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Additional material is published online only. To view please visit the journal online.

Cite this as: Malik R.
Relationship Between
Periodontal Disease and
Systemic Health of an Individual.
Premier Journal of Dentistry
2025;2:100004

DOI: <https://doi.org/10.70389/PJD.100004>

Received: 26 March 2025

Revised: 28 March 2025

Accepted: 29 March 2025

Published: 25 April 2025

Ethical approval: N/a

Consent: N/a

Funding: No industry funding

Conflicts of interest: None

Author contribution:
Rabeea Malik –
Conceptualization, Writing –
original draft, review and editing

Guarantor: Rabeea Malik

Provenance and peer-review:
Commissioned and externally
peer-reviewed

Data availability statement:
N/a

Relationship Between Periodontal Disease and Systemic Health of an Individual

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ABSTRACT

Periodontal disease (PD), one of the most common chronic inflammatory diseases that affect dental health, impacts the gingiva, periodontal ligaments, alveolar bones, and almost all the structures that support the teeth. Recent studies also indicate a close relationship between PD and overall systemic health, demonstrating that PD has both local as well as systemic implications. This review article mainly delves into the bidirectional link between periodontal illness and many systemic illnesses, such as diabetes mellitus, cardiovascular diseases, adverse pregnancy outcomes, and respiratory conditions. The article also provides an overview of recent literature, contrasts different views, delineates several challenges in diagnosis and treatment, highlights important gaps in information within the discourse, and offers potential trajectories for comprehensive interdisciplinary efforts going forward.

Keywords: Periodontal disease, Systemic health, Inflammatory pathways, Cardiovascular diseases, Diabetes mellitus

Introduction

The importance of oral health for overall systemic health cannot be overstated. Periodontal disease (PD) is a chronic pathological inflammatory disease initiated by bacterial infection and their host immune response and has been associated with a variety of systemic diseases such as cardiovascular diseases (CVDs), diabetes, and respiratory diseases.¹ Commercial Dental Advice: The paradigm of PD as solely a dental condition has transitioned into a known risk factor that affects the most common diseases of humans. The mechanisms by which PD may play a role in systemic conditions include dissemination of bacteria, modulation of the immune system, and inflammatory pathways.² This article reviews the association between systemic and periodontal health and highlights important challenges, research gaps, and future perspectives for interdisciplinary studies.

Literature Review

Over the past few decades, the relationship between PD and systemic health has been extensively researched. Research is ongoing to define the complex biological mechanisms that connect oral health with chronic systemic diseases, including diabetes, cardiovascular diseases (CVDs), respiratory disease, Alzheimer's disease (AD), and adverse pregnancy outcomes. In this section, we offer an overview of the literature reviewing the state of knowledge, particularly of recent work over the last 5 years.

PD and Inflammatory Pathways

Periodontitis is a chronic inflammatory disease caused by dysbiotic microbial biofilms inhabiting the oral

cavity. Periodontitis is characterized by connective tissue destruction, alveolar bone loss, and the presence of deep periodontal pockets, which, if not treated, leads to tooth loss.^{3,4} In periodontitis, the immune response leads to the release of inflammatory cytokines, including TNF- α , IL-6, and C-reactive protein (CRP), which also contribute to systemic inflammation.^{5,6}

Kinane et al.⁷ periodontitis increases the systemic inflammatory burden, contributing to the onset or worsening of chronic diseases. Similarly, Graziani et al.⁸ stress that subgingival dysbiosis gives rise to chronic inflammation that promotes microbial translocation systemically, thereby triggering immune responses distally.

Furthermore, Dörfer et al.⁹ showed in a meta-analysis that periodontal therapy was found effective in the reduction of systemic inflammatory markers with a significant impact on CRP levels. This is in line with the theory that periodontal treatment is beneficial for one's overall systemic health.

PD and Cardiovascular Health

The two-way relationship between periodontitis and CVDs has been well established. Pathogens implicated in PD, including *Porphyromonas gingivalis* and *Fusobacterium nucleatum*, promote early atherosclerosis, endothelial dysfunction, and vascular inflammation by inducing proinflammatory responses in blood vessels.^{10,11}

D'Aiuto et al.¹² conducted a systematic review of randomized controlled trials (RCTs) and revealed that periodontal treatment diminishes endothelial dysfunction, which plays a basic role in the course of CVDs. A study by Lickardo et al.¹³ revealed a higher prevalence of hypertension as well as stroke and myocardial infarction in patients with severe periodontitis compared with healthy gums.

