular outcomes such as myocardial infarction or stroke, the available data strongly support its relevance as part of an integrated preventive health strategy.

This reinforces the importance of a multidisciplinary approach involving dentistry, cardiology, preventive medicine, and systemic risk management.

3.6 Future directions: oral microbiome as biomarker and therapeutic target

The oral microbiome is increasingly being explored as a **diagnostic, prognostic, and therapeutic target** in cardiovascular medicine. Advances in **metagenomics**, **metabolomics**, **multi-omics**, and **machine learning** are enabling the identification of oral microbial signatures associated with atherosclerosis, vascular inflammation, and cardiometabolic dysregulation (QIN; ZHANG; WANG, 2026).

Future directions include:

- salivary and oral microbiome-based cardiovascular risk screening,
- targeted microbial modulation,
- precision periodontal medicine,
- probiotic and prebiotic oral interventions,
- and therapeutic approaches aimed at restoring microbial homeostasis.

However, despite this promise, important challenges remain. These include lack of methodological standardization, variability in sampling techniques, interindividual microbiome diversity, and the need for more longitudinal and interventional human studies.

Even so, the oral microbiome–cardiovascular axis represents one of the most innovative and translational frontiers in contemporary periodontology.

Table 1. Main recent studies on the oral microbiome, periodontitis, and cardiovascular disease

Authors / Year	Study Type	Main Focus	Main Contribution
Rahimi; Afshari (2021)	Literature review	Periodontitis and cardiovascular disease	Summarized inflammatory and epidemiological links
Sedghi et al. (2021)	Review	Oral microbiome ecology	Explained oral microbial networks and dysbiosis
Tonelli; Lumngwena; Ntusi (2023)	Narrative review	Oral microbiome in cardiovascular disease	Detailed oral–cardiovascular mechanisms
Carra et al. (2023)	Critical appraisal	Periodontitis and atherosclerotic cardiovascular disease	Evaluated evidence quality and causal plausibility
Kim et al. (2024)	Review	Periodontitis and ASCVD	Mechanistic discussion of endothelial and inflammatory pathways
Lu et al. (2024)	Systematic review and meta-analysis	Periodontitis and metabolic syndrome-related ASCVD	Reinforced cardiometabolic relevance
Rajasekaran et al. (2024)	Review	Oral microbiome and systemic health	Broad systemic implications of oral

			dysbiosis
Wang et al. (2024)	Review	Microbial metabolites and immuno-inflammatory mechanisms	Highlighted metabolic pathways and immunometabolism
Kumar; Dhanasekaran; Venugopal (2025)	Narrative review	Periodontitis-driven atherosclerosis	Detailed cellular and molecular pathways
Mendoza et al. (2025)	Review	Inflammatory mechanisms	Connected periodontal inflammation and cardiorespiratory fitness
Ogawa et al. (2025)	Scoping review	Oral health and cardiovascular disease	Reviewed clinical assessment and prognostic aspects
Pizziolo et al. (2025)	Systematic review	Oral microbiota and tooth loss	Related oral microbial burden to cardiovascular risk
Su; Ni; Lin (2025)	Review	Oral–gut microbiota axis	Introduced oral–gut–cardiovascular metabolic mechanisms
Sui; Yu; Cui (2026)	Predictive model study	Oral microbiome and ASCVD prediction	Proposed microbiome-based cardiovascular prediction
Qin; Zhang; Wang (2026)	Mendelian randomization	Oral microbiota and cardiovascular disease	Explored causal inference using genetic epidemiology

Table 2. Proposed mechanisms linking periodontitis and cardiovascular disease

Mechanism	Biological Description	Cardiovascular Relevance
Inflammatory spillover	Periodontal inflammation increases CRP, IL-6, TNF-α, IL-1β	Endothelial dysfunction, plaque instability
Transient bacteremia	Oral pathogens enter bloodstream during daily activities or dental manipulation	Vascular inflammation and immune activation
Endotoxemia	Lipopolysaccharides and bacterial products circulate systemically	Atherosclerotic signaling and inflammatory burden
Endothelial invasion	Some pathogens can invade endothelial and immune cells	Vascular injury and plaque progression
Oxidative stress	Chronic inflammation enhances ROS generation	Endothelial dysfunction and vascular stiffness
Microbial metabolites	Oral microbiota produce bioactive metabolites affecting host pathways	Cardiometabolic dysregulation and blood pressure effects
Oral–gut axis	Oral pathogens may alter gut	Systemic inflammation

	microbial ecology and barrier integrity	and metabolic disruption
Immunometabolic dysregulation	Microbial products alter immune and metabolic signaling	Pro-atherogenic systemic environment

3 CONCLUSION

Recent literature supports the concept that the relationship between periodontitis and cardiovascular disease extends beyond epidemiological association and involves biologically plausible **inflammatory, microbial, and metabolic pathways**.

Oral microbiome dysbiosis appears to contribute to systemic inflammation, endothelial dysfunction, microbial dissemination, and production of metabolites capable of influencing vascular health and atherosclerotic progression. Among the most relevant pathogens, *Porphyromonas gingivalis* remains a key model organism in mechanistic studies, although current evidence suggests that the broader dysbiotic microbial network is likely more relevant than any single species alone.

