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PERIODONTAL DISEASE IS ASSOCIATED WITH GESTATIONAL DIABETES MELLITUS: A CASE-CONTROL STUDY

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Abstract

Background—Few studies have specifically examined the relationship between periodontal disease and gestational diabetes mellitus (GDM). The objective of this study was to examine whether maternal periodontal disease is associated with GDM.

Methods—A case-control study was conducted of 53 pregnant women with GDM and 106 pregnant women without GDM at Woman's Hospital, Baton Rouge, USA. The periodontal examinations were performed by a calibrated dentist who was blinded on the diabetic status of the pregnant women. Periodontitis was defined as the presence of any site with a probing depth (PD) ≥ 4 mm or a clinical attachment loss (CAL) ≥ 4 mm. The severity of periodontal disease was measured in quartiles of PD and CAL. Univariable analysis and multivariable logistic regression were used to examine the relationships between periodontal disease and GDM.

Results—The percentage of periodontitis was 77.4% in women with GDM and 57.5% in pregnant non-GDM women, with an odds ratio (OR) and 95% confidence interval (CI) of 2.5 (1.2–5.3). After adjusting for confounding variables of maternal age, parity, race, marital status, education, family income, smoking, alcohol consumption, systemic antibiotics in pregnancy, family history of diabetes, income, dental insurance coverage and body mass index, the adjusted OR (95% CI) was 2.6 (1.1–6.1). The adjusted ORs (95% CIs) of GDM comparing the highest-to-lowest quartiles of PD and CAL were 3.8 (1.0–14.0) and 4.5 (1.2–16.9).

Conclusion—This study supports the hypothesis of an association between periodontal disease and GDM.

Keywords

Case-control study; gestational diabetes mellitus; periodontal disease; pregnancy

Periodontal disease is one of the most common chronic disorders of infectious origin known in humans, with a reported prevalence varying between 10 and 90% in adults, depending on diagnostic criteria.[1–5] Periodontal disease refers to an inflammatory condition of the soft tissues surrounding the teeth (i.e., gingivitis) and the destruction of the supporting structures

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of the teeth, including the periodontal ligament, bone, cementum and soft tissues (i.e., periodontitis).[6] There is increasing evidence suggesting that periodontal disease is associated with an increased risk of systemic diseases such as cardiovascular diseases, diabetes mellitus and adverse pregnancy outcomes.[3, 4, 7, 8]

Gestational diabetes mellitus (GDM) is carbohydrate intolerance with onset or first detection during pregnancy.[9] GDM affects approximately 4% of all pregnancies in the U.S., representing about 160,000 cases annually.[10] GDM is associated with significantly increased risks of maternal and infant morbidity, including macrosomia, preeclampsia, preterm birth, shoulder dystocia, birth injury, and need for cesarean section.[9, 11] Women with GDM are at a significantly higher risk of developing type 2 diabetes later in life.[12]

The association between periodontal disease and type 1 or 2 diabetes has been well established. Studies have found that not only type 1 or 2 diabetes increases the risk of developing periodontal disease, but also that periodontal disease may also increase the risk for type 2 diabetes.[13, 14] However, few studies have examined the relationship between periodontal disease and GDM.[3, 4] Periodontal disease induces local and host immune responses and is able to cause transient bacteremia.[6–8] Viable bacteria, bacterial products (e.g., lipopolysaccharide) from the subgingival plaque and pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, IL-8, and C-reactive protein) from the inflamed periodontal tissues can enter the circulation and trigger a maternal systemic inflammatory response.[7, 8] Pregnancy itself is a stressful state with increased inflammatory activity,[15] increased gingival inflammation[16, 17] and increased insulin resistance.[18, 19] It is known that pancreatic β-cell destruction can result from the pro-inflammatory imbalance created by sustained elevation of cytokines (e.g., IL-1β and TNF-α).[20] Studies have shown that there are elevated inflammatory cytokines in patients with GDM and diabetes.[21–25] It is well accepted that infection results in a state of insulin resistance.[26] Therefore, maternal chronic periodontal disease could induce a sustained systemic inflammatory response that may result in a state of insulin resistance. Such an infection-induced insulin resistance in response to periodontal infection could exacerbate the preexisting pregnancy-induced insulin resistance and may cause impaired glucose tolerance and the manifestation of GDM. Despite the biological plausibility for an association between these two disorders, except for our secondary data analysis based on the data from the U.S. Third National Health and Nutrition Examination Survey (NHANES III),[27] few studies have specifically examined the relationship between periodontal disease and GDM. We hypothesized that maternal periodontal disease, as a source of chronic and persistent infection, induces systemic inflammatory responses that result in or exacerbate a state of insulin resistance in pregnancy and thereby contribute to the development of GDM. We conducted a case-control study to test this hypothesis of a relationship between these two diseases. The objective of this study was to examine whether periodontal disease is associated with an increased risk of GDM.

