Revista ARACÊ
ISSN: 2358-2472

THE SYSTEMIC IMPACT OF PERIODONTAL DISEASE: ASSOCIATIONS WITH DIABETES, ALZHEIMER'S, HYPERTENSION, KIDNEY DISEASE, AND GASTROINTESTINAL CONDITIONS

https://doi.org/10.56238/arev7n8-055

Date of submission: 07/14/2025 **Date of publication:** 08/14/2025

Pedro Guimarães Sampaio Trajano dos Santos[1], Rosana Maria Coelho Travassos[2], Luciana Oliveira Leal[3], Maria Regina Almeida de Menezes[4], Alexandre Batista Lopes do Nascimento[5], Verônica Maria de Sá Rodrigues[6], Josué Alves[7], Eliana Santos Lyra da Paz[8], Vanessa Lessa Cavalcanti de Araújo[9], Maria Tereza Moura de Oliveira Cavalcanti[10], Tereza Augusta Maciel[11], Luciano Barreto Silva[12]

ABSTRACT

Objective: This narrative literature review aims to explore the associations between periodontal disease and systemic conditions such as diabetes mellitus, Alzheimer's disease, hypertension, kidney disease, and gastrointestinal disorders.

Methodology: A comprehensive search was conducted across major databases including PubMed, Cochrane Library, EMBASE, and Google Scholar. Keywords used were "Periodontal Disease," "Diabetes," "Alzheimer's," "Hypertension," "Kidney Disease," and "Gastrointestinal Conditions," combined using Boolean operators "AND" and "OR." The selection process involved three stages: removal of duplicates using Zotero, screening of titles and abstracts, and full-text analysis. Only articles relevant to the review's objective were included.

Results: The reviewed studies revealed strong correlations between periodontal disease and systemic conditions. In diabetes, periodontal inflammation exacerbates glycemic control. In Alzheimer's disease, periodontal pathogens may contribute to neuroinflammation. Associations with hypertension, chronic kidney disease, and gastrointestinal conditions such

[1] Undergraduate in Dentistry, Faculdade de Odontologia do Recife. Recife, Pernambuco, Brazil.
E-mail: pedroguimaraessampaio@gmail.com
[2] PhD in Endodontics, Universidade de Pernambuco. Recife, Pernambuco, Brazil.
E-mail: rosana.travassos@upe.br
[3] Graduated in Dentistry, Faculdade Universidade de Passo Fundo-RS. E-mail: llucianalleal@gmail.com
[4] PhD, Universidade de Pernambuco. Recife, Pernambuco, Brazil. E-mail: regina.menezes@upe.br
[5] PhD in Dentistry, Universidade de Pernambuco. Recife, Pernambuco, Brazil.
E-mail: Alexandre.nascimento1@upe.br
[6] PhD in Dentistry, Universidade de Pernambuco. Recife, Pernambuco, Brazil.
E-mail: veronica.rodrigues@upe.br
[7] PhD, Universidade de Pernambuco. Recife, Pernambuco, Brazil. E-mail: Josue.alves@upe.br
[8] PhD in Biological Sciences, Universidade de Pernambuco. Recife, Pernambuco, Brazil.
E-mail: eliana.lyra@upe.br
[9] Professor at Universidade de Pernambuco. E-mail: vanessa.lessa@upe.br
[10] PhD in Dentistry, Universidade de Pernambuco. Recife, Pernambuco, Brazil. E-mail: tereza.moura@upe.br
[11] Master's Degree in Dentistry, Universidade de Pernambuco. Recife, Pernambuco, Brazil.
E-mail: tereza.maciel@upe.br
[12] PhD in Endodontics, Universidade de Pernambuco. Recife, Pernambuco, Brazil.
E-mail: lucianobarreto63@gmail.com

Revista ARACÊ
ISSN: 2358-2472

as inflammatory bowel disease were also identified, suggesting that periodontal inflammation may play a contributory role through systemic inflammatory pathways.

Conclusion: Periodontal disease extends beyond the oral cavity and may influence or be influenced by systemic health. Understanding these connections emphasizes the importance of oral health in the broader context of general health and supports integrated, interdisciplinary care.

