

# Periodontal Disease and Adverse Pregnancy Outcomes

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**Abstract:** *Periodontal disease, or gum disease, is one of the most common chronic inflammatory disorders that affect the tissues surrounding the teeth. Optimal oral health is a critical component to the overall health of pregnant women and their babies. Untreated oral conditions can be a major risk factor for health complications in the developing fetus or newborn infant. Periodontal diseases are considered a risk factor for adverse pregnancy outcomes, including preeclampsia, preterm delivery, low birth weight, and intrauterine growth restriction, and fetal demise affect a significant number of pregnancies and are a major source of both maternal and neonatal morbidity and mortality. This review will assess the relationship between periodontal diseases on adverse birth outcomes as well as importance and safety of maintaining oral health care during pregnancy.*

**Keywords:** Periodontal disease, Adverse pregnancy outcomes, Low birth weight, preeclampsia, pregnancy

## 1. Introduction

Periodontal disease, or gum disease, is one of the most common chronic inflammatory disorders that affect the tissues surrounding the teeth<sup>1</sup>. Periodontal disease results from a complex interplay between the subgingival biofilm and the host immune inflammatory event, which develop in the gingival and periodontal tissues in response to the challenge presented by the bacteria<sup>2</sup>.

The bacteria may initiate the disease, but the progression is host immune-mediated, and several inflammatory cells and enzymes are released which have a detrimental effect on other cells, tissues, and organ systems. There is a shift from healthy nonpathogenic flora to a huge virulent and infectious anaerobic flora in the periodontal disease. These bacteria and their toxins and various pro-inflammatory mediators penetrate into systemic circulation. The penetration of bacterial toxins and host-mediated immunomodulatory mediators into systemic circulation can have a toxic effect on the cells and organs elsewhere in the body. Environmental, physical, social, and host stresses may affect and modify disease expression through a multitude of pathways<sup>3</sup>.

The potential effect of periodontal diseases might be explained by two mechanisms: the translocation of periodontal pathogens to the feto-placental unit, or the effect of inflammatory mediators, such as interleukin-1 (IL-1), IL-6, IL-8, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) or prostaglandin E2 (PGE2), on the fetoplacental unit.<sup>4</sup>

There is a two-way relationship between periodontal disease and systemic disease or condition in an individual. The influence of periodontal infection on systemic disease and condition documented includes coronary heart disease (CHD) and CHD-related events such as angina, infarction, atherosclerosis, and other vascular conditions; stroke; diabetes mellitus; preterm labor, low birth weight delivery, and preeclampsia; and respiratory conditions such as chronic obstructive pulmonary disease<sup>5</sup>. Adverse pregnancy outcomes have been attributed to infections and inflammatory conditions in the vagina and elsewhere in the body. The potential role of chronic bacterial infections elsewhere in the body remote from the fetal-placental unit,

which may influence the health and growth of babies in the placenta, has been studied immensely. This realization that infection in any part of the body can affect the placenta has led to the idea that periodontal disease can be a possibility in adverse pregnancy outcome. Local elevation of pro-inflammatory prostaglandins and cytokines due to "chronic gram-negative infection" in the periodontal diseases can be a risk factor<sup>6</sup>.

Since 2000, research has identified the presence of multiple oral bacterial species found in systemic locations outside of the oral cavity. *Streptococcus mutans* (brain abscess), *Aggregatibacter actinomycetemcomitans* (bacterial endocarditis), and *A. actinomycetemcomitans* and *Porphyromonas gingivalis* (atherosclerotic plaques in the aorta) have all been discovered throughout the body, substantiating the relationship between oral health and systemic health<sup>7</sup>. Studying the direct effect of any one risk factor on the outcomes of preterm birth and LBW babies is challenging because of the many confounding variables that may generate the same outcome<sup>8</sup>.

The establishment of a solid oral health regimen, paired with periodontal treatment recommendations from the patient's dental professional and/or obstetrician, may help prevent negative outcomes. Early prevention and intervention are key<sup>9</sup>.

## 2. Focal Infection Theory Revisited

William Hunter, a British physician in 1900, first developed the idea that oral microorganisms were responsible for a wide range of systemic conditions that were not easily recognized as being infectious in nature. Hunter also identified gingivitis and periodontitis as foci of infection and advocated the extraction of teeth with these conditions to eliminate source of sepsis. He also thought that oral organisms had specific actions on different tissues and that these organisms were acted by producing toxins, thereby resulting in low-grade superinfection that produce systemic effect over prolonged periods. The Hunter theory became widely accepted, thereby leading to wholesale extraction of teeth. The focal infection theory fell into disrepute during the 1940s and 1950s when widespread extraction failed to reduce or eliminate the systemic conditions. However,

Hunter ideas did encourage extensive research in the areas of microbiology and immunology. The Hunter theories are being revived today in light of recent research demonstrating links between oral and systemic health. Today's era of evidence-based medicine and dentistry provides an excellent environment in which to examine the possible relationship between oral infection and systemic disorders<sup>3</sup>.

