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# Periodontal Pathogens and Gestational Diabetes Mellitus

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## Abstract

In previous cross-sectional or case-control studies, clinical periodontal disease has been associated with gestational diabetes mellitus. To test the hypothesis that, in comparison with women who do not develop gestational diabetes mellitus, those who do develop it will have had a greater exposure to clinical and other periodontal parameters, we measured clinical, bacteriological (in plaque and cervico-vaginal samples), immunological, and inflammatory mediator parameters 7 weeks before the diagnosis of gestational diabetes mellitus in 265 predominantly Hispanic (83%) women in New York. Twenty-two cases of gestational diabetes mellitus emerged from the cohort (8.3%). When the cases were compared with healthy control individuals, higher pre-pregnancy body mass index ($p = 0.004$), vaginal levels of *Tannerella forsythia* ($p = 0.01$), serum C-reactive protein ($p = 0.01$), and prior gestational diabetes mellitus ($p = 0.006$) emerged as risk factors, even though the clinical periodontal disease failed to reach statistical significance (50% in those with gestational diabetes mellitus *vs.* 37.3% in the healthy group; $p = 0.38$).

### Keywords

Maternal periodontal disease; gestational diabetes mellitus; *Tannerella forsythia*

## INTRODUCTION

Gestational diabetes mellitus is defined as either onset or first recognition of glucose intolerance during pregnancy (ADA, 2004). Gestational diabetes mellitus is seen in 7% of all pregnancies (over 200,000 cases annually) in the United States (ADA, 2004). Native Americans (5.8-14.3%) (Benjamin *et al.*, 1993; Murphy *et al.*, 1993), Asian/Pacific Islanders (3.9-7.4%) (Berkowitz *et al.*, 1992; Keshavarz *et al.*, 2005; Rosenberg *et al.*, 2005; Thorpe *et al.*, 2005; Silva *et al.*, 2006), and Hispanics (3.5-7.5%) (Forsbach *et al.*, 1988; Berkowitz *et al.*, 1992; Kieffer *et al.*, 1999, 2001; Rosenberg *et al.*, 2005) experience higher prevalence compared with African-Americans (1.7-3.9%) (Dooley *et al.*, 1991; Berkowitz *et al.*, 1992; Kieffer *et al.*, 2001; Rosenberg *et al.*, 2005; Thorpe *et al.*, 2005) and non-Hispanic Whites (2.2-2.6%) (Berkowitz *et al.*, 1992; Rosenberg *et al.*, 2005; Thorpe *et al.*, 2005).

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Risk factors for gestational diabetes mellitus include older maternal age, a higher body mass index (ADA, 2004; Xiong *et al.*, 2001; Keshavarz *et al.*, 2005; Dudhbhai *et al.*, 2006), prior gestational diabetes mellitus (ADA, 2004; Dudhbhai *et al.*, 2006), family history of diabetes among first-degree relatives (ADA, 2004; Keshavarz *et al.*, 2005; Dudhbhai *et al.*, 2006), and being a member of a racial/ethnic group with a high prevalence of diabetes/gestational diabetes mellitus (ADA, 2004). In addition, increased levels of C-reactive protein (Wolf *et al.*, 2003; Leipold *et al.*, 2005), tumor necrosis factor-α (TNF-α) (Kirwan *et al.*, 2002; Winkler *et al.*, 2002; Atègbo *et al.*, 2006), and interleukin-6 (IL-6) (Atègbo *et al.*, 2006) among women with gestational diabetes mellitus suggest a role of infection and inflammation in its etiology (Wolf *et al.*, 2004). The purpose of this study was to examine the relationship between clinical and other periodontal disease parameters (bacteriological, immunological, and inflammatory aspects) and gestational diabetes mellitus.

