

Association Between Periodontitis and Impaired Fasting Glucose and Diabetes

YOUN-HEE CHOI, DDS, PHD^{1,2}
ROBERT E. MCKEOWN, PHD¹
ELIZABETH J. MAYER-DAVIS, PHD³

ANGELA D. LIESE, PHD^{1,4}
KEUN-BAE SONG, DDS, PHD²
ANWAR T. MERCHANT, SCD, DMD^{1,4}

OBJECTIVE—Many studies have reported that periodontal disease is associated with diabetes, but its relation with impaired fasting glucose (IFG) has been understudied. This study investigated the relationship between chronic periodontitis, IFG, and diabetes in the U.S. population.

RESEARCH DESIGN AND METHODS—Participants in the National Health and Nutrition Examination Survey III, aged ≥ 20 years, who received periodontal examinations and provided blood samples ($n = 12,254$) were grouped into quintiles of mean clinical attachment loss (CAL) and pocket depth, with the lowest category being the reference. Plasma fasting glucose was categorized into three groups (normal, < 100 mg/dL; IFG, ≥ 100 but < 126 mg/dL; and diabetic, ≥ 126 mg/dL). Sociodemographic factors and other potential risk factors were obtained by interview or examination. SAS 9.1 was used for statistical analysis accounting for the complex weighted sampling.

RESULTS—Participants in the top quintile category of CAL had higher prevalence odds of IFG (odds ratio [OR] 1.55 [95% CI 1.16–2.07]) and diabetes (4.77 [2.69–8.46]) after adjustment for related confounders, compared with those in the bottom quintile. The highest quintile of pocket depth was positively associated with IFG (1.39 [1.00–1.92]) and diabetes (1.63 [1.10–2.42]) compared with the lowest quintile. ORs for CAL increased from the lowest to the highest quintile (P value test for trend < 0.01) for all outcomes. The ORs for pocket depth also tended to rise across quintiles.

CONCLUSIONS—Chronic periodontitis measured by CAL and pocket depth was positively associated in a linear relation with IFG and diabetes in U.S. adults.

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Diabetes and periodontal health status have long been considered to be biologically linked (1). Advanced chronic periodontitis often coexists with poorly controlled diabetes, such that diabetes is considered to be a risk factor for severe chronic periodontitis (1). A meta-analysis (2) of four studies conducted among adults reported a significant positive association between diabetes (both type 1 and type 2) and periodontal disease. Numerous epidemiological studies (3–5) that have evaluated this relationship hypothesized that diabetes increases the risk of developing chronic periodontitis after controlling for related confounders.

At the same time, there is evidence that the presence of chronic periodontitis may raise the risk of diabetes (6).

Hyperglycemia status impairs gingival fibroblast synthesis, resulting in the loss of periodontal fibers and supporting alveolar bone (7). In addition, advanced glycation end-product accumulation in the periodontium affects phagocytic migration and activity of mononuclear and polymorphonuclear phagocytic cells, leading to the establishment of a more pathogenic subgingival flora (8) and consequent periodontal damage. Based on this evidence, L oe (9) proposed that periodontal disease is another complication of

diabetes. Periodontal infection can increase systemic inflammation in turn, which may induce a chronic state of insulin resistance, contributing to the cycle of hyperglycemia and advanced glycation end-product-protein binding accumulation. Therefore, it can amplify the classical pathway of connective tissue degradation, destruction, and proliferation in diabetes (7).

Studies evaluating the relationship between impaired glucose tolerance (IGT) and periodontal disease among Japanese populations suggested that periodontal disease was positively associated with IGT, but other studies found no association (10–12). However, few studies have evaluated the relationship between impaired fasting glucose (IFG) and chronic periodontitis (13). We therefore investigated the association between chronic periodontitis, IFG, and diabetes in a large group of U.S. adults.

