REVIEW ARTICLE

Bidirectional Relationship between Diabetes Mellitus (DM) and Periodontal Disease

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ABSTRACT

The bidirectional relationship between diabetes mellitus (DM) and periodontal disease (PD) has been increasingly recognized in the literature. DM predisposes individuals to greater risk, prevalence, severity, and progression of periodontitis, while periodontitis adversely affects glycemic control and may exacerbate diabetes. This review synthesizes epidemiological evidence from cohort and cross-sectional studies, explores molecular and immunoinflammatory mechanisms, and discusses clinical implications, including periodontal therapy's impact on glycemic parameters. A systematic search was conducted in major databases, yielding high-quality observational and mechanistic studies. Meta-analytic data indicate that individuals with periodontitis have a ~1.26-fold increased risk of developing diabetes, and diabetics have a ~1.24-fold increased risk of incident periodontitis. Mechanistically, advanced glycation end products (AGEs), chronic inflammation, altered host response, insulin resistance, and dysbiosis link the two conditions. Periodontal treatment has shown modest but clinically meaningful reductions in HbA1c. These findings emphasize the need for integrated medical-dental care and further high-quality interventional trials.

KEYWORDS: diabetes mellitus; periodontal disease; periodontitis; inflammation; advanced glycation end products; glycemic control

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia due to defects in insulin secretion, insulin action, or both. It is associated with multiple systemic complications, including cardiovascular disease, nephropathy, neuropathy, and retinopathy. More recently, periodontal disease (PD), especially chronic periodontitis, has been recognized as both a complication and a potential contributing factor in diabetes (1, 2).

Periodontal disease is a chronic inflammatory disease involving the supporting structures of the teeth (gingiva, periodontal ligament, alveolar bone), triggered by bacterial biofilms and modulated by host immune response (3). Epidemiological and clinical studies over decades have demonstrated a bidirectional relationship: diabetes increases the risk, severity, and progression of periodontal disease, while periodontitis can negatively influence glycemic control and potentially contribute to the development of diabetes (4, 5).

Mechanistically, hyperglycemia leads to accumulation of advanced glycation end-products (AGEs), oxidative stress, altered neutrophil function, and a pro-inflammatory milieu, all of which impair periodontal tissue integrity (6). Conversely, periodontal infection produces systemic inflammation (e.g., elevated IL-6, TNF-α, CRP), which may worsen insulin resistance and metabolic dysregulation (7). Understanding this two-way interaction has critical implications for both medical and dental management.

This review aims to: (1) summarize epidemiological evidence for the bidirectional association; (2) explore molecular and immunological mechanisms underpinning the link; and (3) discuss clinical and therapeutic implications, including effects of periodontal therapy on glycemic control.

METHODS

Search strategy: We searched PubMed/Medline, Web of Science, and Scopus databases for articles published up to August 2025, using combinations of keywords such as “diabetes mellitus”, “periodontal disease”, “periodontitis”, “inflammation”, “advanced glycation end products”, “glycemic control”, and “bidirectional association”. Additional articles were identified by screening references in key reviews.

Inclusion criteria:

- Observational cohort studies, cross-sectional studies, interventional clinical trials, and mechanistic (molecular/animal) studies.
- Studies explicitly addressing the association between DM and PD in either direction (i.e., the effect of diabetes on PD, or of PD on glycemic control or diabetes incidence).
- English-language articles.

Exclusion criteria:

- Case reports, non-peer-reviewed commentary.
- Studies not providing quantitative or mechanistic data relevant to the bidirectional link.

Data extraction and synthesis: We extracted data on study design, population, measures of periodontal disease (e.g., clinical attachment loss, pocket depth, community periodontal index), measures of diabetes/glycemic control (e.g., HbA1c, fasting glucose), follow-up duration, risk estimates, and mechanistic findings. We qualitatively synthesized mechanistic studies and highlighted key pathways.

RESULTS

Epidemiological Evidence

- A systematic review and meta-analysis of 15 prospective cohort studies found a significant bidirectional association: the summary relative risk (SRR) of incident diabetes in people with periodontitis was 1.26 (95% CI 1.12–1.41), and the SRR of incident periodontitis in diabetic individuals was 1.24 (95% CI 1.13–1.37) (8).
- Earlier epidemiologic reviews also documented consistent evidence: diabetics show higher prevalence, severity, and progression of periodontal disease (9).
- In children with type 1 diabetes, clinical studies have demonstrated worsening periodontal parameters (gingival index, plaque index, clinical attachment loss) correlating with poor glycemic control; after periodontal treatment, improvements in HbA1c were observed (10).

