

Diabetes and Periodontitis: A Two Way Relationship

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ABSTRACT

Periodontitis is a destructive inflammatory disease of the supporting tissues of the teeth and is caused by specific microorganisms or group of specific microorganisms resulting in progressive destruction of periodontal ligament and alveolar bone with periodontal pocket formation, gingival recession or both. The link between periodontal disease and systemic diseases has been progressively recognized over the past two decades. Currently there is a large amount of data in epidemiological, clinical and laboratory studies that strongly correlate the role of periodontal pathogens on systemic organs by producing pro-inflammatory cytokines, chemokines and inflammatory mediators. Although the relationship between periodontal disease, inflammation and overall health has been suspected, numerous studies are providing more comprehensive evidence for this link. In this context, diabetes predisposes oral tissues to greater periodontal destruction but several studies have now identified that periodontal disease leads to poor glycemic control. It was hence predicted that there exists a two-way relationship between periodontal disease and diabetes mellitus. The regular use of Dental Air Force home dental cleaning system as an oral hygiene device is optimal for suppressing both periodontal infection and associated systemic diseases (Diabetes) as compared to conventional tooth brushing.

Periodontitis: A Microbial Infection

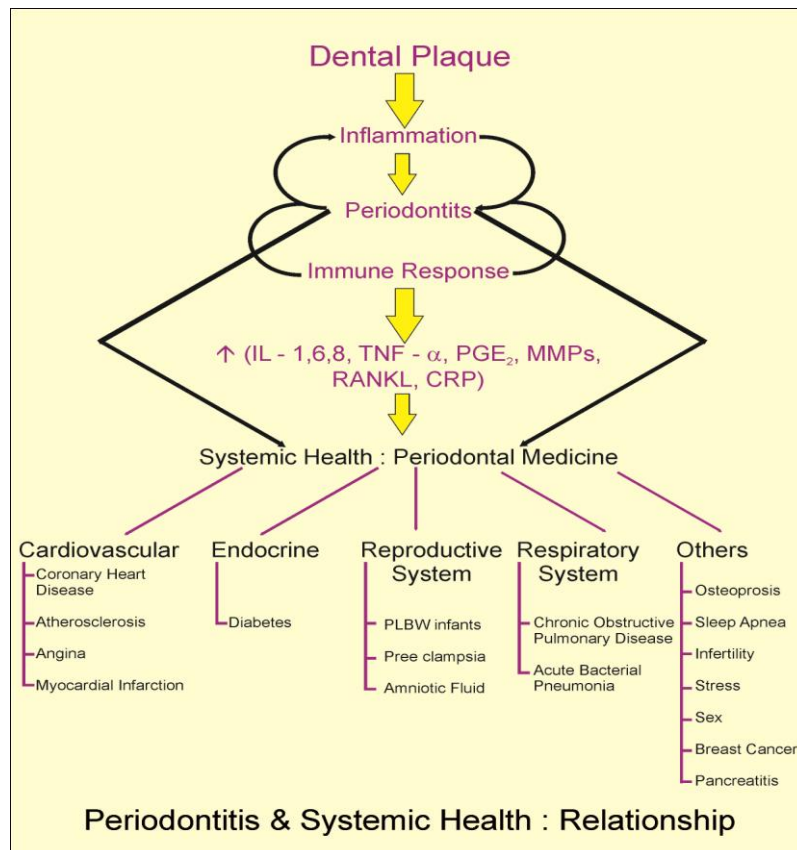
The oral cavity has the potential to harbor at least 600 different bacterial species, and in any given patient, more than 150 species may be present, surfaces of tooth can have as many as a billion bacteria in its attached bacterial plaque and good oral hygiene is the fundamental for oral integrity as it greatly affects the quality of life. [1] Periodontitis is a destructive inflammatory disease of the supporting tissues of the teeth and is caused by specific microorganisms or group of specific microorganisms resulting in progressive destruction of periodontal ligament and alveolar bone with periodontal pocket formation, gingival recession or both. Periodontal diseases are recognized as infectious processes that require bacterial presence and a host response and are further affected and modified by other local, environmental and genetic factors. [2] The host responds to the periodontal infections with an array of events involving both innate and adaptive immunity. [3] Dental plaque in oral cavity is now considered as biofilm, Dental biofilm forms via an ordered sequence of events, resulting in structured and functionally organized species of a rich microbial community and modern molecular biological techniques have identified about 1000 different bacterial species in the dental biofilm, twice as many as can be cultured. Bacteria in a biofilm have a physiology different from that of planktonic cells and live under nutrient limitation and often in a dormant state, thus a biofilm is organized to maximize energy, spatial arrangements and movement of nutrients and byproducts with advantages which includes a broader habitat range for growth, an enhanced resistance to antimicrobial agents and host defense and an enhanced ability to cause disease. [4]