RESEARCH DESIGN AND METHODS

In these analyses, we included participants of the National Health and Nutrition Examination Survey (NHANES) III who were aged ≥ 20 years at the time of data collection. The National Center for Health Statistics conducted this complex, stratified, multistage sample survey from 1988 to 1994 among a representative sample of the U.S. civilian, noninstitutionalized population aged ≥ 2 months. A total of 33,994 individuals participated in the interview; of these, 31,311 underwent a comprehensive physical examination (14). Plasma glucose measurements were conducted for participants aged ≥ 20 years. We considered participants who had plasma glucose measurements and received a periodontal examination ($n = 17,029$). Participants were excluded if they were edentulous ($n = 1,957$), had missing data for plasma glucose level ($n = 1,056$) or clinical attachment loss (CAL) ($n = 1,495$), or if women were pregnant ($n = 267$), leaving 12,254 individuals as the final sample size.

Measurement of periodontal health

Chronic periodontitis is an infectious disease that results in inflammation within the supporting tissues of the teeth,

From the ¹Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, South Carolina; the ²Department of Preventive Dentistry, School of Dentistry, Kyungpook National University, Daegu, South Korea; the ³Department of Nutrition, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; and the ⁴Center for Research in Nutrition and Health Disparities, University of South Carolina, Columbia, South Carolina.

Corresponding author: Anwar T. Merchant, merchant@mailbox.sc.edu.

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Table 1—Participant characteristics and risk-factor distribution by quintiles of CAL and periodontal pocket depth in U.S. adults, NHANES III, 1988–1994

