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Chapter 5

Diabetes as a Risk for Periodontal Disease; Association Studies

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Abstract

Diabetes affects 1/10 adults and periodontal disease 4/10 adults in the U.S., and they are linked. Individuals with diabetes are more likely to suffer from periodontal disease and periodontal disease affects glycemic control and complications of diabetes. The role of diabetes as a risk factor for periodontal disease and other oral conditions will be discussed in this chapter. The fact that type 2 diabetes, especially uncontrolled is a risk factor for periodontal disease has been long recognized, however the role of type 1 diabetes and gestational diabetes in periodontal risk are recently described. Also diabetes as a risk factor for tooth loss has more recently been described and the deleterious effects of tooth loss especially edentulism in comparing the diet of patients with diabetes now is fully appreciated. From longitudinal studies it is clear that diabetes often precedes periodontitis and hence may contribute to the causal pathway of periodontitis. Other oral manifestations of diabetes include increased risk of oral and non-oral (vaginal) fungal infections. In patients with diabetes there is often reduced salivary flow associated with diabetes medications, and neuropathy affecting the salivary glands. This may lead to increased caries. Burning mouth, resulting from diabetes neuropathy, and taste impairment may also be seen. It has long been known that there is delayed wound healing in patients with diabetes, especially if uncontrolled. Hence it is critical to achieve good glycemic control before carrying out surgical procedures or dental implant placement in patients with diabetes. Clinically important factors about the association of diabetes and periodontal disease includes:

- a) Type 1 and type 2 diabetes, as well as gestational diabetes increase the risk for periodontal disease, especially if uncontrolled.
- b) Diabetes also increases the risk of tooth loss which interferes with diet often resulting in poor glycemic control.
- c) Diabetes can result in increased oral fungal infections and fissured tongues. Diabetes can also lead to burning mouth and loss of taste sensation, both of which can interfere with eating resulting in poor nutrition.
- d) Strict control of blood sugar, weight, and adequate exercise can result in good diabetes control and prevention and management of periodontal disease can result in good oral health. Both can be obtained in patients with diabetes to help ensure a longer and healthy life for many patients.

Introduction

Periodontal disease and diabetes mellitus are two of the most common chronic diseases of man and they are linked. The association of periodontal disease and diabetes has been termed a “two-way relationship” with diabetes increasing the risk for periodontal disease and periodontal disease adversely affecting glycemic control and increasing the severity of complications of diabetes.¹

In this chapter we will discuss the evidence for the role of diabetes in increasing the risk for periodontal disease, while in Chapter 7 in this volume, the role of periodontal disease adversely affecting diabetes is discussed.

The Burden of Periodontal Disease and Diabetes Mellitus

Periodontitis affects 42% of adults in the U.S. over 30 years of age.² Mild/moderate periodontitis accounts for 34.4% and severe periodontitis accounts for 7.8% of the total. Data from 37 countries shows that severe periodontitis affect 11.2% of the population on average, ranging from 5% for individuals from Oceania and 20.4% among Latin Americans. It is the 6th most prevalent among 291 diseases assessed globally.^{3,4}

Burden of Diabetes Mellitus

Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia associated with defective insulin production, insulin action or both. In the U.S. 9.4% of adults had diabetes in 2018.⁵ Of these 23.1 million were diagnosed and about 24% were unaware of their diabetes. The prevalence has tripled worldwide from 2006 to 2017.⁶ Overall, type 2 diabetes accounts for 90% of the cases, and type 1 or immune-mediated diabetes and gestational diabetes account for most of the rest.⁹ Other types of diabetes including maturity-onset diabetes of the young and pancreatic disease or drug and chemical induced diabetes are rare.⁸

The prevalence of diabetes varies among the countries of the world, with China, India, and the U.S. having the highest prevalence.⁶ Pre-diabetes or increased risk for diabetes occurs in about 1/3 of U.S. adults. It is defined as a fasting plasma glucose levels of 100-125 mg/dl, and/or elevated HbA1c of 5.7-6.4%. Prediabetes predisposes to manifest diabetes with about 2/3 converting in 3 years.⁵ Hyperglycemia affects one out of six pregnancies worldwide, of which 86.4% are due to gestational diabetes.⁶ A large proportion of women with gestational diabetes will develop diabetes 3-6 years post-partum.⁷

