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RESEARCH ARTICLE

Association between Periodontitis and Diabetes Mellitus in the General Population

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Abstract

Purpose- This study aimed to examine the association between periodontitis and diabetes mellitus.

Methods Participants with natural teeth in one jaw from the Third United States National Health and Nutrition Examination Survey (1988–1994) were included in this analysis. Participants with moderate (>4mm attachment loss in ≥2 mesial sites or 5mm pocket depth in ≥2 mesial sites) or severe (>6mm attachment loss in ≥2 mesial sites and >5mm pocket depth in ≥1 mesial site) periodontitis were classified as having periodontal disease. The rest of the participants were considered without periodontal disease. Diabetes mellitus was defined as fasting glucose ≥126mg/dL, hemoglobin A1c ≥6.5% or the use of antihyperglycemic medications. Multivariable logistic regression was used to examine the association between periodontitis and diabetes mellitus in all study population and subgroups stratified by demographics and comorbidities.

Results This analysis included 13,000 participants [mean age 43.8 ± 19.1 years, 47.5% male, 30% whites]. About 12.7% (n = 1,656) of the study population had periodontitis, and 9.2% (n = 1,200) had diabetes. In a multivariable-adjusted model, presence (vs. absence) of periodontitis was associated with 66% increased odds of diabetes (OR (95% CI):1.66 (1.43–1.94); p < 0.001). Compared to those without periodontitis, the odds of diabetes among those with severe periodontitis was much higher (OR (95% CI): 2.31(1.72–3.11); p < 0.001) than in those with moderate periodontitis (OR (95% CI): 1.54(1.30–1.82); p < 0.001).

Conclusions Periodontitis is associated with prevalent diabetes in a dose-response fashion, suggesting a bidirectional relationship between those two diseases. Patients with periodontal disease should be counseled regarding their elevated risk of diabetes.

Keywords Diabetes mellitus · Periodontitis · NHANES-III

Introduction

The global burden of non-communicable diseases such as diabetes mellitus and periodontitis is growing worldwide [1]. In 2019, diabetes was among the top ten leading causes of morbidity worldwide, with over 2.8% disability-adjusted life years [2]. Similarly, there has been a dramatic increase in the burden of periodontitis in the last decade that made it a global public health problem [3].

Chronic periodontitis has been long identified as a complication of diabetes mellitus and poor glycemic management [4]. Patients with type 2 diabetes are 2.8 times more likely to have severe periodontal disease and 4.2 times more likely to develop alveolar bone loss [5, 6].

Whether periodontitis is also a risk factor for diabetes mellitus in the general population is not well-established, but the association is plausible. Data from prior studies suggest a possible bidirectional association between diabetes and periodontal disorders [7]. That is, diabetes is related to increased development and advancement of periodontitis, whereas periodontal infection is also associated with poorer glycemic control in diabetics. The pathophysiological basis

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of the possible association between periodontal disease and diabetes is that periodontitis triggers a systemic chronic inflammatory state. Chronic inflammation over time is associated with insulin resistance and worsening glycemic control, leading to diabetes [8].

Furthermore, there is emerging evidence that preventing and managing oral health issues in patients with diabetes minimizes the deleterious consequences of hyperglycemia and vice versa [9–12]. Hence, it could be hypothesized that periodontal disease is a risk factor for diabetes. We tested this hypothesis in a large racially diverse sample of individuals enrolled in the United States Third National Health and Nutrition Examination Survey (NHANES-III).

Methods

Study Population

The NHANES-III is one of a series of large-scale national health surveys designed to assess the health and nutritional status of the non-institutionalized U.S. population. Each survey consists of a detailed standardized medical examination in a mobile examination unit preceded by an interview to obtain information on socio-demographic characteristics [13]. This analysis was limited to NHANES-III participants who were ≥ 18 years with one or more natural teeth and had complete data on diabetes.

Oral Examination and Definition of Periodontitis (Independent variable)

