OPEN ACCESS

Saudi Journal of Oral and Dental Research

Abbreviated Key Title: Saudi J Oral Dent Res
ISSN 2518-1300 (Print) | ISSN 2518-1297 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Review Article **Oral Pathology**

Periodontal Manifestations of Prediabetes: An Overview for Dental Clinicians

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DOI: https://doi.org/10.36348/sjodr.2026.v11i04.006 | **Received:** 22.02.2026 | **Accepted:** 16.04.2026 | **Published:** 18.04.2026

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Abstract

Prediabetes is an intermediate glycemic state defined by impaired fasting glucose, impaired glucose tolerance, or mildly elevated glycated hemoglobin (HbA1c 5.7–6.4%) and affects an estimated 374 million people worldwide. Growing evidence supports a bidirectional relationship between prediabetes and periodontitis in adults. Individuals with prediabetes face a significantly higher risk of periodontitis, with disease severity correlating with the advancing stages of clinical attachment loss. Inflamed periodontal tissues generate advanced glycation end-products (AGEs), upregulate matrix metalloproteinase-8 (MMP-8), and sustain a pro-inflammatory cytokine milieu that exacerbates insulin resistance. Non-surgical periodontal therapy reduces active MMP-8 and HbA1c levels in prediabetic patients, potentially delaying the progression to overt type 2 diabetes. Dentists are ideally positioned to identify undiagnosed prediabetes through periodontal assessment and chairside glycemic screening, enabling timely interdisciplinary referrals.

Keywords: prediabetes, periodontitis, advanced glycation end-products, matrix metalloproteinase-8, insulin resistance, HbA1c, non-surgical periodontal therapy.

INTRODUCTION

Prediabetes is a reversible intermediate glycemic state that substantially increases the risk of type 2 diabetes and its systemic complications [1]. Emerging evidence indicates that periodontal disease coexists with and may actively accelerate prediabetes by sustaining a chronic systemic inflammatory burden [2,3]. Despite the growing global prevalence of both conditions, their clinical interplay remains underappreciated in routine dental practices [4]. This review examines the epidemiology, pathogenic mechanisms, and clinical implications of periodontal manifestations in prediabetes for practicing dentists.

Epidemiology and Prevalence of Periodontal Disease in Prediabetes

Prediabetes, defined by impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or HbA1c levels between 5.7% and 6.4%, currently affects an estimated 374 million people worldwide, representing a critical window for preventive intervention [1]. A 2025 meta-analysis of ten observational studies encompassing 38,727 participants confirmed that individuals with prediabetes have a 27% higher risk of periodontitis than normoglycemic controls (OR: 1.27; 95% CI: 1.09–1.48; $p<0.001$), independent of established confounders such as age, BMI, and smoking [1]. National Health and Nutrition Examination Survey (NHANES) data further demonstrate a dose-dependent relationship, with moderate periodontitis associated with an OR of 1.46 (95% CI: 1.29–1.65) and severe periodontitis with an OR of 1.62 (95% CI: 1.31–2.01) for prediabetes [3].

Critically, this risk is not confined to the middle-aged or elderly populations. A cross-sectional study of 400 young adults aged 18–35 years found that non-diabetic hyperglycemia, consistent with prediabetes, was prevalent in 19% of participants, and all periodontal parameters, including plaque index, gingival index, bleeding on probing, probing depth, and clinical

attachment loss, were significantly worse in this group than in normoglycemic controls [4]. Among 1,071 non-diabetic adults enrolled in a population-based study, greater interproximal clinical attachment loss (i-CAL) was associated with a 2.42-fold higher prevalence of prediabetes (PR: 2.42; 95% CI: 1.77–3.08), while greater interproximal probing depth was independently correlated with insulin resistance (HOMA-IR) [5]. In patients presenting for dental care without a prior diabetes diagnosis, up to 47% of those with stage I/II periodontitis harbored undiagnosed prediabetes, as detected by chairside HbA1c testing, with glycemic levels rising progressively across advancing periodontitis stages [6].

