

The relationship between oral health and diabetes mellitus

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The term “diabetes mellitus” is used to identify a group of disorders characterized by elevated levels of glucose in the blood. This elevation is the result of a deficiency in insulin secretion or an increased cellular resistance to the actions of insulin, leading to a variety of metabolic abnormalities involving carbohydrates, fats and proteins. A number of pathological mechanisms related to elevated levels of glucose in the blood have been defined, including the activation of the sorbitol pathway, the formation of advanced glycation end-products (AGEs), the damaging effect of oxidative stress and altered lipid metabolism. These mechanisms have been associated with classical clinical complications of diabetes mellitus such as retinopathy, nephropathy, neuropathy, macrovascular disease and poor wound healing. In 1993, Loe¹ proposed that periodontal disease was the sixth complication of diabetes mellitus. In a 2008 article, Taylor and Borgnakke² identified periodontal disease as a possible risk factor for poor metabolic control in people with diabetes mellitus. This bidirectional relationship between periodontal disease and diabetes mellitus makes diabetes a disorder of importance to dentists and dental hygienists and to patients seen in the dental office.

ABSTRACT



Background. The term “diabetes mellitus” describes a group of disorders characterized by elevated levels of glucose in the blood and abnormalities of carbohydrate, fat and protein metabolism. A number of oral diseases and disorders have been associated with diabetes mellitus, and periodontitis has been identified as a possible risk factor for poor metabolic control in subjects with diabetes.

Methods. The authors reviewed the literature to identify oral conditions that are affected by diabetes mellitus. They also examined the literature concerning periodontitis as a modifier of glycemic control.

Results. Although a number of oral disorders have been associated with diabetes mellitus, the data support the fact that periodontitis is a complication of diabetes. Patients with long-standing, poorly controlled diabetes are at risk of developing oral candidiasis, and the evidence indicates that periodontitis is a risk factor for poor glycemic control and the development of other clinical complications of diabetes. Evidence suggests that periodontal changes are the first clinical manifestation of diabetes.

Conclusions. Diabetes is an important health care problem. The evidence suggests that oral health care providers can have a significant, positive effect on the oral and general health of patients with diabetes mellitus.

Key Words. Diabetes mellitus; oral health; oral candidiasis; periodontitis.

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In this article, we review the association of oral health and diabetes mellitus.

ORAL MANIFESTATIONS OF DIABETES MELLITUS

A number of oral disorders have been associated with diabetes mellitus. The association of diabetes mellitus and periodontal diseases (such as gingivitis and periodontitis) has received the greatest attention and is the focus of this article. In addition to gingivitis and periodontitis, Ship³ listed dental caries, salivary dysfunction, oral mucosal diseases, oral infections such as candidiasis, taste and other neurosensory disorders.

Dental caries. The occurrence of dental caries in patients with diabetes mellitus has been studied, but no specific association has been identified.³ The relationship between dental caries and diabetes mellitus is complex. Children with type 1 diabetes often are given diets that restrict their intake of carbohydrate-rich, cariogenic foods, whereas children and adults with type 2 diabetes—which often is associated with obesity and intake of high-calorie and carbohydrate-rich food—can be expected to have a greater exposure to cariogenic foods. Furthermore, a reduction in salivary flow has been reported in people with diabetes who have neuropathy,⁴ and diminished salivary flow is a risk factor for dental caries. The literature presents no consistent pattern regarding the relationship of dental caries and diabetes.⁵

Salivary dysfunction. Dry mouth, or xerostomia, has been reported in people with diabetes mellitus.⁴ Salivary dysfunction, however, can be difficult to diagnose. Salivary flow may be affected by a variety of conditions, including the use of prescription medications and increasing age, and it appears to be affected by the degree of neuropathy and subjective feelings of mouth dryness that may accompany thirst.⁴ These variables are relevant for adults with diabetes mellitus. Therefore, although no definitive association of diabetes and reduced salivary flow has been identified, this complication has been reported in people with diabetes.