Periodontal examinations were conducted in a mobile examination center (MEC) by six dental examiners who had to be licensed in at least one State. Oral examination was conducted in two phases. Phase 1 was completed from October 1988 to September 199, and phase 2 was from September 1991 to October 1994. Visual, tactile oral health examination was designed to last seven and a half minutes. Periodontal measures were done on randomly assigned half-mouths, one upper quadrant and one lower quadrant selected at the beginning of the examination. Each tooth's buccal and mesial-buccal aspects were scored separately for each periodontal measure: gingival bleeding, calculus, gingival recession, and pocket depth. Loss of attachment was derived from two measurements made at each site: 1 (a) the distance from the free gingival margin to the cementoenamel junction, and2 (b)the distance from the free gingival margin to the bottom of the sulcus (pocket depth). When the gingival margin had receded and the cementoenamel junction was exposed, the first number was scored as a negative value and indicated gingival recession. The loss (level) of attachment variables was calculated by subtracting the recorded distance of the free gingival margin to cementoenamel junction1 from the recorded distance of the free gingival margin to the base of the sulcus2. Periodontal disease was defined based on the Centers for Disease Control and Prevention (CDC) criteria as follows: moderate periodontal disease as at least two mesial sites with > 4mm attachment loss or at least two mesial sites with 5mm pocket depth [not on the same tooth], and severe periodontal disease as at least two mesial sites with > 6mm attachment loss and one or more mesial sites with > 5mm pocket depth. The NHANES-III protocol called for examiners to round their measurements to the nearest millimeter using the color-coded NIDR (National Institute of Dental Research) periodontal probe, which is graduated at 2,4,6,8, 10, and 12 millimeters. Similar to prior work from NHANES-III [14], individuals with either moderate or severe disease were classified as having periodontal disease, while the rest of the participants were considered without periodontal disease. Replicate data were gathered by persons designated as "standards" who visited the field periodically and replicated such examination components as the dental examination. These replicates were used to monitor the measurement process and retrain examiners if necessary.

Outcome Variable

The outcome variable in this study was diabetes mellitus. Diabetes was defined as fasting glucose ≥ 126mg/dL, hemoglobin A1c ≥ 6.5% or the use of an antihyperglycemic medication.

Other variables

Age, sex, race/ethnicity, smoking status, and prior cardiovascular disease (CVD) were self-reported. Hypertension was defined as systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 80 mmHg or use of an antihypertensive medication according to American Heart Association/American College of Cardiology guidelines. Obesity was defined as body mass index ≥ 30kg/m^2. Hyperlipidemia was defined as total cholesterol ☐200mg/dL or triglycerides ☐150mg/dL or use of antihyperlipidemic agents.

Statistical analysis

The characteristics of the study population were compared by periodontal disease status. Continuous variables were reported as mean ± standard deviation. Categorical variables

Table 1 Population Characteristics Stratified by Periodontal Disease

Characteristics	Periodontal Disease		
	None	**Moderate**	**Severe**
(Mean ± SD or n (%))	11,344 (87.3%)	1,371 (10.5%)	285 (2.2%)
Age (years)	41.9 ± 18.8	57.2 ± 16.5*	56.6 ± 13.9*
Men	5150 (45.4%)	824 (60.1%)*	197 (69.1%)*
Race			
White	8015 (70.7%)	916 (66.8%)*	160 (56.1%)*
Non-white	3329 (29.3%)	455 (33.2%)*	125 (43.9%)*
Hypertension	4753 (41.9%)	863 (63.0%)*	203 (71.2%)*
Obesity	2743 (24.2%)	373 (27.2%)*	90 (31.6%)*
Hyperlipidemia	6291 (55.5%)	957 (69.8%)*	212 (74.4%)*
Current smoker	2723 (24.0%)	486 (35.4%)*	122 (42.8%)*
History of CVD	441 (3.9%)	131 (9.6%)*	26 (9.1%)*
Diabetes	873 (7.7%)	253 (18.5%)*	74 (26.0%)*

*p < 0.05 compared with no periodontal disease
CVD = cardiovascular disease (myocardial infarction or stroke)

were reported as frequency and percentage. A student's t-test was used to compare continuous variables, and a chi-square test was used to compare categorical variables.

The association between diabetes and periodontitis was assessed using multivariable logistic regression. Periodontal disease was used in the model in two separate ways: as a binary variable [presence vs. absence of "moderate or severe" periodontitis] and as a 3-level variable [severe periodontitis, moderate periodontitis, and no periodontitis [reference group]. Model 1 was adjusted for age, gender, and race (all entered in the model as binary variables except for age which was entered as a continuous variable). Model 2 was adjusted for variables in Model 1 plus hypertension, obesity, hyperlipidemia, current smoking status, and history of CVD (all entered in the model as binary variables). The choice of potential confounders in the models was based on prior literature and known risk factors for CVD, given the higher prevalence of CVD in diabetes.

To examine the consistency of the results among subgroups, the association between diabetes and periodontitis was evaluated in subgroups stratified by race [whites vs. non-whites], gender, hypertension, obesity, hyperlipidemia, smoking status, and history of CVD. The interaction was tested in models adjusted for variables similar to those in model 2 with the addition of an interaction term between diabetes and each stratifying factor. All statistical analyses were conducted using R Studio version 1.3.1093 (Boston, MA), and p-values were considered significant if < 0.05.

