OBSTETRICS

# Periodontal disease and adverse pregnancy outcomes: is there an association?

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**OBJECTIVE:** We assessed the risk of adverse pregnancy outcomes (preterm birth [PTB], preeclampsia [PRE], fetal growth restriction [FGR], or perinatal death) in women with periodontal disease (PD) compared to those without.

**STUDY DESIGN:** A multicenter prospective cohort study enrolled women from 3 sites between 6 and 20 weeks' gestation. The presence of PD was defined as periodontal attachment loss ≥ to 3 mm on 3 or more teeth. The primary binary composite outcome included PRE, PTB, FGR, or perinatal death. Multivariable logistic regression (MVLR) was used to control for confounders.

**RESULTS:** Three hundred eleven patients with and 475 without PD were included. There was no association between PD and the composite outcome, PRE, or PTB in unadjusted analyses. There was no association between PD and the composite outcome (adjusted odds ratio [AOR], 0.81; 95% confidence interval [CI], 0.58-1.15; $P = .24$), preeclampsia (AOR, 0.71; 95% CI, 0.37-1.36; $P = .30$), or preterm birth (AOR, 0.77; 95% CI, 0.49-1.21; $P = .25$) after adjusting for relevant confounders.

**CONCLUSION:** Despite the body of literature suggesting an association between PD and adverse pregnancy outcomes in urban populations, this large prospective study failed to demonstrate an association.

**Key words:** adverse outcomes, periodontal disease, pregnancy, preterm birth

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There are 4 million deliveries every year in the United States.[1] Approximately 12% are affected by preterm delivery and 5-7% are affected by preeclampsia.[1,2] Preeclampsia is a major contributor to maternal and perinatal morbidity and mortality. Stillbirth and growth restriction are additional adverse pregnancy outcomes that affect many women each year and are difficult to reliably predict. Despite advances in technology, promotion of prenatal care and continued scientific efforts focused on reducing adverse pregnancy outcomes, little reduction has occurred. This is largely due to an incomplete understanding of the etiology of these adverse outcomes. Infection and/or inflammation as a causative factor for these adverse outcomes continue to be at the forefront of etiologic theories. Previous studies have demonstrated a link between infection and/or inflammation and preterm birth, preeclampsia, and other adverse outcomes thought to be in part secondary to poor placentation.[3-6] However, no successful targeted interventions have been developed likely due to the lack of clear inciting agents.

Given the theorized link between infection and/or inflammation and many adverse pregnancy outcomes, it is biologically plausible that periodontal disease may be linked to adverse pregnancy outcomes. Periodontal disease is one of the most common chronic infectious disorders in humans with prevalence between 10 and 60% depending on the definition and the population being studied.[7,8] Within the past decade, several studies have demonstrated an association between periodontal disease and the development of systemic diseases such as atherosclerosis and diabetes.[9,10] The underlying theory is that periodontal disease leads to a chronic systemic inflammatory response that then influences the onset and course of cardiovascular disease and diabetes mellitus. Adverse pregnancy outcomes including preeclampsia, low birthweight, and preterm delivery have also been among the "systemic diseases" studied in association with periodontal disease.[10,11] In addition to biologic plausibility, to further support this possible link, periodontal disease occurs commonly in the general population, but does have an increased prevalence in underserved populations. These are the same populations dispro-

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portionately affected by adverse pregnancy outcomes.

Studies performed to date examining the relationship between periodontal disease and pregnancy outcomes have mostly focused on the relationship between periodontal disease and a single pregnancy outcome, including preterm birth, preterm low birthweight, and low birthweight. Some have demonstrated a positive association,[12-19] while others have failed to demonstrate an association.[12,20-25] Interestingly, many of the studies that have failed to demonstrate an association between periodontal disease and adverse outcomes have been performed in other countries (United Kingdom, Canada, Denmark, and Sri Lanka). Studies that have shown a positive association between periodontal disease and various adverse outcomes have been performed in the United States, in largely urban settings with high proportions of African American patients. This suggests that periodontal disease may have varying associations with adverse pregnancy outcomes in different populations, the etiology of periodontal disease varies in different populations, or that periodontal disease is a marker for other factors that are associated with adverse pregnancy outcomes.