| | CAL | | | | | Pocket depth | | | | |
|------------------------------|------------|------------|------------|------------|------------|--------------|------------|------------|------------|------------|
| | Quintile 1 | Quintile 2 | Quintile 3 | Quintile 4 | Quintile 5 | Quintile 1 | Quintile 2 | Quintile 3 | Quintile 4 | Quintile 5 |
| Total (n = 12,254) | 2,412 | 2,493 | 2,465 | 2,431 | 2,453 | 2,451 | 2,413 | 2,512 | 2,429 | 2,449 |
| Age (%) | | | | | | | | | | |
| 20-44 years | 88.8 | 78.3 | 68.3 | 47.7 | 22.0 | 63.4 | 65.7 | 65.6 | 65.9 | 58.0 |
| 45-64 years | 9.6 | 18.0 | 23.3 | 35.6 | 47.5 | 24.3 | 24.6 | 24.5 | 23.2 | 31.0 |
| ≥65 years | 1.6 | 3.7 | 8.4 | 16.7 | 30.5 | 12.3 | 9.8 | 9.9 | 10.9 | 11.0 |
| Sex (%) | | | | | | | | | | |
| Male | 45.2 | 47.2 | 47.8 | 53.9 | 59.9 | 36.7 | 48.0 | 55.0 | 56.1 | 62.1 |
| Female | 54.8 | 52.8 | 52.2 | 46.1 | 40.1 | 63.3 | 52.0 | 45.0 | 43.9 | 37.9 |
| Race (%) | | | | | | | | | | |
| Non-Hispanic white | 77.6 | 74.9 | 76.0 | 74.3 | 72.0 | 81.4 | 79.5 | 76.7 | 69.6 | 61.2 |
| Non-Hispanic black | 10.2 | 10.6 | 9.9 | 10.2 | 14.7 | 7.2 | 7.4 | 9.5 | 14.4 | 21.4 |
| Mexican American | 6.3 | 6.2 | 5.9 | 5.2 | 4.2 | 4.2 | 4.6 | 6.3 | 6.7 | 7.9 |
| Others | 6.0 | 8.3 | 8.2 | 10.4 | 9.1 | 7.3 | 8.6 | 7.5 | 9.3 | 9.5 |
| Education level (%) | | | | | | | | | | |
| ≤6 years | 2.3 | 3.6 | 3.8 | 5.3 | 9.8 | 3.2 | 2.7 | 4.3 | 5.8 | 9.3 |
| 7-12 years | 43.5 | 43.7 | 48.1 | 52.8 | 60.1 | 44.8 | 42.7 | 47.2 | 53.3 | 63.7 |
| ≥13 years | 54.1 | 52.6 | 48.1 | 41.8 | 30.1 | 52.0 | 54.6 | 48.5 | 40.9 | 27.0 |
| Income poverty ratio (%)* | | | | | | | | | | |
| Lower (≤1.5) | 19.5 | 21.0 | 17.8 | 19.7 | 25.2 | 16.6 | 16.8 | 17.3 | 23.8 | 33.5 |
| Middle (≤3.0) | 29.7 | 31.3 | 32.1 | 31.5 | 34.9 | 26.8 | 30.1 | 32.8 | 34.5 | 37.7 |
| Higher (>3.0) | 50.8 | 47.7 | 50.1 | 48.8 | 39.9 | 56.6 | 53.1 | 49.8 | 41.8 | 28.7 |
| Number of missing teeth (%)† | | | | | | | | | | |
| 0 | 73.0 | 63.4 | 52.9 | 42.9 | 32.9 | 59.9 | 59.0 | 57.0 | 51.3 | 38.3 |
| 1-5 | 24.7 | 32.2 | 40.3 | 47.2 | 43.6 | 33.4 | 33.4 | 34.9 | 41.5 | 44.2 |
| 6-10 | 2.1 | 3.8 | 5.9 | 8.5 | 17.6 | 6.1 | 5.2 | 6.4 | 5.7 | 13.2 |
| ≥11 | 0.2 | 0.7 | 1.0 | 1.5 | 5.9 | 0.7 | 0.8 | 1.7 | 1.4 | 4.3 |
| Smoking (%) | | | | | | | | | | |
| Never smoker | 59.9 | 53.8 | 50.1 | 38.3 | 27.2 | 52.8 | 54.0 | 48.7 | 41.9 | 30.6 |
| Ex-smoker | 16.0 | 20.9 | 24.5 | 31.2 | 32.5 | 25.8 | 23.0 | 25.4 | 23.2 | 23.9 |
| Current smoker | 24.1 | 25.3 | 25.4 | 30.5 | 40.3 | 21.3 | 23.0 | 25.9 | 34.9 | 45.5 |
| Alcohol (%) | | | | | | | | | | |
| Never | 10.2 | 11.5 | 12.6 | 13.6 | 12.1 | 13.1 | 12.3 | 11.4 | 10.7 | 11.8 |
| Former | 24.1 | 27.6 | 27.7 | 1.4 | 38.4 | 31.0 | 26.2 | 29.1 | 57.1 | 34.4 |
| Current | 65.7 | 60.9 | 59.7 | 54.9 | 49.5 | 55.9 | 61.5 | 59.5 | 62.3 | 53.8 |
| Physical activity (%)‡ | | | | | | | | | | |
| Active | 61.6 | 56.1 | 56.5 | 54.3 | 49.4 | 55.7 | 56.0 | 58.6 | 56.1 | 52.8 |
| Moderate | 10.5 | 12.1 | 12.2 | 13.1 | 11.2 | 12.0 | 13.6 | 12.0 | 11.2 | 8.9 |
| Less active | 9.7 | 9.6 | 8.5 | 7.9 | 5.8 | 8.5 | 9.8 | 8.5 | 8.4 | 6.1 |
| Unknown | 18.2 | 22.1 | 22.8 | 24.7 | 33.6 | 23.8 | 20.6 | 20.9 | 24.3 | 32.1 |