Table 2 Association of Periodontal Disease and Diabetes*

Periodontal Disease	Reference Level	Model 1		Model 2	
		Odds Ratio (95% CI)	*p-value*	Odds Ratio (95% CI)	*p-value*
Moderate	No disease	1.53 (1.30–1.80)	< 0.001	1.54 (1.30–1.82)	< 0.001
Severe	No disease	2.46 (1.85–3.28)	< 0.001	2.31 (1.72–3.11)	< 0.001
Moderate or Severe	No disease	1.68 (1.45–1.95)	< 0.001	1.66 (1.43–1.94)	< 0.001

95% CI = 95% Confidence Interval

Model 1 adjusted for age, gender, and race

Model 2 adjusted for model 1 plus hypertension, obesity, hyperlipidemia, tobacco smoking status, and cardiovascular disease (myocardial infarction or stroke)

† Association of moderate or severe periodontal disease and diabetes

* Interaction p-value calculated from model 2

CVD = cardiovascular disease (myocardial infarction or stroke)

Results

A total of 13,000 participants (mean age 43.8 ± 19.1 years, 47.5% male, 70.7% whites) were included in the analysis. The overall prevalence of periodontitis was 12.7% (1371 (10.5%) with moderate periodontitis, and 285 (2.2%)) with severe periodontitis. Table1 shows the characteristics of the study population stratified by periodontal disease status. Compared to individuals without periodontitis, individuals with periodontitis were more likely to be older, non-whites, and had a higher prevalence of cardiovascular risk factors, including obesity, hypertension, hyperlipidemia, current smoking, and prior history of CVD. Generally, individuals with severe periodontitis tended to be slightly older, non-whites, and with a higher prevalence of CVD risk factors than those with moderate periodontitis.

The prevalence of diabetes was highest among individuals with severe periodontitis (n = 74; 26.0%) and lowest among those without periodontitis (n = 87; 7.7%). In a multivariable-adjusted logistic regression model, periodontal disease (moderate or severe vs. no periodontitis) was associated with increased odds of diabetes (OR (95% CI): 1.66, 1.43–1.99; p < 0.001)(Table 2). These results were consistent in subgroups stratified by race, gender, hypertension, obesity, hyperlipidemia, smoking, and history of CVD (Table3).

Compared to those without periodontitis, the odds of diabetes among those with severe periodontitis was much higher (OR (95% CI): 2.31 (1.72–3.11); p < 0.001) than in

Table 3 Association of Periodontal Disease and Diabetes Among Subgroups*

Subgroups		Model 1†	Model 2†	
		Odds Ratio *(95% CI)*	Odds Ratio *(95% CI)*	*Interaction p-value**
Race	*Non-white*	1.46 (1.12–1.89)	1.45 (1.11–1.90)	0.50
	White	1.80 (1.50–2.15)	1.77 (1.47–2.14)	
Gender	*Men*	1.64 (1.35–1.99)	1.64 (1.34-2.00)	0.88
	Women	1.75 (1.39–2.20)	1.68 (1.33–2.13)	
Hypertension	*Present*	1.60 (1.35–1.89)	1.61 (1.35–1.92)	0.08
	Absent	1.79 (1.32–2.42)	1.78 (1.31–2.42)	
Obesity	*Present*	1.44 (1.13–1.84)	1.44 (1.12–1.84)	0.06
	Absent	1.78 (1.48–2.16)	1.83 (1.50–2.22)	
Hyperlipidemia	*Present*	1.59 (1.35–1.89)	1.60 (1.35–1.90)	0.05
	Absent	1.85 (1.35–2.54)	1.86 (1.35–2.56)	
Smoking Status	*Smoker*	1.50 (1.10–2.05)	1.51 (1.11–2.07)	0.45
	Nonsmoker	1.83 (1.54–2.17)	1.72 (1.44–2.04)	
History of CVD	*Present*	1.24 (0.83–1.86)	1.27 (0.84–1.91)	0.09
	Absent	1.72 (1.47–2.02)	1.71 (1.45–2.02)	

Model 1 adjusted for age, gender, and race

Model 2 adjusted for model 1 plus hypertension, obesity, hyperlipidemia, smoking status, and history of cardiovascular disease (myocardial infarction or stroke)

* The association is examined using logistic regression with diabetes as the outcome and periodontal disease as the independent variable.

those with moderate periodontitis (OR (95% CI): 1.54(1.30–1.82); $p < 0.001$) (Table2).