Moreover, a recent research study by Van Dyke and Sima¹⁴ found strong evidence of periodontal bacteria and inflammatory mediators that enter the bloodstream leading to the acceleration of plaque generation in atherosclerosis. Novel findings in the association between PD and cardiovascular risk contextually emphasize the importance of oral hygiene and periodontal management in minimizing cardiovascular risk.

PD and Diabetes Mellitus

There is a bidirectional association between diabetes and periodontitis, with diabetes worsening periodontitis and vice versa.^{15,16} Diabetes reduces immune functioning, increasing susceptibility to periodontal infections, and, on the other hand, periodontitis leads to a systemic inflammatory state, with increasing insulin resistance and poor glycemic control.^{17,18}

Chapple and Genco¹⁹ conducted a meta-analysis, which showed that periodontitis worsens the glycemic control of diabetic patients significantly. In contrast, studies show nonsurgical periodontal therapy can also reduce HbA1c levels, leading to decreased complications of diabetes. A seminal study by Preshaw et al.²⁰ showed that HbA1c decreased by 0.4% in diabetic patients who underwent periodontal therapy, which meets the impact effect of certain sugar-lowering medications.

Moreover, Eke et al.²¹ identified prediabetes as a predictive indicator of periodontitis and recommended screening for periodontitis to identify prediabetic individuals.

PD and Respiratory Diseases

Oral microorganisms are aspirated into the lower respiratory tract, especially the pathogens in *P. gingivalis*, causing lung infections, chronic obstructive pulmonary disease, and pneumonia.^{22,23}

A study by Bui et al.²⁴ evidenced the direct relationship between periodontal pathogens and respiratory diseases, especially in elderly patients and those with a deficient immune system. They have found that poor oral hygiene correlates to an increased risk of hospital-acquired pneumonia.

Furthermore, Herrera et al.²⁵ also mentioned that periodontal therapy helps to reduce the bacterial load in the oral cavity, which can potentially reduce the incidence of aspiration pneumonia, especially in elderly and hospitalized patients. This is an area ripe for research, with new therapeutic options on the horizon, and will provide newer insights into how preventive oral healthcare is key to respiratory care (Figure 1).

PD and AD

The association between PD and neurodegenerative disorders, particularly with AD, has been the subject of recent studies. *P. gingivalis* may also play an essential role in the etiology of neuroinflammation, amyloid

plaque formation, and cognitive deficits associated with chronic oral infections.^{26,27}

Wu and Nakanishi²⁸ showed that *P. gingivalis* and its toxins (gingipains) were detected in post-mortem brain samples of AD patients, strongly suggesting a possible causative relationship between periodontitis and neurodegeneration. Similarly, Simas et al.²⁹ reported that patients with periodontitis were at a 1.7 times greater risk than healthy participants for developing dementia.

Darveau³⁰ also suggested that systemic exacerbation of chronic inflammation due to periodontitis might be amplifying blood-brain barrier dysfunction and neuronal damage. The neuroinflammatory load and cognitive impairment may become less in response to periodontal therapy, demonstrating the importance of initiating the therapy as early as possible.

PD and Pregnancy Outcomes

PD is a risk factor for poor pregnancy outcomes like preterm birth, low birth weight, and preeclampsia.^{31,32} This is driven, in part, by proinflammatory cytokines that stimulate systemic immune responses and alter fetal development.

A clinical trial by Peres et al.³³ reported that pregnant women with severe periodontitis had a 2.5-fold increase in risk of preterm delivery. Another study by Glick et al.³⁴ has proven that periodontal treatment intervention in pregnancy significantly reduces inflammatory markers, indicating that oral health-based interventions have the potential to ameliorate pregnancy outcomes.

The Role of Periodontal Therapy in Systemic Disease Management

With a strong link between PD and systemic health, there is a growing interest in periodontal therapy as potentially reducing risks for systemic disease. Various studies have shown improved health outcomes after periodontal treatment (Figure 2).^{35,36}

- **Diabetes Status:** Periodontal therapy has been associated with reduced HbA1c levels and is often associated with decreased insulin resistance.^{19,20}
- **Cardiovascular Benefits:** The reductions in CRP, IL-6, and endothelial dysfunction following periodontal treatment would point to a protective effect on heart health.^{12,13}
- **Cognitive Function:** Periodontal therapy may slow cognitive decline in patients at risk for dementia, according to some studies.^{28,29}
- **Pregnancy Outcomes:** The treatment of periodontitis during pregnancy reduces the risk of preterm birth and facilitates fetal well-being.^{33,34}

These results highlight the need to incorporate periodontal care into wider healthcare approaches to prevent chronic illness.