Periodontitis and Systemic Health: A Complex Linkage

Association of periodontal infection with organ systems such as cardiovascular system, endocrine system, reproductive system, and respiratory system makes periodontal infection a complex multiphase disease. Inflamed periodontal tissues produce significant amounts of pro-inflammatory cytokines, mainly interleukin1 beta (IL-1 β), IL-

6, PGE₂, and tumor necrosis factor alpha (TNF- α), which may have systemic effects on the host. Periodontitis initiates systemic inflammation and can be monitored by inflammatory markers like C-reactive protein or fibrinogen levels. [5] The link between periodontal disease and systemic diseases has been progressively recognized over the past two decades. Currently there is a large amount of data in epidemiological, clinical and laboratory studies that strongly correlate the role of periodontal pathogens on systemic organs by producing pro-inflammatory cytokines, chemokines and inflammatory mediators. Bacteria and byproducts from the oral cavity are commonly introduced into the bloodstream; the extent of the pathogenic bacterial migration depends on the severity of the gingival inflammation. Oral bacteria have been found in arteries, lungs, the brain, amniotic fluid and pancreas. The vibrant effect of dental plaque- host immune reaction leading to adverse influence on systemic health is illustrated in Fig.1. [6]

Figure 1: Periodontitis and Systemic health Linkage



Diabetes: A Global Disease

The term “diabetes mellitus” (DM) describes a group of disorders characterized by elevated levels of glucose in the blood and abnormalities of carbohydrate, fat and protein metabolism. DM is a metabolic disorder characterized by impaired action, secretion of insulin or both, resulting in hyperglycemia presents with the classical triad of symptoms: Polydipsia, polyuria and polyphagia which are often accompanied by chronic fatigue and loss of weight. [7] Diabetes mellitus is a metabolic disorder characterized by hyperglycemia due to defective secretion or activity of insulin. [8] The hyperglycemia is the result of a deficiency of insulin secretion caused by pancreatic b-cell dysfunction or of resistance to the action of insulin in liver and muscle, or a combination of these. Frequently this metabolic disarrangement is associated with alterations in adipocyte metabolism. Diabetes is a syndrome and it is now recognized that chronic hyperglycemia leads to long-term damage to different organs including the heart, eyes, kidneys, nerves, and vascular system. A conclusive diagnosis of diabetes mellitus is made by assessing glycated hemoglobin levels; in those people with diabetes, sequential fasting plasma glucose levels will be 7 mol/L or more. There are several etiologies for diabetes and although establishing the type of diabetes for each patient is important, understanding the pathophysiology of the various forms of the disease is the key to appropriate treatment.