Table 1—Continued

| | CAL | | | | | Pocket depth | | | | |
|--------------------------------|------------|------------|------------|-------------|-------------|--------------|------------|------------|------------|-------------|
| | Quintile 1 | Quintile 2 | Quintile 3 | Quintile 4 | Quintile 5 | Quintile 1 | Quintile 2 | Quintile 3 | Quintile 4 | Quintile 5 |
| Total (n = 12,254) | | | | | | | | | | |
| BMI (%) | | | | | | | | | | |
| <18.5 (kg/m ²) | 3.5 | 1.6 | 2.1 | 1.6 | 2.1 | 2.8 | 2.1 | 2.3 | 1.8 | 1.7 |
| 18.5–24.9 (kg/m ²) | 52.7 | 44.8 | 41.7 | 38.1 | 34.0 | 49.8 | 46.7 | 39.3 | 41.4 | 31.8 |
| 25–29.9 (kg/m ²) | 26.4 | 33.2 | 35.2 | 34.7 | 37.0 | 29.3 | 32.8 | 36.0 | 32.6 | 35.7 |
| ≥30.0 (kg/m ²) | 17.5 | 20.4 | 21.0 | 25.6 | 26.9 | 18.1 | 18.5 | 22.4 | 24.2 | 30.8 |
| Central adiposity (%)§ | | | | | | | | | | |
| Absent | 76.9 | 70.2 | 65.7 | 58.9 | 51.5 | 71.3 | 69.7 | 65.9 | 60.7 | 54.8 |
| Present | 23.1 | 29.8 | 34.3 | 41.1 | 48.5 | 28.7 | 30.3 | 34.1 | 39.3 | 45.2 |
| Regular dental checkup (%) | | | | | | | | | | |
| Yes | 56.1 | 57.2 | 56.4 | 53.8 | 43.4 | 64.0 | 61.0 | 54.8 | 47.9 | 30.4 |
| No | 43.9 | 42.8 | 43.6 | 46.2 | 56.6 | 36.0 | 39.0 | 45.2 | 52.1 | 69.6 |
| Diabetic status (%) | | | | | | | | | | |
| Normal (n = 7,262) | 81.7 | 76.6 | 69.8 | 59.6 | 46.1 | 71.7 | 72.5 | 68.5 | 67.5 | 56.2 |
| IFG (n = 3,681) | 15.8 | 19.4 | 25.0 | 30.5 | 37.9 | 23.1 | 20.8 | 25.3 | 25.6 | 32.6 |
| Diabetes (n = 1,311) | 2.5 | 4.0 | 5.2 | 9.8 | 16.0 | 5.2 | 6.7 | 6.2 | 6.9 | 11.2 |
| Clinical attachment loss (mm) | 0.2 ± 0.0 | 0.6 ± 0.0 | 0.9 ± 0.0 | 1.4 ± 0.0 | 3.0 ± 0.0 | 0.7 ± 0.0 | 0.8 ± 0.0 | 1.0 ± 0.0 | 1.2 ± 0.1 | 2.2 ± 0.1 |
| Pocket depth (mm) | 1.3 ± 0.0 | 1.3 ± 0.0 | 1.4 ± 0.0 | 1.6 ± 0.0 | 1.9 ± 0.0 | 1.0 ± 0.0 | 1.2 ± 0.0 | 1.5 ± 0.0 | 1.8 ± 0.0 | 2.4 ± 0.0 |
| Plasma glucose level (mg/dL) | 91.2 ± 0.5 | 93.9 ± 0.6 | 96.6 ± 0.8 | 101.7 ± 1.1 | 107.5 ± 1.1 | 95.0 ± 0.6 | 96.9 ± 1.0 | 96.9 ± 0.7 | 97.5 ± 0.8 | 103.6 ± 0.9 |

Data are percentage or means ± SD. *Income-to-poverty ratio: (midpoint family income)/(poverty threshold values based on calendar years and inflation). †Missing due to caries/periodontal disease. ‡The number of missing values was 4,097 categorized by unknown. §Central adiposity present if waist for male subjects ≥101.6 cm and for female subjects ≥88.9 cm. ||At least once a year visit to dental clinic.

