

# Diabetes Mellitus and Periodontitis: A two Way Relationship

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## ABSTRACT

Periodontitis is an inflammatory disease affecting the supporting structures of teeth (periodontal ligament and alveolar bone). Association between diabetes mellitus and periodontal disease is well established. Periodontitis has been reported as one of the microvascular complications of diabetes. Diabetes is a risk factor for periodontitis. Both diseases are thought to share a common pathogenesis. Poor control of diabetes with HBA1c > 8 has adverse effects on the periodontium as well as the response to periodontal therapy. Periodontitis has been shown to adversely effect glycaemic control and periodontal therapy has been postulated to improve glycaemic control in diabetics. An attempt is made herein to review the bidirectional relationship between periodontitis and diabetes mellitus so that periodontal health is considered as an integral part of management of diabetes.

**KEY WORDS:** diabetes mellitus, glycaemic control, periodontal therapy, periodontitis

## INTRODUCTION:

Diabetes Mellitus and periodontal diseases are common chronic diseases observed worldwide. Historically oral infections were thought to be localized to the oral cavity, except in the case of some associated syndromes and some untreated odontogenic infections. A change in paradigm has dispelled this notion, and a whole new concept of the status of oral cavity and its impact on systemic health and disease has evolved. Periodontal infection represents a complication that may be involved in altering the systemic physiology in diabetic patients. Since periodontitis can be more than just a localized oral infection, the effects have been hypothesized to be far-reaching. Severe chronic forms of this disease can result in systemic response to the bacteria and bacterial products that are disseminated due to breakdown of the periodontal apparatus (the ligament attachment around the tooth that includes the gingival tissues and bone). Periodontal disease has been reported as the sixth complication of diabetes along with neuropathy,

nephropathy, retinopathy and micro and macrovascular diseases<sup>[1]</sup>. An association between diabetes and periodontitis is a widely accepted phenomenon that has been shown in numerous studies. The interrelationships between diabetes and periodontal disease provide an example of systemic disease predisposing to oral infection, and once that infection is established, the oral infection exacerbates the progression of systemic disease<sup>[2,3]</sup>.

Hence, this article is an attempt to review the relationship between diabetes mellitus and periodontal disease and the potential mechanisms involved in local and systemic disease progression.

## The two-way relationship between periodontitis and diabetes mellitus:

### *Mechanisms of interaction between diabetes mellitus and periodontal disease:*

Periodontal disease includes both gingivitis and periodontitis. Gingivitis is defined as the condition where inflamed gingival tissues are associated with a tooth with no attachment loss or with previous attachment and bone loss (reduced periodontal support), but is not currently losing attachment or bone. Periodontitis, on the other hand, is defined as an inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms or groups of specific microorganisms, resulting in progressive destruction of the periodontal ligament

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and alveolar bone with pocket formation, recession, or both. It is a multifactorial disease. The development of periodontitis is dependent on many factors, like the microbial challenge, genetic risk factors, environmental and acquired risk factors<sup>[4]</sup>.

