

The Bidirectional Relationship Between Diabetes Mellitus and Periodontal Disease: A Comprehensive Review

Ahmed Ishag^{1,2}, Almoeiz Y. Hammad³, Daris Adouma⁴ and Abdalla S. Aljabry⁴

¹ School of Dentistry, Darfur University College, Sudan

² Department of Periodontology, Faculty of Clinical Medicine and Dentistry, Kampala International University-Uganda

³ Department of Biochemistry, Faculty of Biomedical Sciences, Kampala International University - Uganda

⁴ Department of Dental Public Health, Faculty of Clinical Medicine and Dentistry, Kampala International University-Uganda

⁵ Department of Periodontology, Equator University of Science and Technology, Uganda

Abstract: Diabetes mellitus (DM) and periodontal disease are two highly prevalent chronic inflammatory conditions that exhibit a well-established bidirectional relationship. Diabetes increases the risk and severity of periodontal disease through mechanisms involving hyperglycemia-induced inflammation, oxidative stress, immune dysfunction, and advanced glycation end-product accumulation. Conversely, periodontitis adversely affects glycemic control through systemic dissemination of periodontal pathogens, inflammatory mediators, and subsequent insulin resistance. This review synthesizes current scientific evidence on the epidemiology, pathophysiology, and clinical implications of this bidirectional relationship. Periodontal disease has been recognized as the "sixth complication" of diabetes. Intervention studies demonstrate that non-surgical periodontal treatment can reduce glycated hemoglobin (HbA1c) levels by approximately 0.3-0.5 percentage points, a clinically significant improvement comparable to adding a second oral antidiabetic medication. Furthermore, periodontal therapy reduces systemic inflammatory markers, decreases diabetes-related healthcare costs, and may lower the risk of cardiovascular complications. Despite this robust evidence, periodontitis remains underdiagnosed and undertreated in the context of routine diabetes care. Integrated medical-dental collaboration, early screening, and timely periodontal intervention are essential to optimize outcomes for patients with diabetes and periodontal disease.

Keywords: Diabetes mellitus, periodontitis, bidirectional relationship, glycemic control, HbA1c, periodontal therapy, inflammation, interdisciplinary care

1. Introduction

The oral cavity serves as a mirror of systemic health, and the relationship between oral diseases and systemic conditions has garnered increasing attention over the past three decades. Among the numerous systemic associations identified, the link between periodontal disease and diabetes mellitus (DM) stands out due to its strong, clinically significant, and bidirectional nature [1,2]. Periodontal disease, a chronic inflammatory condition affecting the tooth-supporting structures, and diabetes, a metabolic disorder characterized by persistent hyperglycemia, are both highly prevalent globally and share common risk factors and inflammatory pathways [3,4]. The concept of periodontal disease as a complication of diabetes was first articulated by Löe in 1993, who proposed it as the "sixth complication" of diabetes, following retinopathy, nephropathy, neuropathy, cardiovascular disease, and peripheral arterial disease [5]. Since then, a substantial body of evidence has accumulated demonstrating not only that diabetes increases the risk and severity of periodontal disease but also that periodontitis adversely affects glycemic control and contributes to the development of diabetes-related complications [6-8]. This bidirectional relationship has profound diagnostic and therapeutic implications, underscoring the need for integrated medical-dental care models [9,10].

The global burden of both diseases is staggering. According to the International Diabetes Federation (IDF), approximately 537 million adults were living with diabetes in 2021, and this number is projected to rise to 643 million by 2030 and 783 million by 2045 [11]. Periodontal disease affects an estimated 62% of adults worldwide, with approximately 24% having severe periodontitis [12]. The coexistence of these conditions creates a synergistic burden that significantly impacts quality of life, healthcare costs, and mortality [13,14].

Despite the well-documented evidence, periodontitis remains largely underrecognized and undertreated in routine diabetes management. The American Diabetes Association (ADA) has historically omitted oral health from its Standards of Care, although it does recommend dental referrals [15]. In contrast, the International Diabetes Federation (IDF) and the European Federation of Periodontology (EFP) have published consensus guidelines emphasizing the importance of oral health in diabetes management [16,17]. This disparity highlights the critical need for greater awareness and interdisciplinary collaboration among healthcare providers.

This comprehensive review aims to synthesize the current scientific evidence on the bidirectional relationship between diabetes mellitus and periodontal disease, focusing on epidemiology, pathophysiological mechanisms, clinical implications, and management strategies. By integrating findings from multiple systematic reviews, meta-analyses, and consensus reports, this review provides a holistic perspective on why periodontitis should be included in diabetes management and how interdisciplinary collaboration can improve patient outcomes.

2. Diabetes Mellitus: Classification, Diagnosis, and Complications

2.1 Definition and Classification

Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both [18]. The disease has a multifactorial etiology and lifelong duration, with significant implications for multiple organ systems. According to the American Diabetes Association (ADA) and the World Health Organization (WHO), diabetes is classified into several categories [19]:

Type 1 Diabetes Mellitus (T1DM): Characterized by autoimmune destruction of pancreatic β -cells, leading to absolute insulin deficiency. It accounts for approximately 5-10% of all diabetes cases and is typically presents in childhood or adolescence, although it can occur at any age. Organ-specific autoimmune markers, including glutamic acid decarboxylase antibodies (anti-GAD), are observed in approximately 90% of cases [20].

