

# The two way relationship between diabetes mellitus and periodontal disease

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## ABSTRACT

Periodontitis and diabetes mellitus are common chronic diseases with an established bidirectional relationships. Epidemiological studies have clearly identified that diabetes is a major factor for periodontitis, increasing the risk approximately three-fold compared to non-diabetic individuals, particularly if glycemic control is poor. This article discusses the possibility impact of diabetes on the periodontal patient and the ways in which untreated periodontitis may influence the course of diabetes. Diabetes mellitus is considered a risk factor and associated with an increased prevalence and severity of gingivitis and periodontitis. Inflammation plays an obvious role in periodontal diseases, evidence in literature also supports the role of inflammation as a major component in the pathogenesis of diabetes and diabetes complications. There is also evidence that periodontal disease can worsen a patient's control of diabetes mellitus and proper management of periodontal disease can improve control of diabetes mellitus. The association between diabetes mellitus and periodontal diseases is clear that glycemic control improves periodontal conditions, while the management of periodontal infection improves glycemic control of diabetic patients (HbA1c reduction approximately 0,4%). Periodontal assessment is as important in people with diabetes as it is in people who do not have diabetes and people with diabetes should be made aware of their increased risk for periodontal disease.

Keywords: diabetes mellitus, periodontal diseases, inflammation, glycemic control

## INTRODUCTION

Recently epidemiological studies have shown the tendency to increase incidence rate and prevalence of type 2 diabetes in all over the world. WHO predicts an increase in the number of the people with diabetes in Indonesia from 8.4 million (2000) to about 21.3 million (2030). This report shows an increase the number of people with diabetes 2-3 times by 2035. The current population of Indonesia is 240 million people. The International Diabetes Federation (IDF) predicts an increase in the number of people with diabetes in Indonesia from 9.1 million (2014) to 14.1 million (2035). Indonesia is ranked 5<sup>th</sup> in the world or rise two ranks compared to IDF data in 2013 which is ranked 7<sup>th</sup> with 7.6 million people.<sup>1</sup>

Periodontitis and diabetes are both highly prevalent conditions and the association between this two common diseases has been recognised by dental professionals for many years. Epidemiological studies have clearly identified that diabetes is a major factor for periodontitis, increasing the risk approximately three-fold compared to non-diabetic individuals, particularly if glycemic control is poor.<sup>2</sup> This article discusses the possibility impact of diabetes on the periodontal patient and the ways in which untreated periodontitis may influence the course of diabetes.<sup>3</sup>

## DISCUSSION

### Periodontal disease

Periodontal disease is an infectious, oral condition affecting the supporting structures of the teeth that is caused by the interaction between pathogenic bacteria and the host's immune system. But oral bacteria itself are insufficient for disease initiation; persistent host inflammatory responses is needed before the soft

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and mineralised periodontal tissues become eroded and disease is established. Periodontal diseases comprises gingivitis and periodontitis.<sup>4</sup>

Gingivitis is inflammation of the gum which is most commonly associated with plaque build up around the tooth and is usually reversible with good oral hygiene. If left untreated, gingivitis can lead to periodontitis.<sup>4</sup> Ervasti observed greater gingival bleeding in patients with poorly controlled diabetes than in control subjects without diabetes or in subjects with well-controlled diabetes. Subjects with type 2 diabetes also had greater gingival inflammation than control subjects without diabetes; the highest level of gingivitis was found in subjects with poor glycemic control.<sup>5</sup>

Periodontitis is the more advanced stage of periodontal disease, occurring when microorganisms colonise and progressively destroy the periodontal ligament and alveolar bone, with pocket formation or recession around the diseased teeth. This process is multifactorial and occurs in the presence of microbial challenge alongside other genetic, environmental and acquired risk factors. The destructive tissue changes observed in cases of periodontitis are result of the host's inflammatory response to chronic oral infection and largely irreversible.<sup>2,4</sup> The consequences of periodontitis such as gingival bleeding, compromised aesthetics, recurrent periodontal infections, tooth mobility and tooth loss, may have negative impacts on quality of life, with implications for function, comfort, self-confidence, social interactions and food choices.<sup>2</sup>

## Diabetes

Diabetes is a group of metabolic disorders characterised by hyperglycaemia due to defective secretion or activity of insulin.<sup>2,3</sup> Diabetes mellitus can be classified into 4 broad categories according to signs and symptoms such as type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes mellitus and other specific types diabetes mellitus.<sup>2,3</sup>

