OBSTETRICS

Optimal timing of periodontal disease treatment for prevention of adverse pregnancy outcomes: before or during pregnancy?

Xu Xiong, MD, DrPH; Pierre Buekens, MD, PhD; Robert L. Goldenberg, MD; Steven Offenbacher, DDS, PhD; Xu Qian, MD, PhD

Over the past 2 decades, there has been increasing evidence suggesting associations between periodontal disease and various adverse birth outcomes such as preterm birth, low birthweight, diabetes mellitus, and adverse pregnancy outcomes.1,2 Since Offenbacher et al1 first reported an association between periodontal disease and preterm birth in 1996, substantial evidence has accumulated suggesting that periodontal disease may be associated with an increased risk of various adverse birth outcomes.2 Adverse pregnancy outcomes that have been linked to periodontal disease include preterm birth, low birthweight, miscarriage or early pregnancy loss, preeclampsia, and gestational diabetes mellitus.3

Several large randomized controlled clinical trials failed to find that standard periodontal therapy during pregnancy reduces the incidence of adverse pregnancy outcomes (eg, preterm birth and low birthweight). However, treating periodontal disease during pregnancy may be too late to reduce the inflammation that is related to the adverse pregnancy outcomes. Moreover, periodontal treatment during pregnancy can cause bacteremia, which itself may initiate the pathway leading to the adverse pregnancy outcomes. Finally, the periodontal treatments provided during pregnancy are not always effective in preventing the progression of periodontal disease during pregnancy. Pregnancy may not be an appropriate period for periodontal intervention(s). We hypothesize that periodontal treatment before pregnancy may reduce the rates of adverse pregnancy outcomes. Future randomized controlled trials are needed to test if treating periodontal disease in the prepregnancy period reduces the rate of adverse pregnancy outcomes.

Key words: periodontal disease, prepregnancy periodontal treatment, preterm birth, randomized controlled clinical trial


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Based on our prior systematic review of existing observational studies (eg, case-control, cross-sectional and cohort) on the relationship between periodontal disease and adverse birth outcomes,2 we concluded that there is evidence of an association between periodontal disease and increased risk of preterm birth and low birthweight, especially in economically disadvantaged populations. However, because of potential biases (eg, inconsistent definitions of periodontal disease and pregnancy outcomes, insufficient sample size, or lack of controlling for key confounders), observational studies are unable to offer a clear conclusion about the relationship between periodontal disease and pregnancy outcomes.2 Randomized controlled treatment trials (RCTs) of periodontal disease are likely to offer the best evidence of whether periodontal disease is in the causal pathway leading to adverse pregnancy outcomes.