## MATERIALS & METHODS

The study was approved by the appropriate Institutional Review Boards (New York University School of Medicine, Bellevue Hospital, and GCRC), and written informed consent was obtained from each woman. Inclusion criteria were: (1) gestational age of 15 to 23 wks; (2) singleton gestation; (3) ability to understand and sign the consent form; and (4) having a well-confirmed estimated date of delivery from either the last menstrual period or ultrasound screening. Those who needed antibiotics before dental procedures and those who had taken antibiotics within 2 wks prior to sample collection were excluded.

Initial screening for gestational diabetes mellitus was performed with a one-hour 50-g oral Glucose Challenge Test at an initial pre-natal care visit, and if gestational diabetes mellitus had not yet been diagnosed, at 24 to 28 wks of gestation. If the Glucose Challenge Test value was greater than 140 mg/dL, a three-hour 100-g oral Glucose Tolerance Test was given. If 2 of the 4 values in the Glucose Tolerance Test were at or above the cut-off levels (fasting glucose ≥ 95 mg/dL, one-hour glucose ≥ 180 mg/dL, two-hour glucose ≥ 155 mg/dL, or three-hour glucose ≥ 140 mg/dL), then gestational diabetes mellitus was diagnosed (Carpenter and Coustan, 1982).

Data on brushing, flossing, dental visits, and alcohol, cigarette, and drug use were collected by means of a pre-tested self-administered questionnaire (English or Spanish). Pre-pregnancy body mass index was determined at the time of enrollment. Clinical periodontal data, plaque, blood, and cervico-vaginal samples were collected from each woman. Mean gestational age for oral examination and plaque sample collection was 18.2 wks (SD = 3.4), and for blood and cervico-vaginal sample collection, 17.9 wks (SD = 3.3).

Subgingival pooled plaque samples were collected from the mesial and buccal sites of first molars by means of a sterile metal scalar. When the first molar was not available, either the second molar, third molar, second premolar, or the first premolar (in the order of availability) was used. Samples were placed in 0.1 mL TE buffer (50 mM Tris, 1 mM EDTA, pH 7.6) and stored at -80°C within 4 hrs of collection. Oral examinations were conducted by calibrated dentists using the Periodontal Screening and Recording method and Periowise® probes (Premier Dental Products, Plymouth Meeting, PA, USA). Probing pocket depth in mesial, central, and distal sites of buccal and lingual surfaces and bleeding on probing were recorded on each sampled tooth. Clinical periodontal disease was defined as the presence of at least 1 pocket > 3 mm (beyond the green mark on the probe). Those with signs of periodontal disease were advised to visit their regular dentists and/or were given a referral letter.

Cervico-vaginal samples were collected by a sterile speculum examination. Two polyester-tipped sterile swabs (Fisher Scientific, Hampton, NH, USA) were introduced into the posterior

fornix of the vagina and left in place for 30 sec, then were rotated a minimum of 6 times. By the same technique, third and fourth swabs were then placed intra-cervically to obtain cervical secretions. Every attempt was made to ensure that cervical samples were not contaminated by the vaginal flora. All samples were placed in 0.1 mL TE buffer (50 mM Tris, 1 mM EDTA, pH 7.6) and stored in a -80°C freezer. Cervical samples were not collected at visits during which the woman bled (less than 0.5%).

Blood samples (approximately 6 mL) were drawn by a certified phlebotomist, left at room temperature (20-25°C) for 30 min, and then transferred to a refrigerator (2-8°C) until centrifuged (Drucker Model 614B, Philipsburg, PA, USA) within 2 hrs at 3150 rpm for 20 min. Each specimen was divided into a minimum of 4 0.5-mL aliquots of serum and stored in a -80°C freezer until transportation to labs on dry ice by express mail.

Plaque and cervico-vaginal samples were assayed at The Forsyth Institute (Boston, MA, USA) with DNA probes (Socransky *et al.*, 2004). For vaginal and cervical samples, DNA was extracted before DNA probe assay with the use of a DNeasy® Tissue Kit (QIAGEN Sciences, Germantown, MD, USA) according to the manufacturer's protocol.