MATERIALS AND METHODS

Study population

We conducted a case-control study at Woman's Hospital in Baton Rouge, Louisiana. Woman's Hospital is a state-of-the-art tertiary woman's medical center, delivering more than 8,700 babies each year (the 19th largest delivery service in the country and largest in Louisiana). The hospital includes Level III Regional Obstetrics unit, Maternal-Fetal Medicine Center, Regional Neonatal Intensive Care Unit, and prenatal and women's health education. The study subjects were recruited at the obstetrical clinic at Woman's Hospital where offices approximately 60 private obstetricians-gynecologists. According to the data from our previous study based on NHANES III,[27] we estimated that, at a ratio of 1 case to 2 controls, a total of 53 cases as well as 106 controls would be sufficient to detect an odds

ratio (OR) of 3.00 with 80% power and alpha of 0.05, assuming a frequency of periodontal disease of at least 20% in the control group. Therefore, a total of 53 cases of GDM and 106 controls were recruited at Woman's Hospital, between June 2007 and December 2008. This study was approved by the Institutional Review Boards of Tulane University and Woman's Hospital.

Definition of cases and controls

At Woman's Hospital, all pregnant women undergo a laboratory screening test for GDM between 24–30 weeks or later gestation based on the American College of Obstetricians and Gynecologists' recommendation.[9] Women were first screened for carbohydrate intolerance by performing a standard 1-hour 50-g oral glucose challenge test (GCT). If the glucose level was greater than 135 mg/dl (GCT positive), they then underwent a 3-h, 100-g oral glucose tolerance test (OGTT) after a 10- to 12-h overnight fast.[28] Women whose glucose levels (i.e., fasting, 1-h, 2-h, and 3-h) exceed two or more threshold values on the OGTT are diagnosed as having GDM or cases.[28] Controls are defined as women who passed the GCT at 24–30 weeks and do not have any other types of diabetes.

Pregnant women were asked to participate if they met all of the following criteria: 1) completed GDM screening at gestational age between 24–30 weeks; 2) at least 18 years of age; 3) English-speaking; and 4) agreed to sign a consent form. Women with known pre-gestational type 1 or type 2 diabetes; having not undergone lab screening for GDM; having taken insulin and other anti-diabetic drugs before this pregnancy; having less than 20 teeth; contraindication to probing in a dental examination such as heart disorders, history of fenfluramine-phentermine use; serologically HIV positive; and having had periodontal treatment (scaling or surgery) during the last 3 months were excluded from this study. All eligible pregnant women who were diagnosed with GDM (cases) and without GDM (controls) were invited to take part in the study. All participants gave written informed consent. After consenting, the research staff conducted an in-person, structured questionnaire interview, as well as scheduled another date for a dental examination at the dental clinic at Woman's Hospital.