Inflammatory and Molecular Mechanisms

The biological link between prediabetes and periodontitis involves a self-amplifying cascade centered on advanced glycation end products (AGEs), pro-inflammatory cytokines, and collagenolytic enzymes. Inflamed periodontal tissues function as an endogenous source of AGEs, even in normoglycemic individuals. Serum AGE levels are approximately 2.4 times higher in normoglycemics with periodontitis (15.91 ng/mL) than in those without it (6.60 ng/mL), while gingival crevicular fluid (GCF) AGE concentrations are nearly 2.68-fold greater in periodontitis-affected sites than in healthy gingival tissues [2]. The periodontal pathogen Tannerella forsythia drives this accumulation by producing methylglyoxal, a key AGE precursor, via the enzyme methylglyoxal synthase, with methylglyoxal levels recorded 94.2% higher in diseased sites than in healthy tissue [2].

These AGEs bind to their receptors (RAGEs) on macrophages and endothelial cells, triggering the release of IL-1β, TNF-α, and IL-6, which impair beta-cell function, promote insulin resistance, and disrupt the RANKL/OPG axis to favor alveolar bone resorption [1][2]. The elevated AGE load feeds a vicious cycle: impaired insulin signaling increases free glucose, generating more AGEs and perpetuating both systemic glycemic dysregulation and local periodontal destruction. In rapidly progressing, severe periodontitis (stage III grade C), prediabetic HbA1c levels significantly upregulate MMP-8 expression, and active MMP-8 (aMMP-8), the principal collagenase in the periodontium, correlates positively with prediabetic status (Spearman's rho = 0.646; p = 0.044) [7]. Non-surgical periodontal therapy (scaling and root planing, SRP) consistently reduces GCF levels of IL-1β and IFN-γ in patients with prediabetes and generalized periodontitis, attenuating local inflammation, irrespective of glycemic status [8].

Clinical Implications

The prediabetes–periodontitis interface has direct and actionable implications for clinical dentistry. Non-surgical periodontal therapy (NSPT) achieves a statistically significant reduction in aMMP-8 levels ($p<0.001$) and a mean HbA1c decline of 0.4% in prediabetic and diabetic patients with stage II–IV periodontitis, with the most pronounced response observed in stages III and IV disease [9]. Since 25–37% of individuals with prediabetes will progress to type 2 diabetes within 3–5 years, and up to 70% will do so over a lifetime, timely periodontal intervention may be a strategy to delay this transition [9]. Chairside aMMP-8 point-of-care (PoC) mouthrinse testing delivers quantitative results within five minutes and can simultaneously serve as a marker of periodontal activity and prediabetes-related collagenolytic burden in the dental operatory [7,9].

From a diagnostic perspective, dental visits offer an underutilized screening opportunity. Patients presenting with moderate-to-severe periodontitis and no prior diabetes diagnosis should be assessed using a chairside HbA1c test. In one cross-sectional cohort, up to 47% of patients with stage I/II periodontitis had undiagnosed prediabetes [6], while a population-based NHANES analysis linked severe periodontitis in prediabetic patients to a hazard ratio of 1.81 for all-cause mortality [3]. Systematic monitoring of probing depth, bleeding on probing, and i-CAL in patients with known or suspected prediabetes supports early referral to a physician for metabolic evaluation [5,4]. Dentists who incorporate simple glycemic screening tools alongside comprehensive periodontal examinations are positioned to reduce the dual burden of undiagnosed prediabetes and undertreated periodontal disease in their patients.

CONCLUSION

Prediabetes is independently associated with increased periodontitis severity, distinct inflammatory biomarker profiles, and accelerated periodontal tissue destruction in adults. The dental operatory offers a feasible and underutilized setting for prediabetes risk detection through comprehensive periodontal assessment and chairside glycemic screening. Non-surgical periodontal therapy meaningfully improves both local and systemic inflammatory parameters in prediabetic patients and may delay the progression to overt type 2 diabetes. Integrating periodontal care with systemic metabolic management is an evidence-based strategy that dentists can adopt to improve patient outcomes.

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