Diabetes Complications

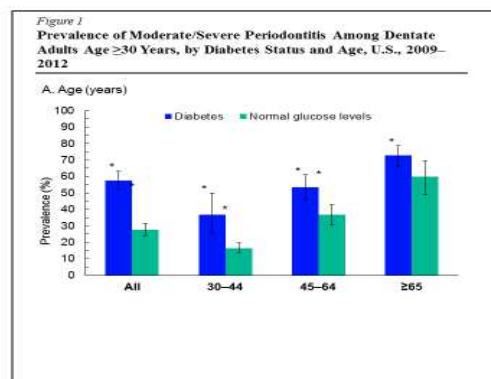
Hyperglycemia, especially of long duration, leads to diabetes complications and these complications are similar for all types of diabetes. Complications of diabetes include

dehydration, hyperosmolar coma, poor wound healing, and diseases such as myocardial infarction, stroke, limb ischemia, kidney failure, retinopathy leading to blindness, neuropathy, neurocognitive decline, and foot infectious which can lead to amputation.⁸ Heart disease and stroke are the main cause of death among those with diabetes. Diabetic retinopathy is the leading cause of blindness, and diabetes is the leading cause of kidney disease in the U.S. Pregnant women with glycemia or gestational diabetes mellitus are at high risk of transgenerational effects on their offspring including obesity, hypertension, and kidney disease.⁶ Periodontal disease which occurs in the majority of adults with diabetes is also a complication of diabetes. The periodontal complications of uncontrolled diabetes are often devastating resulting in increased risk for death, heart disease and stroke at rates 2-4 times higher than in normal individuals.¹⁰

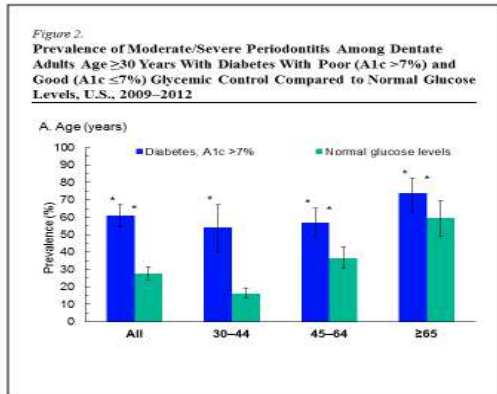
Diabetes and Periodontitis

Cross-Sectional Studies

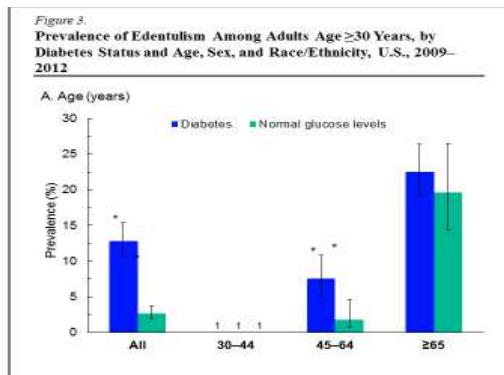
The most recent cross-sectional study defines the relationship of diabetes to periodontal disease in over 10,000 individuals representing over 143 million employed adults in the U.S. examined from 2009-2012.¹¹ The NHANES survey of the U.S. employed population and uses a whole mouth examination of periodontal disease, which gives a true picture of the prevalence of periodontal disease.



From Figure 1, it can be seen that adults ≥ 30 years of age with diabetes suffer from more periodontitis as compared to those with normal glucose levels at all age levels.¹¹



From Figure 2, it can be seen that the prevalence of periodontitis is more severe in those with diabetes with elevated HbA1c levels $> 7\%$, as compared to those with good glycemic control ($HbA1c \leq 7\%$).



From Figure 3 it can be seen that edentulism defined as losing all teeth is greater among those with diabetes and prediabetes for those in the age range of 45-64 years, but not among those 65 years or older.¹¹

The same results were seen with HbA1c as the measure of diabetes, there was more edentulism among those with elevated HbA1c levels as compared to those with good glycemic control. Similar finding was seen when the number of missing teeth were analyzed i.e., more missing teeth in those with diabetes. Missing teeth were also greater in those with worse HbA1c. From this study representation of over 143 million employed adults in the U.S., diabetes and hyperglycemia are associated with more severe periodontitis, edentulism and tooth loss.

Periodontitis in Type 1 Diabetes

Periodontitis in type 1 diabetes was evaluated in a case control study by Cianciola et al. in 1982.¹² These authors assessed the oral health status of 263 subjects with type 1 diabetes as compared to 208 with no diabetes ages 11-18 years. They found 9.8% of those with type 1 diabetes had evidence of periodontitis. This was compared to a comparable group of 11-18-year-olds who had no evidence of diabetes and in whom 3% had evidence of periodontitis. Figure 4 shows radiographs from a 16-year-old female with type 1 diabetes and severe periodontitis from this study. Severe periodontitis especially affecting the molars and incisors can be seen in this patient. The predominant pattern of alveolar bone loss seen in the adolescent in this study of those with type 1 diabetes was molar incisor as seen in Figure 4.

