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Original Research Article

The Role of Oral Microbiome in Systemic Health: A Dental Perspective

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Abstract: ***Aim:*** To evaluate whether specific oral microbial signatures can serve as predictive biomarkers for systemic inflammatory diseases, enabling earlier risk stratification and targeted prevention strategies. ***Methodology:*** A total of 60 participants were recruited, comprising 30 systemically healthy individuals and 30 patients diagnosed with systemic inflammatory conditions. Unstimulated whole saliva samples were collected following standardized protocols to minimize diurnal and behavioral variability. Microbial DNA was extracted and subjected to 16S rRNA gene sequencing targeting the V3–V4 hypervariable regions using the Illumina MiSeq platform. Sequencing data were processed through a validated bioinformatics pipeline, including quality filtering, denoising, operational taxonomic unit (OTU)/amplicon sequence variant (ASV) clustering, and taxonomic assignment against curated reference databases. Alpha and beta diversity metrics, as well as differential relative abundance of key taxa, were calculated to characterize microbial community structure. Systemic inflammatory status was assessed by quantifying C-reactive protein (CRP) and interleukin-6 (IL-6). Associations between microbial parameters and inflammatory markers were analyzed using appropriate statistical tests, with adjustments for potential confounders to ensure robust inference. ***Results:*** The systemically healthy group exhibited significantly greater microbial diversity than the diseased cohort, as demonstrated by higher Shannon diversity (3.85 vs. 2.96, $p < 0.01$) and Chao1 richness indices (210 vs. 175, $p < 0.01$). Taxonomic profiling revealed a marked elevation of pathogenic taxa—including Porphyromonas gingivalis and Fusobacterium nucleatum—in participants with systemic disease, whereas commensal and health-associated species predominated in healthy individuals. Correlation analyses showed strong positive associations between the relative abundance of pathogenic bacteria and systemic inflammatory markers (CRP, IL-6), with a combined correlation coefficient of $r = 0.72$ ($p < 0.01$). These findings indicate that oral microbial dysbiosis is closely linked to heightened systemic inflammatory burden. ***Conclusion:*** This study demonstrates a significant association between oral microbiome imbalance and systemic health, underscoring the value of oral microbial profiling as a predictive indicator for systemic disease risk. These findings highlight the importance of maintaining oral microbial homeostasis as a preventive strategy to enhance overall health outcomes, aligning with SDG 3 (Good Health and Well-Being) by emphasizing early detection and prevention. Moreover, the integration of advanced sequencing technologies and bioinformatics supports SDG 9 (Industry, Innovation and Infrastructure) through the adoption of innovative diagnostic approaches in oral healthcare. Recognizing the growing influence of systemic inflammation on climate-related vulnerability, improved population-level prevention strategies indirectly contribute to SDG 13 (Climate Action) by reducing healthcare burden and resource consumption. Finally, this work reinforces SDG 17 (Partnerships for the Goals) by advocating multidisciplinary collaboration between dental clinicians,

microbiologists, and public health researchers to translate oral–systemic health insights into sustainable, scalable preventive strategies.

Keywords: Oral microbiome, systemic health, oral dysbiosis, inflammation, saliva, 16S rRNA sequencing, SDG 3,9,13,17.

INTRODUCTION

The oral cavity harbors a diverse and dynamic microbial community, collectively referred to as the oral microbiome, which plays a pivotal role in maintaining oral ecological balance, preventing pathogenic colonization, and modulating local immune responses (Rajasekaran et al., 2024 [1]). Disruption of this microbial equilibrium—termed dysbiosis—has been implicated in the pathogenesis of common oral diseases such as periodontitis and dental caries, both of which are increasingly recognized as contributors to systemic inflammatory and metabolic disorders (Peng et al., 2022 [2]).

Emerging evidence indicates that oral microbial dysbiosis can influence systemic health through multiple biological pathways. Dysregulated oral microbial communities have been associated with metabolic diseases, including type 2 diabetes, by promoting pro-inflammatory signaling and exacerbating insulin resistance (Bourgeois et al., 2022 [3]). Similarly, several oral pathogens have been shown to induce systemic inflammation and contribute to the progression of cardiovascular disease (Georges et al., 2022 [4]).