Keywords: Periodontal Disease. Diabetes. Alzheimer's. Hypertension. Kidney Disease. Gastrointestinal Conditions.

O IMPACTO SISTÊMICO DA DOENÇA PERIODONTAL: ASSOCIAÇÕES COM DIABETES, ALZHEIMER, HIPERTENSÃO, DOENÇA RENAL E CONDIÇÕES GASTROINTESTINAIS

RESUMO

Objetivo: Esta revisão narrativa da literatura visa explorar as associações entre doença periodontal e condições sistêmicas, como diabetes mellitus, doença de Alzheimer, hipertensão, doença renal e distúrbios gastrointestinais.

Metodologia: Uma busca abrangente foi conduzida nas principais bases de dados, incluindo PubMed, Cochrane Library, EMBASE e Google Acadêmico. As palavras-chave utilizadas foram “Doença Periodontal”, “Diabetes”, “Alzheimer”, “Hipertensão”, “Doença Renal” e “Condições Gastrointestinais”, combinadas usando os operadores booleanos “AND” e “OR”. O processo de seleção envolveu três etapas: remoção de duplicatas usando Zotero, triagem de títulos e resumos e análise de texto completo. Apenas artigos relevantes ao objetivo da revisão foram incluídos.

Resultados: Os estudos revisados revelaram fortes correlações entre doença periodontal e condições sistêmicas. No diabetes, a inflamação periodontal exacerba o controle glicêmico. Na doença de Alzheimer, patógenos periodontais podem contribuir para a neuroinflamação. Associações com hipertensão, doença renal crônica e condições gastrointestinais, como doença inflamatória intestinal, também foram identificadas, sugerindo que a inflamação periodontal pode desempenhar um papel contributivo por meio de vias inflamatórias sistêmicas.

Conclusão: A doença periodontal se estende além da cavidade oral e pode influenciar ou ser influenciada pela saúde sistêmica. A compreensão dessas conexões enfatiza a importância da saúde bucal no contexto mais amplo da saúde geral e apoia o cuidado integrado e interdisciplinar.

Palavras-chave: Doença Periodontal. Diabetes. Alzheimer. Hipertensão. Doença Renal. Condições Gastrointestinais.

Revista ARACÊ
ISSN: 2358-2472

EL IMPACTO SISTÉMICO DE LA ENFERMEDAD PERIODONTAL: ASOCIACIONES CON DIABETES, ALZHEIMER, HIPERTENSIÓN, ENFERMEDAD RENAL Y AFECCIONES GASTROINTESTINALES

RESUMEN

Objetivo: Esta revisión narrativa de la literatura tiene como objetivo explorar las asociaciones entre la enfermedad periodontal y las condiciones sistémicas como la diabetes mellitus, la enfermedad de Alzheimer, la hipertensión, la enfermedad renal y los trastornos gastrointestinales.

Metodología: Se realizó una búsqueda exhaustiva en las principales bases de datos, incluyendo PubMed, Cochrane Library, EMBASE y Google Scholar. Las palabras clave utilizadas fueron "Periodontal Disease", "Diabetes", "Alzheimer", "Hypertension", "Kidney Disease" y "Gastrointestinal Conditions", combinadas mediante los operadores booleanos "AND" y "OR". El proceso de selección involucró tres etapas: eliminación de duplicados utilizando Zotero, revisión de títulos y resúmenes, y análisis de texto completo. Solo se incluyeron los artículos relevantes para el objetivo de la revisión.

Resultados: Los estudios revisados revelaron fuertes correlaciones entre la enfermedad periodontal y las condiciones sistémicas. En la diabetes, la inflamación periodontal exacerba el control glucémico. En la enfermedad de Alzheimer, los patógenos periodontales pueden contribuir a la neuroinflamación. También se identificaron asociaciones con hipertensión, enfermedad renal crónica y afecciones gastrointestinales como la enfermedad inflamatoria intestinal, lo que sugiere que la inflamación periodontal podría contribuir a través de vías inflamatorias sistémicas.