Type 2 Diabetes Mellitus (T2DM): The most common form, accounting for approximately 90% of all diabetes cases. It is characterized by insulin resistance and relative insulin deficiency. T2DM is strongly associated with obesity, physical inactivity, and genetic predisposition. The onset is typically insidious, and many individuals remain undiagnosed for years [21].

Gestational Diabetes Mellitus (GDM): Defined as glucose intolerance that develops or is first recognized during pregnancy. Women with a history of GDM have an approximately 10-fold increased risk of developing T2DM later in life [22].

Other Specific Types: Include genetic defects of β -cell function or insulin action (e.g., maturity-onset diabetes of the young, MODY), exocrine pancreas diseases, endocrine diseases, drug- or infection-induced diabetes, and genetic syndromes [23].

Prediabetes: A state of intermediate hyperglycemia that does not meet the diagnostic criteria for diabetes but carries an increased risk of progression to T2DM. Prediabetes include impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and elevated HbA1c [24].

2.2 Diagnostic Criteria

The diagnosis of diabetes is based on one of the following criteria [25]:

- Fasting plasma glucose (FPG) ≥ 126 mg/dL (7.0 mmol/L) on two occasions
- Random plasma glucose ≥ 200 mg/dL (11.1 mmol/L) in the presence of hyperglycemia symptoms
- Glycated hemoglobin (HbA1c) $\geq 6.5\%$ (48 mmol/mol)
- 2-hour plasma glucose ≥ 200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT) with 75 g glucose load

Prediabetes is defined as:

- FPG 100-125 mg/dL (5.6-6.9 mmol/L)
- 2-hour OGTT 140-199 mg/dL (7.8-11.0 mmol/L)
- HbA1c 5.7-6.4% (39-47 mmol/mol) [26]

The 10-year risk of diabetes diagnosis is approximately 88% for individuals with FPG of 126 mg/dL and HbA1c of 6.5%, compared to 55% for those with FPG of 126 mg/dL and HbA1c of 5.7-6.5% [27].

2.3 Complications of Diabetes

Chronic hyperglycemia is associated with long-term damage, dysfunction, and failure of various organs, particularly the eyes, kidneys, nerves, heart, and blood vessels [28]. The complications of diabetes are broadly classified into macrovascular and microvascular complications:

Macrovascular Complications:

- Coronary artery disease (CAD)
- Myocardial infarction (MI)
- Stroke
- Peripheral arterial disease (PAD)

Microvascular Complications:

- Diabetic retinopathy
- Diabetic nephropathy
- Diabetic neuropathy

Cardiovascular disease (CVD) is the leading cause of mortality in individuals with diabetes, accounting for over 50% of deaths [29]. Diabetes is associated with a two- to fourfold increased risk of CVD, including coronary artery disease, ischemic heart disease, heart failure, stroke, and peripheral artery disease [30]. Every 20 mg/dL increase in blood glucose increases the risk of heart failure by 23%, and even prediabetic blood sugar levels increase this risk [31].

Other complications include:

- Diabetic ketoacidosis (more common in T1DM)
- Hypoglycemia
- Increased susceptibility to infections
- Delayed wound healing
- Depression and anxiety (frequently observed in patients with T2DM) [32]
- Cognitive impairment and dementia (including Alzheimer's disease, sometimes referred to as "type 3 diabetes") [33]

2.4 Epidemiology of Diabetes

Diabetes is one of the fastest-growing global health emergencies of the 21st century. According to the IDF Diabetes Atlas, 10th edition, approximately 537 million adults (20-79 years) were living with diabetes in 2021, representing 10.5% of the adult population [11]. This number is projected to rise to 643 million by 2030 and 783 million by 2045. The majority of this increase will occur in low- and middle-income countries.

The prevalence of diabetes is higher in urban areas (4.6%) compared to rural areas (2%), reflecting the impact of urbanization, sedentary lifestyles, and dietary changes [34]. T2DM accounts for approximately 90% of all diabetes cases globally [35]. The countries with the highest numbers of people with diabetes are China, India, and the United States [36].

The global economic burden of diabetes is substantial, with healthcare expenditures estimated at \$966 billion in 2021, representing 9% of total global health expenditure [11]. Indirect costs, including lost productivity and premature mortality, further compound this burden.

3. Periodontal Disease: Classification, Pathogenesis, and Epidemiology

3.1 Definition and Classification

Periodontal diseases are chronic inflammatory conditions affecting the soft and hard tissues surrounding the teeth [37]. The 2018 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions introduced a new classification system that categorizes periodontal diseases into three main groups [38]:

1. **Periodontal Health and Gingival Diseases:**
 - Periodontal health and gingival health
 - Gingivitis induced by dental biofilm
 - Gingival diseases not induced by dental biofilm
2. **Necrotizing Periodontal Diseases:**
 - Necrotizing gingivitis
 - Necrotizing periodontitis
 - Necrotizing stomatitis
3. **Periodontitis:**
 - Periodontitis
 - Periodontitis as a manifestation of systemic disease
 - Systemic diseases or conditions affecting the periodontal supporting tissues

Gingivitis is a reversible inflammatory condition of the gingiva caused by dental plaque accumulation. It is characterized by redness, edema, bleeding on probing, and discomfort. Gingivitis can be resolved with improved oral hygiene practices [39].