To this end, we sought to compare the risk of a composite of adverse pregnancy outcomes in women with and without prospectively identified (early in pregnancy) periodontal disease in a multicenter urban population. Our secondary aims were to compare the risk of specific adverse outcomes, preeclampsia and preterm birth, in women with and without periodontal disease.

## Materials and Methods

The Periodontal Infection and Prematurity Study (PIPS) includes a large, randomized controlled trial to study the association between periodontal disease, treatment, and preterm birth. The primary aim of the overall randomized trial is to compare efficacy of scaling and planning treatment of periodontal disease to polishing (placebo) in preterm birth prevention (< 35 week delivery). Additionally, an observational cohort of women without periodontal disease was followed as a comparison group.

We performed a multicenter prospective cohort study. Specifically, we set out to compare women who screened negative for periodontal disease (unexposed group), and were thus ineligible for the trial, to those who screened positive for periodontal disease (exposed group), but were not randomized, because they failed to show up for the follow-up visit when randomization occurred.

Patients for the PIPS study were recruited from 3 centers in Philadelphia: Helen O. Dickens Center at the Hospital of the University of Pennsylvania (HUP), Women and Children's Health Service at Pennsylvania Hospital (PAH), and Albert Einstein Medical Center (AE). Recruitment occurred from October 2004 to October 2007. All of these sites provide prenatal care for underserved populations in Philadelphia, and all enrollment occurred in large prenatal clinics at each site. Trained research nurses from the 3 participating sites enrolled patients for the PIPS trial. Ninety percent of women who deliver at these hospitals enroll in prenatal care at < 20 weeks' gestation at these 3 sites based on a prior study performed by one of the investigators (data not shown).

Inclusion criteria for the PIPS study (randomized and observational components) included women who were 6-20 weeks' gestation (adjusted by ultrasound if necessary). A nurse trained by dental personnel evaluated women for the presence or absence of periodontal disease using predefined criteria. Each study nurse underwent retraining and observation once to twice annually for the duration of the study. A thorough, complete exam was performed on all patients. Specifically, the presence of periodontal disease was defined as periodontal attachment loss greater than or equal to 3 mm on 3 or more teeth. Eligibility for enrollment was determined by presence or absence of periodontal disease (dichotomous yes/no); those with documented periodontal disease were eligible for the randomized trial. Bleeding on probing and severity of periodontal disease at initial screening were not recorded in this study. Those without periodontal disease were eligible to be followed in the observational cohort. Women who received periodontal treatment during the pregnancy, used antibiotic or antimicrobial mouthwash within 2 weeks of enrollment, had a multiple gestation pregnancy, or had known mitral valve prolapse were excluded.

Women identified with periodontal disease were asked to complete a baseline interview and provide consent for enrollment into the trial. Randomization took place at their subsequent visit. Women with periodontal disease who were enrolled initially but who failed to present for randomization formed the exposed cohort in this investigation. Women without documented periodontal disease at the initial visit were asked to complete a baseline interview and provide consent for enrollment into a follow-up study. These women formed the unexposed cohort in this investigation. All data were collected by a structured interview at enrollment and chart review by trained research nurses at the end of the follow-up period. Data collected from these 2 sources included outcomes as described below as well as potential identifiable confounders. Potential confounders that were analyzed include: prior obstetric history, maternal race, age, and socioeconomic status (measured by highest level of educational attainment), site of care, obesity, diabetes and chronic hypertension (prior to pregnancy), tobacco use, drug use, sexually transmitted infection, and bacterial vaginosis. Body mass index (BMI) was determined using height and current weight given by patient at time of interview. Periodontal disease status was not reassessed at the time of delivery in any study group.

The primary study outcome was a binary composite outcome and included the occurrence of any of the following 4 outcomes: preterm birth (spontaneous or indicated delivery at < 37 weeks' gestation), preeclampsia (hypertension after 20 weeks' gestation based on traditional criteria per American College of Obstetricians and Gynecologists [≥ 140/90 mmHg] with proteinuria),[26] fetal growth restriction (< 10% for gestational age based on Alexander growth