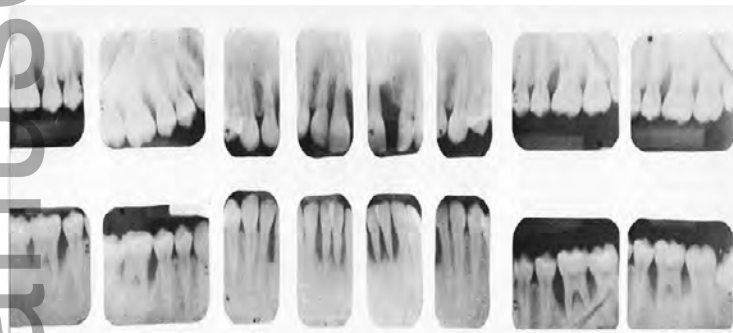


Figure 4. 16-year-old, white female patient. Type 1 diabetes mellitus onset at age 14, duration two years. Note alveolar bone loss localized to first molars, especially mesial surfaces and central incisors. Also note few or no dental caries.¹²

A population-based longitudinal study¹³ showed that those subjects with uncontrolled type 1 diabetes suffered from greater loss of clinical attachment over 5 years. They also found that uncontrolled type 1 diabetes as well as uncontrolled type 2 diabetes was associated with greater tooth loss over the 5-year follow-up period.

Silvestre et al. in 2009¹⁴, showed in a case-control study that those with diabetes had a greater bleeding index as well as more periodontal attachment loss than those with no diabetes. They also found that those with deficient metabolic control and presence of other diabetic complications had higher bleeding indices and greater periodontal pocket depths. They conclude that patients with type 1 diabetes show increased susceptibility to periodontal disease, especially those with poorer metabolic control or with diabetic complications.

Gestational Diabetes Mellitus

Periodontitis and gestational diabetes mellitus was analyzed from the NHANES III data by Novak et al. in 2006.¹⁵ They compared 113 women with gestational diabetes mellitus during their pregnancies to those who were negative for gestational diabetes mellitus or other forms of diabetes. They found that women with gestational diabetes mellitus may be at greater risk for developing more severe periodontal disease than women pregnant without gestational diabetes mellitus. A meta-analysis of 10 studies of periodontitis and gestational diabetes mellitus was carried out by Abariaga and Whitcomb in 2016.¹⁶ They found that there is a 2-fold higher risk of gestational diabetes mellitus among pregnant women with periodontitis compared to those without periodontitis. This was statistically significant ($P=0.009$).

It appears that individuals with most types of diabetes mellitus including type 1, type 2, and gestational diabetes mellitus have more severe periodontitis especially if the diabetes was uncontrolled, than subjects with no diabetes.

Longitudinal Studies

From this long history of cross-sectional and case report studies it is clear that patients with diabetes type 1 and type 2 as well as gestational diabetes suffer from more severe periodontal disease, after adjustment for common risk factors. As strong as the evidence for this association is, there is need to establish the temporal sequence of events, does diabetes proceed periodontitis and hence is a likely risk factor, contributing to the pathogenesis of periodontitis? Alternately is periodontitis a condition which precedes or is concurrent with diabetes? There are a series of longitudinal studies that address these issues.

The earlier onset and greater severity of periodontal disease was documented in a longitudinal study of PIMAs of the Gila River Native American Community.¹⁷ In this study the incidence or number of new cases of periodontitis was 2.6 times greater in those with diabetes type 2, as compared to those individuals with normal glucose levels when followed over 2-3 years. In Figures 5 a,b,c is seen a subject who was non-diabetic at baseline, with little or no periodontal

disease. However she developed type 2 diabetes and severe periodontitis seen on examination about 3 years later (see Figures 5 a,b,c).¹⁷

Figure 5a: 35-year-old female, baseline examination, mild periodontal disease, non-diabetes, radiographs.