Oral mucosal diseases and other oral infections. A number of types of oral mucosal lesions, including lichen planus and recurrent

aphthous stomatitis, have been reported in people with diabetes mellitus. Not all study results have showed this association, and these are relatively common disorders that often are observed in patients who do not have diabetes. In contrast, oral candidiasis has been a more consistent finding in patients with diabetes⁶ (Figure 1). Candidiasis is a manifestation of an immunocompromised state, and a reduction in salivary flow is another risk factor for oral candidiasis.

Taste and other neurosensory disorders. Taste disturbances have been reported in patients with diabetes mellitus,³ but all investigators have not observed this finding. Although patients with diabetes who receive hemodialysis have been reported to have altered taste,⁷ it is a complex symptom, and it may be related to salivary flow

and changes in food intake associated with disease management. Other neurosensory disorders of the oral and perioral tissues, including burning mouth syndrome and dysphagia, have been reported in patients with diabetes.³ Prevalence data are not available. Retinopathy and peripheral neuropathy that affects patients' hands may severely limit a patient's ability to perform oral hygiene procedures.³

Gingivitis and periodontitis.

In contrast to other reported oral manifestations of diabetes mellitus, periodontal disease is a recognized and well-documented complication of diabetes (Figure 2). The evidence supporting this relationship is based on epidemiologic data and animal model studies that help explain the pathophysiology of periodontal disease as a complication of diabetes mellitus.^{8,9} Data suggest that periodontal disease may increase the risk of experiencing poor metabolic control.²

PATHOGENESIS OF PERIODONTITIS AS A COMPLICATION OF DIABETES

Once it was recognized that periodontal disease was more prevalent and more severe in people with diabetes than in people without diabetes, researchers sought specific biological mechanisms

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ABBREVIATION KEY. AGE: Advanced glycation endproduct. GPD: General practice dentist. HbA_{1c}: Glycosylated hemoglobin. NHANES III: Third National Health and Nutrition Examination Survey. RAGE: Receptor for AGE.



Figure 1. Oral candidiasis in a patient with poorly controlled diabetes mellitus. The dorsum of the tongue is erythematous, and numerous hyphae were present microscopically.

to explain the association. Diabetes is believed to promote periodontitis through an exaggerated inflammatory response to the periodontal microflora. The subgingival microflora in patients with periodontitis who have diabetes mellitus generally is equivalent to that observed in patients with periodontitis who do not have a diagnosis of diabetes.^{10,11}

The formation of AGEs occurs when excess available glucose is in contact with structural and other proteins. This process is not driven enzymatically, and once they are formed, AGEs bind to a specific cellular receptor, known as the receptor for AGE (RAGE).⁸ RAGE is found on endothelial cells and monocytes, which is of importance in periodontitis. The binding of AGE and RAGE causes a series of proinflammatory events that might be self-sustaining because AGE-RAGE binding on the surface of endothelial cells induces the expression of vascular cell adhesion molecule-1 that attracts monocytes to the luminal side of the endothelial cells, thus perpetuating the inflammatory response. Graves and colleagues¹² reviewed the pathogenesis of periodontal disease in patients with diabetes and concluded that, in addition to the robust inflammatory response, enhanced apoptosis (the sequence of programmed events leading to cell death) may contribute to periodontitis as a complication of diabetes. If apoptosis is enhanced, the effects, including delayed wound healing, can be detrimental. Therefore, enhanced inflammation leading to tissue destruction and diminished repair of damaged tissue may contribute to the periodontal tissue destruction seen in patients with diabetes.

Taylor¹³ and Taylor and Borgnakke² summarized the clinical studies in which periodontitis as



Figure 2. Periodontal disease in a patient with poorly controlled diabetes mellitus. This palatal view displays granulomatous tissue at the gingival margin, especially evident at teeth nos. 10 and 14. Spontaneous suppuration also is present.

a complication of diabetes mellitus was examined. Taylor¹³ identified 48 studies published in the English language between 1960 and 2000 in which periodontal disease in people with diabetes was evaluated, and the results of 44 studies supported diabetes as a risk factor for periodontitis. There were 41 cross-sectional studies (with results from 37 showing a relationship) and seven prospective studies (with results from all seven showing a relationship). In a subsequent review, Taylor and Borgnakke² identified 17 cross-sectional articles that were published in the English language between 2000 and 2007. The results from 13 supported the conclusion that periodontitis is more prevalent and severe in patients with diabetes mellitus than in patients without diabetes mellitus. Therefore, the results from 57 of the 65 studies support this association.