Periodontitis is a chronic, multifactorial inflammatory disease characterized by progressive destruction of the periodontal ligament and alveolar bone, leading to tooth loss if untreated [40]. The disease results from a complex interaction between dysbiotic bacterial communities and the host immune response.

3.2 Staging and Grading of Periodontitis

The 2018 classification introduced a staging and grading system to provide a more comprehensive diagnosis and personalized treatment planning [41]:

Staging (Severity):

- **Stage I (Initial):** Clinical attachment loss (CAL) 1-2 mm, radiographic bone loss (RBL) <15%, no tooth loss
- **Stage II (Moderate):** CAL 3-4 mm, RBL 15-33%, no tooth loss
- **Stage III (Severe):** CAL ≥5 mm, RBL extending to mid-third of root and beyond, ≤4 teeth lost due to periodontitis
- **Stage IV (Severe with potential loss of dentition):** CAL ≥5 mm, RBL extending to mid-third of root and beyond, ≥5 teeth lost due to periodontitis

Grading (Progression):

- **Grade A (Slow):** No loss over 5 years, RBL/age ratio <0.25
- **Grade B (Moderate):** <2 mm over 5 years, RBL/age ratio 0.25-1.0
- **Grade C (Rapid):** ≥2 mm over 5 years, RBL/age ratio >1.0

Diabetes is incorporated as a grade modifier, with HbA1c <7.0% indicating Grade B and HbA1c ≥7.0% indicating Grade C [42].

3.3 Pathogenesis of Periodontal Disease

The pathogenesis of periodontitis involves a complex interplay between microbial dysbiosis and the host immune response [43]. The subgingival microbiome harbors at least 700 bacterial species, along with viruses, fungi, and archaea [44]. Key periodontal pathogens include:

- *Porphyromonas gingivalis* (Pg)
- *Aggregatibacter actinomycetemcomitans* (Aa)
- *Tannerella forsythia* (Tf)
- *Treponema denticola* (Td)

P. gingivalis has been described as "a master of immune subversion" due to its sophisticated mechanisms to evade host immune detection and destruction [45]. The bacterium produces various virulence factors, including lipopolysaccharide (LPS), gingipains (cysteine proteases), and fimbriae, which facilitate tissue invasion and immune evasion.

The host inflammatory response, rather than the bacteria themselves, is primarily responsible for periodontal tissue destruction. The inflammatory cascade involves:

1. **Initial innate immune response:** Polymorphonuclear leukocytes (PMNs) migrate to the gingival sulcus and release proteolytic enzymes and reactive oxygen species (ROS) [46].
2. **Adaptive immune response:** Activation of T and B lymphocytes, leading to plasma cell differentiation and antibody production [47].
3. **Cytokine and mediator release:** Pro-inflammatory cytokines, including interleukin-1 β (IL-1 β), IL-6, tumor necrosis factor- α (TNF- α), and prostaglandin E2 (PGE2), induce connective tissue degradation and bone resorption [48].
4. **Matrix metalloproteinases (MMPs):** MMP-8, MMP-9, and MMP-13 degrade collagen and other extracellular matrix components [49].
5. **RANKL/OPG system:** Receptor activator of nuclear factor kappa-B ligand (RANKL) promotes osteoclast activation and bone resorption, while Osteoprotegerin (OPG) acts as a decoy receptor [50].

3.4 Epidemiology of Periodontal Disease

Periodontal disease is one of the most common chronic conditions worldwide. According to the Global Burden of Disease (GBD) study, severe periodontitis was the 11th most prevalent condition globally in 2010, affecting approximately 743 million people [12]. A recent systematic review and meta-analysis estimated the global prevalence of periodontitis at 62%, with severe periodontitis affecting approximately 24% of adults [12].

The prevalence of periodontitis increases with age, with the highest rates observed in adults aged 30-50 years and older [40]. Other risk factors include:

- **Modifiable:** Smoking, poor oral hygiene, diabetes, obesity, unhealthy diet, alcohol consumption, stress [3]
- **Non-modifiable:** Age, genetic predisposition, race/ethnicity, socioeconomic status [4]

In individuals with diabetes, the prevalence of periodontitis is significantly higher. Among those with T2DM, prevalence estimates range from 70-80%, with some studies reporting rates exceeding 90% [21,22]. A meta-analysis of 53 studies found that T2DM increases the risk of developing periodontitis by 34% and is associated with greater disease severity, including two additional missing teeth, greater attachment loss, and deeper periodontal pockets [21].

4. Pathophysiological Mechanisms Linking Diabetes and Periodontal Disease

The bidirectional relationship between diabetes and periodontal disease is mediated by complex interrelated mechanisms involving inflammation, oxidative stress, immune dysfunction, and microbial dysbiosis [6]. Figure 1 illustrates the conceptual model of these interactions.

4.1 Effect of Hyperglycemia on Periodontal Tissues

4.1.1 Inflammation and Immune Dysregulation

Hyperglycemia induces a state of chronic low-grade inflammation that exacerbates periodontal tissue destruction [7]. Key mechanisms include:

Advanced Glycation End-Products (AGEs): Chronic hyperglycemia leads to the non-enzymatic glycation of proteins and lipids, forming AGEs. The binding of AGEs to their receptor (RAGE) on cell surfaces activates pro-inflammatory signaling cascades, including NF- κ B, leading to increased production of IL-1 β , TNF- α , and IL-6 [8]. AGEs also increase the respiratory burst in PMNs, potentially increasing localized tissue damage in periodontitis [8].