Serum samples were analyzed for IgG antibodies against cell-surface antigens of *Porphyromonas gingivalis* and *Tannerella forsythia* by a modified (Craig *et al.*, 2002) enzyme-linked immunosorbent assay at the New York University College of Dentistry laboratories (Ebersole *et al.*, 1985). C-reactive protein, IL-6, and TNF-α levels were measured at Yale University (New Haven, CT, USA) with the commercially available Immulite® chemiluminescent enzyme immunometric assay (Diagnostic Products Corp., Los Angeles, CA, USA). Gestational diabetes mellitus status was masked to all laboratories.

In a nested case-control fashion, gestational diabetes mellitus cases were compared with healthy control individuals by parametric and non-parametric methods (SAS Version 9.1, SAS Institute, Cary, NC, USA). Bacteriological levels were transformed to $\log_{10}$ values (after the addition of 0.5 to raw values to replace zeros). Odds Ratios and 95% Confidence Intervals were calculated. Bacteriological and cytokine levels were treated as continuous variables. Following bivariate estimation of risk, multivariable logistic regression analysis was performed with adjustment for prior gestational diabetes mellitus (factor with the highest odds ratio) and the use of one other variable in the model to assess the independent effect of the latter. Inclusion of more than 2 independent variables in each model resulted in unstable models. Two-sided type I error probability $\leq 0.05$ was considered as the level of significance.

## RESULTS

Seventy-six percent of the participants had only a high school education, and 43% were married. Thirty-percent had a self-reported annual family income under $5,000, 52%, $5,000-$24,999, 14%, $25,000-$49,000, and only 4% had an income over $50,000.

The prevalence of gestational diabetes mellitus was 8.3% (total of 22; 15 with GDMA1, and seven with GDMA2). Three additional women were diagnosed as GDMA2 *vs.* type B, indicating that they probably were diabetic prior to pregnancy and were excluded from the analyses. Mean gestational age at gestational diabetes mellitus diagnosis was 24.9 wks (SD = 7.8).

Group comparisons are shown in Tables 1-4. Women with gestational diabetes mellitus were older ($p = 0.07$), had a significantly higher pre-pregnancy body mass index ($p = 0.004$), and a history of prior gestational diabetes mellitus ($p = 0.006$). More women with gestational diabetes mellitus were current/previous smokers ($p = 0.09$). Their oral hygiene practices and dental-care-seeking patterns were similar (Table 1). Women with gestational diabetes mellitus

delivered at an earlier gestational age (p = 0.004), and had a higher incidence of premature rupture of membranes (p = 0.04), and chorioamnionitis (p = 0.04; Table 2).

Women with gestational diabetes mellitus also had higher vaginal levels of *T. forsythia* (p = 0.01), but their clinical periodontal disease, though higher (50%), was not significantly different from that in the non-gestational diabetes mellitus control individuals (37.3%; p = 0.38). *P. gingivalis* (p = 0.39) and *T. forsythia* (p = 0.73) specific serum IgG samples were not statistically significantly different between the two groups. Although the women with gestational diabetes mellitus had higher levels of C-reactive protein, TNF-α, and IL-6, only C-reactive protein levels reached statistical significance (p = 0.01; Table 3).

Higher vaginal levels of *T. forsythia* (OR = 1.27; 95% CI = 1.05-1.55), higher C-reactive protein levels (OR = 2.01; 95% CI = 1.02-3.96), prior gestational diabetes mellitus (OR = 8.48; 95% CI = 2.19-32.82), and higher pre-pregnancy body mass index (OR = 1.17; 95% CI = 1.08-1.27) were all significantly associated with gestational diabetes mellitus. In the multivariable analysis that adjusted for prior gestational diabetes mellitus, higher pre-pregnancy body mass index (OR = 1.16; 95% CI = 1.07-1.26) and vaginal levels of *T. forsythia* (OR = 1.31; 95% CI = 1.06-1.60) still remained significant.