Tsai and colleagues¹⁴ analyzed the Third National Health and Nutrition Examination Survey (NHANES III) database to examine the relationship of glycemic control (as assessed by means of fasting plasma glucose and glycosylated hemoglobin [HbA_{1c}]) to the presence of severe periodontitis. This analysis included 4,343 adults between the ages of 45 and 90 years. Diabetic status was defined on the basis of both the level of glycemic control on the day of the examination (assessed by means of fasting plasma glucose) and during the prior two to three months (as assessed by means of HbA_{1c}). With use of multivariable modeling to control for other risk factors for periodontitis, the odds ratio of having periodontitis in adults with poorly controlled diabetes mellitus was 2.9 compared with that in adults without diabetes mellitus. Furthermore, for people who had diabetes mellitus but better glycemic control, the odds ratio was 1.56. This

study is important because of the nationally representative population and the consideration of multiple complicating variables.

Another aspect of the relationship between diabetes mellitus and periodontitis was presented in a series of studies in which researchers examined the oral manifestations of diabetes in children and adolescents. In one, Lalla and colleagues¹⁵ examined 350 children and adolescents with diabetes mellitus and 350 children and adolescents without diabetes mellitus (all 6-18 years of age). They used three definitions of periodontal disease, which incorporated attachment loss, gingival bleeding or both. With use of multiple regression analysis to account for a variety of variables, the investigators observed greater prevalence of periodontal disease and tissue inflammation in children with diabetes mellitus than in children without diabetes mellitus regardless of the definition used.

The mean odds ratio for the three definitions of periodontal disease was 2.96. This same database was used to examine the effect of diabetes-associated variables on periodontal conditions.¹⁶ Using a fully adjusted model, researchers found that mean HbA_{1c} during the two years before the examination was associated with periodontal destruction (odds ratio, 1.31; 95 percent confidence interval, 1.03-1.66; $P < .03$). This association was not seen for duration of diabetes mellitus or body mass index-for-age percentile. These study results are important because they show periodontal disease as the first clinical complication of diabetes mellitus (the children and adolescents with diabetes mellitus did not have evidence of other clinical complications of diabetes mellitus) and demonstrate a relationship between poor long-term metabolic control and periodontal manifestations of diabetes mellitus. Similar relationships have been seen between HbA_{1c} and other clinical complications in longitudinal evaluations of patients with diabetes.^{17,18}

INFLUENCE OF PERIODONTITIS ON DIABETES MELLITUS

Researchers examining the influence of periodontitis on diabetes have assessed how treatment of periodontitis influences glycemic control. Taylor

and Borgnakke² reviewed the influence of periodontitis on glycemic control in diabetes mellitus, as well as the association of periodontitis and other clinical complications of diabetes mellitus.

The effect of periodontitis on diabetes mellitus is believed to result from the nature of the inflammatory response in the periodontal tissues. A number of proinflammatory cytokines produced in inflamed periodontal tissue, including tumor necrosis factor- α , interleukin 6 and interleukin 1, antagonize insulin.¹⁹ These mediators gain access to the circulation via the periodontal microcirculation and can affect tissues and organs at distant sites.

In a literature review, Taylor and Borgnakke² found that in seven randomized controlled trials researchers examined the effect of periodontal therapy on glycemic control, and the results from four demonstrated a positive effect as indicated

by a reduction in HbA_{1c}. In four of the seven studies, antibiotics were used systemically (three studies) or were delivered locally (one study), and the results from three of the four studies (two systemic, one local) indicated a beneficial effect. Taylor and Borgnakke² also examined 13 periodontal treatment studies that were not randomized controlled trials and found that the results of eight indicated a beneficial effect of treatment on glycemic control.

A number of observational studies provide further evidence

to support the concept that periodontitis can adversely effect glycemic management. Taylor and colleagues²⁰ reported that when they compared patients with and without periodontitis who had moderate-to-good glycemic control, the patients with periodontitis had a greater likelihood of having poor glycemic control two years later.

