

# Type 2 Diabetes Mellitus as a Risk Factor for Periodontal Disease

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It has long been recognised that patients with type 2 diabetes mellitus (T2DM) tend to suffer from advanced forms of periodontal disease, particularly if they have poor glycaemic control. Many studies have reported T2DM to be a risk factor for periodontitis, with diabetic populations demonstrating increased gingival inflammation, probing depths, attachment loss and alveolar bone destruction compared with non-diabetic controls. T2DM is increasingly viewed as an inflammatory condition, and dysregulated immune-inflammatory responses in patients with T2DM may increase susceptibility to periodontal disease by disrupting local cytokine networks in the periodontium. Cytokines such as interleukin-6 (IL-6) and tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) play a role in the pathogenesis of both diseases, and together with other mediators such as the IL-1 family of cytokines and adipokines may, in part, provide a mechanistic link between T2DM and periodontitis. Altered neutrophil function and deposition of advanced glycation endproducts (AGEs) are also likely to play key roles in increasing susceptibility to periodontitis in patients with T2DM. Emerging data have recently suggested that periodontal treatment may have a favourable impact on glycaemic control. Such findings, if confirmed, would present opportunities for the dental team to become increasingly involved in the general management of patients with both periodontal disease and T2DM.

**Key words:** periodontal disease, risk factors, type 2 diabetes mellitus

## INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a common, complex disease with a variable clinical presentation and is associated with significant complications affecting both quality and length of life. In 2000, approximately 150 million people worldwide were affected by T2DM, which is now viewed as a rapidly growing global epidemic predicted to affect 300 million people by 2025 (Zimmet et al, 2001). Prevention and management of T2DM and its associated complications have become major health-care challenges throughout the world, particularly in developing economies (Narayan et al, 2000).

The term 'diabetes' encompasses a group of metabolic disorders characterised by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. The vast majority of cases of diabetes fall into two broad categories, type 1 and type 2. Type 1 diabetes mellitus (T1DM) is caused by an absolute deficiency of insulin secretion and can be identified by the presence of serological markers indicating autoimmune destruction of the  $\beta$  cells of the pancreas. In T2DM, the focus of this review, the main causal processes are insulin resistance (i.e. an inability of the body to respond normally to insulin) and failure of pancreatic  $\beta$  cells to produce sufficient insulin. The subsequent hypergly-



caemia has wide ranging molecular and cellular effects resulting in oxidative stress, upregulation of pro-inflammatory responses and vascular changes that collectively predispose individuals to the classic diabetes complications of retinopathy, nephropathy, neuropathy, macrovascular disease and atherosclerosis.

T2DM tends to present mainly in middle age and later life, and early symptoms can be vague; thus many patients remain undiagnosed, whereas others are diagnosed by chance during investigations for other conditions. T2DM is a heterogeneous condition, and arises from interactions between environmental stressors (such as obesity, sedentary lifestyle and high calorie food intake) and genetic susceptibility that result in increased insulin resistance and the clinical manifestations of disease.

#### THE ASSOCIATION BETWEEN T2DM AND PERIODONTITIS

A number of case reports, cross-sectional studies, and a few longitudinal studies have reported an increased prevalence of periodontal disease in patients with T2DM. Indeed, periodontal disease has been termed the sixth complication of diabetes (Loe, 1993) and it is now widely accepted in the periodontal community that T2DM is an important risk factor for periodontal disease.

Epidemiological surveys of non-diabetic individuals have found that advanced periodontitis severe enough to threaten tooth retention affects approximately 10–15% of adults in Western populations (Brown et al, 1996; Kelly et al, 2000). Key steps in the pathogenesis of periodontal disease include acquisition of a pathogenic microflora and the development of a dysregulated, destructive host immune-inflammatory response to the presence of the subgingival biofilm. The majority of destruction seen in periodontitis is mediated by infiltrating inflammatory cells (including neutrophilic polymorphonuclear leukocytes (PMNL), macrophages, T- and B-lymphocytes) and modified resident periodontal cells including fibroblasts and epithelial cells. These cells secrete elevated quantities of pro-inflammatory mediators, including interleukins and prostaglandins, in addition to destructive enzymes such as matrix metalloproteinases (MMPs).