Type 1 diabetes (insulin dependent diabetes) describes a condition in which there is a failure to produce insulin as a result of autoimmune destruction of the insulin producing  $\beta$ -cells in the pancreas. Genetic susceptibility is a major risk factor in type 1 diabetes and in susceptible individuals, the onset diabetes appears to be triggered by environmental factors such as a viral infections and diet, rather than related to lifestyles. The onset of type 1 diabetes usually in childhood or young adult, constitutes about 5-10% of all cases, but accounts for > 90% of diabetes cases in young people < 25 years old.<sup>2,3</sup>

Type 2 diabetes (non-insulin-dependent diabetes) result from insulin resistance; reduced responsiveness of the cells in the body to insulin, leading to a reduced capacity to transfer glucose out of the circulation and into cells which lead to hyperglycemia. In the early stages, insulin secretion by the  $\beta$ -cells of the pancreas may be normal, but this can diminish over time, leading to insulin deficiency as well as insulin resistance. Type 2 diabetes constitutes 90-95% of all cases and typically associated with lifestyle such as overweight/obesity, lack of exercise and genetic factors. The management of type 2 diabetes involves combinations of lifestyle change, weight loss, dietary modification, oral hypoglycemic drugs and insulin injections in severe cases. The age of onset type 2 diabetes was previously considered to be in the 40s and 50s, but increasing numbers of cases in younger age groups are now being identified.<sup>2,3</sup>

## The effect of diabetes on periodontal disease

The complications of diabetes are related to long-term elevation of blood glucose concentrations (hyperglycemia). Hyperglycemia results in the formation of advanced glycation end-products (AGE) which act to "prime" endothelial cells and monocytes, making them more susceptible to stimuli that induce the cells to produce inflammatory mediators. There is speculation that AGE-enriched gingival tissue has greater vascular permeability, experiences greater breakdown of collagen fibers and show accelerated destruction nonmineralized connective tissue and bone. Periodontitis has been referred as sixth complication of diabetes. In terms of oral manifestations, the patients may experience delayed wound healing, xerostomia, increased susceptibility to periodontal diseases.<sup>3,7</sup>(see Table 1)

Table 1. Oral complication of diabetes mellitus<sup>3,7</sup>

Long term diabetic complication	Oral manifestation
Microvascular disease	Xerostomia
	Increased susceptibility of oral tissue to trauma
	Increased opportunistic infections (eg candidiasis)
	Greater accumulation of plaque
	Greater risk of caries
	Delayed wound healing
Peripheral neuropathy	Increased susceptibility to periodontal disease
	Oral paresthesia (including burning mouth or tongue)
	Altered taste sensations

Epidemiological studies have consistently shown that diabetes is associated with increased risk factor for gingivitis and periodontitis, and the glycemic control appears to be an important determinant in this relationship.<sup>2,6</sup> The magnitude of the increased risk of periodontitis is known to be dependent on the level of glycemic control, as it is with the risk of all complications of diabetes. Thus in well controlled diabetes with HbA1c of around 7% (53mmol/mol) or lower, there appears to be little effect of diabetes on the risk for periodontitis. Overall, the increased risk of periodontitis in patients with diabetes is estimated to be between 2-3 fold – that is, it increases the risk for periodontitis by 2-3 times.<sup>2</sup>

Diabetes increases the prevalence, extent and severity of periodontitis. It has been reported that patients with diabetes may present to dental professional with multiple recurring periodontal abscesses. Thus, there is nor normally any particular characteristic clinical presentation of periodontitis in patients with diabetes other than the normal clinical features of the condition.<sup>2</sup> In addition to the effects of diabetes on periodontitis, various other oral conditions may also be associated with diabetes. Many patients with diabetes may also take calcium channel blocker drugs such as amlodipine and nifedipine for hypertension, and this may result in gingival overgrowth in some cases. Occasionally, medications can also have other oral manifestations, such as lichenoid mucosal reactions to metformin. Other oral consequences of diabetes may include xerostomia resulting in increased risk for caries, candidal infections and chronic mouth ulcers.<sup>2</sup>