Oxidative Stress: Hyperglycemia increases the production of reactive oxygen species (ROS) through various pathways, including mitochondrial dysfunction, increased polyol pathway flux, and activation of protein kinase C [9]. ROS-induced oxidative stress impairs insulin secretion and action, creating a vicious cycle. In periodontal tissues, oxidative stress contributes to tissue destruction and impaired healing [9].

Impaired Neutrophil Function: Diabetes is associated with defects in PMN chemotaxis, phagocytosis, and bactericidal activity [10]. These defects impair the host's ability to control bacterial growth, leading to more severe periodontal destruction. Additionally, defective PMN apoptosis leads to increased retention of PMNs in periodontal tissues, causing greater tissue destruction through continuous secretion of MMPs and ROS [10].

Cytokine Dysregulation: Hyperglycemia enhances the expression of pro-inflammatory cytokines and MMPs in periodontal tissues [6]. Gingival crevicular fluid (GCF) levels of PGE2 and IL-1 β are higher in patients with diabetes and periodontitis compared to non-diabetic individuals with similar periodontal status [7]. A study found significantly higher GCF IL-1 β levels in T2DM patients with HbA1c >8% than in those with HbA1c <8%, indicating that glycemic control directly influences local inflammatory burden [8].

Altered Bone Metabolism: Diabetes adversely affects bone metabolism through multiple mechanisms. AGEs have detrimental effects on bone repair and formation, reducing extracellular matrix production [8]. Diabetes enhances osteoclastogenesis by increasing RANKL release and reduces new bone formation by enhancing apoptosis of bone-forming cells and lowering periodontal ligament stem cell proliferation and differentiation [50].

4.1.2 Microbial Dysbiosis

The composition of the subgingival microbiome is significantly different in normoglycemia and hyperglycemia [11]. Diabetes is associated with:

- Reduced microbial diversity
- Increased abundance of pathogenic species (e.g., *Corynebacterium*, *Lactobacillus*, *Saccharibacteria*)
- Decreased abundance of beneficial species (e.g., *Prevotella*, *Filifactor*) [11]

The degree of glycemic control influences the oral microbiome, with higher HbA1c levels associated with greater reductions in diversity and increased proportions of carbohydrate-utilizing species such as *Veillonellaceae* and *Prevotellaceae* [12]. These microbial shifts favor the development of dysbiosis and exacerbate periodontal inflammation.

4.2 Effect of Periodontitis on Glycemic Control

4.2.1 Systemic Inflammation and Insulin Resistance

Periodontitis contributes to impaired glycemic control through the systemic dissemination of periodontal pathogens and inflammatory mediators [13]. Key mechanisms include:

Bacteremia and Endotoxemia: Chronic periodontitis-associated bacteremia and the release of bacterial products, particularly LPS, into the bloodstream trigger systemic inflammatory responses [13]. LPS activates Toll-like receptors (TLRs) on immune cells, leading to the production of pro-inflammatory cytokines that interfere with insulin signaling [14].

Inflammatory Cytokines: Elevated levels of IL-6, TNF- α , and C-reactive protein (CRP) are observed in patients with periodontitis [14]. These cytokines impair insulin signaling by:

- Inhibiting hepatic glycogen synthesis
- Increasing hepatic gluconeogenesis
- Blocking the insulin receptor substrates via production of branched-chain amino acids (BCAA)
- Reducing glucose-induced insulin production [15]

Insulin Resistance: Periodontitis-induced systemic inflammation promotes insulin resistance in hepatic and adipose tissues [16]. A study demonstrated that periodontal treatment reduces insulin resistance and improves insulin sensitivity in T2DM [16].

Gut Dysbiosis: Swallowed periodontal bacteria can induce gut dysbiosis, leading to endotoxemia and changes in the blood metabolome that further impair glucose metabolism [17].

4.2.2 Effect of Periodontitis on Diabetes Complications

Periodontitis negatively influences glucose control in existing T2DM and contributes to incident T2DM and diabetes complications in a dose-response manner [18]. Moderate-to-severe periodontitis has been associated with:

- Increased macroalbuminuria
- End-stage renal disease
- Atherosclerotic plaque calcification
- Carotid intima-media thickening
- Cardiovascular mortality [19]

A longitudinal study of Pima Indians found that severe periodontitis was associated with a 6-fold increased risk of poor glycemic control over a 2-year period [20]. Another study demonstrated that periodontitis was associated with ischemic heart disease and diabetic nephropathy in individuals with T2DM [20].

4.3 Mechanisms Linking Periodontitis to Cardiovascular Disease in Diabetes

The relationship between periodontitis and cardiovascular disease in individuals with diabetes is particularly concerning, as cardiovascular disease is the leading cause of mortality in this population [29]. Several mechanisms have been proposed:

Endothelial Dysfunction: Periodontal pathogens and their products can translocate into the systemic circulation, causing endothelial dysfunction and promoting atherogenesis [18]. *P. gingivalis* has been detected in atherosclerotic lesions, providing direct evidence of this mechanism [18].

Systemic Inflammation: Periodontitis contributes to a persistent low-grade inflammatory state, characterized by elevated levels of IL-6, TNF- α , and CRP [14]. These inflammatory mediators promote endothelial dysfunction, activate immune and vascular cells, and increase the production of pro-thrombotic factors [14].