Although not predictors of gestational diabetes mellitus, premature rupture of membranes (OR = 4.64; 95% CI = 1.46-14.77) and chorioamnionitis (OR = 3.76; 95% CI = 1.18-12.05) during the current pregnancy were significantly associated with gestational diabetes mellitus.

## DISCUSSION

Clinical periodontal disease has been previously associated with gestational diabetes mellitus in cross-sectional (Novak *et al.*, 2006; Xiong *et al.*, 2006) or case-control studies (Millar and Offenbacher, personal communication). In our study, we measured clinical and other periodontal-disease-related parameters at least 7 wks prior to the diagnosis of gestational diabetes mellitus.

The prevalence of gestational diabetes mellitus (8.3%) was higher compared with the 4.1%-5.4% previously reported for Hispanics (Berkowitz *et al.*, 1992; Kieffer *et al.*, 1999, 2001), perhaps due to the higher Glucose Tolerance Test cut-off levels previously used (fasting glucose ≥ 105 mg/dL, one-hour glucose ≥ 190 mg/dL, two-hour glucose ≥ 165 mg/dL, or three-hour glucose ≥ 145 mg/dL).

Pre-pregnancy body mass index and prior gestational diabetes mellitus are known risk factors for gestational diabetes mellitus (Xiong *et al.*, 2001; ADA, 2004; Keshavarz *et al.*, 2005; Dudhbhai *et al.*, 2006). Additionally, gestational diabetes mellitus has been linked to pre-eclampsia (Xiong *et al.*, 2001; Khatun *et al.*, 2005), cesarean delivery (Xiong *et al.*, 2001; Keshavarz *et al.*, 2005; Khatun *et al.*, 2005; Johns *et al.*, 2006), premature rupture of membranes (Xiong *et al.*, 2001; Yang *et al.*, 2002), and preterm delivery (Xiong *et al.*, 2001; Yang *et al.*, 2002; Hedderson *et al.*, 2003). However, other than delivering at an earlier gestational age and having a higher incidence of premature rupture of membranes and chorioamnionitis, no other pregnancy outcomes were significantly associated with gestational diabetes mellitus in our study, perhaps due to the smaller study size.

Elevated C-reactive protein levels, IL-6, and TNF-α in women with gestational diabetes mellitus have been shown to suggest a role of inflammation in the etiology of gestational diabetes mellitus. It is known that IL-6 and TNF-α interfere with insulin signaling, and are also insulin antagonists. Therefore, sustained elevated levels of IL-6 and TNF-α can interfere with carbohydrate metabolism, and consequently cause glucose intolerance that can result in gestational diabetes mellitus. In our study, women with gestational diabetes mellitus had higher

C-reactive protein, TNF-α, and IL-6 levels, though only the C-reactive protein levels reached statistical significance. Similarly, clinical measures of periodontal disease in the gestational diabetes mellitus group were higher (though not significant, due to study limitations). As such, it can be argued that periodontal-disease-induced inflammatory mediators may further aggravate insulin resistance, perhaps exacerbate the pre-existing pregnancy-induced insulin resistance, and further impair glucose tolerance.

Higher vaginal levels of *T. forsythia* were significantly associated with gestational diabetes mellitus, even with our small sample ($p = 0.01$). However, the plaque levels of *T. forsythia*, a more plausible periodontal disease parameter, were not significantly associated with gestational diabetes mellitus. The most likely explanation for this is the study's inadequate power to show differences in plaque levels of *T. forsythia* between women with gestational diabetes mellitus and those without it. The same is true for cervical levels. This may be due to the higher prevalence of *T. forsythia* in plaque (60%) and cervical samples (30%), compared with the lower prevalence of *T. forsythia* in vaginal samples (13%) among control women. Others have observed an increased incidence of chorioamnionitis and premature rupture of membranes, which are clinical conditions associated with increased inflammatory cytokines and oxidative stress that can occur with gestational diabetes mellitus and increased oral *T. forsythia* colonization (Sawamoto *et al.*, 2005; Biri *et al.*, 2006). A literature review reported on the presence of *T. forsythia* in other extra-oral host tissues, such as atheromatous plaque, coronary stenotic artery plaque, atherosclerotic vessels, occluded arteries in persons with Buerger disease, and bronchial tissues in embalmed cadavers (Tanner and Izard, 2006), lending support to the possibility of the presence of these organisms in extra-oral sites.

