

Periodontal disease and diabetes

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Article points

1. Periodontitis is caused by long-term build-up of plaque where the gum meets the teeth, and is characterised by inflammation and bleeding of the gum as well as progressive destruction of the periodontal ligament and alveolar bone which, if left untreated, results in teeth loosening and eventual loss.
2. People with diabetes, particularly those with poor glycaemic control, are at increased risk of periodontitis; conversely, treatment of periodontitis can result in small improvements in HbA_{1c}.
3. Both clinicians and people with diabetes need to be aware of the risk of periodontitis, and routine screening for the disease should be made available.

Key words

- Periodontal disease
- Periodontitis

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Periodontal diseases (gingivitis and periodontitis) are common inflammatory diseases of the supporting structures of the teeth. Periodontitis is the more serious of the two conditions. If untreated, it can lead to destruction of the periodontal ligament and alveolar bone, resulting in teeth loosening and eventual loss. Proper oral hygiene is the cornerstone of periodontal disease prevention. People with diabetes have a three-fold increased risk of developing periodontitis compared with those without the condition. This risk is significantly greater in individuals with poor glycaemic control. Many people with diabetes are unaware of this increased risk and may have undetected gingivitis or periodontitis due to the painless nature of the diseases, and diagnosis and treatment in this population is often delayed or absent. Treating periodontal disease may result in improved glycaemic control. There is a need for greater awareness of the relationship between periodontal disease and diabetes in both people with diabetes and members of their healthcare delivery teams.

Periodontal diseases are those that affect the supporting structures of the teeth. They are highly prevalent, with advanced periodontitis affecting around 10% of adults. People with diabetes (both type 1 and type 2) are at increased risk of developing periodontitis, and the risk increases as glycaemic control worsens. There is evidence that periodontitis can have negative impacts on glycaemic control and that treating the disease can result in reductions in HbA_{1c}. It is, therefore, important that oral health is assessed and periodontal disease detected and treated in people with diabetes. However, medical and dental professionals do not typically practise collaboratively, and healthcare systems do not assess the quality of periodontal management of people with diabetes; thus, optimal management of both conditions may be compromised.

What is periodontal disease?

Periodontal diseases are a group of inflammatory conditions that affect the structures that support the teeth: the gingiva (gum), periodontal ligament (which anchors the teeth to the alveolar bone) and the alveolar bone (the part of the jaw bone that invests and supports the teeth). In broad terms, there are two main categories of periodontal disease: gingivitis and chronic periodontitis (typically referred to simply as periodontitis), the latter of which is the topic of interest in this article. Gingivitis is inflammation that is localised to the gingiva only and does not involve destruction of the deeper supporting tissues. It is highly prevalent (probably affecting the majority of people) and is characterised by red, inflamed gums that bleed easily (for example, when brushing the

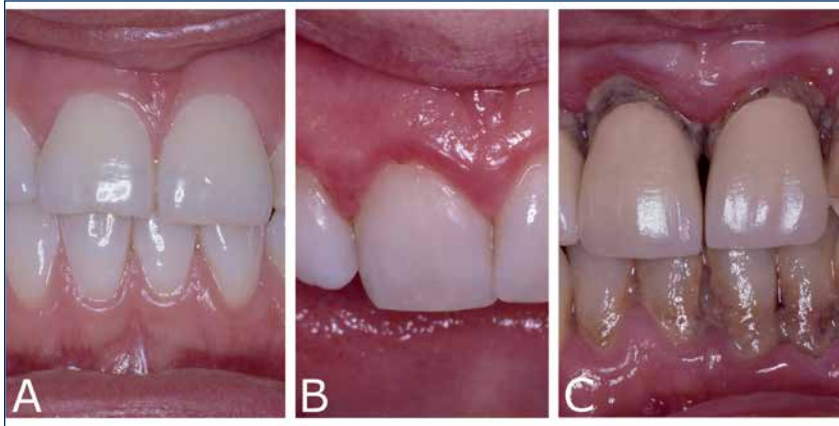


Figure 1. Clinical appearance of healthy gums, gingivitis and periodontitis. (A) Healthy gingival tissues are pink, with no evidence of swelling or bleeding. (B) Gingivitis is characterised by inflammation (redness and swelling) of the gingival tissues, particularly at the gingival margin. (C) Periodontitis is characterised by poor oral hygiene, marked gingival inflammation and gingival recession, indicative of underlying breakdown of the periodontal tissues.

teeth; *Figure 1*). It is completely reversible with improved oral hygiene.