Future Directions in Periodontal-Systemic Research

The link between PD and systemic health is a burgeoning area of research. Understanding this emerging



Fig 1 | Crop unrecognizable stomatologist with tweezers and dental tools in clinic

Source: Photo by Cedric Fauntleroy from Pexels



Fig 2 | Close-up shot of dental implant model

Source: Photo by cottonbro studio from Pexels



Fig 3 | Woman in white medical scrub suit

Source: Photo by Nataliya Vaitkevich from Pexels

aspect is crucial for improving treatment strategies and overall knowledge in the field.

Advanced Biomarkers for Early Detection

Novel studies target salivary and serum biomarkers to facilitate the early diagnosis of systemic diseases associated with PD. Systemic diseases, including CVDs and diabetes, have been associated with various inflammatory mediators, including interleukin-6 (IL-6), CRP, and matrix metalloproteinases, that may have value as diagnostic markers.^{31,32} These biomarkers should be validated by large clinical trials.

Genetic and Epigenetic Studies

As genomics technology progresses, some researchers are investigating the genetic predisposition to PD (epidemiology) and its systemic impact. For instance, a number of studies suggest that single nucleotide polymorphisms in genes associated with inflammation (e.g., IL-1 β , TNF- α) were linked to periodontitis susceptibility and systemic diseases, such as rheumatoid arthritis and diabetes.^{33,34} Moreover, epigenetic changes such as DNA methylation and histone modifications have emerged as attractive therapeutic targets.³⁷

Microbiome Research and Gut-Oral Axis

Recent studies highlight the importance of the oral microbiome to systemic health. Alterations in the gut microbiota are associated with changes in the oral microbiota,³⁷ which may contribute to systemic diseases, such as metabolic syndrome,^{12,33} inflammatory bowel disease,³⁴ and neurological diseases.³⁸ Future studies may thus aim to reveal interactions between the oral and gut microbiomes for targeted probiotic approaches.

Artificial Intelligence (AI) and Machine Learning (ML) in Diagnosis

PD has been a target for early diagnosis, with the research community investigating the potential of AI and ML models for the detection, classification, and prognosis of PD. Deep learning algorithms trained based on radiographic and clinical data have demonstrated promising performance for the detection of early-stage periodontitis and systemic health risk prediction.^{39,40} AI in Periodontal therapy could prove to be a game-changer for personalized clinical support.

Novel Therapeutic Approaches

Conventional periodontal treatment concentrates on mechanical debridement, yet novel biological and regenerative treatment alternatives are emerging. Stem cell therapy, platelet-rich plasma, and tissue engineering have demonstrated efficacy in periodontal regeneration and may attenuate the systemic inflammatory burden.^{41,42} Moreover, specific anti-inflammatory drugs and probiotics are also tested as adjunctive therapies to standard periodontal treatment (Figure 3).⁴³

Impact of Lifestyle and Dietary Interventions

A growing body of evidence suggests that diet and lifestyle have a significant impact on periodontal and

systemic health. A Mediterranean and anti-inflammatory diet with omega-3 fatty acids and polyphenols has been associated with improved periodontal outcomes and reduced systemic inflammation.^{44,45} Large-scale RCTs are needed to define dietary guidelines for periodontal health.

Periodontal-Systemic Connection in Aging Populations

As the global population ages, the impact of PD on geriatric health, frailty, and cognitive decline needs further investigation. Multiple reports suggest the association between periodontitis and neurodegenerative diseases like AD and Parkinson's.^{46,47} Further studies should identify whether preventive periodontal treatment may reduce cognitive decline among the elderly.