The smaller number of women with gestational diabetes mellitus (22) was a limitation of our study. Original data came from a prospective study designed to evaluate the association between maternal periodontal parameters and preterm birth and was not powered to evaluate the association between periodontal disease and gestational diabetes mellitus. However, under the fixed values of the available 22 cases and 240 control individuals (three were excluded due to possible prior diabetes), one-sided $\alpha = 0.05$, and 13% exposure frequency (vaginal *T. forsythia* prevalence) among control individuals, the study had 80% power, but only to detect a four-fold increase in the risk of gestational diabetes mellitus. In contrast, a two-sample *t* test with a 0.05 two-sided significance level will have 80% power to detect an effect size of 0.64 when the sample sizes in the two groups are 22 and 240, respectively. An effect size of 0.64 is considered a moderate-to-large effect in general (Cohen, 1992).

The use of periodontal screening and recording may explain why clinical periodontal disease was not significant. Pre-pregnancy body mass index, although significant, was based on individual recall. This might have diluted the true association due to random misclassification of body mass index. It is also possible that we failed to detect other true risk factors (*i.e.*, age) due to small study size. Similarly, our inability to show significant differences in *T. forsythia* in plaque and cervical samples may not threaten the internal consistency of our findings. Last, although gestational diabetes mellitus diagnosis was made 7 wks after the collection of plaque, blood, and cervico-vaginal samples, the date of gestational diabetes mellitus diagnosis does not necessarily mean the date of gestational diabetes mellitus onset. Future studies should measure periodontal parameters prior to the true onset of gestational diabetes mellitus.

Strengths of our study include the data on multiple parameters related to periodontal disease collected prior to gestational diabetes mellitus diagnosis and independent evaluation of biological samples at different laboratories that were masked to gestational diabetes mellitus status.

We conclude that the presence of *T. forsythia* in vaginal flora is a potential risk factor for gestational diabetes mellitus, but this should be confirmed in future studies before consideration of its clinical significance, due to the study limitations discussed above.

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**Table 1**

Demographic, Pre-pregnancy, Behavioral, and Dental Characteristics of Study Participants

| Characteristic | GDM[§] | Non-GDM | p |
|---|---|---|---|
| *Demographics* | | | |
| Age: Mean yrs (SD) | 28.7 (5.3) | 26.6 (5.8) | 0.07[b] |
| Ethnicity: N (%) | | | |
| Hispanic | 17 (77) | 200 (83) | 0.55[a] |
| Non-Hispanic | 5 (23) | 40 (17) | |
| Race: N (%) | | | |
| White | 17 (77) | 204 (85) | |
| Black | 2 (9) | 26 (11) | 0.19[a] |
| Asian | 3 (14) | 10 (4) | |
| *Pregnancy-related* | | | |
| Pre-pregnancy Body Mass Index: Mean (SD) | 30.5 (7.9) | 25.5 (4.4) | 0.004[b*] |
| Family history of diabetes: (%) | 13.6 | 8.6 | 0.59[a] |
| GDM[§] in a prior pregnancy: (%) | 18.2 | 2.6 | 0.006[a*] |
| Pre-eclampsia in a prior pregnancy: (%) | 9.1 | 3.0 | 0.17[a] |
| PTD[¶] in a prior pregnancy: (%) | 9.1 | 4.6 | 0.30[a] |
| C-section in a prior pregnancy: (%) | 18.2 | 13.6 | 0.52[a] |
| *Behavioral* | | | |
| Smoking (%) | | | |
| Current | 4.8 | 0.5 | 0.09[a] |
| Previous | 28.6 | 19.9 | |
| Never | 66.7 | 79.6 | |
| Alcohol use (%) | | | |
| Current | 0.0 | 0.5 | 1.00[a] |
| Previous | 40.0 | 39.2 | |
| Never | 60.0 | 60.4 | |
| Drug use (%) | | | |
| Current | 0.0 | 0.0 | 1.00[a] |
| Previous | 4.8 | 5.9 | |
| Never | 95.2 | 94.1 | |
| *Dental habits* | | | |
| Brushing (*per* day): Mean (SD) | 2.2 (0.4) | 2.3 (0.6) | 0.19[b] |
| Flossing (*per* week): Mean (SD) | 3.7 (5.0) | 3.9 (5.3) | 0.92[b] |
| Dental visits (*per* year): Mean (SD) | 1.1 (0.9) | 1.3 (2.6) | 0.75[b] |