The Table presents a summary of 13 clinical trials published to date to examine if periodontal treatment during pregnancy reduces the incidence of adverse pregnancy outcomes. Earlier RCTs showed very promising results of periodontal treatment during pregnancy. These RCTs, which tended to be conducted in low socioeconomic status populations or low- and middle-income countries (eg, Chile and India),6,10 were pilot studies,5,7,9 or had relatively small sample sizes,6,14 suggested that periodontal treatment during pregnancy led to significant reductions in the rates of preterm birth and low birthweight. However, several large RCTs conducted in high-income countries (eg, United States and Australia) failed to find that periodontal therapy during pregnancy reduced the incidence of preterm birth and low birthweight.1,13,16 A metaanalysis of the nine clinical trials4,6,7,9,10,13-16 that had preterm birth as an outcome suggested that periodontal treatment did not significantly reduce the rate of preterm birth (pooled relative risk [RR], 0.82; 95% confidence interval [CI],
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<tr>
<td>Mitchell-Lewis et al, 2001 USA&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Oral prophylaxis group: 74 Control group: 90</td>
<td>60% African American, 39% Hispanic, all of low socioeconomic status</td>
<td>Oral prophylaxis group was enrolled during pregnancy and received oral intervention. Control group is recruited postpartum</td>
<td>PLBW: 13.5% in oral prophylaxis group, 18.9% in control group, RR: 0.72 (0.4–1.47)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>There was a 28% reduction in PLBW in the periodontally treated group, but it was not statistically significant.</td>
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<td>Lopez NJ et al, 2002 Chile&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Periodontal disease treatment group: 200 Nontreatment group: 200</td>
<td>Low socioeconomic status</td>
<td>≥4 teeth with ≥1 sites with PD ≥4 mm and with CAL ≥3 mm</td>
<td>PLBW: RR: 0.18 (0.05–0.6)&lt;sup&gt;a&lt;/sup&gt; PTB: RR: 0.19 (0.04–0.85)&lt;sup&gt;a&lt;/sup&gt; LBW: RR: 0.16 (0.02–1.33)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Periodontal disease is an independent risk factor for PLBW.</td>
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<td>Jeffcoat MK et al, 2003 USA&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Group 1: prophylaxis plus placebo capsule, n = 123; Group 2: SRP plus placebo capsule, n = 123; Group 3: SRP and metronidazole capsule (250 mg for 1 wk), n = 120</td>
<td>African-American: 85% Married: 13.4%</td>
<td>≥3 sites with CAL ≥3 mm</td>
<td>PTB &lt;37 wks: RR: 0.5 (0.2–1.3) PTB &lt;35 wks: RR: 0.2 (0.02–1.4)</td>
<td>Performing SRP in pregnant women with periodontitis may reduce PTB. Metronidazole therapy did not improve pregnancy outcome.</td>
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<td>Sadatmansouri S et al, 2006 Iran&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Periodontal treatment group: SRP and 0.2% chlorhexidine mouth rinse for 1 wk: 15 Controls: 15</td>
<td>All women with moderate or advanced periodontitis</td>
<td>PLBW: 4 cases (26.7%) in controls vs 0 (0%) in treatment group (P &lt; .05)</td>
<td>Periodontal therapy results in a reduction in PLBW.</td>
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<tr>
<td>Michalowicz BS et al, 2006 USA&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Periodontal disease treatment group: 413 Control group: 410</td>
<td>White: 28.6% Black: 45.2% Hispanic: 42.5%</td>
<td>≥4 teeth with PD ≥4 mm and CAL ≥2 mm and BOP ≥35%</td>
<td>PTB: RR: 0.93 (0.63–1.37) LBW: RR: 0.92 (0.61–1.39)&lt;sup&gt;a&lt;/sup&gt; SGA: RR: 1.04 (0.68–1.58)</td>
<td>Treatment of periodontitis in pregnant women does not significantly reduce rates of PTB, LBW, or SGA.</td>
</tr>
<tr>
<td>Offenbacher S et al, 2006 USA&lt;sup&gt;f&lt;/sup&gt;</td>
<td>Intervention group (SRP and sonic toothbrush): 35 Control group: 32</td>
<td>African American: 60.81%; White: 25.68%; Asian: 1.35%; Other race: 16.67%</td>
<td>≥2 sites measuring ≥5 mm PD plus periodontal attachment loss of 1 to 2 mm at ≥1 sites with PD ≥5 mm</td>
<td>PTB 25.7% in intervention group; 43.8% in control group. aOR: 0.26 (0.08–0.85)</td>
<td>Results from this pilot study (67 subjects) provide further evidence supporting the potential benefits of periodontal treatment on pregnancy outcomes.</td>
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<td>Taranum F et al, 2007 India&lt;sup&gt;g&lt;/sup&gt;</td>
<td>Treatment group: 99 Control group: 89</td>
<td>Mean age: 23.0 ± 3.3 in treatment group; 22.9 ± 3.6 in control group</td>
<td>With ≥20 completely erupted teeth, excluding the third molars; or with ≥2 mm attachment loss at ≥50% of examined sites</td>
<td>PTB 53.5% in treatment group; 76.4% in control group (P &lt; .001). RR: 0.70 (0.56–0.87)&lt;sup&gt;a&lt;/sup&gt; LBW 26.3% in treatment group; 53.9% in control group (P &lt; .002). RR: 0.49 (0.33–0.71)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Nonsurgical periodontal therapy can reduce the risk for preterm births in mothers who are affected by periodontitis.</td>
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<td>Gazolla CM et al, 2007 Brazil&lt;sup&gt;h&lt;/sup&gt;</td>
<td>Treatment group: 266 Control group: 62</td>
<td>White: 48.44% Black: 34.89% Other: 16.67%</td>
<td>Disease status was classified according to PD and CAL: P1: ≥4 teeth with PD of 4 to 5 mm and CAL of 3 to 5 mm at the same site; P2: ≥4 teeth with PD and CAL of 5 to 7 mm at the same site; P3: ≥4 teeth with PD and CAL &gt;7 mm at the same site</td>
<td>Preterm and/or LBW 7.5% in treatment group; 79.0% in control group. RR: 0.10 (0.06–0.15)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Periodontal disease was related significantly to preterm low birthweight.</td>
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Periodontal treatment during pregnancy and adverse pregnancy outcomes