Conclusión: La enfermedad periodontal se extiende más allá de la cavidad oral y puede influir o verse influida por la salud sistémica. Comprender estas conexiones enfatiza la importancia de la salud bucal en el contexto más amplio de la salud general y apoya la atención integral e interdisciplinaria.

Palabras clave: Enfermedad Periodontal. Diabetes. Alzheimer. Hipertensión. Enfermedad Renal. Afecciones Gastrointestinales.

Revista ARACÊ
ISSN: 2358-2472

1 INTRODUCTION

Periodontal disease, a chronic and multifactorial inflammatory condition affecting the supporting tissues of the teeth, has historically been confined to the domain of dental pathology. However, the past few decades have witnessed a paradigm shift in its conceptualization, increasingly framing periodontal disease as a potential contributor to systemic morbidity (Preshaw et al., 2012; Li et al., 2000). This reconceptualization stems from the recognition of the oral cavity as a critical interface between environmental exposures, host immunity, and microbial ecosystems (Hajishengallis, 2015).

The biological plausibility of systemic involvement is supported by robust mechanistic pathways. Periodontal inflammation fosters a persistent state of low-grade systemic inflammation, characterized by elevated circulating cytokines, bacteremia, and oxidative stress, which may influence or exacerbate pre-existing systemic conditions (Chapple & Genco, 2013; Tonetti et al., 2013). Furthermore, the microbial dysbiosis characteristic of periodontal pockets, especially the proliferation of keystone pathogens such as Porphyromonas gingivalis, has been implicated in distant tissue dysfunction through mechanisms including endotoxemia, immune priming, and molecular mimicry (Hajishengallis et al., 2012; How et al., 2016).

This narrative review seeks to synthesize and critically evaluate existing literature exploring the associations between periodontal disease and five major systemic conditions: diabetes mellitus, Alzheimer's disease, hypertension, chronic kidney disease, and gastrointestinal disorders. These associations are examined not only through epidemiological patterns but also via pathophysiological mechanisms that suggest bidirectional relationships and potential causal links. By highlighting these interactions, we aim to underscore the clinical and public health relevance of periodontal health within the broader context of systemic disease management.

2 METHODOLOGY

This review is a narrative literature review; therefore, it is necessary to search online databases to obtain the maximum number of relevant articles related to the current topic. Thus, online searches were conducted in the following databases: PubMed, Cochrane Library, EMBASE, and Google Academy. Furthermore, to obtain only results related to the topic addressed in this article, the following descriptors were used: Periodontal Disease, Diabetes, Alzheimer's, Hypertension, Kidney Disease, and Gastrointestinal Conditions.

Revista ARACÊ
ISSN: 2358-2472

Boolean terms such as "AND" and "OR" were also used in the PubMed searches. The results obtained from online searches underwent a three-phase screening process: the first phase involved exporting the results to Zotero, where duplicate articles were removed. The second phase consisted of reading the abstracts and titles of the articles, eliminating those that did not fit the review. The third phase involved reading the article in its entirety, eliminating those that were not relevant to the present study and retaining those that were useful. Rother's (2007) study was used to guide the development of this study, as it addresses the differences between a systematic review and a narrative review, highlighting their approaches, characteristics, structures, and composition.

3 RESULTS

The scientific literature consistently supports a multifaceted association between periodontal disease and systemic conditions, grounded in shared immunoinflammatory mechanisms, microbial translocation, and systemic dissemination of pro-inflammatory mediators. Below, we detail the specific pathophysiological and epidemiological links established between periodontitis and five major systemic diseases.

3.1 DIABETES MELLITUS

The bidirectional relationship between diabetes and periodontitis is one of the most extensively characterized in the field of periodontal-systemic research. Chronic periodontal inflammation exacerbates insulin resistance via elevated levels of pro-inflammatory cytokines such as IL-6 and TNF-α, as well as through systemic endotoxemia. Hyperglycemia, in turn, promotes periodontal tissue breakdown via impaired neutrophil function, collagen crosslinking by advanced glycation end-products (AGEs), and microvascular dysfunction.