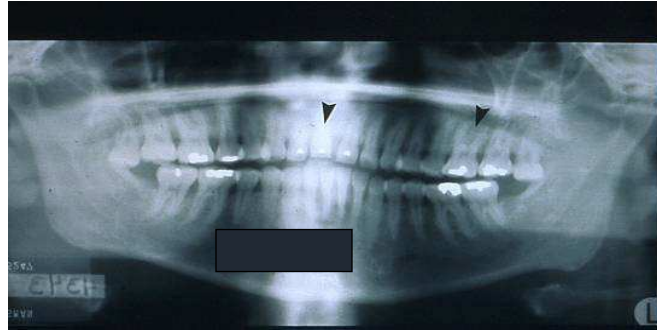


Figure 5b: 38-year-old female severe periodontitis, uncontrolled diabetes type 2, radiographs.

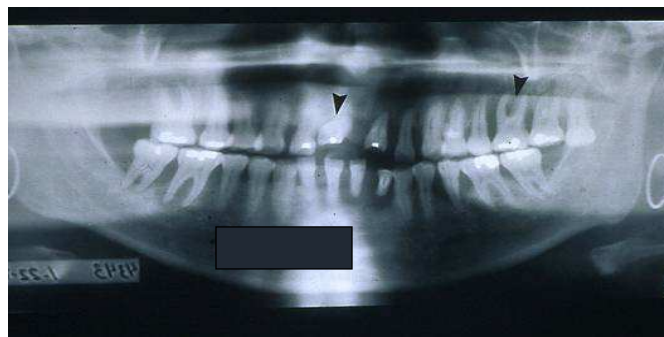
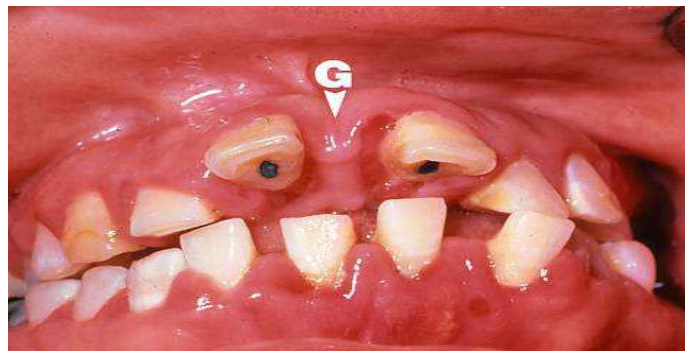


Figure 5c: 38-year-old female, severe periodontitis, uncontrolled diabetes, clinical photo.



This has been confirmed and extended in a population-based study in Germany.¹³ They studied a large population over 5 years and found that individuals with uncontrolled diabetes type 2 had greater progression of pocket depth and clinical attachment level compared to those with controlled or no diabetes.

In another longitudinal study, comparing progression of periodontal disease after periodontal therapy was presented by Costa et al. in 2013.¹⁸ They followed patients for 5 years after periodontal therapy who were on a periodontal maintenance therapy program. They found that the progression of periodontitis was significantly higher among patients with diabetes and poor glycemic control (mean HbA1c 9.1%) as compared to those with diabetes and good control (mean HbA1c 6.1%), and to non-diabetics. The results from this study can be seen in Figure 6.

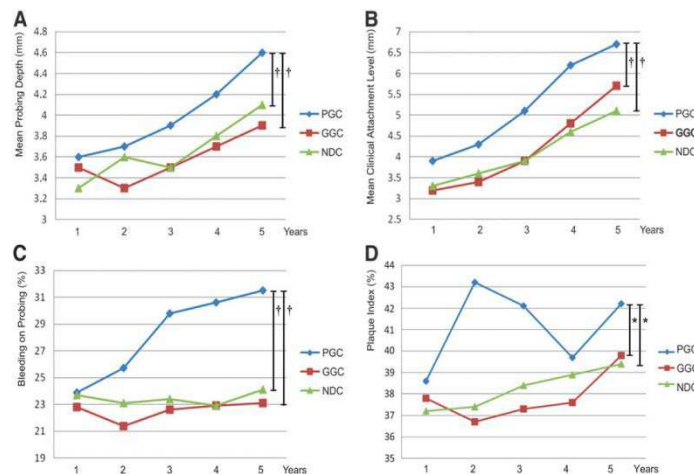


Figure 6. Change in pocket depth (PD) (A), clinical attachment loss (AL) (B), bleeding on probing (BOP) (C), and plaque index (PI) (D) during 5 years of periodontal maintenance therapy. Baseline: Poor Glycemic Control (PGC) = GGC = Non-Diabetic Control (NDC) ($P > 0.05$), except clinical AL: PGC > Good Glycemic Control (GGC) = NDC ($P < 0.039$). Final examination: PGC > GGC ($P < 0.001$); *† PGC > NDC ($P < 0.01$); *† and GGC = NDC ($P > 0.05$). *Statistically significant increase in PI per year, using ANOVA and Bonferroni post hoc analysis ($P < 0.05$). †Statistically significant increase in PD, clinical AL, and BOP per year, using Welch test and Tamhane post hoc analysis ($P < 0.05$). (From Costa et al., 2013).¹⁸

They also found that tooth loss was greater over the 5-year period in those diabetics with poor glycemic control compared to those with good control or those with no diabetes.