Periodontitis is a more serious condition in which the inflammation extends into the deeper tissues supporting the teeth. It is characterised by ongoing gingival inflammation and bleeding from the gingival tissues, as well as progressive destruction of the periodontal ligament and the alveolar bone. This results in gingival recession and reduced support for the teeth, which subsequently become mobile and eventually may become so loose that they spontaneously exfoliate or require extraction. Significantly, the tissue damage that characterises periodontitis is largely irreversible. Periodontitis is very slowly progressing in most cases and, like gingivitis, is usually painless; thus, many people with periodontitis may not realise that they have the condition until the bone loss becomes so advanced that teeth start to become loose.

It is not usually possible to assess the extent of tissue breakdown in periodontitis by visual inspection alone. Instead, a periodontal probe is used to measure how much tissue breakdown has occurred and X-rays are taken to assess the amount of alveolar bone loss. This underscores the importance of regular dental check-ups to assess periodontal health. Given that periodontitis results in inflamed gingiva, gingival recession and tooth mobility, it is not surprising that the condition has significant impacts on many

aspects of daily living and quality of life, including reduced self-confidence and negative effects on food choices and social interactions (O'Dowd et al, 2010; Durham et al, 2013).

Periodontal diseases (gingivitis and periodontitis) are among the most common maladies known to man, likely affecting the vast majority of the world's population. The prevalence of advanced periodontitis in most of the populations that have been studied ranges from 5% to 15% of affected adults (Dye, 2012). In the UK, the 2009 Adult Dental Health Survey for England, Wales and Northern Ireland identified that 8% of adults have advanced periodontitis (White et al, 2011). The main risk factors for periodontitis are tobacco smoking and diabetes. The importance of diabetes will be discussed in detail in this article, but it is also important to note that smoking cessation is a fundamentally important component of periodontal treatment (Warnakulasuriya et al, 2010).

Associations between diabetes and periodontitis

Epidemiological studies have consistently reported increased prevalence and severity of periodontitis in populations with diabetes compared with people without the condition. In broad terms, the risk of periodontitis is increased approximately three-fold in people with diabetes (Mealey and Ocampo, 2007), and the risk is greater with poor glycaemic control (i.e. those with $HbA_{1c} >75$ mmol/mol [$>9\%$]; Tsai et al, 2002). In well-controlled diabetes ($HbA_{1c} \leq 53$ mmol/mol [$\leq 7\%$]), there appears to be little evidence for an increased risk of periodontitis. In the US, the Pima Indian population, in which there is a particularly high prevalence of diabetes, has been studied in detail, with consistent findings of increased periodontitis prevalence in those with type 2 diabetes (Nelson et al, 1990; Taylor et al, 1998). Type 1 diabetes also increases the risk of periodontitis and affected children often show early signs of increased periodontal tissue destruction (Lalla et al, 2007). Therefore, it is important to be aware of the increased risk of periodontitis in all people with diabetes and, in particular, those with poor glycaemic control, regardless of age.