Whereas traditional thinking previously maintained that periodontal disease is a local inflammatory

condition (i.e. the upregulated, maladapted inflammatory response remains localised to the periodontium), more recent investigations have raised the possibility of associations between periodontitis and various systemic conditions (Mattila et al, 1989; DeStefano et al, 1993; Offenbacher, 1996), including diabetes (Iacopino, 2001; Taylor, 2001). Indeed, periodontal disease is now widely recognised as a complication of diabetes (Salvi et al, 1997b) and epidemiological evidence supports associations between diabetes and increased prevalence and severity of periodontal disease (Taylor, 2001). Although the majority of studies have been cross-sectional in design, typically describing findings from small convenience samples, there is a smaller subset of population-based studies that strongly support associations between diabetes and periodontal disease (Nelson et al, 1990; Shlossman et al, 1990; Emrich et al, 1991; Taylor et al, 1998).

Several of these studies have focused on the Pima Indians, a population suffering from very high prevalence rates of T2DM. In this population, diabetic subjects were 2.8 times and 3.4 times more likely to have periodontal disease compared with non-diabetic controls when periodontitis was defined by clinical attachment loss or radiographic bone loss respectively (Emrich et al, 1991). The increased risk for periodontal disease could not otherwise be explained by age, gender or oral hygiene. In another study of the Pima Indians, the prevalence of periodontal disease was 60% in 720 subjects with T2DM and 36% in 1,553 subjects without diabetes (Nelson et al, 1990). The incidence of periodontal disease over an interval of approximately 2.6 years was also determined in a subset of individuals with no evidence of periodontal disease at the start of the monitoring period ( $n = 701$ , of whom 56 had T2DM). The incidence of periodontal disease in that time period was 2.6 times higher in the subjects with T2DM than that observed in the non-diabetic controls (Nelson et al, 1990).

T2DM patients with poor glycaemic control have a much greater risk of progressive alveolar bone loss (odds ratio, OR 11.4) than well controlled T2DM patients (OR 2.2) compared with non-diabetic subjects (Taylor et al, 1998). Interestingly, this study also provided evidence to support a possible negative effect of periodontitis on glycaemic control, as subjects with moderate or well controlled T2DM at

baseline who also had severe periodontitis were approximately 6 times more likely to have poor glycaemic control at 2 years follow-up than the subjects who did not have severe periodontitis at baseline (Taylor et al, 1998).

Observations such as these lend support to the concept of a 'bi-directional' relationship between T2DM and periodontal disease, with T2DM being associated with increased prevalence and severity of periodontal disease, and periodontitis being associated with poorer glycaemic control. There are, however, very few clinical studies that have investigated this premise in a convincing manner, highlighting the need for further population-based investigations to characterise both periodontal status in patients with T2DM and the impact of periodontitis on glycaemic control. The principal findings of recent key studies that have investigated associations between periodontal disease and T2DM are summarised in Table 1.

#### MECHANISMS THAT LINK T2DM AND PERIODONTAL DISEASE

The observed epidemiological associations between periodontitis and T2DM may arise from common pathological defects that result in increased susceptibility to both diseases. Periodontitis and diabetes share common pathogenic pathways and both conditions can be thought of as upregulated or maladapted responses of the immune system to environmental stressors acting on the host. Current concepts of periodontitis suggest that susceptible individuals mount an aggressive, upregulated immune-inflammatory response to the presence of plaque, with environmental stressors such as smoking adversely affecting pathogenic processes (Pihlstrom et al, 2005). Environmental stressors that have been implicated in T2DM include over-eating and lack of physical exercise. Environmental stressors mediate their effects via cells (macrophages, PMNL, fibroblasts) that secrete inflammatory mediators such as cytokines into the environment, which act locally and systemically, potentially affecting both disease processes.