Periodontal disease measurements and definitions

A full-mouth periodontal examination was performed on all study participants, and measurements were taken at six sites per tooth (mesio-buccal, mesio-lingual, disto-buccal, disto-lingual, mid-buccal and mid-lingual), using a manual UNC-15 probe*. The clinical measures of periodontal conditions included probing depth (PD), gingival recession, clinical attachment loss (CAL), and bleeding on probing (BOP). PD was defined as the distance in millimiters from the gingival margin to the apical part of the pocket. Gingival recession was determined by measuring the distance from the cemento-enamel junction to the gingival margin in millimeters. The CAL was calculated from recession and probing depth (PD) measurements and represents the distance from the cemento-enamel junction to the most apical portion of the sulcus/pocket in millimeters. BOP was assessed when probing to the base of the sulcus, 6 surfaces per tooth, and is expressed as the percentage of bleeding sites over the total tooth surfaces. Third molars were not included in the analysis. In order to eliminate inter-examiner variability, all periodontal measurements were performed by one dentist (R.D.). Prior to the enrollment of patients for the study, this dentist was calibrated on five volunteers (not pregnant women) by an experienced periodontist as the standard examiner (S.V.). In addition, to reduce the intra-variability of dental examinations during the course of study, this dentist was recalibrated by the same periodontist under the same protocol in the middle of the study (i.e., after nine months of the total of 18-month period of

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recruitment). Inter- and intra-examiner reliability, as assessed by weighted Kappa coefficients (within ±1mm) were 0.82–0.88. Intra-class correlation coefficients were 0.81–0.86. The dentist was blinded on the diabetic status of the pregnant women.

There is no universally accepted standard for periodontal disease diagnosis.[3, 4] In most previous studies on periodontal disease and pregnancy outcomes, definitions that combined PD and/or CAL over a certain threshold (e.g., ≥ 4 mm) have been used.[3–5] For this study, periodontitis was defined *a priori* as presence of any sites exhibiting PD ≥ 4 mm or CAL ≥ 4 mm as we applied in our previous study.[27] The severity of periodontal disease was measured in quartiles of the mean levels of PD and CAL. In addition, we also used the criteria from the study by Offenbacher et al on periodontal disease and adverse pregnancy outcomes, which defined periodontal disease as any site with PD ≥ 4 mm and CAL ≥ 3 mm and severe periodontal disease as at least 4 sites with PD ≥ 5 mm and 4 sites with CAL ≥ 3 mm.[29]

In addition to the dental examination, other information was obtained from a personal interview of the participants before the dental examination, including socio-demographic (e.g., age, race/ethnicity, pre-pregnancy weight/height, body mass index (BMI)), socioeconomic status (e.g., education, family income), pregnancy and medical history (e.g., parity, previous history of GDM, systemic antibiotics use in pregnancy, treatment of oral disorders in pregnancy), prenatal care (e.g., gestational age at the first of prenatal care visit), health behaviors (e.g., smoking, alcohol consumption in pregnancy), family history (e.g., mother or sisters with diabetes), and oral hygiene and habits (e.g., frequency of dental care visit, dental cleaning, brushing teeth, flossing teeth, dental insurance coverage).

Statistical analysis

Univariable analysis was performed to compare the different periodontal disease measurements, as well as characteristics of study population between the cases and controls. Chi-square tests were used to examine differences in proportions (e.g., periodontitis) and t-tests were used to examine difference in means (e.g., number of sites with BOP, PD and CAL). Chi-square tests for linear trend were used to examine the relationship between periodontal disease severity measured in quartiles of PD and CAL and GDM. Multivariable logistic regression was used to examine the association between periodontal disease and GDM and to adjust for potential confounding variables, including maternal age, parity, race, marital status, education, family income, smoking, alcohol consumption, systemic antibiotics in pregnancy, family history of diabetes, income, dental insurance coverage and BMI. The adjusted odds ratio (OR) and its 95% confidence interval (CI) were derived from the coefficients of the logistic models and the standard errors. Using the lowest quartile of PD or CAL as referent, a dose-response relation was analyzed to examine whether adjusted ORs (95% CIs) of GDM increased with increasing quartiles of PD and CAL, respectively. Data were analyzed using SPSS 16.0 for Windows (SPSS, Inc. Chicago, Ill).