The first association between periodontal disease and preterm low birth weight babies was documented by Offenbacher and colleagues in 1996 using a case-control study design. The study by Offenbacher et al.<sup>10</sup> suggested that maternal periodontal disease could lead to a sevenfold increased risk of delivery of a preterm low birth weight infant. Human case-control studies have demonstrated that women who have low birth weight infants as a consequence of either preterm labor or premature rupture of membranes tend to have more severe periodontal disease than mothers with normal birth weight infants<sup>12</sup>.

### 3. Pregnancy and its Outcomes

Pregnancy by itself does not cause periodontal diseases, but the hormonal changes during pregnancy accentuate the gingival response to plaque and modify resultant clinical picture.<sup>3</sup>

Diverse pregnancy outcomes usually include several different Disease outcomes following pregnancy, including low-birth Weight ( $\leq 5.5$  lbs), very low birth weight ( $\leq 3.3$  lbs), preterm birth/delivery ( $\leq 37$  weeks of gestation) or very preterm ( $\leq 32$  weeks of gestation) birth, preeclampsia (maternal hypertension/proteinuria), and miscarriage/ still births. While several of these outcomes can be interdependent, it is still unclear if they share common pathological processes or associated risk factors. One of the common risk factors for adverse pregnancy outcomes is maternal infection, which is believed to account for most of preterm delivery cases (25% to 40%).<sup>12</sup>

Preeclampsia is a multisystem disorder that occurs during pregnancy and the post-partum period. Affecting both the mother and the fetus, preeclampsia is defined as a first-time hypertension episode and proteinuria in a previously normotensive woman. Women with preeclampsia are at an increased risk for maternal and/or fetal morbidity and mortality<sup>13</sup>. Preeclampsia occurs in up to 7.5% of pregnancies worldwide<sup>14</sup>.

Women with preeclampsia are at an increased risk for life-threatening events, such as placental abruption, acute renal failure, cerebral hemorrhage, hepatic failure or rupture, pulmonary edema, disseminated intravascular coagulation, and progression to eclampsia (development of seizures after severe preeclampsia). Globally, 10% to 15% of maternal deaths are attributed to preeclampsia<sup>15</sup>.

Pyogenic granuloma (PG) or pregnancy tumor is a non-specific inflammatory lesion of the skin and mucous membranes. PG occurs in both males and females as inflammatory lesion on skin or mucous membrane. PG occurs approximately 0.5–2.0% of pregnant women with

gingival lesions developing in interdental gingiva. They are also called pregnancy tumors or granuloma gravidarum.<sup>3</sup>

Clinical complaints with pregnancy-associated pyogenic granulomas include gingival bleeding, tenderness, and esthetic problems. Treatment may include surgical removal, especially if the lesion is large and symptomatic<sup>16,17</sup>. However, in many cases, the lesions undergo partial or complete resolution after delivery, especially if local irritants are removed<sup>18</sup>.

Gestational diabetes mellitus (GDM) refers to the detection of glucose intolerance or raised blood glucose level, for the first time during pregnancy in a woman. Gestational diabetes occurs in approximately 7% of women during pregnancy, and it is a multifactorial disease. GDM has been associated with a long list of risk factors<sup>19</sup>. The increased blood sugar levels make the pregnant woman more susceptible for periodontal diseases.