In the context of periodontal disease, cytokines (such as the interleukin-1 (IL-1) cytokine family) are central to the initiation and maintenance of immune responses to periodontal bacteria. However, inappropriate cytokine secretion, whether quantitative

(i.e. excessive cytokine release) and/or qualitative (e.g. imbalance between the proportions of pro- and anti-inflammatory cytokines), is a manifestation of dysregulated immune responses and results in destruction of periodontal tissues and the clinical signs of disease. As the inflammatory front induced by the plaque biofilm extends laterally and apically, infiltrating inflammatory cells such as PMNL, monocytes/macrophages and lymphocytes are recruited to the area, occupying a considerable volume of the soft tissues and extending close to the alveolar bone. The local release of proteolytic enzymes (including MMPs) to accommodate the emigration and accumulation of inflammatory cells results in connective tissue breakdown, and osteoclastic activity is enhanced so that the alveolar bone retreats from the extending area of inflammation. Key cytokines that drive inflammatory processes in the periodontium include IL-1 $\beta$  and tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ), and local overproduction of these cytokines is a major contributor to alveolar bone destruction. Although it is clear that these pro-inflammatory cytokines are of central importance in periodontal pathogenesis, it is becoming increasingly appreciated that local networks of a range of pro- and anti-inflammatory cytokines are critical in determining the nature of the immune-inflammatory response to the plaque challenge. In broad terms, it is reasonable to propose that substantial changes in immunologically active molecules as a result of systemic disease (e.g. T2DM) might perturb finely balanced cytokine networks within the periodontium, with a consequent effect on localised immune responses and altered susceptibility to periodontal disease. This hypothesis has been strengthened by the concept of T2DM as an inflammatory condition, which will now be considered.

#### Both T2DM and periodontitis are inflammatory conditions

Although insulin resistance and pancreatic  $\beta$ -cell dysfunction continue to be recognised as the central causal processes in the development of T2DM, other perspectives have recently evolved. It is now recognised that a low-grade systemic inflammation precedes the development of both T2DM (Freeman et al, 2002; Duncan et al, 2003) and cardiovascular disease (CVD) (Ross, 1999), indicating a possible inflammatory basis for both diseases. Plasma concentrations of IL-6 and TNF- $\alpha$  are increased in obese individuals and in those with T2DM



Table 1 Principal and recent studies investigating links between periodontal disease and T2DM