Numerous interventional studies and meta-analyses have shown that nonsurgical periodontal therapy (NSPT), particularly scaling and root planing (SRP), can significantly improve metabolic control, resulting in a clinically meaningful reduction in glycated hemoglobin (HbA1c) in patients with type 2 diabetes (Chapple & Genco, 2013; Preshaw et al., 2012; Teeuw et al., 2010). These findings have led to international consensus statements recognizing periodontal therapy as a component of diabetes management.

Revista ARACÊ
ISSN: 2358-2472

3.2 ALZHEIMER'S DISEASE

Emerging evidence indicates a plausible mechanistic connection between periodontitis and neurodegenerative processes. The detection of periodontal pathogens, particularly Porphyromonas gingivalis, in post-mortem brain tissues of individuals with Alzheimer's disease suggests microbial translocation across the blood–brain barrier. The virulence factors of P. gingivalis, notably gingipains, have been shown in murine models to induce neuroinflammation, promote amyloid-β accumulation, and accelerate tau hyperphosphorylation, all of which are hallmarks of Alzheimer's pathology (Dominy et al., 2019).

Additionally, elevated peripheral inflammatory markers associated with periodontitis, such as IL-1β and CRP, are capable of triggering microglial activation and chronic neuroinflammation, thereby contributing to neuronal loss (Kamer et al., 2020; Chen et al., 2017). While causal inference remains under investigation, these findings support the hypothesis of a periodontal–neurological axis.

3.3 HYPERTENSION

Periodontal disease has been implicated in the pathogenesis of primary hypertension through several vascular and inflammatory mechanisms. The persistent low-grade inflammation characteristic of periodontitis induces endothelial dysfunction, oxidative stress, and increased arterial stiffness. Inflammatory mediators released from periodontal tissues, such as IL-6, TNF-α, and CRP are known to impair nitric oxide bioavailability and promote vasoconstriction.

A comprehensive meta-analysis and systematic review demonstrated that periodontitis is independently associated with elevated systolic and diastolic blood pressure (Munoz Aguilera et al., 2020). Furthermore, clinical trials have shown that intensive periodontal therapy can lead to modest but significant reductions in blood pressure in hypertensive patients, particularly in those with severe periodontitis (Tonetti et al., 2013; Vidal et al., 2020).

3.4 CHRONIC KIDNEY DISEASE (CKD)

The interaction between CKD and periodontitis appears to be synergistic and bidirectional. CKD patients display increased susceptibility to periodontal inflammation due to uremia-induced immune dysfunction and impaired wound healing. In contrast, periodontal

Revista ARACÊ
ISSN: 2358-2472

disease contributes to the systemic inflammatory burden, accelerating the progression of renal impairment.

Epidemiological data, including results from the ARIC study, show a significant association between periodontitis and reduced glomerular filtration rate (GFR) (Kshirsagar et al., 2007). Elevated systemic levels of IL-6, fibrinogen, and CRP, all of which are upregulated in both CKD and periodontitis, point to a common inflammatory pathway. Furthermore, Fisher and Taylor (2009) proposed predictive models indicating periodontitis as an independent risk factor for CKD onset and progression.

3.5 GASTROINTESTINAL DISORDERS

Recent studies have explored the oral–gut axis, emphasizing the impact of oral dysbiosis on intestinal immune homeostasis. Pathogens associated with periodontitis, including Fusobacterium nucleatum and P. gingivalis, have been shown to migrate to the gastrointestinal tract and contribute to the exacerbation of mucosal inflammation.

In murine models, oral administration of these pathogens induces colitis-like pathology through activation of Th17-mediated immune responses and disruption of intestinal epithelial integrity (Atarashi et al., 2017; Kitamoto et al., 2020). Clinical studies have also observed correlations between periodontal disease and the severity of inflammatory bowel disease (IBD), suggesting that oral pathogens may modulate gut microbiota composition and immune tone systemically (Schmidt et al., 2019).

4 DISCUSSION

The systemic repercussions of periodontal disease reflect a complex interplay between localized oral inflammation and broader physiological pathways, underscoring the paradigm shift in how chronic oral infections are conceptualized within the biomedical sciences. Far from being restricted to the confines of the periodontium, periodontal inflammation engages in multidirectional communication with systemic immune and vascular networks, influencing distant organ systems through a variety of molecular and cellular mechanisms.