RESULTS

Table 1 presents the socio-demographic, socioeconomic status, pregnancy and medical history, prenatal care, health behaviors, family history, and oral hygiene and habits of 53 cases of GDM and 106 controls. There was no difference in gestational age at enrollment between the cases and the controls. Women with GDM had significantly higher mean maternal age and BMI than women without GDM ($p < 0.01$). Women with GDM were more likely to be married, but had higher percentage of lower family income <$ 20,000 as compared to the controls ($p < 0.05$). There were no significant differences in parity, race/ethnicity, education, smoking or drinking alcohol at time of recruitment, patients' mother or sister (s) with diabetes, oral hygiene and health conditions (i.e., frequency of visit to dentist,

dental cleaning, brushing teeth, flossing teeth, and dental or oral disorder treatment during pregnancy) between the two groups.

Table 2 presents the clinical periodontal parameters between the cases and control groups. In the study population, the number of teeth ranged from 20–28, with average number of 27 ± 1.7 (standard deviation) teeth. There was no significant difference in number of teeth between the cases and controls. The PD measures ranged 1–7 mm, and the CAL measures ranged 1–7 mm. The number of sites with bleeding on probing ranged 0–80 sites and the average percentage of sites with bleeding on probing ranged 0–50%. The frequency of women with GDM who had at least one site with BOP (92.5%) was higher than that in women without GDM (80.2%), $p<0.05$. The number of sites with BOP and percentage of sites with BOP (i.e., measures of gingivitis) were higher in the cases than in the controls ($p=0.06$). The mean levels of PD or CAL were significantly higher in the cases than in the controls ($p<0.05$). When the primary definition of periodontal disease was used (presence of any sites exhibiting PD ≥ 4 mm or CAL ≥ 4 mm), the prevalence of periodontitis was 77.4% in women with GDM and 57.5% in the control group, with an OR of 2.5; 95 % CI: 1.2–5.3, $p<0.05$. After adjusting for maternal age, parity, race, marital status, education, family income, smoking, alcohol consumption, systemic antibiotics in pregnancy, family history of diabetes, income, dental insurance coverage and BMI, periodontitis was associated with a significantly increased risk of GDM, with adjusted OR of 2.6 (1.1–6.1), $p<0.05$.

When both the cases and controls were divided into four groups according to quartiles of PD and CAL, there were trends toward that women with GDM were more distributed among higher quartile groups of PD or CAL, while women without GDM were more classified among the lower quartile groups of PD or CAL ($p_{Trend}<0.05$). Using the lowest quartile as referent, the adjusted ORs (95% CIs) of GDM with increasing quartiles of PD from quartile 2 to quartile 4 were 2.4 (0.7–8.0), 3.9 (1.2–13.2), and 3.8 (1.0–14.0), respectively. The adjusted ORs (95% CIs) of GDM with increasing quartiles of CAL from quartile 2 to quartile 4 were 2.9 (0.9–9.9), 4.2 (1.2–14.3), and 4.5 (1.2–16.9), respectively.

The results were also consistent when periodontal disease and severity of periodontal disease were defined by using the criteria from the study by Offenbacher et al.[29] Periodontitis in general and severe periodontitis were associated with a significantly increased risk of GDM, with adjusted ORs of 2.3 (1.0–5.3) and 2.7 (1.1–6.7), respectively.

DISCUSSION

Our study shows that periodontal disease is associated with an increased risk of GDM, and there is a ‘dose–response’ relation of an increased risk GDM with increasing severity of periodontal disease. This study confirms the finding of our previous study based on the cross-sectional study data of NHANES III.[27] Dasanayke et al. found an increase of clinical periodontal disease in women with GDM compared to women without GDM; but this increase did not reach statistical significance.[30]

