

# Association between Diabetes and Periodontitis

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**Abstract:** *Periodontal disease is known as the sixth complication of diabetes. Lately, numerous clinical and epidemiologic reports have shown that local periodontal inflammation induces systemic micro-inflammation, contributing to insulin resistance and increasing the risk of cardiovascular diseases. Although diabetes and periodontal diseases may seem like very different diseases, dentists have known for a long time that people with diabetes are further likely to get gum disease. Also, their periodontal disease may be worse and tougher to treat equated with people who do not have diabetes. If a person's blood sugar levels are under good control, periodontal treatment is expected to be more successful. Periodontal diseases may also have an effect on diabetes according to results of some clinical studies, making blood sugar control more difficult. It's clear that periodontal health is an important key factor for the overall health of a person with diabetes.*

**Keywords:** Diabetes, Periodontitis, Type 1 diabetes mellitus, Type 2 diabetes mellitus, Advanced glycation end products

## 1. Introduction

Gum disease is one of the most common diseases seen in humans. In its most severe form, known as periodontitis, the periodontium that support the teeth are destroyed over time, leading to loss of teeth. Periodontitis affects about half of all adults and as many as 85% of people over 65-years of age.

Scientists are now finding that gum disease may also have an effect on diabetes, making blood sugar control more difficult. It remains clear and that keeping the gums healthy is an vital part of conservation of the overall health of a person with diabetes.

### Diabetes mellitus

Diabetes mellitus (DM) is a chronic disease, characterized by hyperglycaemia due to a defect in insulin secretion by pancreatic  $\beta$  cells, a decrease in insulin sensitivity, or a combination of both. The current classification of diabetes is based upon the pathophysiological mechanisms of each form of the disease.<sup>1,2</sup> Type 1 diabetes results from autoimmune destruction of pancreatic  $\beta$  cells, typically leading to a complete loss of insulin secretion. This form is usually present in children and adolescents. The lack of insulin production in patients with type 1 diabetes makes the use of exogenous insulin necessary to sustain life, hence the former name "insulin-dependent diabetes."<sup>2</sup> Type 2 diabetes previously called non-insulin dependent diabetes results from insulin resistance, which alters the availability of endogenously produced insulin in the target cells.<sup>1,2</sup> Type 2 diabetic patients can be undiagnosed for many years as the hyperglycaemia appears gradually and often without symptoms.<sup>3</sup>

The disease is characterized by an increased susceptibility to infection, poor wound healing, and increased morbidity and mortality associated with disease progression. Diabetes is also recognized as an important risk factor for more severe and progressive periodontitis, infection or lesions resulting in the destruction of tissues and supporting bone that form the attachment around the tooth. Both diseases are thought to share a common pathogenesis that involves an enhanced inflammatory response that can be observed at the local and

systemic level.<sup>4-9</sup> The inflammatory response is mainly caused by the chronic effects of hyperglycaemia and specifically the formation of biologically active glycosylated proteins and lipids that promote inflammatory responses.<sup>10-11</sup> Systemic implications of DM due to prolonged hyperglycaemia include damage to blood vessels and impaired immune function.<sup>13</sup>

Diagnostically, the World Health Organization outlines the following criteria for DM: fasting plasma glucose levels  $\geq 7.0$  mmol/L; plasma glucose  $\geq 11.1$  mmol/L two hours after administration of 75g oral glycaemic load; and glycosylated haemoglobin (HbA1c)  $\geq 6.5\%$ .<sup>14</sup>

### Periodontitis

Periodontitis involves the progressive destruction of the attachment apparatus of involved teeth due to an exaggerated inflammatory response. This includes loss of alveolar bone, apical migration of junctional and pocket epithelium and eventual pathological exfoliation of periodontally compromised teeth.<sup>15-16</sup> The solidarity existing in the pathogenesis for both diseases aid as a starting point in understanding how they affect each other and why it is important for dentists to work with physicians to set sterner HbA1c targets to enable periodontal health. Numerous studies in various populations have demonstrated that individuals with diabetes tend to have a higher prevalence of and more severe periodontitis than nondiabetics.<sup>17</sup>

Periodontal disease is the most prevalent oral complication in patients with type 2 DM.<sup>18-19</sup>

In a classic cross-sectional study, type 1 diabetes has been associated with a fivefold increased prevalence of periodontitis in teenagers<sup>20</sup> and with greater bleeding index, probing pocket depth and clinical attachment level.<sup>21,22</sup>

Today, chronic periodontitis has been identified as the sixth complication of diabetes alongside retinopathy, nephropathy, neuropathy, macrovascular disease and poor wound healing.<sup>23</sup>