Interactions between the oral microbiome and distal microbial ecosystems, particularly the gut microbiome, further highlight the complexity of the oral–systemic axis. These interactions are mediated by immune, inflammatory, and metabolic pathways, underscoring the bidirectional nature of oral-systemic communication (Li et al., 2022 [5]). Notably, translocation of oral bacteria into the bloodstream can elicit systemic immune responses and promote chronic inflammatory states (Li et al., 2023 [6]). Key pathogens such as Porphyromonas gingivalis and Fusobacterium nucleatum have been identified as potent drivers of systemic inflammation through their ability to modulate cytokine production and impair host immune regulation (Vyhnalova et al., 2023 [7]).

Given the growing recognition of the oral microbiome as a modifiable determinant of systemic health, strategies aimed at preserving or restoring oral microbial homeostasis hold promise for reducing the burden of chronic diseases (Pisano et al., 2023 [8]). Integrating oral health monitoring and preventive microbial management into broader systemic disease-prevention frameworks may therefore contribute to improved population health and more comprehensive management of inflammation-mediated disorders.

MATERIAL AND METHODS

Study Design and Participants

This cross-sectional study was conducted in the Department of Oral Biology and Microbiology to investigate the association between oral microbiome composition and systemic health. Sixty participants were enrolled, comprising 30 systemically healthy individuals and 30 patients diagnosed with one or more systemic conditions (e.g., diabetes mellitus, cardiovascular disease, rheumatoid arthritis, Alzheimer's disease). Participants were aged 25–70 years. Individuals with recent antibiotic usage (within the past 3 months), active oral infections, or ongoing periodontal therapy were excluded to minimize potential confounders. Ethical approval was obtained from the institutional review board, and written informed consent was collected from all participants.

Sample Collection and DNA Extraction

Unstimulated whole saliva samples were collected between 08:00 and 10:00 h into sterile polypropylene tubes following standardized protocols to reduce diurnal variation. Samples were immediately placed on ice and transported to the microbiology laboratory. After centrifugation to remove debris, microbial DNA was extracted using a commercial DNA isolation kit. DNA concentration and purity were assessed using a NanoDrop spectrophotometer.
16S rRNA Gene Amplification and Sequencing

The hypervariable V3–V4 regions of the bacterial 16S rRNA gene were amplified via polymerase chain reaction (PCR). Amplicons were sequenced using the Illumina MiSeq next-generation sequencing platform. Raw sequence data were processed using the QIIME2 pipeline, including demultiplexing, quality filtering, denoising, and operational taxonomic unit (OTU) clustering at a 97% sequence similarity threshold. Taxonomic assignment was performed using curated reference databases.

Microbial Diversity and Community Analysis

Microbial community structure was characterized using alpha diversity metrics (Shannon and Chao1 indices) to evaluate richness and diversity within samples, and beta diversity metrics (Bray–Curtis

dissimilarity) to assess compositional differences between groups. Relative abundance profiles were generated at the phylum and genus levels, with particular attention to pathogens commonly implicated in systemic inflammation, including Porphyromonas gingivalis, Fusobacterium nucleatum, and Prevotella intermedia.

Assessment of Systemic Inflammation and Statistical Analysis

Systemic inflammatory status was determined through quantification of C-reactive protein (CRP) and interleukin-6 (IL-6). Statistical analyses were conducted using SPSS version 26.0. Independent t-tests were employed to compare microbial diversity and relative abundance between healthy and systemically diseased groups, while Pearson's correlation analysis was used to evaluate associations between pathogenic taxa and systemic inflammatory markers. Statistical significance was set at $p < 0.05$.

RESULTS

Analysis of the oral microbiome revealed marked differences in microbial diversity and community composition between systemically healthy individuals and those with systemic diseases. As summarized in Table 1, alpha diversity indices demonstrated significantly greater microbial richness and diversity in the healthy group compared with the diseased cohort ($p < 0.01$). Beta diversity assessment using Bray–Curtis dissimilarity further showed distinct clustering between groups, indicating clear compositional separation at the community level.