Whether periodontal disease is a causal risk factor for GDM or a result of GDM remains to be determined. It is well established that periodontal disease is more prevalent in type 1 or 2 diabetics compared to healthy controls.[13, 14, 31] Periodontitis has been referred to as the sixth complication of diabetes[32] and this has been attributed to consequences of long duration of elevated blood glucose levels (hyperglycemia).[31] Impaired insulin resistance, vascular changes, altered oral microflora, abnormal collagen metabolism, and the consequent hyperglycemia and hyperlipidemia of diabetes result in metabolic alterations which then exacerbate the bacteria-induced inflammatory periodontitis.[13, 32] The observed association between periodontal disease and GDM might be explained by GDM causing

periodontitis, similar to type 1 or 2 diabetes. However, compared to type 1 or 2 diabetes, GDM only represents an early stage of glucose dysregulation and a temporary impaired glucose tolerance that occur in later pregnancy. The elevated glucose levels in the majority of women diagnosed with GDM will usually return to normal after birth.[33] Therefore, the hyperglycemia of GDM may be too mild and of too short a duration to have a significant effect on gingival tissues and to cause a destruction of the supporting structures (i.e., tissue and bone) of the teeth manifested as periodontitis. An alternative explanation is that periodontal disease may be a cause, instead of the result, of GDM. Periodontal infection, a local and chronic sub-clinical inflammation, triggers a maternal systemic inflammatory response.[3, 7] Since pregnancy itself is a stressful state with increased inflammatory activity[15] and marked insulin resistance,[19] such an infection-induced insulin resistance in response to maternal periodontal infection may thus worsen the preexisting pregnancy-induced insulin resistance that may cause impaired glucose tolerance and the manifestation of GDM.[27] Finally, there may be a common genetic cause for both periodontal disease and GDM that results in the observed association between the two disorders. Although there is lack of clear correlation between the gene polymorphisms and GDM,[33] a few studies suggested that cytokines such as TNF-α, IL-6, and IL-1 polymorphisms may be associated with the risk of insulin resistance or type 2 diabetes[34] as well as periodontal disease.[35] Therefore, there is a possibility that pre-existing genetic polymorphisms result in imbalances between the pro vs. anti-inflammatory cytokine systems predisposing to both periodontal disease and GDM simultaneously.

Our study population may appear relatively periodontally healthy compared to other studies that examined the relationship of periodontal disease to adverse pregnancy outcome[36, 37] because of the low average BOP, PD and CAL. This may reflect the fact that our study population had relatively high socioeconomic status. For example, 61 % of the recruited women had university or graduate level of education (Table 1). In our study we examined a population of young women (most in the age range of 25–35 years) that were not selected for periodontal disease severity. Very little information exists on periodontal disease and bleeding on probing on women of that age. According to Albandar et al study, women of ages from 30–39 years old showed an average of 9.5% sites that bleed,[38] which is comparable to our findings. More studies are needed to further examine the association between periodontal disease and GDM in other populations, such as populations with greater severity of periodontal disease or different socioeconomic status.

Several measures were taken to ensure validity as well as to limit potential biases of the study. First, periodontal examinations were performed by only one examiner to eliminate inter-examiner variability in periodontal probing measurements. Furthermore, this examiner was calibrated prior to the study enrollment, and re-calibrated in the middle of the study recruitment by an experienced periodontist to reduce intra- examiner variability in the periodontal probing measurements. This examiner was also blinded on the diabetic status of the pregnant women throughout the study to reduce potential measurement errors that may occur when knowing the diabetic status of study subjects. Second, to avoid potential bias due to the selection of arbitrary criteria to define periodontal disease,[3–5] we used more ***objective*** approaches to assess periodontal disease and its association with GDM by 1) comparing the mean levels of periodontal indices (e.g., number of sites with BOP, PD and CAL) between the cases and controls, and 2) by categorizing each subject according to the quartiles determined by the distribution of PD and CAL to examine whether the risk of GDM increases with an increasing severity of periodontal disease (or dose-response relation, all the tests for a linear trend analysis are statistically significant, Table 2). Our results were consistent even when we used the periodontal disease definitions from another study (Offenbacher et al)[29](Table 2). Third, Woman's Hospital is the largest hospital in Louisiana with about 8,700 deliveries annually with greater than 90% of pregnant women in the region