Author, Year	Subjects	Age	Study design	Principal findings
Mattout et al, 2006	71 T2DM, 2073 controls	35–65	Cross-sectional	Significantly more attachment loss in T2DM patients. More gingival inflammation in T2DM after controlling for plaque levels
Jansson et al, 2006	191 T2DM	55 ± 5	Cross-sectional	20% of the T2DM patients had periodontal disease. These subjects also had significantly higher HbA1c (7.1%) than periodontally healthy T2DM patients (6.5%)
Peck et al, 2006	23 T2DM	59 ± 10	Cross-sectional	Periodontal disease affected 42% of those with poor glycaemic control (HbA1c > 8.0%) compared with 18% of those with good control (HbA1c < 8.0%)
Campus et al, 2005	71 T2DM 141 controls	60 ± 10	Cross-sectional	T2DM patients had significantly more missing teeth, pockets > 4 mm, bleeding on probing and plaque than non-diabetic control patients
Lu and Yang, 2004	72 T2DM 92 controls	54	Cross-sectional	Gingival inflammation and attachment loss were significantly higher in the T2DM patients than the control patients
Engelbreton et al, 2004	45 T2DM	32–69	Cross-sectional	T2DM patients with poor glycaemic control (HbA1c > 8.0%) had significantly higher GCF IL-1β levels than better controlled T2DM patients
Tsai et al, 2002	4343 T2DM	45–90	Cross-sectional	Poorly controlled T2DM patients had a significantly higher prevalence of periodontal disease than those without T2DM (OR: 2.9, 95% CI: 1.4, 6.0)
Sandberg et al, 2000	102 T2DM 102 controls	65 ± 8	Cross-sectional	Significantly more T2DM patients (44.8%) had interproximal alveolar bone loss > 1/3 root length compared with control subjects (25.5%)
Cutler et al, 1999	28 T2DM 7 controls	~28–66	Cross-sectional	Probing depths, attachment loss and gingival inflammation were all significantly elevated in T2DM patients compared with controls
Taylor et al, 1998	24 T2DM 338 controls	15–57	Prospective	Radiographic bone loss (up to 1/4 root length) was more prevalent in T2DM patients (67%) compared with controls (44%)
Emrich et al, 1991	254 T2DM 930 controls	15–55+	Cross-sectional	Prevalence of periodontal disease was higher in T2DM patients compared with non-diabetic controls or subjects with impaired glucose tolerance
Shlossman et al, 1990	736 T2DM 2483 controls	5–45+	Cross-sectional	Periodontal disease was more prevalent in T2DM patients than in controls
Nelson et al, 1990	720 T2DM 1553 controls	15–55+	Cross-sectional and prospective	83% of T2DM patients demonstrated interproximal bone loss compared with 19% of controls. In follow-up appointments, the incidence of periodontitis was 60 new cases per 1000 person-years in T2DM patients compared with 17 new cases in controls



(Dandona et al, 2004). Hyperglycaemia and excessive food intake result in cellular oxidative stress and resultant inflammatory changes, and hyperglycaemia also results in increased circulating IL-6, IL-18 and TNF- $\alpha$  concentrations, particularly in subjects with impaired glucose tolerance (Dandona et al, 2004).

Serum TNF- $\alpha$  is elevated in patients with T2DM, and the source of this may be adipose tissue and/or may be due to increased systemic TNF- $\alpha$  produced indirectly as a result of the diabetic state, for example from the stimulation of leukocytes by advanced glycation end-products (AGEs, see below). Increased circulating IL-6 is also associated with insulin resistance and prospective studies suggest that serum IL-6 concentrations predict future occurrence of T2DM (Pradhan et al, 2001).

Obese individuals have been reported to have increased serum concentrations of TNF- $\alpha$  and IL-6 (Ziccardi et al, 2002). Obesity is associated with increased morbidity and mortality (Calle et al, 1999; Rashid et al, 2003) and is a risk factor for a number of diseases, including CVD and T2DM (Kopelman, 2000). Although the traditional role attributed to adipose tissue is energy storage in the form of lipid, adipose tissue is now increasingly viewed as an active endocrine organ that synthesises a wide range of molecules involved in the complex network of physiological control systems regulating food consumption and energy balance (Trayhurn and Beattie, 2001). Collectively, these molecules secreted by adipocytes are referred to as adipokines.

TNF- $\alpha$  and IL-6 are therefore classed as adipokines by virtue of the fact that they are synthesised by adipocytes in increased levels in metabolic disorders. Of course, these molecules are also familiar to dentists as cytokines with well-defined roles in inflammation and immunity. Other adipokines include leptin, adiponectin, resistin and visfatin, the roles for which are beginning to be established. For example, leptin activates inflammatory responses by acting as an acute-phase reactant and a stimulator of neutrophil chemotaxis and function. Leptin can also mediate pro-inflammatory responses by stimulating cytokine secretion by other cells such as monocytes (Sanchez-Margalet et al, 2003).