Clinical Presentation of Diabetes

Type 1 diabetes

The onset of type 1 diabetes is usually rather abrupt when compared to that of type2. The classic signs and symptoms of diabetes are polyuria, polydipsia, and polyphagia; however, others may be present. [9] Sustained

hyperglycemia causes osmotic diuresis, leading to polyuria. This increased urination causes a loss of glucose, free water, and electrolytes in the urine, with consequent polydipsia. Postural hypotension may be present secondary to decreased plasma volume, and weakness can occur as a result of potassium wasting and catabolism of muscle proteins. Weight loss often takes place despite the patient's excessive sense of hunger (polyphagia) and frequent food intake. Blurred vision is a consequence of the exposure of the lens and retina to the hyperosmolar state. If the insulin deficiency is acute, as often occurs in type 1 diabetes, these signs and symptoms develop abruptly. When ketoacidosis is present, greater hyperosmolarity and dehydration are present causing nausea, vomiting, and anorexia with various levels of altered consciousness. Type 1 diabetes mellitus encompasses diabetes resulting primarily from destruction of the beta-cells in the islets of Langerhans of the pancreas and this condition often leads to absolute insulin deficiency. The cause may be idiopathic or due to a disturbance in the autoimmune process. The onset of the disease is often abrupt, and patients with this type of diabetes are more prone to ketoacidosis and wide fluctuations in plasma glucose levels.

Type 2 diabetes

Patients with type 2 diabetes can be initially asymptomatic or may have symptoms of polyuria and polydipsia. Others may present initially with pruritis or evidence of chronic or acute skin and mucosal infections such as candidal vulvovaginitis or intertrigo. Typically, type 2 diabetic patients are obese and may present with neuropathic or cardiovascular complications, hypertension, or microalbuminuria. Because type 2 diabetes can remain undiagnosed for many years, these patients may have significant diabetic complications even at the time of initial diagnosis. The causes of type 2 diabetes mellitus range from insulin resistance with relative insulin deficiency to a predominantly secretory defect accompanied by insulin resistance. The onset is generally more gradual than for type 1, and this condition is often associated with obesity. In addition, the risk of type 2 diabetes increases with age and lack of physical activity, and this form of diabetes is more prevalent among people with hypertension or dyslipidemia. People with type 2 diabetes constitute 90% of the diabetic population.

Gestational diabetes mellitus (GDM)

Is glucose intolerance that begins during pregnancy. The children of mothers with GDM are at greater risk of experiencing obesity and diabetes as young adults. [10] As well, there is a greater risk to the mother of developing type 2 diabetes in the future. A wide variety of relatively uncommon conditions fall into the category of "other specific types." These consist mainly of specific genetically defined forms of diabetes and diabetes associated with other diseases or drug use.

Periodontitis and Diabetes: A Two Way Relationship

Although the relationship between periodontal disease, inflammation and overall health has been suspected, numerous studies are providing more comprehensive evidence for this link. In this context, diabetes predisposes oral tissues to greater periodontal destruction but several studies have now identified that periodontal disease leads to poor glycemic control. It was hence predicted that there exists a two-way relationship between periodontal disease and diabetes mellitus. [7] Although diabetes is a metabolic disorder and periodontitis is an infectious disease, the relationship occurs through the ability of both conditions to induce an inflammatory response leading to the production of inflammatory mediators. These pro-inflammatory cytokines such as Interleukin-6 impair the glucose stimulated release of insulin from the pancreas. In fact, periodontal disease has been considered as the sixth complication of diabetes. [7] Periodontal therapy, on the other hand, can stabilize glycemic control and reduce complications from unstable blood sugar levels.

People with type 1 diabetes are at greater risk of developing gingivitis. Both children and adults with poor metabolic control show a tendency toward higher gingivitis scores. The prevalence of gingivitis in children and adolescents is nearly twice that observed in populations of children and adolescents without diabetes. Studies indicate that the severity and extent of gingivitis are significantly increased in young patients with diabetes. The association of diabetes with gingivitis in children and adolescents is so widely accepted that diabetes mellitus-associated gingivitis is included as a specific entity in the most recent classification of periodontal diseases. [11] Unlike gingivitis, periodontitis is uncommon in children younger than 12 years, even among those with diabetes. In adolescence, periodontitis does occur, but the extent of attachment loss is usually minimal. The prevalence of periodontal disease in juveniles with type 1 diabetes has been reported to be 9.8 percent, compared with 1.7 percent in those without diabetes. The discrepancies between these two patient populations may be related to different levels of metabolic/glycemic control and other factors, such as different gene pools, which appear to have a strong relationship with rapid periodontal breakdown.