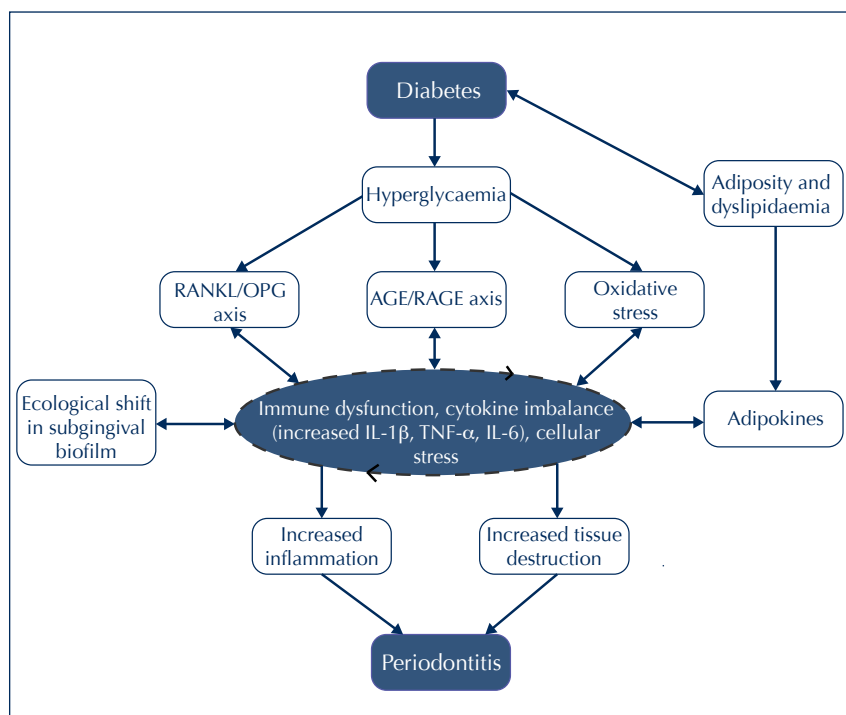
Pathophysiology of periodontitis in people with diabetes

Periodontitis is a chronic inflammatory condition that results from the build-up of dental plaque (biofilm) on the tooth surfaces, specifically in the region where the gum meets the tooth. The bacterial biofilm initiates inflammation in the gingival tissues that, in the early stages, results in gingivitis (inflammation of the gingiva, characterised by red, swollen gums that bleed easily). The inflammatory response aims to reduce the bacterial challenge but, if oral hygiene is poor, the continued presence of bacteria perpetuates the inflammation, which progressively becomes more destructive and damaging. Complex inflammatory networks develop in the gingival and periodontal tissue, involving multiple inflammatory cell types (neutrophils, macrophages and T and B lymphocytes), producing large quantities of inflammatory mediators, including cytokines such as interleukin-1 β (IL-1 β), IL-6, tumour necrosis factor- α (TNF- α), receptor activator of nuclear factor- κ B ligand, prostaglandins such as prostaglandin E₂ and destructive enzymes such as the matrix metalloproteinases (MMPs; such as MMP-8, MMP-9 and MMP-13; Preshaw and Taylor, 2011). T cell regulatory cytokines, such as IL-12 and IL-18, and chemokines also play a role in the inflammatory response.

The ongoing inflammation involves aspects of both innate and adaptive immune functioning, and includes both resident cells in the periodontal tissues (for example, fibroblasts, which are activated to break down collagen, and osteoclasts, which resorb alveolar bone) and infiltrating inflammatory cells (for example, neutrophils, macrophages). The accumulation of large numbers of infiltrating inflammatory cells, and their release of tissue-destructive enzymes and inflammatory mediators, is responsible for the great majority of the tissue damage that we recognise clinically as periodontitis. It is now clear that there is significant heterogeneity between individuals with regard to the nature of the inflammatory response that develops, with certain people appearing to be particularly susceptible to periodontitis and experiencing more advanced tissue breakdown at an earlier age than others (Kinane et al, 2011).

Diabetes is also recognised as a chronic

inflammatory disease. Dysregulated immune responses play a key role in the pathogenesis of diabetes (both type 1 and type 2) and are associated with physiological and metabolic changes, such as the formation of advanced glycation end-products (AGEs). Elevated levels of cytokines such as TNF- α and IL-6 are found in diabetes and obesity (Dandona et al, 2004), and increased serum levels of IL-6 and C-reactive protein have been shown to be linked to the future development of diabetes (Schmidt et al, 1999). Although the precise mechanisms linking periodontitis and diabetes are, as yet,