Mechanistic Insights

- Hyperglycemia in diabetes promotes formation of AGEs, which bind to RAGE (receptors for AGEs) on immune and endothelial cells, triggering increased production of pro-inflammatory cytokines (IL-1β, IL-6, TNF-α) and oxidative stress, impairing periodontal tissues (11).
- Altered immune response: diabetes impairs neutrophil chemotaxis and phagocytosis, which reduces microbial clearance in the periodontal pocket (11).
- Insulin resistance: systemic inflammation arising from periodontitis may exacerbate insulin resistance—elevated cytokines (IL-6, TNF-α) from periodontal infection can interfere with insulin signaling pathways (6, 8).
- Microbial dysbiosis: dysregulated host response in diabetes may modify subgingival microbiota, favoring pathogenic species; conversely, periodontitis may lead to bacteremia, systemic endotoxin exposure, and further metabolic stress (12).
- Vascular and microvascular complications: diabetes-related microvascular damage (capillary basement membrane thickening, impaired perfusion) may impair healing and tissue turnover in periodontal tissues (6, 8).

Clinical Implications / Intervention Studies

- Clinical trials have shown that non-surgical periodontal therapy (scaling and root planing, sometimes with adjuncts) can lead to modest but significant reductions in HbA1c (typically 0.3%–0.6%) over 3–6 months (2, 8).
- Given the bidirectional link, several authors advocate for integrated care: dental assessment in diabetic patients, screening for diabetes in periodontal patients, and co-management between dental and medical professionals (8).
- Recent narrative reviews emphasize the role of HbA1c as a key biomarker bridging the two conditions, and suggest novel interventions (e.g., host-modulation therapy, photodynamic therapy) (13).

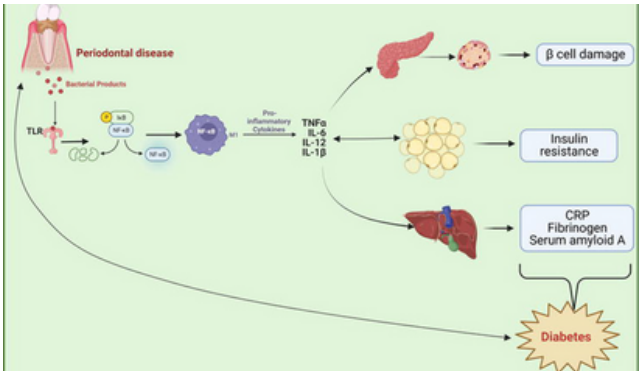

Figure 1.
The bidirectional and pathophysiological mechanisms involved in periodontal and TIIDM (Alluri et al, 2023 Intechopen).

DISCUSSION

The findings of this review reinforce the strong bidirectional relationship between diabetes mellitus (DM) and periodontal disease (PD), confirming what many epidemiological, clinical, and mechanistic studies have suggested over the past several decades. The pathophysiological interplay between these two chronic inflammatory conditions involves a complex and mutually reinforcing cycle of immune dysregulation, metabolic impairment, microbial dysbiosis, and oxidative stress.

Epidemiologic evidence consistently supports this two-way relationship. Large prospective cohort studies demonstrate that individuals with diabetes especially those with poorly controlled glycemia are at significantly increased risk for the development and progression of periodontitis . Conversely, individuals with periodontitis exhibit an increased risk of incident diabetes independent of traditional risk factors (14). The systematic review and meta-analysis by Stöhr et al. showed that individuals with periodontitis had a 26% higher risk of developing diabetes, while diabetic individuals had a 24% higher risk of developing periodontitis, strongly supporting the concept of bidirectionality (15). Earlier epidemiological analyses further highlight that the severity of periodontal destruction correlates with duration of diabetes, glycemic control, and presence of diabetic complications, particularly microvascular disease (16).

From a mechanistic standpoint, hyperglycemia plays a central role. Chronic elevation of blood glucose leads to increased formation of advanced glycation end products (AGEs), which bind to receptors for AGEs (RAGE) expressed on various cells including endothelial cells, immune cells, and periodontal fibroblasts (17). AGE–RAGE interaction triggers nuclear factor-κB (NF-κB) activation, promoting transcription of pro-inflammatory cytokines such as TNF-α and IL-1β, which contribute to periodontal tissue breakdown (5,11). This pro-inflammatory environment also impairs collagen metabolism, alters wound healing, and increases oxidative stress—all of which predispose diabetic individuals to more severe periodontitis (18).