Leptin levels are directly correlated to adipose tissue mass and act centrally, inducing a decrease in

food intake and an increase in energy consumption (Otero et al, 2006). Consistent with having increased amounts of adipose tissue, obese individuals also have high circulating levels of leptin coupled with resistance to its actions in the control of food intake and energy expenditure (Munzberg and Myers, 2005). Research has demonstrated an association between high leptin levels and an increased risk of developing T2DM (McNeely et al, 1999; Boyko et al, 2000). Recent reports have suggested that leptin is present in the gingiva in concentrations that inversely correlate with probing depths (Johnson and Serio, 2001). Furthermore, gingival crevicular fluid (GCF) leptin levels have been reported to be higher in non-smokers than smokers, and higher in shallow pockets than deep pockets in non-smokers (Bozkurt et al, 2006). The implications of these preliminary data are unclear, but suggest that leptin may have a role in periodontal pathogenesis.

C-reactive protein (CRP) is also classed as an adipokine, as not only is it synthesised in the liver, but it is also produced by adipocytes (Lau et al, 2005). CRP production is regulated primarily by circulating IL-6 levels and thus is influenced by adipocytes, which secrete significant quantities of IL-6. CRP levels are elevated in obese individuals and in those with T2DM. In cross-sectional studies, periodontitis has been associated with elevated CRP levels (Noack et al, 2001), and CRP has been shown to decrease following periodontal therapy (D'Aiuto et al, 2004). The association of elevated CRP levels with periodontal disease and subsequent decreases in CRP after therapy are taken to indicate that the inflammatory response to periodontitis contributes to the overall inflammatory challenge throughout the body. However, the precise role of CRP (whether produced by adipocytes or the liver) in periodontal pathogenesis in patients with T2DM remains to be elucidated.

It can be said, therefore, that relationships between cytokine networks and T2DM are likely to be complex. Research supports a contributory role for circulating inflammatory cytokines in insulin resistance. For example, binding of TNF- $\alpha$  and IL-6 to receptors in muscle cells or hepatocytes can directly interfere with insulin signalling (Ruan and Lodish, 2003; Senn et al, 2003; Kolb and Mandrup-Poulsen, 2005) and consequently dampen the cellular response to insulin (Senn et al, 2003).



Given that our knowledge of the importance of inflammation in the pathogenesis of T2DM is relatively recent, it is perhaps not surprising that few studies of periodontal disease and T2DM have investigated markers of inflammation. In one study, a trend for increasing GCF IL-1 $\beta$  concentrations was identified as diabetes control decreased (Cutler et al, 1999). Also, poorly controlled T2DM patients with untreated periodontitis were reported to have significantly higher GCF IL-1 $\beta$  levels than T2DM patients with moderate or good glycaemic control (Engebretson et al, 2004). In another study involving culture of human monocytes, production of prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) and IL-1 $\beta$  in response to challenge with LPS from *Porphyromonas gingivalis* was significantly higher in monocytes from diabetic patients compared to non-diabetics with periodontitis (Salvi et al, 1997c).

In summary, therefore, studies of inflammatory mediators in periodontal disease and diabetes suggest that individuals with diabetes, particularly those with poor glycaemic control, can be considered 'hyper-responding' individuals who mount a dysregulated immune-inflammatory response against plaque bacteria, resulting in increased tissue damage and the clinical signs of disease. Dysregulation of cytokine networks may underpin a wide range of systemic disorders and provide a basis for cross-susceptibility between T2DM and periodontal disease.

#### PMNL function

Impaired or dysregulated PMNL function may be a further mechanistic link between T2DM and periodontitis. The role of PMNL in the maintenance of periodontal health is highlighted by studies that have reported impaired chemotaxis in aggressive forms of periodontitis (Sigusch et al, 2001). Reduced PMNL function has also been found in patients with T2DM, including impaired chemotaxis (Mowat and Baum, 1971; Gustke et al, 1998), adherence (Bagdade et al, 1978), and phagocytosis (Marhoffer et al, 1992). Studies have correlated both periodontitis and diabetes with defective PMNL chemotaxis; diabetic patients with severe periodontitis had depressed PMNL chemotaxis compared with both diabetic patients with mild periodontitis and non-diabetics with mild or severe periodontitis (Manouchehr-Pour et al, 1981; Bissada et al, 1982).