giving births at this hospital. The cases and controls were recruited in a period of one and half years from a large pool of approximately 13,050 pregnant women during their routine prenatal care visits. The controls were selected from the same sources as the cases from the pregnant women who participated in their routine prenatal care. This limits potential selection bias that may occur in a single hospital-based case-control study.[39] Finally, GDM diagnosis was made by following the stricter Carpenter & Coustan guidelines.[28] The study was powered with sufficient sample size to assess the relationship between the two diseases with adjustment for several important confounding variables (e.g., socioeconomic status, BMI, family history of diabetes, systemic antibiotics in pregnancy, oral hygiene and behaviors, and dental insurance coverage).

It is estimated that 35–60% of women with GDM will develop type 2 diabetes within 10 years.[12] Diabetes, especially type 2, has become one of the most common chronic diseases in the U.S.[40] GDM thus provides a window of opportunity for early interventions to prevent later development of type 2 diabetes in young women. Women with a previous history of GDM after birth have a sustained higher prevalence of periodontitis compared to those without diabetes.[27] Since women with GDM are at higher risk of developing type 2 diabetes[12] and periodontal disease has been implicated as a risk factor for type 2 diabetes,[13, 14, 31] periodontal disease may contribute to future development of diabetes in women with a previous history of GDM.[27] Periodontal disease is preventable and curable. If periodontal disease is confirmed as a risk factor for GDM in future studies, this will open the doors to intervention studies. Improving oral health and treating periodontal disease before or during pregnancy may not only reduce maternal and infant morbidity associated with GDM during pregnancy but also prevent type 2 diabetes later in life.

CONCLUSIONS

This study supports the hypothesis of an association between periodontal disease and GDM. Further prospective studies are needed to examine whether periodontal disease is a causal risk factor for GDM.

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Table 1

Characteristics of Study Population

Maternal Characteristics	Controls (n=106)	Cases (n=53)	p-value
Gestational age at recruitment (weeks, mean ± SD)	30.8±3.8	30.8±4.7	0.930
Maternal age (years, mean ± SD)	27.1±5.9	29.9±5.6	0.004
BMI (mean ± SD)	25.7±6.2	31.6±8.1	0.000
Parity			0.207
0	32 (30.2%)	11 (20.8%)	
≥1	74 (69.8%)	42 (79.2%)	
Race			0.460
Whites	49 (46.2%)	30 (56.6%)	
Blacks	55 (51.9%)	22 (41.5%)	
Other	2 (1.9%)	1 (1.9%)	
Marital status			0.005
Married	58 (54.7%)	37 (69.8%)	
Single	43 (40.6%)	9 (17.0%)	
Other	5 (4.7%)	7 (13.2%)	
Education			0.252
Primary or high school	46 (43.4%)	16 (30.2%)	
University	49 (46.2%)	29 (54.7%)	
Graduate school	11 (10.4%)	8 (15.1%)	
Family income*			0.013
< $20,000	15 (14.2%)	12 (22.6%)	
$20,000–$75,000	30 (28.3%)	24 (45.3%)	
> $75,000	31 (29.2%)	12 (22.6%)	
Last visit for dental cleaning*			0.268
Within 6 months	38 (35.8%)	15 (28.3%)	
6–12 months	18 (17.0%)	13 (24.5%)	
2 years	17 (16.0%)	14 (26.4%)	
>2 years	16 (15.1%)	7 (13.2%)	
Never	4 (3.8%)	0 (0.0%)	
Brushing teeth			0.858
≥2 times per day	79 (74.5%)	40 (75.5%)	
Once per day	26 (24.5%)	12 (22.6%)	
A few times per week	1 (0.9%)	1 (1.9%)	
Any dental insurance coverage in pregnancy*			0.064
Yes	66 (62.3%)	31(58.5%)	
No	30 (28.3%)	19 (35.8%)	
Dental or oral disorders treated in pregnancy	7 (6.6%)	4 (7.5%)	0.825
Smoking at the time of recruitment	4 (3.8%)	2 (3.8%)	1.000
Drinking alcohol at the time of recruitment	3 (2.8%)	2 (3.8%)	0.748
Mother or sister(s) with diabetes	14 (13.2%)	7 (13.2%)	0.602