#### Pathogenic Mechanism

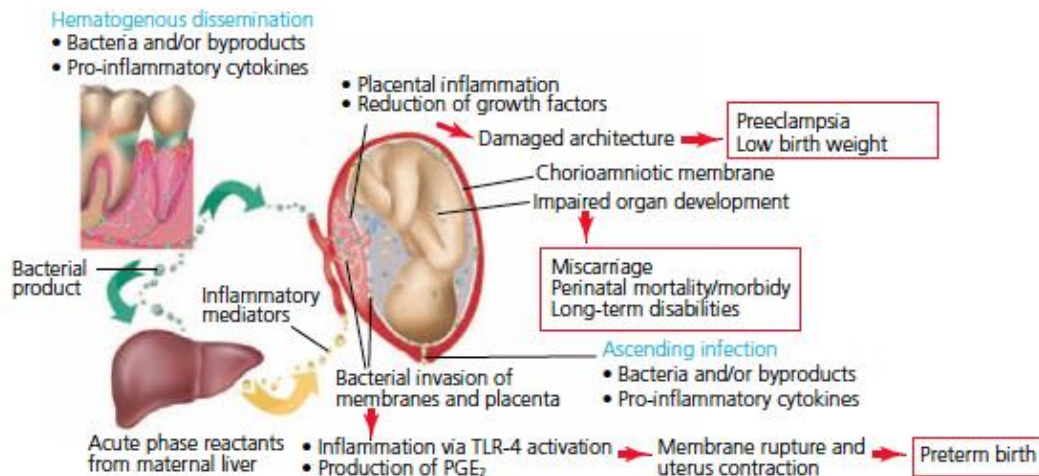
Recent studies have revealed that the placenta is not sterile but instead has a unique microbiome.<sup>20,21</sup> Stout et al. identified gram-positive and gram-negative intracellular bacteria in the basal plate of the human placenta<sup>21</sup>.

Although oral bacteria do not enter systemic circulation constantly, daily oral activities (e.g. tooth brushing and flossing) and dental treatments (e.g. scaling and root planing) often cause bacteremia<sup>22</sup>. Therefore, the fetomaternal units, especially invasive trophoblasts, are exposed to oral bacteria by chance. Not only nonpathogenic oral bacteria but also pathogenic bacteria could translocate to the placenta<sup>4</sup>.

Periodontal disease-associated bacteria have been linked to adverse pregnancy outcomes. Important periodontal pathogens, such as *P. gingivalis*, *F. nucleatum*, and *C. rectus*, have been detected in human placentas of women with preterm delivery, preeclampsia, and in the amniotic fluid of women with premature labor<sup>31</sup> or premature labor with intact membranes. In fact, the human placenta harbors a mix of bacteria (microbiome) similar to the micro biome in an adult human's mouth. Fetal exposure to periodontal pathogens from maternal oral biofilms also has been demonstrated by measuring fetal immunoglobulin M, which specifically reacts to *P. gingivalis* and *C. rectus*, suggesting adaptive immune responses developed by the fetus against oral bacteremia from the mother<sup>9</sup>.

Increased vascular permeability during pregnancy may facilitate the systemic circulation of the pathogens and their toxic byproducts to the fetoplacental unit. This type of bacterial challenge induces the release of inflammatory cytokines, which can result in premature rupture of the membrane and early intrauterine contractions. Consequently, placental infection/inflammation is a key pathogenesis feature of most pregnancy complications. Laboratory evidence suggests that placental cells develop inflammation when exposed to *F. nucleatum* and *C. rectus*<sup>23</sup>. Moreover, evidence derived from animal experiments has demonstrated bacterial translocation, placental inflammation, increased

fetal resorption (similar to miscarriage), and/or growth restriction in response to infection with oral pathogens.<sup>24-26</sup>



**Figure 1:** Various Factors Responsible for Adverse Pregnancy Outcomes

During pregnancy, the placenta invades and grows through support of the maternal uterine tissue. Because of its high vascularity, the placenta is able to exchange nutrients from the maternal tissue and carry it to the fetus via the umbilical cord. The fetus is in the amniotic fluid, surrounded by the amniotic sac. As the fetus continues to grow, there is less space and nutrients available for its growth. As pregnancy progresses, the levels of prosta glandin E2 and inflammatory cytokines, such as TNF-alpha and IL-1 beta, rise steadily until they induce the rupture of the amniotic sac and cause uterine contraction, cervical dilation, and normal delivery.<sup>27</sup> Thus, the pathway of inflammatory signaling controls normal childbirth.

Increased levels of IL-6, CRP, and TNFalpha also interfere with insulin signaling and cause glucose intolerance that can result in gestational diabetes<sup>28</sup>.

Periodontal diseases are infectious diseases that occur at a distance from the fetoplacental unit. As in any infection, there is an increase in the local inflammatory response against the bacteria and their virulence factors in the oral cavity. Eventually these cytokines, as well as the bacteria, can enter the blood circulation and disseminate throughout the body—triggering a systemic inflammatory response.<sup>24,29</sup>

#### 4. Effect of Periodontal Therapy on Pregnancy Outcomes

Encouraging prevention and minimizing oral diseases before and during pregnancy are key to reducing adverse pregnancy outcomes. The pregnancy period is a time when women are highly motivated to adopt healthy behaviors, providing an opportunity to emphasize the importance of effective oral self-care<sup>30</sup>.