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<td>Radnai M et al, 2008</td>
<td>Oral hygiene treatment group: 80 Control group: 79</td>
<td>Nonsmoking women</td>
<td>N/A</td>
<td>Mean birthweight: 3005.3 g in treatment group; 2644.2 g in control group (P &lt; .0001). Delivery time: 37.0 wk in the treatment group; 36.4 wk in control group (P = .059)</td>
<td>Periodontal treatment might have contributed to a more optimal date of delivery and to achieving a larger birthweight.</td>
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<tr>
<td>Offenbacher S et al, 2009</td>
<td>Treatment group: 903 Control group: 903</td>
<td>White: 61.0% Black: 37.6% Other: 1.4% ≥20 teeth, with ≥3 sites with CAL ≥3 mm</td>
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<tr>
<td>Radnai M et al, 2009</td>
<td>Intervention group (oral hygiene instruction and periodontal therapy): 41 Control group: 42</td>
<td>All white women Mean age: 29.1 ± 6.4 in treatment group; 28.9 ± 5.4 in control group.</td>
<td>Periodontitis: ≥4 mm PD at ≥1 site, and BOP for ≥50% of teeth.</td>
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<td>Periodontal therapy did not reduce the incidence of preterm delivery</td>
</tr>
<tr>
<td>Herrera JA et al, 2009</td>
<td>Intervention group: 28 Control group: 32</td>
<td>All mild preeclampsia subjects Mixed ethnic backgrounds: 61.67% Black: 35.00% Indigenous: 3.33% Low socioeconomic level: 83.33%</td>
<td>Periodontal diagnosis was established according to the report consensus criteria of the American Academy of Periodontology.</td>
<td></td>
<td>Periodontal treatment completed before the 35th wk appeared to have a beneficial effect on birthweight and time of delivery</td>
</tr>
<tr>
<td>Newnham JP et al, 2009</td>
<td>Treatment group: 538 Control group: 540</td>
<td>White: 73.65% Asian: 16.23% Aboriginal: 4.17% African: 3.71% Hispanic: 1.11% Other: 1.11%</td>
<td></td>
<td></td>
<td>The evidence provided by the present study does not support the hypothesis that treatment of periodontal disease during pregnancy in this population prevents preterm birth, fetal growth restriction, or preeclampsia.</td>
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</table>

**Notes:**
- BOP: bleeding on probing; CAL: clinical attachment loss; GA: gestational age; IUGR: intrauterine growth restriction; LBW: low birthweight; N/A: not available; OR: odds ratio; PD: probing depth; PLBW: preterm low birthweight; PTB: preterm birth; RR: risk ratio; SGA, small-for-gestational age; SRP: scaling and root planing.
- a Computed from data; b Reversed from original OR form.
0.64–1.06; \( P > .05 \) (Table and Figure 1). A metaanalysis of the 5 clinical trials\(^4,6,10,13,14\) that had low birthweight as an outcome suggested that treatment of periodontal disease during pregnancy may reduce the rate of low birthweight (pooled RR, 0.64; 95% CI, 0.40–1.00; \( P = .05 \)) (Table and Figure 2).

Despite the fact that recent large RCTs failed to demonstrate that periodontal therapy during pregnancy reduced the incidence of preterm birth and low birthweight,\(^4,13,16\) several other explanations need to be explored before a conclusion can be drawn about whether periodontal disease treatment can reduce the risk of preterm birth and other pregnancy outcomes.\(^13,17\) One important aspect is the timing of periodontal treatment. All the published RCTs to date tested periodontal treatment during pregnancy. However, treating periodontal disease during pregnancy may be too late to reduce the local and systemic inflammation that is related to the adverse birth outcomes.\(^17\) It has been hypothesized that once the inflammatory cascade is activated during pregnancy, interventions targeting this pathway may be ineffective in reducing the rates of adverse pregnancy outcomes (eg, preterm birth).\(^17\) Moreover, oral mechanical manipulation (eg, dental procedures) that can cause bacteremia may even initiate the pathway by which periodontal infection causes adverse pregnancy outcomes.\(^3\) Periodontal treatment itself thus may trigger a systemic inflammatory cascade during pregnancy (through bacteremia), which may dilute the beneficial effects of the therapy. In addition, the periodontal treatment provided during pregnancy (usually 1 treatment course during 1 or 2 appointments) was not always effective in preventing the progression of periodontal disease during pregnancy,\(^13\) suggesting that further periodontal maintenance throughout gestation may be needed. Thus, pregnancy may not be an appropriate period for periodontal intervention(s). By contrast, the preconceptional period may be an optimal period for interventions. Periodontal treatment either before pregnancy (for nulliparous women) or in the period between pregnancies (for multiparous women) may reduce the rates of adverse pregnancy outcomes. However, to date, no RCT has examined whether or not treating periodontal disease among preconceptional women (eg, women who plan to conceive within 1 year) reduces the rate of adverse pregnancy outcomes.