[a] Fisher's Exact Test.

[b] Wilcoxon Rank Sum Test.

[*] Statistically significant.

[§] GDM = gestational diabetes mellitus.

[¶] PTD = Preterm delivery.

**Table 2**

Pregnancy Outcomes of Study Participants

| Characteristic | GDM[§] | Non-GDM | p |
|---|---|---|---|
| Gestational age (wks): Mean (SD) | 37.4 (2.8) | 38.8 (2.5) | 0.004[b*] |
| Birthweight (g): Mean (SD) | 3039.0 (676.9) | 3293.4 (628.3) | 0.14[b] |
| Baby gender: N (%) | | | |
| Male | 12 (57) | 105 (46) | 0.37[a] |
| Female | 9 (43) | 122 (54) | |
| Apgar 1: Mean (SD) | 8.3 (2.1) | 8.5 (1.3) | 0.81[b] |
| Apgar 5: Mean (SD) | 8.5 (2.1) | 8.8 (1.3) | 0.34[b] |
| Mode of delivery (%) | | | |
| Vaginal | 68.2 | 74.6 | 0.61[a] |
| C-section | 31.8 | 25.4 | |
| Premature rupture of membranes (%) | 25.0 | 8.6 | 0.04[a*] |
| Chorioamnionitis (%) | 25.0 | 9.2 | 0.04[a*] |
| Pre-eclampsia (%) | 10.0 | 2.7 | 0.14[a] |

[a] Fisher's Exact Test.

[b] Wilcoxon Rank Sum Test.

[*] Statistically significant.

[§] GDM = gestational diabetes mellitus.

**Table 3**

Periodontal Disease Parameters of Study Participants

| Variable | GDM[§] | Non-GDM | p |
|---|---|---|---|
| Clinical periodontal disease (%) | 50.0 | 37.3 | 0.38[a] |
| Maternal serum IgG levels against | | | |
| *P. gingivalis* (% high)[c] | 90.9 | 82.3 | 0.39[a] |
| *T. forsythia* (% high)[c] | 86.4 | 88.7 | 0.73[a] |
| Bacteriological data ($log_{10}$): Mean (SD) | | | |
| Plaque | | | |
| *C. rectus* | 2.5 (2.9) | 3.5 (2.6) | 0.22[b] |
| *F. nucleatum* ssp. *nucleatum* | 4.3 (2.2) | 4.5 (2.2) | 0.22[b] |
| *T. forsythia* | 2.9 (3.0) | 3.2 (2.9) | 0.64[b] |
| *P. gingivalis* | 1.6 (2.8) | 2.5 (2.8) | 0.32[b] |
| *T. denticola* | 2.3 (2.7) | 2.8 (2.7) | 0.33[b] |
| Vaginal | | | |
| *C. rectus* | 1.9 (2.5) | 1.2 (2.2) | 0.14[b] |
| *F. nucleatum* ssp. *nucleatum* | 2.7 (2.5) | 2.7 (2.3) | 0.41[b] |
| *T. forsythia* | 1.3 (2.4) | 0.3 (1.6) | 0.01[b*] |
| *P. gingivalis* | 0.6 (2.0) | 0.4 (1.7) | 0.48[b] |
| *T. denticola* | 0.6 (1.9) | 0.8 (2.0) | 0.71[b] |
| Cervical | | | |
| *C. rectus* | 1.8 (2.4) | 1.8 (2.3) | 0.91[b] |
| *F. nucleatum* ssp. *nucleatum* | 1.9 (2.5) | 2.9 (2.3) | 0.17[b] |
| *T. forsythia* | 1.2 (2.3) | 1.0 (2.1) | 0.57[b] |
| *P. gingivalis* | 1.6 (2.4) | 1.1 (2.1) | 0.18[b] |
| *T. denticola* | 0.7 (2.0) | 0.8 (2.0) | 0.96[b] |
| Inflammatory markers: Mean (SD) | | | |
| C-reactive protein (mg/dL) | 0.6 (0.6) | 0.3 (0.4) | 0.01[b*] |
| TNF-α (pg/mL) | 16.1 (12.5) | 13.2 (10.3) | 0.27[b] |
| IL-6 (pg/mL) | 4.6 (3.4) | 4.3 (4.5) | 0.42[b] |