Discussion

In this analysis from the NHANES-III, we showed that periodontal disease is associated with over 66% increased odds of diabetes. This association was consistent across different subgroups of the study participants. A dose-response relationship between the severity of periodontal disease and the risk of diabetes was also observed. These findings call for the need to increase the awareness of the link between diabetes mellitus and oral health.

The impact of periodontitis on diabetes is likely explained by low-grade inflammation [15]. As periodontitis evolves, penetration of host tissues by subgingival bacteria or their by-products occurs. This triggers a systemic inflammatory response, leading to an acute phase protein response characterized by higher inflammatory markers, such as interleukin-1beta and interleukin-6, and C-reactive protein [16, 17]. Higher levels of inflammation contribute to insulin resistance, which is a risk factor for developing diabetes or worsening diabetes control [8]. A dose-dependent association between the severity of periodontitis and levels of inflammation has been found in adults with diabetes mellites [18]. This could explain the dose-response relationship we observed in our study.

Parallel to what we observed of increased odds of diabetes among those with periodontal disease, it has been reported that the risk of periodontitis is significantly higher among patients with diabetes [19]. Prior reports have shown that diabetes is associated with an increased risk of periodontitis onset and progression in adults [20, 21]. Mechanistically, diabetes influences periodontitis initiation and progression by causing a hyperinflammatory response, impairing bone repair processes, and producing advanced glycation end products [22]. Diabetes also has a significant effect on teeth bone formation and resorption; it contributes to the reduction of bone-forming cells [osteoblast apoptosis] through various mechanisms and enhancement of bone-eating cells [osteoclastogenesis] [23]. These prior findings and our results suggest a bidirectional relationship between periodontitis and diabetes, with each causing the other [7].

The concept of a bidirectional relationship is supported by prior studies that showed an association between periodontal disease and diabetes [24, 25], which agrees with our study. Nonetheless, primary care providers largely ignore this two-way relationship [26]. However, unlike our study, these prior studies were limited by small sample size or a lack of enough racial and gender diversity. Sharing common risk factors such as older age, male sex, minority race or ethnicity, low socioeconomic status, genetic predisposition, smoking, obesity, low physical activity level, and an unhealthy diet could partially explain the reciprocal relationship between periodontal disease and diabetes. Until

a clear explanation for the interplay between periodontal disease and diabetes is further investigated, communication between dental and medical professionals is probably needed to manage both disorders better.

In the United States, nearly half of adults have periodontal diseases [27], and one in ten has diabetes [28]. These high rates and reciprocal correlation between periodontal disease and diabetes highlight the need for innovative preventive measures to tackle both disorders. Integrating diabetes care with primary dental care and vice versa could be one of these approaches. Evidence from randomized clinical trials and other sources has shown that routine oral health assessment and treatment of periodontitis effectively manage diabetes [29, 30]. Non-surgical removal of supra- and subgingival bacterial plaque with scalers or ultrasonic devices (scaling and root planing [SRP]) with adjuvant local and systemic antibiotics showed effectiveness in lowering serum levels of HbA1c and FBS in diabetic patients (30–35).This suggests that periodontal therapy, even beyond SRP, such as routine oral assessment and dental hygiene, could be an essential measure for better glycemic control and reducing the incidence of diabetic-related complications with more studies needed for extended periods. Nevertheless, more studies are needed to examine the cost-effectiveness of community-based real-world programs to reduce diabetes and periodontal disease simultaneously.

Limitations

Our results should be read in the context of certain limitations. Given the cross-sectional design nature of our analysis, issues like residual confounding and temporality could not be avoided despite our effort to overcome. Also, the periodontal examination in the NHANES-III was not a complete mouth examination. This might impact the accuracy of the assessment of the burden of periodontal disease. Finally, although we categorized periodontitis according to severity, this may not be an adequate representation of the complexity of the disease. Our study has several strengths that are worth mentioning as well. This includes the large sample size, racially diverse population, representation of women, a large proportion of participants over 65 years old, and standardized data collection.

Conclusions

Using the NHANES-III data, we found that periodontal disease is associated with an increased odds of diabetes. This association was consistent across different subgroups of the study population. A dose-response relationship between the severity of periodontal disease and the risk of diabetes was also observed.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40200-022-01010-6.

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Data Availability and Codes: The dataset that supports this study are openly available at the National Center for Health Statisticshttps://www.cdc.gov/nchs/nhanes/nh3data.htm.

Statements and Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Compliance with ethical standards NHANES-III protocol was approved by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC) Research Ethics Review Board, and all participants provided written informed consent.

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