Periodontal disease may have a significant impact on the metabolic state of diabetes. The presence of PD increases the risk of worsening glycemic control in time. Taylor [12], in a cohort study of patients with diabetes with severe PD for two years, found a relative risk six times more the probability of worsening glycemic control in

comparison to periodontally healthy diabetics. Inflammation has been suggested to cause increased insulin resistance.

Different biologic mechanisms have been proposed to explain the basis of this relationship. [13] Despite the fact that these mechanisms have been investigated, little progress has been made in the understanding of the molecular basis of the relationship between periodontitis and diabetes, in particular at a genomic level. Bioinformatics can play a central role in the analysis and interpretation of genomic and proteomic data. [14] Recently, a bioinformatics method defined as the "leader gene approach" was proposed. [15]

Hypotheses for the Association between Diabetes and Periodontitis

It is possible to propose at least two hypotheses for testing the relationship between periodontitis and diabetes. The first proposes a direct causal or modifying relationship in which the consequent hyperglycemia and hyperlipidemia of diabetes result in metabolic alterations which may then exacerbate the bacteria-induced inflammatory periodontitis.

The second hypothesis proposes that an unfortunate combination of genes (gene sets) could result in a host who, under the influence of a variety of environmental stressors, could develop both periodontitis and diabetes. This view is supported by the observation of common immune mechanisms involved in the pathogenesis of both diabetes and periodontitis; their genetic association with the HLA region of chromosome 6, where a number of genes involved in the immune response are situated; and the bidirectional association indicating that, not only is the prevalence of periodontitis higher in diabetics than in non-diabetics, but also that the prevalence of diabetes is higher in persons with periodontitis than in controls. It is of course possible that the two mechanisms proposed in the hypotheses are not independent but that they can function together in what is obviously a complicated set of events.

Periodontal Management in Diabetes Patients

The dental practitioner is extremely likely to encounter periodontal patients who suffer from undiagnosed or poorly controlled diabetes mellitus or others who are diagnosed and well maintained. More stringent medical standards have narrowed the criteria for good metabolic control, with the result that an increased number of periodontal patients may now fall into the inadequately controlled category. To properly evaluate periodontal patients, the dental clinician must be aware of the general and oral signs and symptoms of diabetes mellitus. Appropriate dental practice requires a thorough oral examination and an appropriate medical history. The medical history format must include questions about patient's family history of diabetes mellitus and any general symptoms that may raise the practitioner's level of suspicion regarding this disease. The oral examination should identify oral features suggestive of diabetes mellitus, and the presence of any such features may indicate a need for medical consultation.

The well-controlled diabetes mellitus patient with periodontal disease is often an acceptable candidate for complete periodontal therapy, including surgical procedures when indicated. As discussed previously, however, the presence of medical complications associated with diabetes mellitus should be carefully evaluated and considered in any periodontal therapeutic decision. In most instances periodontal surgical therapy should be carefully planned and coordinated with the patient's physician to insure minimal disruption of metabolic diabetes mellitus control. Most authorities recommend that periodontal surgery be scheduled in the morning after breakfast and medication administration. Treatment procedures should be short (2 hours or less), as atraumatic as possible and should not significantly interfere with the patient's normal dietary intake. Patient anxiety should be managed to minimize endogenous epinephrine release, because epinephrine may increase insulin utilization and deplete insulin levels more quickly. In most instances preoperative oral sedation is suitable for this purpose. In the event that general anesthesia or intravenous conscious sedation techniques are necessary or if extensive surgical procedures are likely to alter the patient's dietary intake, then changes in the type 1 patient's insulin intake may be necessary under the guidance of the patient's physician. Decisions regarding the prophylactic use of antibiotics in conjunction with periodontal surgery are best made on a case by- case basis since there is no evidence-based information to indicate that antibiotic premedication is necessary. [16] The poorly controlled type 1 patient is not a good candidate for periodontal therapy other than necessary emergency services. Medical coordination is probably indicated for any type of periodontal therapy and hospitalization may be required for emergency care. If time permits, microbiological testing is desirable to identify putative periodontal pathogens prior to antibiotic therapy. If stable metabolic control is achieved, routine periodontal therapy may be considered with close medical monitoring.