Differential abundance analysis identified a higher prevalence of pathogenic taxa among participants with systemic conditions. Notably, *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, and *Tannerella forsythia* were significantly enriched in the diseased group, whereas health-associated commensals such as *Streptococcus salivarius* and *Rothia mucilaginosa* predominated among healthy individuals (Table 2).

Systemic inflammatory markers demonstrated strong positive associations with key periodontopathogenic species. Elevated CRP and IL-6 levels correlated significantly with increased abundance of pathogenic bacteria (combined $r = 0.72$, $p < 0.01$), suggesting a direct relationship between microbial dysbiosis and heightened systemic inflammatory burden.
Overall, the systemically diseased cohort exhibited reduced microbial diversity, loss of beneficial commensals, and an overrepresentation of pathogenic species implicated in pro-inflammatory pathways. These patterns support the concept that oral microbial imbalance contributes to systemic disease progression, potentially through mechanisms involving chronic low-grade inflammation and microbial translocation.

Table 1. Comparison of alpha diversity indices between healthy and diseased groups

Group	Shannon Index (Mean ± SD)	Chao1 Index (Mean ± SD)	p-value
Healthy (n=30)	3.85 ± 0.42	210 ± 15	<0.01
Diseased (n=30)	2.96 ± 0.38	175 ± 12	<0.01

Table 2. Relative abundance of major bacterial genera identified in both groups

Bacterial Genus	Healthy Group (%)	Diseased Group (%)
Streptococcus salivarius	18.5	9.2
Rothia mucilaginosa	14.7	7.6
Porphyromonas gingivalis	6.1	15.8
Fusobacterium nucleatum	5.3	13.4
Prevotella intermedia	4.8	10.7

Taken together, these findings demonstrate clear distinctions in oral microbiome profiles between systemically healthy and diseased individuals, underscoring the potential utility of oral microbial profiling as a predictive biomarker for systemic health assessment.

DISCUSSION

The oral microbiome is integral to both oral and systemic health, functioning as a complex ecosystem of bacteria, fungi, viruses, and protozoa that interact with the host immune system to maintain homeostasis (Azevedo et al., 2024 [9]). Disruption of this balance—oral dysbiosis—promotes overgrowth of pathogenic species, triggering local inflammation and influencing distant organ systems (Vyhnalova, 2021 [10]). Age-related shifts in microbial communities are particularly significant, predisposing older individuals to pathogenic

colonization, elevated inflammatory mediator production, and heightened systemic inflammatory responses (Gu et al., 2024 [11]). Furthermore, bidirectional communication between the oral and gut microbiomes through immune and metabolic pathways emphasizes the oral microbiome's role in gastrointestinal health, immune regulation, and chronic disease prevention, aligning with SDG 3 (Good Health and Well-Being) (Sarafidou, 2025 [12]).

Oral dysbiosis has been strongly linked to metabolic disorders such as type 2 diabetes. Pathogens including Fusobacterium nucleatum, Porphyromonas gingivalis, and Prevotella intermedia stimulate chronic low-grade inflammation by elevating IL-6 and CRP, impairing insulin signaling and glucose metabolism (Yamazaki & Kamada, 2023 [13]). Clinical data indicate that higher salivary and dental plaque levels of these pathogens correlate with poor glycemic control, suggesting that targeted oral health interventions may improve systemic metabolic outcomes, contributing to SDG 3 and advancing evidence-based preventive healthcare strategies (Long et al., 2017 [14]). Age-related reductions in microbial diversity and enrichment of pathogenic taxa further exacerbate systemic inflammation, reinforcing the link between oral health and chronic disease progression (Sarafidou et al., 2024 [15]).