Diabetes may also result in increased periodontal susceptibility via impaired PMNL apoptosis (Graves

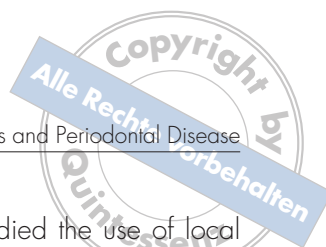
et al, 2006). Apoptosis (programmed cell death) is a mechanism by which superfluous or damaged cells are selectively removed by phagocytic cells, and is an important process in tissue homeostasis. Diabetic patients have been reported to have defects in neutrophil apoptosis (Tennenberg et al, 1999), which may result in increased retention of PMNLs within the periodontal tissues and contribute to tissue destruction by non-specific release of MMPs and reactive oxygen species (ROS), providing a further mechanism for increased susceptibility to periodontal disease in T2DM.

#### Advanced glycation endproducts

In a hyperglycaemic environment, numerous proteins including collagen undergo a non-enzymatic glycosylation process to form advanced glycation endproducts (AGEs). There is evidence that supports a role for AGEs via their interaction with cellular AGE receptor (RAGE) in exacerbating diabetic complications including periodontal disease (Jakus and Rietbrock, 2004; Takeda et al, 2006).

Binding of AGE to RAGE on monocytes and macrophages has been associated with an upregulation of pro-inflammatory cytokines, such as IL-1 $\beta$ , TNF- $\alpha$ , and IL-6 (Lalla et al, 2001). Monocytes from patients with diabetes also produce significantly greater amounts of TNF- $\alpha$ , IL-1 $\beta$  and PGE<sub>2</sub> in vitro than non-diabetic controls (Salvi et al, 1997a; Salvi et al, 1997c). The presence of RAGE in the gingival tissues (specifically endothelial cells lining small blood vessels and the basal cell layer of the epithelium) in both diabetic and non-diabetic subjects has been confirmed by immunohistochemistry (Katz et al, 2005).

AGE formation also results in the production of ROS, and AGEs detected in the gingival tissues of diabetic patients have been shown to increase oxidant stress in these tissues when compared with non-diabetic individuals (Schmidt et al, 1996). Enhanced oxidant stress and the subsequent endothelial cell changes that occur may lead to vascular injury common to diabetic complications, including periodontal disease (Schmidt et al, 1994; Vlassara, 2001). AGEs also enhance the respiratory burst of PMNL NADPH oxidases (which are active in the phagosome during phagocytosis) (Wong et al, 2003). This mechanism may contribute significantly to local tissue damage in the periodontium of patients with T2DM, given the



known importance of PMNL in periodontal tissue breakdown resulting from extracellular release of their lysosomal contents.

The irreversible nature of AGE formation and the interaction with RAGE creates environments in which cells are constantly exposed to these products, resulting in heightened inflammatory responses. Studies support the view that AGE-mediated events are of primary importance in the pathogenesis of diabetic complications such as retinopathy, nephropathy, neuropathy and atherosclerosis. They may also be involved in changes within the periodontium, rendering T2DM patients with poor glycaemic control and elevated AGE production more susceptible to periodontal disease. Increased susceptibility to periodontal disease in patients with poorly controlled T2DM may be partly attributed to (i) increased AGE deposition as a result of hyperglycaemia and subsequent increased activation of immune-inflammatory events via RAGE, and (ii) the enhanced respiratory burst in PMNL. This lends further support to the concept of the diabetic hyper-responder who mounts an upregulated periodontal immune-inflammatory response to plaque bacteria, leading to increased tissue destruction.