Interactions between periodontitis and diabetes

A two-way relationship between periodontitis and diabetes has been described, with each condition having adverse impacts on the other. For example, periodontitis has been associated with worse long-term glycaemic control in people with type 2 diabetes (Taylor et al, 1996), as well as increased risk of diabetic nephropathy (macroalbuminuria and end-stage renal disease) and cardiorenal mortality (ischaemic heart disease and diabetic nephropathy combined; Saremi et al, 2005; Shultis et al, 2007). Periodontitis has also been associated with longitudinal HbA_{1c} increases in people who do not have diabetes, suggesting that periodontal inflammation may influence the risk of developing diabetes (Demmer et al, 2010).

A large number of studies have evaluated the impact of periodontal therapy on glycaemic control in people with diabetes. The standard (non-surgical) treatment for periodontitis is dental cleaning (referred to as root surface debridement) to reduce and disrupt the bacterial biofilm that develops in the subgingival environment, together with motivation and empowering of the individuals to improve their self-performed plaque control (oral hygiene) on a daily basis. Whereas many of the individual studies have been underpowered, a number of meta-analyses (including a review by the Cochrane Collaboration) have consistently shown that non-surgical periodontal treatment is typically associated with reductions in HbA_{1c} of around 4.4 mmol/mol (0.4%; Janket et al, 2005; Darré et al, 2008; Simpson et al, 2010; Teeuw et al, 2010; Liew et al, 2013; Sgolastra et al, 2013). The majority of treatment studies have focused on type 2 diabetes. One recent randomised controlled trial did not show this effect on HbA_{1c} (Engelbretson et al, 2013); however, the study has been criticised for achieving a relatively poor clinical outcome following the periodontal therapy, suggesting that there was limited potential for the (suboptimal) periodontal treatment to impact glycaemic control (Borgnakke et al, 2014).

Collectively, the systematic reviews and meta-analyses suggest that periodontal therapy is associated with improvements in glycaemic control. Mean reductions in HbA_{1c} of

Figure 2. Proposed mechanisms linking the pathogenesis of periodontitis and diabetes (Taylor et al, 2013). Hyperglycaemia results in the formation of AGEs in the periodontal tissues, and interaction between these compounds and their receptor (RAGE) leads to altered inflammatory responses and increased secretion of pro-inflammatory cytokines. Hyperglycaemia also leads to oxidative stress via increased generation of reactive oxygen species, and disturbed RANKL/OPG ratios also contribute to altered inflammatory responses. Production of adipokines associated with adiposity, such as leptin, further contribute to upregulated inflammation. A state of chronic inflammation develops, which is initiated and perpetuated by the plaque biofilm in the subgingival environment, and characterised by immune dysfunction and pro-inflammatory responses. The net result is exacerbated periodontal tissue destruction, and increased progression and severity of periodontal disease. It is important to be aware that there is considerable inter-individual variation in periodontitis susceptibility and that other risk factors, such as smoking, also contribute to this.

AGE: advanced glycation end-product; IL: interleukin; OPG: osteoprotegerin; RAGE, receptor for AGEs; RANKL: receptor activator of nuclear factor- κ B ligand; TNF- α : tumour necrosis factor- α .

not fully understood, inflammation is likely to be a common underlying factor. Diabetes increases levels of IL-1 β and TNF- α in the periodontal tissues (Salvi et al, 1997; Engelbretson et al, 2004), and periodontitis is associated with elevated plasma TNF- α levels in type 2 diabetes (Engelbretson et al, 2007). Formation of AGEs and their interaction with their receptor in the periodontal tissues, together with oxidative stress and the accumulation of reactive oxygen species, also contribute to increased periodontal inflammation in people with diabetes. Some of the key mechanisms that are likely to play a role in the pathogenesis of periodontitis in people with diabetes are shown in Figure 2.

approximately 0.4%, though relatively modest, may yield significant clinical benefits, as every 1% decrease is associated with measurable reductions in the risk of diabetes complications (Stratton et al, 2000). Furthermore, periodontal treatment is a relatively straightforward intervention that does not routinely involve additional drug therapies, thereby avoiding the risk of drug interactions and side-effects associated with pharmacological therapies for diabetes. The precise mechanisms by which periodontal treatment leads to improved glycaemic control are not known, but it is plausible that they are related to the reduction of local and systemic inflammation.