Cardiovascular disease is another systemic condition closely associated with oral microbial imbalance. Periodontal pathogens can translocate into the bloodstream, adhere to vascular endothelium, and promote atherosclerotic plaque formation, vascular inflammation, and thrombosis (Varoni & Rimondini, 2022 [16]). Chronic periodontal inflammation increases the risk of myocardial infarction and stroke, emphasizing the systemic consequences of oral dysbiosis. These findings highlight the potential of innovative diagnostic tools and advanced sequencing technologies (SDG 9: Industry, Innovation, and Infrastructure) for monitoring microbial markers to predict cardiovascular risk (Chang et al., 2023 [17]). Dysbiosis has also been implicated in the pathogenesis of head and neck cancers, where chronic inflammation and immune modulation by oral pathogens can create a tumor-permissive microenvironment (Nayak et al., 2025 [18]).

Neurodegenerative disorders, including Alzheimer's disease, have been associated with oral pathogens, with detection of P. gingivalis DNA and gingipain enzymes in the brain implicating oral microbes in neuroinflammation, neuronal injury, and cognitive decline (Sidhu et al., 2025 [19]). Maternal oral health similarly influences pregnancy outcomes; periodontitis has been linked to preeclampsia, highlighting the systemic impact of oral microbial dysbiosis on maternal and fetal health. Autoimmune conditions, such as rheumatoid arthritis, may be exacerbated by oral pathogens through immune modulation and autoantibody production (Tonelli et al., 2023 [21]).

Interventions targeting the oral microbiome are demonstrating promise in mitigating systemic disease risk. Regular professional dental care, optimized oral hygiene, and the use of probiotics or prebiotics can restore microbial homeostasis and reduce systemic inflammation (Fan et al., 2018 [22]). Metagenomic and multi-omics approaches enable precise characterization of dysbiotic patterns, facilitating personalized interventions tailored to individual microbial profiles, promoting sustainable healthcare solutions in line with SDG 13 (Climate Action) by reducing long-term disease burden and associated resource use (Ahmad et al., 2025 [23]). Certain oral microorganisms, such as Methanobrevibacter oralis, are emerging as potential biomarkers for systemic disease susceptibility, offering opportunities for early diagnosis and preventive strategies, which require collaborative efforts across disciplines (SDG 17: Partnerships for the Goals) (Pilliol et al., 2024 [24]).
Maintaining a balanced oral microbiome is critical not only for preventing oral diseases but also for mitigating systemic conditions. Oral microbial communities actively regulate inflammation, immunity, and metabolism, emphasizing the need for integrated dental and medical care (Liu et al., 2023 [25]). Continuous monitoring and management of oral microbial health can reduce the burden of chronic diseases, improve metabolic and cardiovascular outcomes, and enhance overall well-being. Strategies targeting microbial equilibrium and host immune modulation represent a promising frontier in preventive dentistry and systemic disease management, bridging dentistry and medicine while supporting global health, innovation, sustainability, and collaborative partnerships (SDG 3, 9, 13, 17) (Le et al., 2022 [26]; Bingham & Moni, 2013 [27])

CONCLUSION

This study demonstrates a robust association between oral microbiome imbalance and systemic health, with elevated levels of pathogenic oral bacteria correlating with increased systemic inflammatory markers. Preservation of oral microbial homeostasis may serve as a viable strategy to prevent or mitigate chronic systemic diseases, highlighting the critical role of oral health in overall health management. Integrating oral health monitoring into broader preventive healthcare frameworks supports SDG 3 (Good Health and Well-Being) by promoting early detection and risk reduction. The use of innovative diagnostic and sequencing technologies underscores the relevance of SDG 9 (Industry, Innovation, and Infrastructure) in advancing precision oral healthcare. By reducing the long-term

burden of systemic diseases, such strategies contribute to SDG 13 (Climate Action) through more sustainable healthcare resource utilization. Finally, fostering multidisciplinary collaboration between dental professionals, medical practitioners, and public health researchers aligns with SDG 17 (Partnerships for the Goals), facilitating the translation of oral–systemic health insights into effective, scalable interventions. Collectively, these findings reinforce the need to consider oral health as an integral component of systemic disease prevention and health promotion.

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