#### DOES PERIODONTAL TREATMENT INFLUENCE DIABETES CONTROL?

Recently, a small number of studies have begun to investigate the effect of periodontal treatment on glycaemic control. A randomised clinical trial of T2DM patients assessed the efficacy of different combinations of systemic doxycycline, topical antiseptics, and ultrasonic root surface instrumentation in the treatment of periodontitis (Grossi et al, 1997). All participants ( $n = 113$ ) had poorly controlled T2DM and severe periodontitis. At 3 months, a statistically significant reduction in mean HbA1c (glycated haemoglobin, an indicator of glycaemic control with a lower score indicating better control) was seen in the doxycycline-treated group. The placebo groups had smaller and non-significant reductions in HbA1c. The improvements in glycaemic control accompanied gains in attachment level, but by 6 months, with no further periodontal treatment, HbA1c concentrations in all study groups returned to levels comparable to those seen pre-treatment.

Iwamoto and co-workers studied the use of local delivery minocycline as an adjunct to non-surgical periodontal therapy in a non-randomised investigation of circulating TNF- $\alpha$  levels and HbA1c in patients with T2DM and chronic periodontitis ( $n = 12$ ) or gingivitis ( $n = 1$ ) (Iwamoto et al, 2001). After 3 months, they found a significant reduction in mean HbA1c, from 8.0% pre-treatment to 7.1% post-treatment. In a further study of 44 patients with T2DM, the majority of whom suffered from gingivitis or mild periodontitis, decreases in HbA1c from 7.3% to 6.5% were reported over 3 months in the 22 patients who received non-surgical periodontal therapy, compared with a (non-significant) increase in HbA1c from 7.0% to 7.3% in the 22 control patients who did not receive treatment (Kiran et al, 2005).

In another study, changes in glycaemic control associated with periodontal treatment were assessed in a group of subjects with T2DM and periodontitis (Stewart et al, 2001). The treatment group ( $n = 36$ , all T2DM patients) received root surface instrumentation and extraction of unsalvageable teeth. The control group ( $n = 36$ ) were also T2DM patients, but had not responded to the invitation to attend for dental assessment, and their medical records were reviewed for HbA1c data instead; however, their periodontal status and dental treatment record were not known. Statistically significant reductions in HbA1c were observed in both the treatment group (from 9.5% to 7.6%) and control group (from 8.5% to 7.7%), although the reasons for the decrease in HbA1c in the control patients are not known.

The limited number of published studies investigating the effect of periodontal treatment on glycaemic control in T2DM patients highlights the need for further randomised clinical trials that use validated measures of periodontal status, account for confounding variables, and are adequately powered to detect differences in periodontal and metabolic responses to treatment. In a recent meta-analysis of 10 intervention studies to quantify the effects of periodontal therapy on HbA1c, a weighted mean HbA1c decrease of 0.66% was observed in T2DM patients following periodontal treatment, though this did not achieve statistical significance (Janket et al, 2005). This suggests that there is a possibility that periodontal therapy may have an impact on diabetes control, but this remains to be confirmed in larger studies.



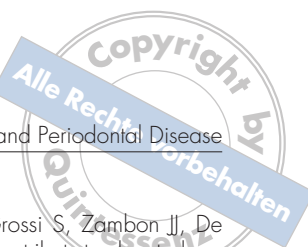
## CONCLUSIONS

Epidemiological data clearly demonstrate links between periodontal disease and T2DM, and diabetic individuals with poor glycaemic control are particularly at risk for periodontitis. Shared susceptibility between these common, complex, inflammatory diseases involves pathogenic pathways common to both conditions. The precise mechanisms linking the diseases remain to be fully elucidated, and probably include roles for key inflammatory cytokines, adipokines, AGEs and PMNL. The concept of diabetes as an inflammatory state further strengthens the hypothesis that these two diseases are linked via dysregulated inflammatory and immune responses that result in increased susceptibility to both conditions. Emerging data suggest that treating periodontal disease may have a beneficial effect on glycaemic control in patients with T2DM and highlight the need to incorporate a thorough oral and periodontal examination into management protocols for patients with diabetes.

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