Increased Adhesion Molecules: Endothelial cells express higher levels of adhesion molecules such as VCAM-1 and ICAM-1 in response to periodontal inflammation, both of which are closely associated with atheroma formation [19].

Pro-thrombotic State: Chronic inflammation stimulates the production of fibrinogen and plasminogen activator inhibitors, increasing the likelihood of arterial thrombosis [19].

Epidemiological studies support these mechanistic findings. The Pittsburgh Epidemiology of Diabetes Complications study, which included over 300 individuals with T1DM, identified periodontitis as a significant predictor of coronary artery disease and major

cardiovascular events [29]. A large-scale study involving approximately 4,300 individuals with diabetes from the NHANES database found a significant association between periodontitis and both cardiovascular-related and all-cause mortality [30].

5. Clinical Evidence for the Bidirectional Relationship

5.1 Epidemiological Evidence

The association between diabetes and periodontal disease has been extensively studied in cross-sectional, case-control, cohort, and intervention studies [1]. Key findings include:

Pima Indian Studies: The Pima Indian population, which has a high prevalence of T2DM, has been instrumental in establishing the association between diabetes and periodontal disease. Early studies by Shlossman et al. found increased prevalence of periodontitis in diabetic versus non-diabetic individuals [20]. Emrich et al. reported that T2DM patients were 2.8-fold more likely to develop clinical attachment loss and 3.4-fold more likely to show radiographic bone loss [20]. Nelson et al. found periodontitis in 60% of individuals with T2DM versus 36% of non-diabetics [20].

Meta-analyses: A systematic review and meta-analysis of 53 studies found that T2DM increases the risk of developing periodontitis by 34% [21]. In cases of severe periodontitis, the risk may increase by 53% [21]. Another meta-analysis of 15 studies confirmed a bidirectional association between periodontal disease and diabetes [2].

Prevalence in Diabetes: The prevalence of periodontal disease among individuals with diabetes varies by diabetes type. In T1DM, a recent meta-analysis reported a prevalence of approximately 18.5% with an odds ratio of 2.5 compared to the general population [22]. In T2DM, prevalence estimates range from 70-80%, with some studies reporting rates greater than 90% [21,22].

Gestational Diabetes: A systematic review and meta-analysis of 10 studies found that periodontitis increases the risk of gestational diabetes by 66% [23].

5.2 Effect of Periodontal Treatment on Glycemic Control

Intervention studies have consistently demonstrated that periodontal treatment improves glycemic control in patients with diabetes [24]. A landmark Cochrane review of 35 randomized controlled trials involving 3,249 participants found that periodontal treatment resulted in an absolute reduction in HbA1c of approximately 0.43% at 3-4 months, 0.30% at 6 months, and 0.50% at 12 months [24]. This magnitude of HbA1c reduction is clinically significant, comparable to the effect of adding a second oral antidiabetic medication to metformin [25].

For clinical perspective, a 1 percentage point reduction in HbA1c may reduce diabetes mortality by 21%, myocardial infarction by 14%, and microvascular complications by 37% [26]. Therefore, the 0.5 percentage point reduction achieved through periodontal therapy could translate into substantial clinical benefits.

Key studies include:

Kiran et al. (2005): A randomized controlled trial in 44 patients with T2DM and periodontal disease found that non-surgical periodontal treatment achieved a 50% reduction in bleeding prevalence at 3 months and an increase in glycemic control of 0.8% compared to untreated controls [27].

Faria-Almeida et al. (2006): A 6-month controlled clinical trial in 20 patients demonstrated that periodontal treatment significantly enhanced metabolic control, with improvements in both clinical and metabolic (HbA1c) variables in the treated group [28].

Simpson et al. (2022): The Cochrane review found that treating periodontitis leads to an HbA1c reduction of about 0.43% at 3-4 months, 0.30% at 6 months, and 0.50% at 12 months [24].

Kaur et al. (2015): A study of 100 T2DM patients with chronic periodontitis found significant improvements in periodontal parameters and a 10.8% reduction in HbA1c at 3 and 6 months [31]. However, patients with poor baseline glycemic control showed less clinical improvement.

Baeza et al. (2020): A systematic review and meta-analysis of 9 studies found that scaling and root planing (SRP) was effective in improving metabolic control and reducing systemic inflammation in patients with T2DM [32].

5.3 Effect of Periodontal Treatment on Inflammatory Markers

Periodontal treatment decreases levels of several inflammatory biomarkers that are risk factors for diabetes complications [33]. Statistically significant decreases in C-reactive protein (CRP) concentration from baseline to each 3-monthly visit up to 1 year have been reported following periodontal therapy [33]. Reductions in IL-6, TNF- α , and MMPs have also been observed [34]. These reductions in systemic inflammation may contribute to improved glycemic control and reduced cardiovascular risk.

5.4 Effect of Periodontal Treatment on Healthcare Costs

Periodontal therapy has been associated with reduced healthcare costs for individuals with diabetes [35]. Studies have demonstrated:

- Decreased expenses for diabetes-care and other medical care, including pharmaceuticals and hospitalizations [35]
- Cost reductions of US\$75 to US\$237 following periodontal treatment [36,37]
- Reduced productivity loss due to illness [38]

A study analyzing dental and medical claims data found that periodontal treatment was associated with decreased diabetes mellitus-related treatment costs [39]. These findings support the notion that periodontal care is not only clinically effective but also cost-effective.