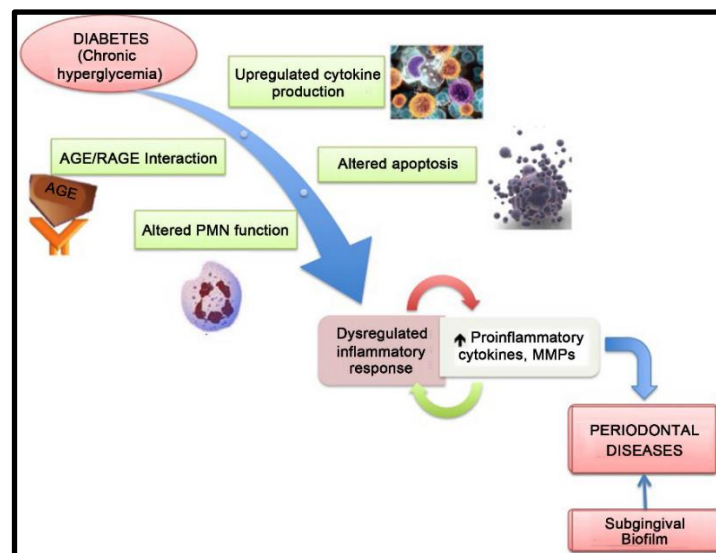


Figure 1. Illustration of the mechanisms of interaction between diabetes and periodontal diseases.

The most widely accepted hypothesis is that diabetes increases inflammatory responses of the periodontal tissues. Exacerbated and dysregulated inflammatory responses are the key to the proposed two-way relationship between diabetes and periodontal diseases. AGE: advanced glycosylation end-products; MMP: extracellular matrix metalloproteinases; PMN: polymorphonuclear leukocytes; RAGE: receptor of advanced glycosylation end products.<sup>8</sup>

The mechanisms that link diabetes and periodontitis are not completely understood, but involve aspects of inflammation, immune functioning, neutrophil activity, and cytokine biology. Both type 1 and type 2 diabetes are associated with elevated levels of systemic markers of inflammation. Diabetes increases inflammation in periodontal tissues, with higher levels of inflammatory mediators such as interleukin-1 $\beta$  (IL-1 $\beta$ ) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ). Periodontal disease has been associated with higher levels of inflammatory mediators such as TNF- $\alpha$  in people with diabetes. Accumulation of reactive oxygen species, oxidative stress, and interactions between advanced glycation end products (AGEs) in the periodontal tissues and their receptor (RAGE / receptor advanced glycation end products) all contribute to increased inflammation in the periodontal tissues diabetes patients.<sup>2,8,9</sup> (see Figure 1)

#### The effect of periodontitis on diabetes

Recent investigations have attempted to determine if the presence of periodontal disease influences the control of diabetes. Grossi suggested that effective control of periodontal infection in diabetic patients reduces the level of AGEs in the serum. The level of glycemic control seems to be the key factor. Tervonen & Karjalainen followed diabetic patients and nondiabetic control for 3 years found that the level of periodontal health in diabetic patients with good or moderate control of their condition was similar to that

in the nondiabetic controls. Those with poor control had more attachment loss and were more likely to exhibit recurrent disease. So we can conclude that prevention and control of periodontal disease must be considered an integral part of diabetes control.<sup>3</sup>

Diabetes not only is a risk factor for periodontal diseases but periodontal disease can also have a negative effect on glycemic and metabolic control in diabetic patients.<sup>8</sup> Evidence to support a negative impact of periodontal disease on diabetes was first postulated following studies of the Gila River Indian Community with a high prevalence of diabetes. It was noted that severe periodontitis was associated with increased risk of poor glycemic control (HbA1c > 9.0%) at follow-up (minimum of 2 years later), suggesting that periodontitis may be compromising diabetes control. Other studies reported increased prevalence of diabetes complications, such as cardiovascular complications, retinopathy, neuropathy and proteinuria in people with advanced periodontitis.<sup>3,8</sup>

Changes in HbA1c in non-diabetic individuals who were monitored for a period of 5 years have also been associated with the presence of periodontitis. In a longitudinal study, the (non-diabetic) participants with the most advanced periodontitis at baseline were found to have 5 times greater increase in their HbA1c values over five years (change in HbA1c  $0.106 \pm 0.03\%$ ) compared to those who did not have periodontitis at baseline (change in HbA1c  $0.023 \pm 0.02\%$ ). In conclusion, current scientific evidence suggests that there is an increased risk of developing diabetes in individuals with severe periodontitis, in comparison with subjects with good periodontal health or only slight periodontitis.<sup>3</sup>