The gingival capillaries of diabetic patients not only have significantly greater basement membrane thickness<sup>[5,6]</sup> but also other aberrations such as disruption of the membrane, presence of collagen fibres within the true membrane, and swelling of endothelium<sup>[7]</sup>. It has been hypothesized that the above changes may impede oxygen diffusion, metabolite waste elimination, leukocyte migration, and diffusion of immune factors and thus contribute to increased periodontitis in diabetic patients. Gram negative bacteria have Lipopolysaccharides present in their bacterial cell wall which are potent inducer of inflammatory mediators like TNF alpha from monocytes and macrophages resulting in severe insulin resistance<sup>[4]</sup>. Defects in polymorphonuclear leukocyte (PMN) chemotaxis in diabetic patients is responsible for their increased susceptibility to periodontal infection<sup>[8]</sup>. Altered collagen metabolism would be expected to contribute to periodontal disease progression and delayed wound healing in diabetics<sup>[9]</sup>. Increased thickness of gingival capillary endothelial cell basement membranes and the walls of small blood vessels may be seen in diabetic individuals. This thickening may impair exchange of oxygen and metabolic waste products across the basement membrane. AGE accumulation results in increased cross-linking of collagen, reducing collagen solubility and decreasing turnover rate. Increased collagenase activity in diabetes mellitus results in greater degradation of newly formed, more soluble collagen. The net effect is a predominance of older, highly crosslinked AGE-modified collagen. In the capillaries, this accumulation of highly cross-linked collagen in the basement membrane increases membrane thickness. These events may play a role in altering the tissue response to periodontal pathogens, resulting in increased severity and progression of periodontitis<sup>[10]</sup>. Poorly controlled diabetic patients exhibit increased levels of beta - glucuronidase enzyme in GCF. It may be derived from polymorphonuclear cells accumulated in the gingiva due to enhanced inflammation. This enzyme causes damage to the collagen tissue and also results in severe periodontal destruction. Salivary calcium levels were found to be higher in uncontrolled DM patients as compared to controls. It aids in dental calculus formation and increases the severity of periodontal

destruction. MMP levels were significantly higher in diabetic patients with periodontal destruction as compared to non-DM patients. Expression of these enzymes may result in enhanced collagenolytic activity, tissue destruction and poor healing<sup>[11]</sup>. HLA-DR4 molecules on peripheral blood antigen cells of diabetic patients may signal greater susceptibility to periodontitis<sup>[12]</sup>. In summary, the increased risk to periodontal disease in diabetes is triggered by the plaque biofilm and the hyperglycaemic state, both of which result in a series of synergistic inflammatory reactions, with release of inflammatory mediators and cytokines causing tissue destruction and an impairment in healing responses.

### **Effect of Diabetes on the Periodontium:**

Large epidemiological studies have shown that diabetes increases the risk of alveolar bone loss and attachment loss approximately three-fold when compared to nondiabetic individuals<sup>[13]</sup>. Diabetes may result in impairment of neutrophil adherence, chemotaxis, and phagocytosis, which may facilitate bacterial persistence in the periodontal pocket and significantly increase periodontal destruction. Formation of advanced glycation end-products, a critical link in many diabetic complications, also occurs in the periodontium, and their deleterious effects on other organ systems may be reflected in periodontal tissues as well. Matrix metalloproteinases are critical components of tissue homeostasis and wound healing, and are produced by all of the major cell types in the periodontium. Production of matrix metalloproteinases such as collagenase increases in many diabetic patients, resulting in altered collagen homeostasis and wound healing within the periodontium.

### **Influence of Diabetes Mellitus on the Outcome of Periodontal Therapy:**

Diabetes Mellitus being a state of altered metabolism has effect on periodontal inflammation as well as response to periodontal treatment. Diabetic patients are known to have altered wound healing, greater chance of recurrence of periodontal disease, rapid deterioration without intervention; especially in poorly controlled diabetics. The conclusion drawn from most of the studies indicate that subjects with well-controlled diabetes exhibit clinical healing similar to non-diabetics, at least in the short term. On the basis of the available findings, there is no substantial evidence that suggests individuals with diabetes would require more thorough and aggressive

periodontal therapy than standard periodontal therapy. However, with poorly controlled diabetics, periodontal health appears to deteriorate more rapidly than in healthy individuals. Therefore, assessment of patients' metabolic status is important in determining the prognosis and recall interval for periodontal therapy<sup>[14]</sup>.