6. Interprofessional Collaboration in Diabetes and Periodontal Disease Management

6.1 The Case for Integrated Care

The evidence strongly supports the need for integrated medical-dental care models for patients with diabetes and periodontal disease [40]. Key arguments include:

1. **High Prevalence of Undiagnosed Diabetes:** Almost half of people with diabetes and 90% of those with prediabetes are unaware of their condition [11]. The dental setting can serve as a valuable point of identification for these individuals.
2. **Bidirectional Benefits:** Treating periodontal disease improves glycemic control and improving glycemic control benefits periodontal health [2]. This reciprocal relationship creates opportunities for mutual benefit through integrated care.
3. **Cost-Effectiveness:** Periodontal therapy reduces healthcare costs for diabetes care and other medical care [35].
4. **Legal Considerations:** As patients become increasingly aware of the importance of periodontal health for general health, failure to refer for periodontal examination and treatment may have legal consequences [41].

6.2 Screening for Diabetes in the Dental Setting

The dental setting is increasingly recognized as an ideal location for diabetes screening [42]. Two systematic reviews and meta-analyses of studies involving finger prick blood sampling among dental patients denying hyperglycemia calculated a T2DM prevalence of 1.7%-46.4% and prediabetes prevalence of 23.3%-68.0% [43]. Gingival crevicular blood from periodontal pockets is also a valid screening tool due to its high correlation with serum glucose concentration [44]. Hyperglycemia screening in the dental setting has been found to be cost-effective [45].

Tools such as the Finnish Diabetes Risk Score (FINDRISC) and periodontal disease risk scores are significantly correlated [46]. The IDF-EFP Oral Health Checklist facilitates early detection in medical settings by linking periodontal risk with systemic health and guiding referral [16].

6.3 Screening for Periodontal Disease in the Medical Setting

Conversely, medical settings can facilitate periodontal disease screening. The American Academy of Periodontology (AAP) recently created a 38-page report and 3 infographics that include diabetes [47]. The International Diabetes Federation (IDF) acknowledged the importance of good oral health in diabetes management by including an oral health section in the 9th edition of the IDF Diabetes Atlas [48]. The IDF and EFP published a consensus document with guidelines upon a joint workshop [16,17].

However, the ADA's Standards of Care in Diabetes still cites dated oral health-related references and does not consider periodontitis as part of ongoing diabetes management [15]. This is despite the ADA emphasizing a holistic approach to diabetes care in its consensus statement with the European Association for the Study of Diabetes (EASD) [15].

6.4 Barriers to Integrated Care

Despite the evidence, integrated care is rarely practiced [40]. Barriers include:

- **Time constraints:** Both medical and dental providers cite lack of time as a barrier to addressing oral health [40]
- **Lack of knowledge:** Many healthcare providers have limited knowledge about the bidirectional relationship between diabetes and periodontal disease [40]
- **Cost and insurance coverage:** Financial barriers, particularly in lower-income populations, limit access to dental care [49]
- **Lack of equipment:** Some dental practices lack the equipment for chairside glucose screening [42]
- **Patient cooperation:** Some patients are reluctant to undergo screening or treatment [42]

6.5 Models of Integrated Care

Several models of integrated care have been proposed or implemented:

Marshfield Clinic Health System (MCHS): An exception to the rarity of integrated care, MCHS has implemented a model that integrates medical and dental care for patients with diabetes [50].

Oral Care Protocol for Primary Diabetes Care: A pilot cluster-randomized controlled trial in the Netherlands implemented an oral care protocol for primary diabetes care, demonstrating feasibility and potential benefits [40].

Community Health Worker Strategy: A randomized controlled trial in Taiwan found that nonsurgical periodontal treatment with community health worker support had positive effects on periodontal treatment outcomes, oral health-related quality of life, and oral self-care behaviors in patients with T2DM [31].

6.6 Recommendations for Interprofessional Collaboration

Based on the available evidence, the following recommendations are proposed:

1. **Medical Providers Should:**
 - Include oral health assessment in routine diabetes care
 - Refer patients with diabetes to dental professionals for comprehensive periodontal examination
 - Educate patients about the bidirectional relationship between diabetes and periodontal disease
 - Consider periodontal disease as a potential contributor to poor glycemic control
 - Collaborate with dental professionals in managing patients with both conditions
2. **Dental Providers Should:**
 - Screen patients for diabetes and prediabetes using chairside tests
 - Educating patients about the importance of glycemic control for periodontal health
 - Provide timely periodontal treatment for patients with diabetes

- Communicate with medical providers about patients' periodontal status and treatment outcomes
- Encourage patients with diabetes to maintain regular dental visits

3. **Healthcare Systems Should:**

- Integrate medical and dental records
- Provide reimbursement for diabetes screening in dental settings
- Support interprofessional education and collaboration
- Develop clinical pathways for integrated care

7. Clinical Management of Patients with Diabetes and Periodontal Disease

7.1 Periodontal Treatment in Patients with Diabetes

7.1.1 Non-Surgical Periodontal Therapy

Non-surgical periodontal treatment (NSPT), also known as "deep cleaning," is the cornerstone of periodontal therapy [1]. It includes:

- **Scaling and Root Planing (SRP):** Removal of soft and hardened plaque (calculus) above and below the gum line
- **Oral Hygiene Instruction:** Education on proper tooth brushing, flossing, and other plaque control measures
- **Risk Factor Modification:** Counseling on smoking cessation, dietary improvement, and glycemic control

NSPT can be provided by dental hygienists or dentists in general dental offices, although severe cases should be referred to specialists [1]. The treatment typically requires multiple visits and may be performed under local anesthesia.