A central pathophysiological axis involves the translocation of periodontal pathogens and their virulence factors into the bloodstream, initiating or exacerbating systemic inflammatory responses. Lipopolysaccharides (LPS), proteases, and other microbial byproducts originating from subgingival biofilms can traverse compromised epithelial barriers

Revista ARACÊ
ISSN: 2358-2472

and interact with Toll-like receptors and other components of the innate immune system, thereby amplifying the production of pro-inflammatory cytokines such as IL-6, TNF-α, and CRP. These mediators, while essential to acute immune responses, become deleterious when chronically elevated, contributing to endothelial dysfunction, insulin resistance, and neuroinflammation.

In diabetes mellitus, this systemic inflammatory burden compounds existing metabolic dysregulation, creating a self-perpetuating cycle in which hyperglycemia enhances periodontal tissue destruction through the formation of advanced glycation end-products and impaired neutrophil function. This bidirectionality necessitates integrated management strategies, recognizing the mutual reinforcement between glycemic control and periodontal status.

The neurological implications of periodontal disease represent an emerging frontier. The neuroinflammatory model posits that chronic peripheral infections may influence central nervous system homeostasis via both hematogenous dissemination and the modulation of immune privilege in the brain. Microglial activation in response to circulating inflammatory mediators and microbial products may underlie the cognitive decline observed in neurodegenerative conditions. While direct causality remains a subject of ongoing inquiry, the biological plausibility of this link is reinforced by experimental evidence of bacterial DNA and virulence factors within the central nervous system in affected individuals.

Vascular dysfunction, a unifying mechanism across numerous systemic diseases, is particularly relevant in the context of hypertension and renal impairment. Endothelial injury resulting from systemic inflammation compromises vasodilation and promotes atherogenesis, conditions that may be exacerbated by chronic oral infections. Furthermore, the renal system, with its highly vascularized and filtration-dependent architecture, is particularly susceptible to systemic inflammatory insults. Periodontal disease may thus contribute to the acceleration of renal functional decline, particularly in individuals with pre-existing susceptibility.

The gastrointestinal tract, with its vast immune network and microbial interface, also emerges as a potential site of impact. Dysbiosis in the oral cavity can influence gut microbiota composition through microbial translocation and immune modulation, potentially exacerbating or even initiating gastrointestinal pathologies such as inflammatory bowel disease. Moreover, the concept of a unified mucosal immunity, wherein immunological stimuli in one mucosal site influence distant mucosal surfaces, adds a theoretical framework to support these observed associations.

Revista ARACÊ
ISSN: 2358-2472

Critically, these interrelations challenge the traditional compartmentalization of medicine and dentistry. The oral cavity must be regarded as an integral part of systemic health, with periodontal disease acting not merely as a consequence of chronic disease but as a potential contributor to their onset, progression, and severity. This perspective reinforces the imperative for interdisciplinary collaboration, not only in clinical practice but also in public health planning and health policy design.

From a translational perspective, the integration of periodontal screening and intervention into routine medical care for high-risk populations could represent a low-cost, high-impact strategy for mitigating systemic disease burden. However, such integration demands a robust body of longitudinal and mechanistic evidence, as well as a shift in professional training, healthcare infrastructure, and patient education. The complexity of these interactions also raises important methodological considerations. Many of the existing studies are observational in nature, susceptible to confounding and reverse causality. Future research must prioritize well-designed prospective cohorts and interventional trials with standardized diagnostic criteria and outcomes. Furthermore, the incorporation of omics technologies including genomics, proteomics, and microbiomics may offer deeper insights into individual susceptibility profiles and mechanistic pathways.

In sum, periodontal disease represents a paradigmatic example of how localized pathologies can exert systemic effects through shared inflammatory, immunological, and microbial pathways. Recognizing and addressing this systemic impact requires a convergence of scientific disciplines, clinical specialties, and health systems in pursuit of genuinely integrative care.