The results of two longitudinal studies of the Gila River Indian Community in Arizona support the relationship between poor periodontal health and risk for clinical complications of diabetes mellitus. Saremi and colleagues²¹ studied 628 adults 35 years or older who had diabetes mellitus for a median of 11 years. Using a fully adjusted model, the researchers found that the risk of death from cardiac or renal disease for people with severe periodontitis was 3.2 times higher than that of

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people with no, mild or moderate periodontitis. Shultis and colleagues²² examined periodontitis as a risk factor for renal complications of diabetes mellitus, including nephropathy and end-stage renal disease. They used the same definitions of periodontal disease as did Saremi and colleagues²¹ and observed similar findings. Using a fully adjusted model, they found that the incidence of nephropathy was 2.0 to 2.6 times greater in people who had moderate or severe periodontitis or who were edentulous than it was in those who had no or mild periodontitis. The incidence of end-stage renal disease was even higher for patients with moderate or severe periodontitis and for edentulous people, with hazard rates ranging from 2.3 to 4.9. It has not been determined whether periodontal therapy will reduce the incidence of renal disease in people with diabetes mellitus.^{2,22}

A number of related questions have been raised regarding the data supporting a bidirectional relationship between diabetes mellitus and periodontitis.²³ Periodontitis is a clinical complication of diabetes mellitus. Furthermore, approximately 30 percent of people with diabetes mellitus have undiagnosed diabetes mellitus. Therefore, the dental office is a health care site that can help identify undiagnosed diabetes mellitus, which can lead to better management of the care of patients with diabetes.

To examine the topic of diagnosing diabetes in the dental office, Borrell and colleagues²⁴ used the NHANES III database to develop a predictive model for identifying undiagnosed diabetes mellitus. They used self-reported information and a periodontal examination in their analysis. The self-reported data included a family history of diabetes mellitus and a history of hypertension and hypercholesterolemia. Probabilities of undiagnosed diabetes mellitus were calculated for people who were 45, 50, 55 and 60 years of age. Data were reported separately by sex and for African-American, Mexican-American and white subjects. For 45-year-old people who had a family history of diabetes, hypertension and hypercholesterolemia and who had periodontitis, probabilities ranged from 53 (Mexican-American men) to 27 percent (white women). As age increased, all probabilities increased. The primary conclusion from this study was that the dental office could be a location at which previously undiagnosed diabetes mellitus can be identified.

DIABETES MANAGEMENT IN THE DENTAL OFFICE

Dentists' willingness to be involved in primary health care activities in the dental office, including managing the care of patients with diabetes mellitus, has been assessed. Study investigators have reported on the attitudes, orientations and practice behaviors of general practice dentists (GPDs) and periodontists regarding these activities. In one study, investigators reported on the attitudes and behaviors of GPDs regarding their active involvement in managing the care of patients with diabetes mellitus and in smoking cessation activities.²⁵ The results indicated that most GPDs reported a lack of confidence in their ability to screen patients for diabetes mellitus, viewed active management of care of patients with diabetes mellitus as peripheral to their role as health care professionals and thought that their colleagues and patients did not expect them to perform such activities. When the types of activities GPDs actually perform were explored, the practitioners reported performing more assessment and advising activities than active management activities.

In a subsequent study, the researchers compared the attitudes and behaviors of GPDs and periodontists regarding patients with diabetes mellitus or patients who smoke.²⁶ Periodontists were chosen as the comparative group because diabetes and smoking are the two most important risk factors for periodontitis. Although periodontists tended to identify risk and management behaviors for patients who have diabetes mellitus or smoke more frequently than did GPDs, both groups of dentists tended more to engage in activities that could be classified as inquiring and discussing, as opposed to actively managing these risk factors. Researchers found that proactive management of the care of patients was not performed routinely.

CONCLUSIONS

Diabetes mellitus is a disease of which the general public and practicing dentists and dental hygienists should be aware. On the basis of the available data, we can conclude that practicing dentists and dental hygienists can have a significant, positive effect on the oral and general health of patients with diabetes mellitus. Since approximately eight percent of the U.S. population is thought to have diabetes mellitus, preva-

lence increases with age, and our population is aging, a greater role for the oral health care team in the management of the care of patients with diabetes mellitus is both warranted and appropriate.²⁷ Although many aspects of this new component of dental practice need to be developed, it is an opportunity the profession should embrace. ■

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