In general, all diabetes mellitus patients should be encouraged to maintain meticulous oral hygiene and to receive supportive periodontal therapy at intervals necessary to sustain a high level of periodontal health. Patients should be carefully monitored for dental caries and home and office use of fluoride caries preventive agents is recommended. Diabetes mellitus-related xerostomia should be managed on a case-by-case basis, but in general patients should be encouraged to adhere to strict diabetes mellitus metabolic control and to avoid smoking or the

use of alcohol (including mouthrinses with high alcohol content) and caffeine-containing beverages. Artificial saliva substitutes and frequent ingestion of water may be of benefit. A pilocarpine-containing drug (Salagen A) has recently been approved by the Food and Drug Administration for management of xerostomia resulting from therapeutic radiation exposure and Sjögren's syndrome. The benefits of this drug in managing diabetes mellitus or drug induced xerostomia have not yet been studied, and it should only be prescribed with the consent of the patient's diabetologist. There is some evidence to suggest that oral hygiene products containing the detergent sodium lauryl sulfate may be irritating to the mucous membranes of xerostomic patients, and this agent should be avoided if xerostomia is a problem for the diabetes mellitus patient. Patients should be encouraged to stimulate salivary flow by the use of sugarless gum or natural salivary stimulants such as chewing raw carrots and celery.

Frequent monitoring for the overgrowth of oral fungal organisms such as *Candida albicans* is indicated, and on occasion the prophylactic use of topical antifungal agents may be necessary. Most topical oral antifungal agent contains chlorine dioxide and chlorhexidine. Improvement in burning mouth and altered taste sensation may occur when diabetes mellitus metabolic control is established or when xerostomia and associated candidiasis are controlled.

Placement of implants in diabetic patients is a matter of great interest to periodontists. Successful implantation has been described in well-controlled individuals with diabetes mellitus^[17], but two recent studies of uncontrolled diabetes mellitus in animals have suggested an altered pattern of bone formation in relation to implants. In view of these studies, plus clinical evidence of delayed healing in diabetic patients, it is doubtful that the uncontrolled or poorly controlled diabetes mellitus patient is a suitable candidate for implant placement.

CONCLUSION

The epidemiological associations between periodontitis and diabetes could be the result of at least two similar but distinct pathogenic pathways: a direct causal relationship in which the consequences of diabetes act as modifiers of periodontal disease expression or alternatively, a common pathological defect which results in a host susceptible to either, or both, diseases. Regular oral hygiene plays a vital role in lowering the pro inflammatory cytokines and further studies have provided evidence that control of periodontal infection has an impact on improvement of glycemic control evidenced by a decrease in demand for insulin and decreased HbA1c.^[18, 19, 20, 7] In the study subjects using Dental Air Force home dental cleaning system as oral hygiene device showed more reduction in HbA1c from base line to six month i.e. from 5.56 ± 0.51 to 5.26 ± 0.52 as compared to subjects using conventional tooth brushing.^[21] The regular use of Dental Air Force home dental cleaning system as oral hygiene device is optimal for suppressing both periodontal infection and associated systemic diseases (Diabetes) as compared to conventional tooth brushing.

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