5 CONCLUSION

Periodontal disease plays a significant role beyond the oral cavity, with associations identified in systemic conditions such as diabetes, Alzheimer's, hypertension, chronic kidney disease, and gastrointestinal disorders. These findings emphasize the necessity of integrated care approaches that consider oral health as an essential component of general health.

REFERENCES

Atarashi K, Tanoue T, Shima T, et al. Oral immune tolerance induction by colonic dendritic cells. Nature. 2017;550(7674):447–451.

Revista ARACÊ
ISSN: 2358-2472

Chapple IL, Genco RJ. Diabetes and periodontal diseases: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. J Clin Periodontol. 2013;40(Suppl 14):S106–S112.

Chen CK, Wu YT, Chang YC. Association between chronic periodontitis and the risk of Alzheimer's disease: a retrospective, population-based, matched-cohort study. Alzheimers Res Ther. 2017;9(1):56.

Dominy SS, Lynch C, Ermini F, et al. Porphyromonas gingivalis in Alzheimer's disease brains: Evidence for disease causation and treatment with small-molecule inhibitors. Sci Adv. 2019;5(1):eaau3333.

Fisher MA, Taylor GW. A prediction model for chronic kidney disease includes periodontal disease. J Periodontol. 2009;80(1):16–23.

Hajishengallis G. Periodontitis: from microbial immune subversion to systemic inflammation. Nat Rev Immunol. 2015;15(1):30–44.

Hajishengallis G, Darveau RP, Curtis MA. The keystone-pathogen hypothesis. Nat Rev Microbiol. 2012;10(10):717–725.

How KY, Song KP, Chan KG. Porphyromonas gingivalis: An Overview of Periodontopathic Pathogen below the Gum Line. Front Microbiol. 2016;7:53.

Kamer AR, Pirraglia E, Tsui W, et al. Periodontal disease associates with higher brain amyloid load in normal elderly. Neurobiol Aging. 2020;82:120–127.

Kitamoto S, Nagao-Kitamoto H, Jiao Y, et al. The inter-kingdom interaction between P. gingivalis and Candida albicans exacerbates oral infection. PLoS Pathog. 2020;16(5):e1008664.

Kshirsagar AV, Craig RG, Beck JD, et al. Periodontal disease is associated with renal insufficiency in the Atherosclerosis Risk in Communities (ARIC) study. Am J Kidney Dis. 2007;49(5):596–603.

Li X, Kolltveit KM, Tronstad L, Olsen I. Systemic diseases caused by oral infection. Clin Microbiol Rev. 2000;13(4):547–558.

Munoz Aguilera E, Suvan J, Buti J, et al. Periodontitis is associated with hypertension: a systematic review and meta-analysis. Cardiovasc Res. 2020;116(1):28–39.

Preshaw PM, Alba AL, Herrera D, et al. Periodontitis and diabetes: a two-way relationship. Diabetologia. 2012;55(1):21–31.

Ricardo AC, Athavale A, Chen J, et al. Periodontal disease, chronic kidney disease and mortality: results from the Third National Health and Nutrition Examination Survey. BMC Nephrol. 2015;16:97.

Rother ET. Revisão sistemática x revisão narrativa. Acta Paul Enferm. 2007;20(2):5–6.

Revista ARACÊ
ISSN: 2358-2472

Schmidt TS, Raes J, Bork P. The human gut microbiome: from association to modulation. Cell. 2019;172(6):1198–1215.

Teeuw WJ, Gerdes VE, Loos BG. Effect of periodontal treatment on glycemic control of diabetic patients: a systematic review and meta-analysis. J Clin Periodontol. 2010;37(12):1110–1116.

Tonetti MS, Van Dyke TE. Periodontitis and atherosclerotic cardiovascular disease: Consensus report of the Joint EFP/AAP Workshop. J Clin Periodontol. 2013;40(Suppl 14):S24–S29.

Vidal F, Figueredo CM, Cordovil I, Fischer RG. Periodontal therapy reduces plasma levels of interleukin-6, C-reactive protein, and fibrinogen in patients with severe periodontitis and refractory arterial hypertension. J Periodontol. 2020;91(4):519–530.