along with progressive loss of gingival attachment with or without resorption of supporting bone and is characterized by pocket formation and/or gingival recession (15). Periodontal damage is assessed by periodontal pocket depth and CAL. Pocket depth is the distance from the base of the periodontal pocket to the free gingival margin. CAL is the distance from the cemento-enamel junction to the base of the periodontal pocket. A CAL of 1–2 mm is considered to be slight, 3–4 mm moderate, and ≥5 mm severe (15). Dental examiners trained on the NHANES protocol examined all participants at mobile examination centers. Periodontal health assessment was based on CAL and pocket depth measurements made at two sites (midbuccal and mesio-buccal) on every tooth in each of two randomly chosen quadrants, one in maxilla and the other in mandible as described in the NHANES procedures manuals (14). In total, 28 sites and 14 teeth per individual were measured if the subject had no history of tooth removal excluding third molars.

We calculated mean CAL and pocket depth for each individual and then grouped participants into quintiles of mean CAL and pocket depth. The lowest quintile was the reference. This categorization was used because there is no consensus on a single accepted method to define chronic periodontitis in epidemiological studies. Although various definitions to categorize CAL and pocket depth have been used (16), it does not impose an assumption of linearity during modeling, is easier to interpret, and it captures the range of variation of the variables.

Hyperglycemia

The American Diabetes Association criteria (17) for plasma fasting glucose levels and interview data from NHANES III were used to categorize respondents into three groups (normal defined as glucose <100 mg/dL [5.6 mmol/L], IFG as glucose ≥100 but <126 mg/dL [7.0 mmol/L], and diabetes as glucose ≥126 mg/dL). Individuals self-reporting a diagnosis of diabetes by a doctor (“Has the doctor ever told you that you have diabetes?”) were also included in the diabetic group irrespective of plasma fasting glucose. These three groups made up the outcomes used in the statistical analyses.

Covariate information

Information on sociodemographic factors, general health, and oral health behaviors

was obtained by interview at participants' home. Age, sex, race/ethnicity, income-to-poverty ratio, education years, smoking history, drinking habits, physical activity, and frequency of regular dental visits were derived from interview data. Leisure time physical activity was assessed by questions of frequency and type of activity and was converted into metabolic equivalents (METs). BMI, as an index of total body adiposity, was based on examination data and computed by dividing weight in kilograms by the square of height in meters (kg/m^2). Waist circumference to assess central obesity was measured using a steel measuring tape to the nearest 0.1 cm at the high point of the iliac crest at minimal respiration when the participant was in a standing position. The number of missing teeth was obtained from dental examination.

The covariates were categorized as follows. Age was classified into three groups (20–44, 45–64, and ≥ 65 years), race/ethnicity into four groups (non-Hispanic white, non-Hispanic black, Mexican American, and others), income into three groups by tertiles of the income-to-poverty ratio (14) (≤ 1.5 , > 1.5 to ≤ 3.0 , and > 3.0), education years into three groups (less than junior high school, ≤ 6 years; junior high and high school, ≤ 12 years; and more than high school, ≥ 13 years), the number of missing teeth into four groups (0, 1–5, 6–10, and ≥ 11), smoking into three groups (never, past, and current), alcohol consumption into three groups (never, former, and current), and physical activity into three groups based on METs (active, ≥ 6 ; moderate, ≥ 4 and < 6 ; and less active, < 4). BMI was classified into four groups (kg/m^2) (obese, ≥ 30 ; overweight, ≥ 25 and < 30 ; normal, < 25 and ≥ 18.5 ; and underweight < 18.5). Central adiposity was said to be present if waist circumference was ≥ 101.6 cm for male subjects and ≥ 88.9 cm for female subjects. People who had regular dental checkups were defined as those who had visited dental clinics at least once a year. Continuous variables were categorized as above to avoid assuming a linear relation with the outcomes and for ease of interpretation.

Statistical analysis

SAS, version 9.1 (SAS Institute, Carey, NC) was used for data management and statistical analyses. SAS survey procedures were used to take into account the complex weighted sampling design and yield unbiased parameter estimates and standard errors. Sample weights, cluster,

and strata variables were included in all analyses. A statistical significance α level was considered at 0.05.