Implications for diabetes care teams

Good oral health is integral to achieving and sustaining good general health. Given the pandemic of predominantly type 2 diabetes and the increased risk of periodontitis in people with diabetes, it is essential that these people and their healthcare professionals are aware of the links between these conditions so that the best outcomes can be delivered at the lowest cost. The care and management of people with both periodontitis and diabetes require a life-long commitment to modifying lifestyle and behaviours in order to control the condition and prevent clinical deterioration. Patient motivation and empowerment are central to effective management strategies for both conditions, and are impossible to attain without self-management skills. With education on the importance of oral health and ongoing self-management support, including the skills to brush their teeth and use dental floss most effectively, people with diabetes can incorporate proper oral hygiene and prevention into their daily routine.

Unfortunately, many people with diabetes remain unaware of their increased risk of developing periodontal disease (Allen et al, 2008), and many may already have undetected gingivitis or periodontitis. Non-dental healthcare professionals are also generally unaware of the links between periodontitis and diabetes, as medical and dental professionals do not typically practise in clinics together. Furthermore, national guidance documents and care pathways do not

usually refer to the importance of achieving and maintaining oral and periodontal health in people with diabetes. It is likely that the organisational barriers that exist between the dental and medical professions in most healthcare systems are hindering our ability to deliver high-value, integrated and team-based medical and dental care to people with diabetes and multimorbidity (Bissett et al, 2013).

It is important that people with diabetes are made aware of the potential impact that their diabetes may have on their oral and periodontal health. Health promotion messages should emphasise the importance of maintaining good oral health and should be consistent across all of the professionals within an individual's healthcare journey. At the very least, a simple query by the (non-dental) healthcare professional about any problems the individual may have in the mouth, such as bleeding gums or loose teeth, could lead on to discussion about the increased risk of periodontitis, as well as a recommendation to be seen by a dental professional.

We advocate that periodontal assessment, by dental professionals, should be undertaken as a routine in people with diabetes to assess for both periodontitis and the other potential oral complications of diabetes, such as dry mouth, candidal infections, burning mouth, and dental caries. A rapid screening tool, the Basic Periodontal Examination, is commonly employed by dental professionals to assess periodontal status. If periodontitis is detected, a more detailed assessment is performed and the necessary treatment is pursued. Non-surgical periodontal therapy is generally very effective when performed well, with a major emphasis on patient self-care (in terms of optimising oral hygiene) as well as root surface debridement to reduce the bacterial challenge. Systemic antibiotics are not usually indicated in the treatment of periodontitis in people with diabetes.

Conclusions

Diabetes and periodontitis are inextricably linked as chronic inflammatory diseases that adversely influence each other. The risk of periodontitis is increased approximately three-fold in people with diabetes, particularly if the latter condition

Page points

1. Many people with diabetes, and even their healthcare professionals, are unaware of the increased risk of periodontitis associated with the condition, and the barriers between medical and dental practitioners in most healthcare systems further restrict the ability to deliver effective care in this population.
2. Diabetes specialists can improve care by warning their patients about the risk of periodontitis, enquiring about their oral health and promoting good oral hygiene.
3. To further improve care, routine, regular periodontal assessment by dental professionals is advocated in people with diabetes.

“People with diabetes should be informed about their increased risk of periodontitis and, at the very least, advised to visit a dental professional for periodontal assessment.”

is poorly controlled, and there is evidence that advanced periodontitis compromises glycaemic control. Periodontal treatment has been associated with improved glycaemic control and reductions in HbA_{1c} of around 0.4%. People with diabetes should be informed about their increased risk of periodontitis and, at the very least, advised to visit a dental professional for periodontal assessment. Indeed, international dental societies recommend periodontal assessment as an indispensable component of the comprehensive diabetes evaluation. ■

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