The dilemma of performing periodontal treatment during pregnancy to reduce the APOs has not been answered. Periodontal treatment even if undertaken during pregnancy will not be thorough and completely eradicate the disease process, due to fear of bacteraemia which may cause APO.

Pre-conception period is most appropriate time for periodontal treatment. Periodontal treatment to create a healthy mouth before conception may reduce the occurrence of APOs. The local and systemic inflammation caused by periodontal pathogens may not be controlled by periodontal treatment during pregnancy. Periodontal treatment before pregnancy (for nulliparous women) or in the period between pregnancies (for multiparous women) may reduce APOs<sup>31</sup>.

It has been known for many years that nonsurgical periodontal therapy is effective in reducing the increased amount of periodontal inflammation associated with pregnancy. Data clearly show that this therapy is safe and does not trigger an increase in adverse pregnancy outcomes. It has not been shown that routine nonsurgical periodontal therapy decreases the incidence of these outcomes. In general, women assigned to the periodontal treatment groups showed statistically significant improvements in their periodontal assessments<sup>3</sup>.

#### 5. Oral Health Care during Pregnancy

In 2012, the National Maternal and Child Oral Health Resource Center published Oral Health Care during Pregnancy: A National Consensus Statement. This report, in addition to statements released by the American Academy of Periodontology (AAP) and the American College of Obstetricians and Gynecologists (ACOG), document the necessity and importance of maintaining maternal oral health during pregnancy as well as promoting a collaborative effort between prenatal providers and oral health practitioners to promote oral health education, preventive care, and dental treatment during the gestational period. Most importantly, these consensus statements aim to reassure the safety of preventive care and therapeutic treatment during pregnancy. Radiographic exposures (with proper shielding of the thyroid and abdomen) for diagnostic procedures do not pose any harmful risk to the developing embryo or fetus and are considered safe throughout the entire pregnancy. Routine prophylaxis, scaling and root planing, restorative procedures, and local anesthesia administration, are also all considered safe and may be

performed on pregnant women at any time during pregnancy<sup>32</sup>.

## 6. Conclusion

Gingival inflammation and tissue response toward the microbial plaque is exaggerated during pregnancy due to the hormonal factors and is accepted by the scientific community. Pregnant women with previously existing periodontal disease will have increased destruction of the periodontal structures. The gingival changes observed during pregnancy return to normal limits immediately after delivery of the baby, if the local irritants are removed; this phenomenon is called as “immune reconstitution syndrome.” Gestational diabetes which occurs in certain pregnant women can increase the risk for periodontal diseases, and it should be well controlled by treating gynecologist. Preeclampsia if not detected and treated can cause serious condition eclampsia leading to convulsions, coma, and death of the mother<sup>3</sup>.

A 2011 systematic review found a positive association between periodontal diseases and adverse pregnancy outcomes in nine out of 11 studies<sup>33</sup>. The authors concluded that there was not enough evidence to support the theory that maternal periodontal treatment can decrease the risk of preterm birth or low-birth weight, but they did recommend that pregnant women be instructed on the importance of maintaining their periodontal health and that obstetricians be encouraged to refer patients for periodontal treatment as part of routine prenatal evaluations. While periodontal treatment during pregnancy is safe and leads to better periodontal conditions, strong evidence shows that scaling and root planing does not reduce the overall rates of preterm birth and low-birth weight.<sup>34,35</sup>

Similarly, several systematic reviews and meta-analyses do not support the theory that periodontal treatment reduces the risk of preterm birth. Conversely, two meta-analyses found a significant reduction in the risk of preterm birth following periodontal treatment in a subgroup of high-risk women. The latter suggests that women at elevated risk of adverse pregnancy outcomes may benefit from periodontal treatment, and that they should be screened for periodontal diseases<sup>9</sup>.

Periodontal diseases go unnoticed in the initial stages of disease process. The inflammatory load of periodontal disease can enter the systemic circulation and can be a risk factor for several host tissues and physiological activities. There is definite link between periodontal diseases and adverse pregnancy outcomes, through direct or indirect mechanisms. The direct action of perio-pathogenic organisms on amnion and indirect action through systemic circulation by production of inflammatory mediators can be risk for adverse pregnancy outcomes<sup>3</sup>.

In spite of the controversial results, prevention remains the ultimate goal in the association between periodontal diseases and adverse pregnancy outcomes. Consequently, the dental hygiene team has a great opportunity to directly impact the oral and systemic health of pregnant women.

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