The distribution of sociodemographic factors and other potential risk factors across categories of CAL and pocket depth was estimated to observe the descriptive relation between these factors. To explore the crude association between hyperglycemic status and periodontal measures (CAL and pocket depth), mean plasma glucose levels and percentage of individuals in normal, IFG, and diabetes categories were calculated for each quintile of CAL and pocket depth. To examine the multivariable association between quintiles of CAL and pocket depth and IFG and diabetes status, four different multiple logistic regression models for each outcome such as IFG and diabetes were built and adjusted odds ratios (ORs), 95% CIs, and *P* values calculated. The first model was adjusted for age and sex. Race/ethnicity, education degree, and household income level were added in the second model. Smoking, alcohol habits, the number of missing teeth, and dental checkups were added to the third model. Finally, physical activity, BMI, and central adiposity were added to the fourth model. The Mantel extension χ^2 test was used to evaluate linear trend across quintile categories.

RESULTS—The distribution of potential risk factors across categories of CAL and pocket depth is shown in Table 1. Participants in the highest quintile of CAL were more likely to be older, male, and non-Hispanic black and in lower education and income levels than those in the lowest quintile of CAL. This pattern was very similar in pocket-depth quintiles. Participants in the fifth quintile of CAL had more missing teeth, were more likely to smoke, be overweight or obese, have more central adiposity, be less physically active, and visit the dentist less frequently than those in the first quintile. The trend for pocket depth was similar. All tests for distributional difference were statistically significant.

Fasting plasma glucose levels were higher in the top versus bottom categories of CAL (107.5 vs. 91.2 mg/dL) and pocket depth (103.6 vs. 95.0 mg/dL). Likewise, there were proportionately more participants with IFG and diabetes in the highest versus lowest categories of CAL (IFG, 37.9 vs. 15.8%; diabetes, 16.0 vs. 2.5%) and pocket depth (IFG, 32.6 vs. 23.1%; diabetes, 11.2 vs. 5.2%) (Table 1).

The highest quintile of CAL had higher prevalence odds of IFG (OR 1.55 [95% CI 1.16–2.07], *P* for trend < 0.01) and diabetes (4.77 [2.69–8.46], *P* for trend < 0.01) after adjusting for age, sex, education, income, race, smoking, alcohol intake, missing teeth, dental visits, BMI, central adiposity, and physical activity (Table 2) compared with the lowest quintile. Likewise, comparing extreme quintiles, pocket depth was positively associated with IFG (1.23 [0.86–1.76], *P* for trend < 0.01) and diabetes (1.63 [1.10–2.42], *P* for trend < 0.01) after accounting for the same confounders as the regression models for CAL (Table 3).

CONCLUSIONS—Chronic periodontitis measured by CAL and pocket depth was positively associated with IFG and diabetes in a dose-dependent manner among free-living U.S. adults after adjustment for potential confounders. This is important because IFG is more common among U.S. adults than diabetes (18) and is associated with increased risk of diabetes (19).

The periodontal disease/IFG relationship is relatively understudied. Prospective (11) and cross-sectional (12) studies conducted in Japanese populations showed that periodontal disease was associated with increased risk of IGT. Nevertheless, some epidemiological studies (4,20) did not show any association between prediabetes and periodontitis risk. The study by Noack et al. (4) with negative results included 100 adults aged 40–70 years, of whom 27 had normal fasting glucose and 56 had IGT; the study was underpowered to detect any difference in IGT by periodontal status. Saito et al. (20) conducted their study among a larger sample ($n = 584$) of adult women, of whom 108 had IGT. However, in that study CAL and pocket depth were divided into two groups (high and low) and did not evaluate the full range of the data. Periodontitis was positively linked with IFG in a recent study (13) from Israel. Periodontitis presence was associated with increased A1C after 5 years of follow-up in a German population free of diabetes (21). To our knowledge, this is the first study to find empirical evidence of the relation between chronic periodontitis and IFG in the U.S. population. It is plausible that hyperglycemia resulting from IFG may raise the risk of periodontal disease but also that chronic systemic inflammation from periodontal disease may stimulate inflammatory cytokines