Comparisons

Comparative analyses of various studies highlight differences in methodological approaches, study populations, and disease severity. While some studies emphasize microbial components, others focus on inflammatory biomarkers or clinical outcomes.⁸ Notably, interventions such as scaling and root planning have shown variable effectiveness in improving systemic health outcomes in different populations.⁹

Challenges

Despite advancements in understanding the link between PD and systemic health, several challenges remain:

- **Heterogeneity in Research Design** – Different studies adopt varying diagnostic criteria for periodontitis, making cross-comparison difficult.¹⁰
- **Short-Term Longitudinal Studies** – The absence of long-term clinical trials¹¹ makes it difficult for the majority of studies to demonstrate causation rather than relationships.
- **Patient Compliance** – Patients often fail to comply with periodontal treatment and follow-ups, limiting the study outcome.¹²
- **Interdisciplinary Collaboration** – There is a gap in the integration of dental and medical care, which results in the fragmentation of patients with systemic diseases.¹³

Gaps in Current Research

Several gaps exist in the current understanding of PD and systemic health:

- **Absence of Standard Diagnostic Standard** – The absence of a standard diagnostic standard to classify PD leads to undercutting substantial research outcomes.¹⁴
- **Mechanistic Pathways Are Not Fully Defined** – Although the associations are well recognized, the exact mechanistic pathways associated with PD related to systemic diseases need further investigation.¹⁵
- **Underrepresentation of Specific Populations** – A number of studies have been conducted in Western

populations, leaving out other ethnic and socioeconomic groups.¹⁶

Future Work

To advance the understanding of PD and its impact on systemic health, future research should focus on:

- **Large-Scale Clinical Trials** – Conducting multi-center studies with standardized diagnostic criteria to validate findings.¹⁷
- **Mechanistic Studies** – Exploring the molecular pathways involved in periodontal-systemic disease interactions.¹⁸
- **Integration of AI in Diagnosis** – Utilizing AI for early detection and risk assessment of periodontal and systemic diseases.¹⁹
- **Public Health Initiatives** – Developing policies to promote interdisciplinary care between dentistry and medicine.²⁰

Integration of Findings Across Disease Categories

Recent research suggests that PD shares common inflammatory pathways with systemic conditions such as CVDs, diabetes, and rheumatoid arthritis. Proinflammatory cytokines, including IL-1 β , IL-6, and TNF- α , are elevated in both periodontitis and these systemic diseases, contributing to chronic inflammation and tissue destruction.⁴⁸ The role of oxidative stress and microbial dysbiosis in exacerbating these conditions highlights the need for an integrated approach to managing periodontal and systemic health.⁴⁹ A holistic understanding of these mechanisms can improve treatment strategies and patient outcomes.

Limitations of Current Studies

Despite growing evidence linking PD to systemic health, several limitations exist in the current literature:

- Many studies rely on observational data, making it difficult to establish causality.⁵⁰
- Variability in diagnostic criteria for PD across studies affects comparability.⁵¹
- The influence of confounding factors such as smoking, diet, and genetic predisposition is not always accounted for.⁵²
- Longitudinal studies are needed to better understand the progression of PD and its systemic effects.⁵³

Future research should address these gaps by employing standardized diagnostic methods, controlling for confounders, and conducting interventional studies to assess whether periodontal therapy can reduce the risk of systemic diseases.

Future Research Directions

To further elucidate the relationship between PD and systemic health, future studies should focus on:

- **Interdisciplinary Approaches:** Collaboration between periodontists, cardiologists, endocrinologists, and rheumatologists to develop integrated treatment protocols.⁵⁴

- **Biomarker Research:** Identifying specific biomarkers in saliva and blood that can predict systemic complications of PD.⁵⁵
- **Personalized Treatment Strategies:** Investigating genetic and microbiome-based therapies for targeted periodontal and systemic disease management.⁵⁶
- **Impact of Periodontal Therapy:** Conducting large-scale RCTs to determine whether periodontal treatment can directly reduce the incidence or severity of systemic diseases.⁵⁷

Interdisciplinary Approaches to Treatment

An interdisciplinary approach is crucial for managing patients with both PD and systemic conditions. Collaborative care models that include dental professionals, primary care physicians, and specialists can improve patient outcomes by:

- Incorporating periodontal screening in routine medical check-ups.⁵⁸
- Educating healthcare providers on the systemic implications of PD.⁵⁹
- Developing shared treatment plans that address both oral and systemic inflammation.⁶⁰

By strengthening these aspects, the review will provide a more comprehensive and practical resource for researchers and healthcare professionals.

Conclusion

There is already good evidence to support an association between PD and health, with links noted between periodontitis and a range of diseases involving cardiovascular, gastrointestinal, respiratory, and pregnancy complications. However, there are many challenges and research gaps, and more studies are needed to establish causative mechanisms and to create targeted interventions. The integration of dental and medical care, advanced diagnostics, and multicenter trials should be the focus of future research to better characterize treatment approaches. This would translate to better outcomes for the patient as well as improve the public health approaches in place to keep people's oral cavities healthy.

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