[a] Fisher's Exact Test.

[b] Wilcoxon Rank Sum Test.

[c] Mean is ≥ 2 standard deviations.

[*] Statistically significant.

[§] GDM = gestational diabetes mellitus.

**Table 4**

Effects of Periodontal Disease and Other Parameters on Gestational Diabetes Mellitus—Bivariate and Multivariable Logistic Regression Analysis

| Variables | OR | 95% CI |
|---|---|---|
| Bivariate model[a] | | |
| Clinical periodontal disease (yes *vs.* no) | 1.68 | 0.52-5.43 |
| *P. gingivalis* IgG (high *vs.* low) | 2.15 | 0.48-9.58 |
| *T. forsythia* IgG (high *vs.* low) | 0.80 | 0.22-2.91 |
| Plaque bacteria | | |
| *C. rectus* | 0.87 | 0.74-1.02 |
| *F. nucleatum* ssp. *nucleatum* | 0.97 | 0.80-1.17 |
| *T. forsythia* | 0.97 | 0.83-1.12 |
| *P. gingivalis* | 0.89 | 0.76-1.05 |
| *T. denticola* | 0.93 | 0.79-1.10 |
| Vaginal bacteria | | |
| *C. rectus* | 1.13 | 0.94-1.36 |
| *F. nucleatum* ssp. *nucleatum* | 1.01 | 0.84-1.22 |
| *T. forsythia* | 1.27 | 1.05-1.55* |
| *P. gingivalis* | 1.08 | 0.86-1.36 |
| *T. denticola* | 0.93 | 0.74-1.18 |
| Cervical bacteria | | |
| *C. rectus* | 1.00 | 0.82-1.20 |
| *F. nucleatum* ssp. *nucleatum* | 0.84 | 0.70-1.01 |
| *T. forsythia* | 1.04 | 0.85-1.28 |
| *P. gingivalis* | 1.13 | 0.93-1.36 |
| *T. denticola* | 0.98 | 0.78-1.23 |
| C-reactive protein | 2.01 | 1.02-3.96* |
| TNF-α | 1.02 | 0.99-1.06 |
| IL-6 | 1.01 | 0.93-1.11 |
| GDM[§] in a prior pregnancy (yes *vs.* no) | 8.48 | 2.19-32.82* |
| Pre-pregnancy Body Mass Index | 1.17 | 1.08-1.27* |
| Multivariable models[†] | | |
| Model 1: Pre-pregnancy Body Mass Index | 1.16 | 1.07-1.26* |
| Model 2: Vaginal *T. forsythia* | 1.31 | 1.06-1.60* |

[a] Bacterial and cytokine levels were entered as continuous variables.

[†] Models 1 and 2 had prior pregnancy GDM (since it was the strongest predictor in the bivariate model) plus one other independent variable as shown.

* Statistically significant associations.

[§] GDM = gestational diabetes mellitus.