Table 2—Dose-response relationship between periodontal attachment loss and IFG and diabetes

| | Quintile (1–5) for attachment loss (reference: quintile 1, n = 2,412) | | | | P for trend |
|------------------------------------------------------------------------------------|-----------------------------------------------------------------------|---------------------------|---------------------------|---------------------------|-------------|
| | Quintile 2 (n = 2,493) | Quintile 3 (n = 2,465) | Quintile 4 (n = 2,431) | Quintile 5 (n = 2,453) | |
| Hyperglycemia | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | |
| Median attachment loss (quintile 1: 0.19) | 0.54 | 0.93 | 1.44 | 2.71 | |
| IFG* | | | | | |
| Adjusted for age and sex | 1.10 (0.81–1.49) | 1.51 (1.14–1.99) | 1.63 (1.21–2.20) | 1.70 (1.31–2.21) | <0.01 |
| Additionally adjusted for education, income, and race | 1.09 (0.80–1.49) | 1.46 (1.09–1.96) | 1.56 (1.13–2.14) | 1.63 (1.24–2.16) | <0.01 |
| Additionally adjusted for smoking, alcohol intake, missing teeth, and dental visit | 1.06 (0.77–1.47) | 1.44 (1.07–1.93) | 1.59 (1.13–2.23) | 1.65 (1.24–2.21) | <0.01 |
| Additionally adjusted for BMI, central adiposity, and physical activity | 0.97 (0.69–1.35) | 1.34 (1.00–1.78) | 1.54 (1.08–2.18) | 1.55 (1.16–2.07) | <0.01 |
| Diabetes† | | | | | |
| Adjusted for age and sex | 1.93 (1.17–3.18) | 2.53 (1.38–4.64) | 4.33 (2.34–8.02) | 6.16 (3.54–10.73) | <0.01 |
| Additionally adjusted for education, income, and race | 2.11 (1.28–3.48) | 2.70 (1.49–4.91) | 4.76 (2.50–9.08) | 5.89 (3.24–10.72) | <0.01 |
| Additionally adjusted for smoking, alcohol intake, missing teeth, and dental visit | 2.00 (1.21–3.32) | 2.55 (1.40–4.62) | 3.84 (2.36–6.24) | 5.30 (3.01–9.31) | <0.01 |
| Additionally adjusted for BMI, central adiposity, and physical activity | 1.77 (1.04–3.03) | 2.21 (1.17–4.17) | 3.38 (2.06–5.54) | 4.77 (2.69–8.46) | <0.01 |

*Excluding subjects with diabetes. †Excluding subjects with IFG.

(C-reactive protein, tumor necrosis factor α , and interleukin-6), leading to insulin resistance and hyperglycemia (22). Periodontitis is associated with increased risk of developing diabetes in the U.S. population (6). Our findings imply that people

with IFG may need to be evaluated for periodontal health. It is also possible that periodontal treatment may reduce the risk of IFG, and this effect may extend to diabetes. However, this needs to be verified in future studies.

Notwithstanding the significance of the present study, several limitations should be mentioned. First, NHANES III data are cross-sectional so it is not possible to ascertain whether periodontitis led to hyperglycemia or vice versa.