7.1.2 Adjunctive Therapies

In some cases, adjunctive therapies may be considered:

- **Systemic Antibiotics:** May be beneficial in cases involving gram-negative periodontal pathogens, particularly in young individuals with generalized severe disease or refractory disease [32]
- **Local Antimicrobials:** Subgingival delivery of antimicrobial agents may provide additional benefits in specific sites
- **Host Modulation:** Sub-antimicrobial dose doxycycline may be considered where indicated [32]

7.1.3 Surgical Periodontal Therapy

In cases where non-surgical therapy proves insufficient, surgical intervention may be warranted:

- **Flap Surgery:** Elevation of gingival flaps to access deep pockets for debridement
- **Osseous Recontouring:** Reshaping of bone to eliminate deep pockets and establish a more maintainable architecture
- **Regenerative Procedures:** Use of enamel matrix derivatives, bone grafts, and guided tissue regeneration to restore lost periodontal structures [32]

7.1.4 Periodontal Maintenance

Following active treatment, patients transition into a structured periodontal maintenance program [50]. Maintenance visits typically occur at 3- to 4-month intervals and involve:

- Clinical monitoring of periodontal status
- Reinforcement of oral hygiene practices
- Removal of new biofilm deposits
- Assessment of glycemic control and coordination with medical providers

The frequency and nature of maintenance appointments may be modified based on the patient's individual risk profile and response to therapy [50].

7.2 Glycemic Control in Patients with Periodontal Disease

7.2.1 Medical Management of Diabetes

Optimal glycemic control is essential for both diabetes management and periodontal health [25]. Treatment approaches include:

- **Lifestyle Modifications:** Diet, exercise, weight management
- **Pharmacotherapy:** Oral antidiabetic agents (e.g., metformin, sulfonylureas, DPP-4 inhibitors, SGLT2 inhibitors) and insulin
- **Regular Monitoring:** HbA1c testing, self-monitoring of blood glucose
- **Complication Screening:** Regular eye, kidney, and foot examinations

7.2.2 Target HbA1c Levels

The American Diabetes Association recommends an HbA1c target of <7.0% for most adults with diabetes [25]. However, targets should be individualized based on:

- Duration of diabetes
- Age and life expectancy
- Comorbidities
- Risk of hypoglycemia
- Patient preferences

For patients with periodontal disease, achieving HbA1c <7.0% may be particularly beneficial, as this level is associated with reduced risk of periodontal progression and improved response to periodontal therapy [42].

7.3 Considerations for Dental Treatment in Patients with Diabetes

7.3.1 Pre-Treatment Assessment

Before initiating dental treatment, a thorough medical history should be obtained, including:

- Type and duration of diabetes
- Current medications and glycemic control
- History of hypoglycemia
- Presence of diabetes complications (cardiovascular, renal, neurological)
- Recent HbA1c levels

7.3.2 Management of Hypoglycemia Risk

Patients with diabetes, particularly those on insulin or sulfonylureas, are at risk of hypoglycemia during dental procedures [41].

Preventive measures include:

- Scheduling appointments in the morning after breakfast
- Confirming that the patient has taken their usual medications
- Having glucose sources available (e.g., orange juice, glucose tablets)
- Monitoring for signs of hypoglycemia (e.g., sweating, tremors, confusion)

7.3.3 Infection Control and Wound Healing

Patients with diabetes may have impaired immune function and delayed wound healing [41]. Considerations include:

- Use of prophylactic antibiotics for invasive procedures in patients with poorly controlled diabetes
- Meticulous infection control practices
- Post-operative follow-up to monitor healing
- Coordination with medical providers for glycemic management

7.3.4 Dental Implants in Patients with Diabetes

Dental implants are a viable option for tooth replacement in patients with diabetes, but outcomes may be affected by glycemic control [41]. Patients with hyperglycemia experience:

- Greater risk for peri-implantitis (15-fold risk reported in metabolic syndrome)
- Higher implant failure rates compared to non-diabetic individuals
- Greater failure rates in T1DM than in T2DM

Therefore, optimal glycemic control and careful patient selection are essential for successful implant outcomes [41].

8. Discussion

8.1 Synthesis of Evidence

The evidence presented in this review unequivocally supports a bidirectional relationship between diabetes mellitus and periodontal disease. Diabetes increases the risk and severity of periodontal disease through multiple mechanisms, including hyperglycemia-induced inflammation, oxidative stress, immune dysfunction, and microbial dysbiosis. Conversely, periodontitis adversely affects glycemic control through systemic dissemination of periodontal pathogens and inflammatory mediators, leading to insulin resistance and contributing to diabetes complications.

The clinical significance of this relationship is underscored by the finding that periodontal treatment can reduce HbA1c levels by approximately 0.5 percentage points, a magnitude comparable to adding a second oral antidiabetic medication [24,25]. This reduction is clinically meaningful, as a 1 percentage point reduction in HbA1c is associated with a 21% reduction in diabetes mortality, 14% reduction in myocardial infarction, and 37% reduction in microvascular complications [26].