### Role of AGE

One of the major characteristics of diabetic complications is a change in microvascular integrity, which underlies end-organ damage, such as that responsible for retinopathy and nephropathy.<sup>24</sup> People with diabetes, especially those with poor glycaemic control, accumulate high levels of irreversibly glycated proteins called advanced glycation end products (AGEs) in the tissues, including the periodontium.<sup>25-26</sup> AGEs are a primary link between numerous diabetic complications because they induce marked changes in cells and extracellular matrix components. These changes, including abnormal endothelial cell function, capillary growth and vessel proliferation also occur in the periodontium of some people with diabetes.<sup>24-27</sup> The accumulation of AGEs in patients with diabetes also increases the intensity of the immunoinflammatory response to periodontal pathogens because inflammatory cells such as monocytes and macrophages have receptors for AGEs (RAGE).<sup>25</sup> Interactions between AGEs and their receptors (RAGE) on inflammatory cells result in the increased production of proinflammatory cytokines such as IL-1 $\beta$  and TNF- $\alpha$ .<sup>28</sup> This interaction may be the cause of the marked elevation in gingival crevicular fluid levels of IL-1 $\beta$  and TNF- $\alpha$  seen in subjects with diabetes compared with those without diabetes and it may contribute to the increased prevalence and severity of periodontal diseases found in numerous studies of populations of people with diabetes.<sup>29</sup>

In poorly controlled diabetic patients, collagen becomes cross-linked resulting in a marked reduction of solubility.<sup>30</sup> At the ultrastructural level, collagen homeostasis is altered, thereby affecting its turnover. AGE have an adverse effect on bone collagen at the cellular level and this may result in alterations in bone metabolism.<sup>31-33</sup> Glycation of bone collagen may affect bone turnover, leading to reduced bone formation.<sup>34</sup> This, in turn, reduces osteoblastic differentiation and ECM production.<sup>35-36</sup> However, the role of the AGE–collagen complex in bone resorption is not so clear. Some studies have reported significant levels of osteoclasts and increased osteoclast activity in diabetic patients,<sup>37-40</sup> whereas other studies have reported decreased bone resorption under similar conditions.<sup>41-43</sup>

Chronic periodontal diseases also have the potential to exacerbate insulin resistance and worsen glycaemic control, while periodontal treatment that decreases inflammation may help diminish insulin resistance.<sup>44</sup>

### Effect of periodontal treatment on diabetes

Reduction in HbA1C is an established outcome measure of successful diabetes treatment. Evidence derived from RCTs shows that periodontal treatment results in a mean reduction in HbA1C of 0.36% (95% CI 0.19, 0.54) at 3 months (Engelbreton & Kocher 2013). This result is consistent with previous meta-analyses. Levels of HbA1C reduction obtained within the short term following periodontal interventions are equivalent to those achieved by adding a second drug into a pharmacological regime. If such reductions following periodontal therapy can be sustained over the longer term, then this may contribute to reduced diabetes-associated morbidity and mortality.<sup>46</sup>

In a recent study of subjects with type 2 diabetes and periodontitis, Iwamoto and colleagues found that periodontal treatment resulted in a significant reduction in serum levels of TNF- $\alpha$  that was accompanied by a significant reduction in mean HbA1c values (from 8.0 to 7.1 percent).<sup>45</sup>

Treatment of periodontitis is associated with HbA1c reductions of approximately 0.4%. Thus oral and periodontal health should be promoted as integral components of diabetes management.<sup>47</sup>

### Role of dental professional

It has been suggested that oral health is a neglected area of global health and an editorial in *The Lancet* proposed that promoting and improving oral health should be part of the routine agenda of healthcare policymakers and clinicians.<sup>48</sup> Periodontal disease and diabetes are directly and independently associated chronic diseases of high prevalence in the population and the global prevalence of type 2 diabetes, in particular, is rising dramatically. In 2000, the US Surgeon General referred to a ‘silent epidemic’ of oral and dental diseases and stressed the importance of oral health as being essential for general health and well-being.<sup>49</sup>

Routine periodontal assessment should be performed in all patients, including those with diabetes. Ask the patient about their level of glycaemic control: many will be able to tell you their most recent HbA1c measurements. If the patient does not have periodontitis, then long term preventive care and monitoring should be undertaken (that is, same as for all patients). Diabetic patients should also be evaluated for the other potential oral complications of diabetes, including caries, dry mouth, burning mouth, candidal infections and co-morbidities such as those associated with medications. If periodontitis is diagnosed, it should be managed as appropriate. This would typically involve (similar to non-diabetic patients) patient education and empowerment, oral hygiene instructions, non-surgical therapy (root surface debridement), surgical intervention (if required) and monitoring of the treatment outcomes. Effective periodontal treatment is particularly important in people with diabetes, given that periodontitis has potential negative impacts on glycaemic control and diabetes complications and that periodontal treatment has been associated with improvements in HbA1c. In most cases, conventional (non-surgical) periodontal treatment is very effective in diabetic patients, including optimisation of plaque control to control the inflammation that leads to periodontal destruction along with a major emphasis on self-management and patient education.<sup>50</sup>

## 2. Conclusion

Diabetes increases the risk for periodontitis predominantly if poorly controlled and evidence suggests that advanced periodontitis also compromises glycaemic control. Periodontal treatment has been linked with improvements in glycaemic control, with HbA1c drops of approximately 0.4% specified in systematic reviews and meta-analyses, though more research is mandatory to investigate this further. Oral health as well as periodontal health is a fundamentally important factor of general health and particularly so in diabetes. It would be thoughtful to identify

diabetes within the dental setting. Similarly, in the medical setting, patients with diabetes should be assessed for the presence of periodontitis. The dental team has an important role to play in the management of people with diabetes. An evolving role for the dental team is foreseen through the use of relatively simple screening tools, they may help to detect patients at high risk of diabetes.

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