Table 3—Dose-response relationship between periodontal pocket depth and IFG and diabetes

| | Quintile (1–5) for pocket depth (reference: quintile 1, n = 2,451) | | | | P for trend |
|------------------------------------------------------------------------------------|--------------------------------------------------------------------|---------------------------|---------------------------|---------------------------|-------------|
| | Quintile 2 (n = 2,413) | Quintile 3 (n = 2,512) | Quintile 4 (n = 2,429) | Quintile 5 (n = 2,449) | |
| Hyperglycemia | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | |
| Median pocket depth (quintile 1: 1.00) | 1.25 | 1.50 | 1.75 | 2.25 | |
| IFG* | | | | | |
| Adjusted for age and sex | 0.86 (0.69–1.08) | 1.14 (0.89–1.46) | 0.98 (0.78–1.23) | 1.40 (1.08–1.23) | <0.01 |
| Additionally adjusted for education, income, and race | 0.89 (0.68–1.13) | 1.12 (0.86–1.47) | 0.92 (0.73–1.17) | 1.40 (1.05–1.87) | 0.03 |
| Additionally adjusted for smoking, alcohol intake, missing teeth, and dental visit | 0.88 (0.67–1.14) | 1.08 (0.82–1.42) | 0.92 (0.72–1.18) | 1.39 (1.00–1.93) | 0.07 |
| Additionally adjusted for BMI, central adiposity, and physical activity | 0.82 (0.62–1.08) | 1.00 (0.76–1.32) | 0.87 (0.67–1.12) | 1.23 (0.86–1.76) | <0.01 |
| Diabetes† | | | | | |
| Adjusted for age and sex | 1.60 (1.13–2.25) | 1.15 (0.87–1.53) | 1.49 (0.99–2.24) | 2.66 (1.92–3.68) | <0.01 |
| Additionally adjusted for education, income, and race | 1.69 (1.14–2.49) | 1.25 (0.87–1.81) | 1.62 (1.06–2.48) | 2.28 (1.65–3.15) | <0.01 |
| Additionally adjusted for smoking, alcohol intake, missing teeth, and dental visit | 1.47 (0.97–2.24) | 1.26 (0.86–1.84) | 1.63 (1.05–2.53) | 2.06 (1.48–2.88) | <0.01 |
| Additionally adjusted for BMI, central adiposity, and physical activity | 1.40 (0.91–2.18) | 1.16 (0.74–1.73) | 1.44 (0.92–2.25) | 1.63 (1.10–2.42) | <0.01 |

*Excluding subjects with diabetes. †Excluding subjects with IFG.

Second, NHANES III used a partial mouth examination, so that approximately half the teeth existing in mouth were examined and was thus subject to random sampling error. Third, the categorization of CAL and pocket depth into quintiles might not correspond to meaningful clinical categories of periodontitis. Last, our study population only included individuals with one or more teeth so that the association between periodontitis and prediabetes and diabetes cannot be generalized to edentulous persons even though they may have had a history of periodontal disease.

The present study also has several strengths. First, we used quintiles of mean CAL and pocket depth in these analyses because quintiles captured the range of periodontal damage in this population, did not depend on any a priori or arbitrary cut point, did not impose any distributional assumptions during modeling, and facilitated in the detection of a dose response relation. Although CAL and pocket depth measures are universally used to assess periodontal damage, and there are explicit clinical definitions of chronic periodontitis, there is no consensus on the optimal way to categorize CAL and pocket depth in epidemiological studies although many approaches are suggested (16). Studies using these predetermined definitions of periodontal disease did not find a clear linear relation with type 2 diabetes and prediabetes (6,11). Second, the association persisted after sequential adjustment for many potential confounders. Adjustment for obesity, central adiposity, and physical inactivity would tend to attenuate the strengths of the association between chronic periodontitis and IFG because these variables may lie on the causal pathway (23). Third, the finding has implications for diabetes prevention. IFG is more common than diabetes, but its progression to diabetes can be prevented through lifestyle interventions (24). Further research in this area may ultimately lead to new strategies to prevent IFG from its progressing to diabetes. Finally, the NHANES data were collected with careful quality control, the sample was large enough to give us good power to evaluate the relations, and it was representative of the U.S. adult population.

In conclusion, chronic periodontitis assessed by CAL and pocket depth is positively associated in a dose-response way with increased prevalence odds of

IFG and diabetes in a representative sample of U.S. adults. Additional epidemiological studies need to be conducted to characterize this association further. People with IFG may need to be evaluated for periodontal health status.

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