Furthermore, periodontal therapy reduces systemic inflammatory markers, decreases diabetes-related healthcare costs, and may lower the risk of cardiovascular complications [33,35,39]. These findings support the inclusion of periodontal disease in diabetes management as a novel, economical tool for improving glycemic control and reducing complications.

8.2 Implications for Clinical Practice

The evidence has several important implications for clinical practice:

1. **Screening:** Dental professionals should screen patients for diabetes and prediabetes, and medical professionals should screen patients with diabetes for periodontal disease.
2. **Referral:** Patients with diabetes should receive at least annual dental checkups, and those with periodontal disease should be referred for appropriate treatment.
3. **Treatment:** Periodontal treatment should be considered an adjunct to standard diabetes care, with the potential to improve glycemic control and reduce complications.
4. **Collaboration:** Medical and dental professionals should collaborate in patient-centered care for their mutual patients with or at risk for hyperglycemia.
5. **Education:** Both medical and dental curricula should include content on the bidirectional links between oral health and systemic health.

8.3 Implications for Health Policy

The evidence supports several policy recommendations:

1. **Integration of Medical and Dental Records:** Healthcare systems should integrate medical and dental records to facilitate communication and coordination of care.
2. **Reimbursement for Screening:** Dental practices should be reimbursed for diabetes screening services.
3. **Coverage for Periodontal Treatment:** Insurance coverage should include periodontal treatment for patients with diabetes, recognizing its role in glycemic control and complication prevention.
4. **Interprofessional Education:** Medical and dental schools should implement interprofessional education programs to foster collaboration.
5. **Public Awareness:** Public health campaigns should raise awareness of the bidirectional relationship between diabetes and periodontal disease.

8.4 Limitations of Current Evidence

While the evidence is strong, several limitations should be acknowledged:

1. **Heterogeneity of Studies:** Studies vary in their definitions of periodontitis, diagnostic criteria, and outcome measures, limiting comparability [50].
2. **Short Follow-up:** Most intervention studies have follow-up periods of 3-12 months, limiting assessment of long-term effects [24].
3. **Confounding Factors:** Observational studies may be subject to confounding by factors such as smoking, socioeconomic status, and other comorbidities.
4. **Generalizability:** Findings from specific populations (e.g., Pima Indians) may not be generalizable to all populations.
5. **Lack of Standardized Protocols:** There is no standardized protocol for periodontal treatment in patients with diabetes, and the optimal frequency and intensity of treatment remain unclear.

8.5 Future Research Directions

Future research should address:

1. **Long-term Outcomes:** Randomized controlled trials with longer follow-up periods (>12 months) are needed to assess the sustained effects of periodontal therapy on glycemic control and diabetes complications.
2. **Dose-Response Relationship:** Studies should investigate the optimal frequency and intensity of periodontal treatment for improving glycemic control.
3. **Patient Subgroups:** Research should identify which subgroups of patients with diabetes are most likely to benefit from periodontal treatment.
4. **Mechanistic Studies:** Further research is needed to elucidate the precise mechanisms linking periodontitis and diabetes, including the role of specific pathogens and inflammatory mediators.
5. **Cost-Effectiveness:** More studies are needed to assess the cost-effectiveness of integrated care models in different healthcare systems.
6. **Intervention Studies:** Randomized controlled trials of integrated medical-dental care models are needed to demonstrate effectiveness.

9. Conclusion

Diabetes mellitus and periodontal disease are two highly prevalent chronic inflammatory conditions that exhibit a well-established bidirectional relationship. Diabetes increases the risk and severity of periodontal disease through mechanisms involving hyperglycemia-induced inflammation, oxidative stress, immune dysfunction, and AGE accumulation. Conversely, periodontitis adversely affects glycemic control through systemic dissemination of periodontal pathogens and inflammatory mediators, leading to insulin resistance and contributing to diabetes complications.

Periodontal disease has been recognized as the "sixth complication" of diabetes, and the evidence supports its inclusion in diabetes management. Non-surgical periodontal treatment can reduce HbA1c levels by approximately 0.5 percentage points, a clinically significant improvement comparable to adding a second oral antidiabetic medication. Furthermore, periodontal therapy reduces systemic inflammatory markers, decreases diabetes-related healthcare costs, and may lower the risk of cardiovascular complications. Despite this robust evidence, periodontitis remains underdiagnosed and undertreated in the context of routine diabetes care. Integrated medical-dental collaboration, early screening, and timely periodontal intervention are essential to optimize outcomes for patients with diabetes and periodontal disease. Medical and dental professionals are strongly encouraged to collaborate in patient-centered care for their mutual patients with or at risk for hyperglycemia.

The importance of keeping disease-free, natural teeth for proper biting and chewing, smiling, self-esteem, and pain avoidance cannot be overestimated. The great importance of a healthy oral cavity free of infection and subsequent inflammation, especially periodontitis that if untreated will cause loosening and eventually loss of affected teeth—has largely gone unnoticed by the medical community. It is time for this to change. Through sustained efforts in knowledge translation, professional education, and health system integration, the medical and dental professions can work in concert to address the common inflammatory basis of diabetes and periodontal disease, improving patient outcomes across disciplines.

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