Over the years, there have been many attempts at reducing the incidence of preterm births and other adverse pregnancy outcomes. These attempts have included various strategies to improve maternal nutritional status (increasing calories, protein, iron and folate, and other minerals, and vitamin intake), attempts to treat various genitourinary tract infections (bacterial vaginosis, Chlamydia, urinary tract infection), cervical cerclage to prevent or treat incompetent cervix, as well as the use of prostaglandin agents to prevent contractions or reduce inflammation.\(^18,19\) Attempts at treating premature labor have included the use of various tocolytic agents (alcohol, beta-adrenergic agents, MgSO4, calcium channel blockers), as well as antibiotics and bed rest, fluid administration, and narcotics.\(^18,19\) For the most part, these attempts have failed, as evidenced by results from randomized trials as well as the observation that preterm birth rates in most developed countries have not decreased despite their use. Exceptions might include the use of cerclage and prostaglandin agents in well-defined populations.\(^20\) Even with the expanded use of these interventions, however, there is unlikely to be an important decrease in the overall preterm birth rate.

Periodontal disease, because of its high prevalence, strong association with preterm birth in many studies and in the metaanalyses, and plausible biologic pathway,\(^2,3\) despite the negative RCT results of 1 type of treatment during pregnancy, remains an inviting target for reducing preterm birth. Because pregnancy may not be an appropriate period for periodontal intervention(s) and there is a lack of knowledge of whether
Prepregnancy periodontal treatment may reduce the risk of adverse pregnancy outcomes, future RCTs are needed to test if prepregnancy periodontal therapy can reduce the incidence of adverse pregnancy outcomes. In such a RCT, prepregnancy women (eg, women who plan to conceive within 1 year) would be eligible to participate in a periodontal examination. Women who meet the criteria for periodontal disease will then be randomized into 2 groups: intervention or periodontal treatment group vs non-intervention or control group. Women in both groups will be followed up through their pregnancy until they give birth. The rates of pregnancy outcomes (eg, preterm birth and low birthweight) will be compared between the 2 groups. Compared with the RCTs conducted in pregnant women in a hospital setting, a preconceptional trial may be more difficult to enroll because most women do not receive preconceptional care in this country. Additional efforts may be needed to recruit preconceptional women at community levels (eg, marriage registration offices, churches).

Such a trial of prepregnancy periodontal treatment in the reduction of adverse pregnancy outcomes would have the following potential benefits on both scientific and applicable aspects to the improvement of maternal and child health:

- Prepregnancy periodontal therapy can be more intensive than what can be provided during pregnancy (eg, the use of adjunctive antibiotics) and can lead to better resolution of periodontal disease. An adoptive treatment model can be used to titrate all preconceptional women to a relative state of periodontal health before conception. Furthermore, preconception periodontal maintenance would be less intensive and designed to maintain health, throughout the hormonal and immunomodulatory stresses of pregnancy.

- Prepregnancy treatments might provide a more definitive conclusion as to whether periodontal disease is a causal risk factor for preterm birth and other adverse pregnancy outcomes.

- If the effect of prepregnancy periodontal treatment is confirmed, it would contribute to a better understanding of the etiologic pathway and biologic mechanism of how subclinical infections like periodontal disease lead to an increased risk of preterm birth and other adverse pregnancy outcomes.

- Preterm birth and other adverse pregnancy outcomes are the leading causes of infant morbidity and mortality worldwide. To date, few risk factors have been identified that are modifiable and amenable to intervention strategies for reducing their incidence. Because periodontal disease is preventable and curable, if the effect of prepregnancy periodontal treatment is confirmed, improving oral health and treating periodontal disease before pregnancy may lead to a reduction in rates of preterm birth and infant morbidity and mortality worldwide.

- Finally, the prepregnancy periodontal treatment strategy would be applicable to many low- or middle-income countries (eg, India and China), where there is little or no access to preventive or restorative dental care. The prepregnancy periodontal treatment mainly includes scaling and root planing (in combination with personal oral hygiene), which are nonsurgical periodontal procedures and can be performed by oral health professionals (eg, dentists or dental hygienists) after receiving appropriate training. In addition, if the periodontal treatment is performed before pregnancy, it will avoid potential risks to the pregnancy (fetus) and will be more acceptable and less stressful to women. If the effect of prepregnancy periodontal treatment is confirmed, this intervention could be recommended for application in low- or middle-income countries to improve both oral health and maternal and child health.

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