The oral microbiome–periodontitis–cardiovascular axis therefore represents a clinically significant and scientifically promising area with implications for prevention, diagnosis, and interdisciplinary patient care. Further robust clinical and translational studies are still needed to clarify causality and to support future microbiome-based therapeutic strategies.

4 REFERENCES

CARRA, Maria Clotilde et al. **Periodontitis and atherosclerotic cardiovascular disease: a critical appraisal**. *Periodontology 2000*, [S. l.], 2023. DOI: 10.1111/prd.12528. PMID: 37997210.

GUPTA, Vandana et al. **Cardiovascular biomarkers in periodontitis: a systematic review and meta-analysis**. *Oral Diseases*, [S. l.], 2025. DOI: 10.1111/odi.70084. PMID: 40887818.

KIM, June Yeon et al. **Periodontitis and atherosclerotic cardiovascular disease**. *Molecules and Cells*, [S. l.], v. 47, n. 12, p. 100146, 2024. DOI: 10.1016/j.mocell.2024.100146. PMID: 39515611.

KUMAR, Rithwik; DHANASEKARAN, Anuradha; VENUGOPAL, Priyanka. **A narrative review on bridging the gap between periodontitis and cardiovascular disease: exploring the cellular and molecular mechanisms of periodontitis-driven atherosclerosis**. *Molecular Biology Reports*, [S. l.], v. 52, n. 1, p. 690, 2025. DOI: 10.1007/s11033-025-10806-7.

LU, Lijie et al. **The role of periodontitis in the development of atherosclerotic cardiovascular disease in participants with the components of metabolic syndrome: a**

systematic review and meta-analysis. *Clinical Oral Investigations*, [S. l.], v. 28, n. 6, p. 339, 2024. DOI: 10.1007/s00784-024-05731-1. PMID: 38801482.

MENDOZA, Michael F. et al. **More than just a toothache: inflammatory mechanisms linking periodontal disease to cardiovascular disease and the protective impact of cardiorespiratory fitness**. *Biomedicines*, [S. l.], v. 13, n. 7, p. 1512, 2025. DOI: 10.3390/biomedicines13071512.

OGAWA, Masato et al. **Oral health and cardiovascular disease: a scoping review of assessment methods, risk factors, and prognosis**. *Circulation Reports*, [S. l.], v. 7, n. 4, p. 223-230, 2025. DOI: 10.1253/circrep.CR-24-0187.

PIZZIOLO, Pillar Gonçalves et al. **The role of oral microbiota and tooth loss in cardiovascular disease risk: a systematic review**. *Biofouling*, [S. l.], v. 41, n. 7, p. 649-663, 2025. DOI: 10.1080/08927014.2025.2518280.

QIN, Si-Da; ZHANG, Yi-Wen; WANG, Jing-Zhi. **Evaluating the association between oral microbiota and cardiovascular diseases: evidence from Mendelian randomization analysis**. *Journal of Geriatric Cardiology*, [S. l.], v. 23, n. 1, p. 36-44, 2026. DOI: 10.26599/1671-5411.2026.01.001. PMID: 41777408.

RAHIMI, Alireza; AFSHARI, Zohreh. **Periodontitis and cardiovascular disease: a literature review**. *ARYA Atherosclerosis*, [S. l.], v. 17, n. 5, p. 1-8, 2021. DOI: 10.22122/arya.v17i0.2362.

RAJASEKARAN, John J. et al. **Oral microbiome: a review of its impact on oral and systemic health**. *Microorganisms*, [S. l.], v. 12, n. 9, p. 1797, 2024. DOI: 10.3390/microorganisms12091797.

SEDGHI, Lea et al. **The oral microbiome: role of key organisms and complex networks in oral health and disease**. *Periodontology 2000*, [S. l.], v. 87, n. 1, p. 107-131, 2021. DOI: 10.1111/prd.12393.

SUI, Qiuli; YU, Jie; CUI, Shuping. **An oral microbiome model for predicting atherosclerotic cardiovascular disease**. *Frontiers in Cellular and Infection Microbiology*, [S. l.], v. 15, p. 1707599, 2026. DOI: 10.3389/fcimb.2025.1707599.

SU, Shuling; NI, Xiaobin; LIN, Yongluan. **The oral-gut microbiota axis in cardiovascular diseases: mechanisms, therapeutic targets, and translational challenges**. *Frontiers in Cellular and Infection Microbiology*, [S. l.], v. 15, p. 1658502, 2025. DOI: 10.3389/fcimb.2025.1658502.

TONELLI, Andrea; LUMNGWENA, Evelyn N.; NTUSI, Ntobeko A. B. **The oral microbiome in the pathophysiology of cardiovascular disease**. *Nature Reviews Cardiology*, [S. l.], v. 20, p. 386-403, 2023. DOI: 10.1038/s41569-022-00825-3.

WANG, Zheng et al. **The oral microbiota, microbial metabolites, and immuno-inflammatory mechanisms in cardiovascular disease**. *International Journal of*

Molecular Sciences, [S. l.], v. 25, n. 22, p. 12337, 2024. DOI: 10.3390/ijms252212337. PMID: 39596404.