Maternal Characteristics	Controls (n=106)	Cases (n=53)	p-value
Systemic antibiotics use in pregnancy	23 (21.7%)	20 (37.7%)	0.069

* Excluding missing values (i.e., answered as ‘do not know’, or refused to answer the questions)

Table 2

Periodontal Disease and Gestational Diabetes Mellitus

Periodontal measurements	Controls (n=106)	Cases (n=53)	p-value OR (95% CI)	p-value for trend aOR (95% CI)†
Number of teeth (mean ± SD)	27±1.7	27±1.7	0.665	
At least one site with bleeding on probing	85 (80.2%)	49 (92.5%)	0.045	
Number of sites with bleeding on probing (mean ± SD)	10.7±14.3	15.5±15.9	0.060	
Percentage of sites with bleeding on probing (mean ± SD)	6.7±9.0	9.5±9.6	0.068	
PD (mm, mean ± SD)	1.8±0.4	2.0±0.3	0.028	
CAL (mm, mean ± SD)	1.8±0.4	2.0±0.3	0.022	
Periodontitis (any PD or CAL≥4mm)			0.014	
No	45 (42.5%)	12 (22.6%)	1.0 (referent)	1.0 (referent)
Yes	61 (57.5%)	41 (77.4%)	2.5 (1.2–5.3)	2.6 (1.1–6.1)
PD (mm, cutoff for quartile) (mean ± SD)			0.028	0.011
Quartile 1 (<1.57 mm) (1.46 ± 0.08)	32 (30.2%)	8 (15.1%)	1.0 (referent)	1.0 (referent)
Quartile 2 (1.57 mm) (1.71 ± 0.08)	30 (28.3%)	10 (18.9%)	1.3 (0.5–3.8)	2.4 (0.7–8.0)
Quartile 3 (1.85 mm) (2.00 ± 0.08)	21 (19.8%)	19 (35.8%)	3.6 (1.3–9.8)	3.9 (1.2–13.2)
Quartile 4 (2.14 mm) (2.41 ± 0.26)	23 (21.7%)	16 (30.2%)	2.8 (1.0–7.6)	3.8 (1.0–14.0)
CAL (mm, cutoff for quartile) (mean ± SD)			0.020	0.007
Quartile 1 (<1.62 mm) (1.48 ± 0.10)	33 (31.1%)	7 (13.2%)	1.0 (referent)	1.0 (referent)
Quartile 2 (1.62 mm) (1.73 ± 0.07)	29 (27.4%)	11 (20.8%)	1.8 (0.6–5.2)	2.9 (0.9–9.9)
Quartile 3 (1.86 mm) (2.03 ± 0.09)	22 (20.8%)	20 (37.7%)	4.3 (1.6–11.8)	4.2 (1.2–14.3)
Quartile 4 (2.17 mm) (2.43 ± 0.26)	22 (20.8%)	15 (28.3%)	3.2 (1.1–9.2)	4.5 (1.2–16.9)
Periodontitis (Offenbacher S, et al)[29]			0.033	
No	42 (39.6%)	12 (22.6%)	1.0 (referent)	1.0 (referent)
Yes	64 (60.4%)	41 (77.4%)	2.2 (1.1–4.8)	2.3 (1.0–5.3)
Periodontitis (Offenbacher S, et al)[29]			0.034	0.012
No	42 (39.6%)	12 (22.6%)	1.0 (referent)	1.0 (referent)
Mild	17 (16.0%)	6 (11.3%)	1.2 (0.4–3.8)	1.3 (0.4–4.3)
Severe	47 (44.3%)	35 (66.0%)	2.6 (1.2–5.7)	2.7 (1.1–6.7)

†OR adjusted for maternal age, parity, race, marital status, education, smoking, alcohol consumption, systemic antibiotics in pregnancy, family history of diabetes, income, dental insurance coverage, and BMI.