### **Role of Periodontitis on Glycaemic Control:**

The interest in the effect of periodontal disease on diabetes may be due to the finding that acute infections alter the endocrinologic-metabolic status, leading to difficulty in controlling blood sugar and increased insulin resistance. Chronic infection may result in poor metabolic control of blood sugar and increased insulin requirements. Evidence suggests that periodontal diseases can induce or perpetuate an elevated systemic chronic inflammatory state, as reflected in increased serum C-reactive protein, interleukin-6, and fibrinogen levels seen in many people with periodontitis<sup>[15]</sup>. Inflammation induces insulin resistance, and such resistance often accompanies systemic infections. Periodontal infection can induce elevated serum interleukin-6 and tumour necrosis factor-alpha levels, and may play a similar role as obesity in inducing or exacerbating insulin resistance. Studies involving mechanical periodontal treatment alone reported improvement in periodontal status only (ie. no change in glycaemic control), while studies including systemic antibiotics accompanying mechanical therapy reported an improvement in both periodontal status and glycaemic control. It has been hypothesized that these different results due to antibiotic use (especially doxycycline) may involve several mechanisms, including an antimicrobial effect. Thus, good control of serum glucose in diabetic patients appears to be a desirable goal in preventing certain infections and to ensure maintenance of normal host defense mechanisms that determine resistance and response to infection<sup>[16]</sup>.

### **Effects of Periodontal Therapy on Glycaemic Control:**

This topic has been of interest since last few decades. With better understanding of inflammatory mediators, role of periodontal treatment in controlling blood glucose levels has been studied. It is known that infections are often accompanied by tissue insulin resistance (Vki-Jarien 1989). Grossi et al. (1996) have suggested that chronic Gram-negative infections and chronic endotoxemia, such as is seen in periodontal disease could also induce insulin resistance and a

worsening of metabolic control in diabetic patients. In view of these facts, it has been hypothesized that control of periodontal infections improves metabolic control of diabetics. Periodontal treatment may involve scaling, root planning and flap surgery with or without the use of systemic or local antibiotics. It is hypothesized that successful periodontal therapy appears to reduce circulating TNF- $\alpha$  levels significantly in both systemically healthy periodontitis patients<sup>[17]</sup> and diabetic patients. TNF- $\alpha$  produced from a diposetissuesin insulin-resistant type 2 diabetes patients. In a study by Martorelli de Lima AF et al<sup>[18]</sup> it was found that with antimicrobial periodontal therapy, there was significant reduction in the number of microorganisms in periodontal pockets, circulating TNF- $\alpha$  levels and HbA1c value. A recent study by Martorelli de Lima and co-workers<sup>[18]</sup> demonstrated that the adjunctive use of locally delivered doxycycline improved the periodontal attachment levels of diabetic patients with periodontitis as compared with controls who received scaling and root planing. Similar results were shown with adjunctive systemic doxycycline, in addition to non-surgical periodontal therapy<sup>[19]</sup>.

### **CONCLUSION:**

The evidence supports viewing the relationship between diabetes and periodontal disease as bidirectional; that is, diabetes is associated with increased occurrence and progression of periodontitis, and periodontal infection is associated with poor glycaemic control in people with diabetes. While treating periodontal infection in diabetics is clearly an important component of oral health, it may also have an important role in establishing and maintaining glycaemic control. Further studies may be helpful to determine, if early development of gingival inflammation and periodontal disease in patients with diabetes represents a risk for development of other complications. Many variables need to be considered including type of diabetes, glycaemic control and preexisting periodontal disease. While dental profession recognizes the relationship of periodontal disease and diabetes mellitus, the level of awareness by the medical profession is not as apparent. Large body of evidence indicates that improved glycaemic control in patients with type 1 and type 2 diabetes results in fewer micro and macrovascular complications and reduced rate of progression of existing complications. These studies which do not include oral findings clearly suggest that appropriate glycaemic control may improve periodontal

manifestations of diabetes. Furthermore, studies in periodontal literature which have examined this question have concluded that good glycaemic control is associated with improved periodontal status<sup>[17]</sup>. With the current focus on the relationship of periodontal disease and certain systemic disorders, it is time to develop an appropriate agenda regarding the periodontal disease- diabetes mellitus relationship.

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