Conversely, periodontal disease contributes to systemic inflammation, which may worsen insulin resistance and glycemic control. Elevated circulating levels of IL-6, TNF-α, CRP, and lipopolysaccharides from periodontal pathogens can impair insulin receptor signaling and promote hepatic insulin resistance (6,8). These inflammatory mediators reduce insulin sensitivity at the cellular level by interfering with insulin receptor substrate pathways, leading to metabolic dysfunction and potentially accelerating the progression from impaired glucose tolerance to diabetes (8). This mechanism provides a plausible explanation for epidemiological findings that periodontitis increases the risk of diabetes onset.

Another important component of the interaction is immune dysregulation. Individuals with diabetes exhibit impaired neutrophil chemotaxis, phagocytosis, and microbial killing, contributing to ineffective control of periodontal pathogens (19). At the same time, the subgingival microbial ecosystem in diabetic individuals shifts toward more virulent and proteolytic bacterial species such as Porphyromonas gingivalis which further exacerbate periodontal destruction (20). This dysbiosis–inflammation–hyperglycemia cycle underscores the complexity of the bidirectional relationship.

Periodontal therapy has emerged as a potential strategy to improve systemic metabolic outcomes. Numerous clinical trials have demonstrated that non-surgical periodontal therapy (scaling and root planing) leads to modest reductions in HbA1c, typically in the range of 0.3% to 0.6% over several months (21). Although small, such reductions are clinically meaningful because they correspond to a decreased risk of diabetic complications. The mechanism likely involves suppression of systemic inflammatory mediators after periodontal treatment, thereby improving insulin sensitivity. However, results across trials vary due to differences in study design, adjunctive therapies used, baseline glycemic control, and duration of follow-up. Some studies report little or no change in HbA1c following periodontal treatment, suggesting that while periodontal therapy may support metabolic control, it is not a substitute for medical diabetes management.

Children with type 1 diabetes represent another important group. Studies in this population demonstrate that poor glycemic control is strongly associated with worsening periodontal parameters, and that periodontal therapy can improve both oral health and metabolic status (22). These findings underscore that the bidirectional relationship is not limited to type 2 diabetes or adults but is relevant across age groups and diabetes types.

Clinical implications of this evidence are profound. First, periodontal evaluation should be a routine component of comprehensive diabetes management. Professional guidelines increasingly emphasize integrating oral health into diabetes care to reduce long-term complications (16). Second, dental professionals should be aware that periodontitis may be an early indicator of undiagnosed diabetes; thus periodontal screening offers an opportunity for medical referral and early detection (23). Third, interdisciplinary collaboration between dentists, diabetologists, primary care physicians, and nutritionists is essential to optimize outcomes for patients affected by both diseases.

Despite strong evidence, several gaps remain. Many studies differ significantly in diagnostic criteria for both diabetes and periodontitis, contributing to heterogeneity (9). Most mechanistic studies rely on in vitro models or animal experiments, which may not reflect human physiology fully (21). Long-term randomized controlled trials are needed to determine whether sustained periodontal therapy can reduce incidence of diabetes or diabetic complications. Moreover, emerging therapies such as host modulation, probiotics, and photodynamic therapy warrant further investigation for their potential systemic benefits (24).

In summary, the evidence overwhelmingly supports a pathophysiological cycle between diabetes and periodontal disease: hyperglycemia exacerbates periodontal inflammation, and periodontal inflammation worsens metabolic control. Breaking this cycle through effective periodontal care may offer a valuable adjunctive strategy for diabetes management. Future research should prioritize interdisciplinary approaches, standardized diagnostic criteria, and long-term outcomes to better understand how oral-systemic health can be integrated into comprehensive patient care.

Limitations in the current literature include methodological heterogeneity (different definitions of periodontitis, different diagnostic criteria for diabetes), residual confounding, and high inter-study variability. Mechanistic studies, while compelling, often rely on in vitro or animal models, and translation to human clinical outcomes needs further validation.

CONCLUSION

The bidirectional association between diabetes mellitus and periodontal disease is well-supported by epidemiological and mechanistic evidence. Diabetes contributes to increased risk, severity, and progression of periodontitis, while periodontitis can impair glycemic control and potentially increase diabetes risk. Periodontal therapy has modest but beneficial effects on glycemic parameters, highlighting the therapeutic potential of oral interventions in systemic disease management. Given the public health implications, integrated medical-dental care and further interventional research are strongly warranted.

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