As described above there is greater edentulousness and partial tooth loss in individuals with diabetes based on cross-sectional studies. The longitudinal study by Demmer et al. in 2012¹³ shows that great tooth loss occurred in both type 1 and type 2 diabetes when uncontrolled, as compared to groups with controlled or no diabetes. Loss of teeth in individuals with diabetes is of great potential significance as it often interferes with proper nutrition.

Based on the cross-sectional and longitudinal studies it is reasonable to conclude that diabetes mellitus is a risk factor for periodontitis, and that diabetes proceeds periodontitis likely contributing to its pathogenesis. Evidence for mechanisms by which diabetes increases the risk for periodontal diseases is summarized in a large number of studies in Chapter _____ in this volume of Periodontology 2000.

Common Risk Factors

Periodontal disease and diabetes share many risk factors, both modifiable and non-modifiable.¹⁹ The modifiable risk factors common to diabetes and periodontal disease include smoking, excessive alcohol consumption, obesity, physical inactivity and excessive refined sugar consumption. It should be noted that periodontal disease is also a risk factor for worsening diabetes, and diabetes for more severe periodontitis.

The non-modifiable risk factors common to diabetes and periodontal disease include higher age, male gender, minority race/ethnicity, low socio-economic status, and genetic predisposition.²⁰ It is clear then that in management of periodontal disease, especially in patients with diabetes, strict attention to modifying smoking, excessive alcohol consumption, obesity, physical activity and high refined sugar consumption will benefit management of both diseases. This can perhaps be best accomplished by a team approach including the dentist and physician and their respective staffs.

Other Oral Manifestations of Diabetes

There is evidence of a greater predominance of fissured tongue and oral candidiasis in patients with diabetes.^{21,22} Also, in patients with diabetes, decreased salivary secretion, and increased levels of cariogenic organisms may predispose patients, especially those with Type 1 diabetes, to dental caries.²³ Xerostomia may result from thirst common in patients with diabetes. Xerostomia may also result from sensory nerve dysfunction as a neural complication of diabetes. Xerostomia may also be caused by medications taken by patients with diabetes.

Burning mouth may result from diabetic neuropathy, and treatment of patients for xerostomia may be effective for burning mouth. Neuropathy can also result in taste impairment in patients with diabetes.²⁴ Taste impairment, burning mouth along with increased tooth loss can seriously affect the ability to maintain a proper diet, which is critical to glycemic control in a patient with diabetes. Hence, it is important to prevent tooth loss and stress adequate nutrition in such patients.

Impaired Wound Healing in Patients with Diabetes

Delayed wound healing including oral wounds and lesions has been well known to occur in patients with diabetes. The factors involved in increasing oral disease include: hypoxia, dysfunction in fibroblasts and epidermal cells, impaired angiogenesis and neovascularization, high levels of metalloproteases, damage from reactive oxygen species and advanced glycation end products, neuropathy and multiple levels of decreased host immune resistance.²⁵ Most of these factors are accentuated in non-controlled diabetes, and they adversely affect dental procedures that require wound healing.

Dental management of patients with diabetes requires special attention to their treatment planning and management, especially post treatment. Proactive coordination of care with their physician to help ensure proper glycemic control is critical to long term successful periodontal and implant therapy. Patients should be assessed regularly for periodontal disease, and in those periodontally healthy, strict preventive measures instituted to prevent periodontal disease. If the patient with diabetes has periodontal disease, it should be treated definitively reducing all periodontal pockets, establishes glycemic control and control of other complications managed in coordination with the patient's physician. Good glycemic control and modification of common risk factors such as smoking and obesity, as well as complete periodontal therapy and regular periodontal maintenance will help the patient achieve a lifetime of good oral as well as general health.

Summary

Periodontal disease and diabetes are of great interest to clinicians', and they are common diseases of adults. Periodontal disease affects 4/10 adults, and diabetes 1/10 adults, and they are

linked. Diabetes increases the severity of periodontal disease and periodontal disease in diabetics leads to poor glycaemic control and more severe complications such as death from heart and kidney diseases.

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