#### The effect of periodontal treatment on diabetes control

Researchers have attempted to demonstrate the effect of periodontal treatment on metabolic control in diabetes, as the periodontal treatment has been seen to improve not only the clinical and immunological parameters of periodontitis but also long-term glycemic control in diabetes.<sup>8</sup> Systematic reviews and meta-analyses have been published which investigated the outcomes of these studies and a consistent finding has been that periodontal treatment is associated with reductions in HbA1c of the order of 0.4%. Cochrane studies review similarly identified a reduction in HbA1c of approximately 0.4% following non-surgical periodontal therapy. Although such an improvement in HbA1c may appear to be relatively modest, it may have very significant clinical impacts because every 1% reduction in HbA1c is associated with a measurably reduced risk for diabetes complications.<sup>3,9</sup>

Kiran et al randomly assigned of 44 type 2 diabetes patients with periodontal disease into 2 groups: treatment group (full mouth SRP) and non-treatment group (only oral hygiene instructions) which obtained that 50% reduction in prevalence of gingival bleeding in the treatment group after 3 months. HbA1c levels in treatment group decreased significantly (from 7.31% to 6.51%, approximately 10.94% of the baseline level) whereas the control group showed 4.42% increases in HbA1c levels although these were not statistically or clinically significant.<sup>8</sup>

Faria-Almeida et al demonstrated treatment of periodontal diseases (conventional SRP) significantly improves metabolic control of diabetes on 6 months clinical study of 20 patients divided into 2 groups (type 2 diabetes and non-diabetics) with moderate generalized chronic periodontitis. An improvement in all clinical variables was observed, with no statistically significant differences between the groups, with the exception of probing depth. The improvement observed in blood HbA1c level confirmed positive metabolic response to periodontal treatment, with a lower values at 3 and 6 months after periodontal treatment.<sup>8</sup>

In spite of the promising results of these studies, it should be noted that few randomized clinical studies have been conducted and the results are variable and at times contradictory. Generally, the results indicate that periodontal treatment improves glycemic control in type 2 diabetes, although some do not report any improvement.<sup>8</sup> Hence, it is now considered that there is sufficient evidence to justify further research into the contribution of periodontal treatment to metabolic control in diabetic patients and associated with additional medications taken as integral part of diabetes therapy management.<sup>3,8</sup>

#### Implication for the dental professional

Clearly oral and periodontal healthcare must form an integral part of diabetes management. An improved understanding of the relationship between diabetes and periodontal disease must be disseminated not only among healthcare professionals but also among diabetes patients. It is necessary to train professionals and inform patients about the benefits of oral health in relation to diabetes.<sup>8</sup>

Regarding increased susceptibility to the periodontitis in people with diabetes, this has a number of implications for dental management. It is important that diabetic patients are aware of the potential impact

their condition may have on their oral and periodontal health. Patients who are newly diagnosed with diabetes should be told about this impact and we should continue to urge our medical clinicians are unaware the link between periodontitis and diabetes and the periodontal treatment potential benefits for diabetic patients.<sup>3,9</sup>

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 instruction, non-surgical therapy, and monitoring of treatment outcomes. Effective periodontal treatment is particularly important in diabetes patients, given that periodontitis has potential negative impacts on glycemic 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>3,9</sup>

## CONCLUSION

The association between diabetes and periodontal diseases is clear that glycemic control improves periodontal conditions, while the management of periodontal infection improves metabolic status of diabetic patients. Considering the issue of high prevalence and severity of both diseases and the possibility impact for patient's health, the endocrinologist should play a key role in referring patients to dentist on a regular basis in order to monitor risk factors such as the ongoing presence of bacterial plaque in periodontal pockets. Healthcare professionals should also remember that disordered glucose metabolism can affect the development and severity of periodontal diseases.

Diabetes increases the risk for periodontitis and evidence suggests that advanced periodontitis also compromises glycemic control. Periodontal treatment has been associated with improvements in glycemic control (HbA1c reductions approximately 0,4%), though more research is required to investigate this further. Periodontal assessment is as important in people with diabetes as it is in people without diabetes and people with diabetes should be made aware of their increased risk for periodontal disease. The dental team has an important role to play in the management of people with diabetes. An emerging role for the dental team is envisaged in which, through the use of relatively simple screening tools, they may help to identify patients at risk of diabetes.

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