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#### **Adverse Pregnancy Outcomes and Maternal Periodontal Health**

Erin A. Kierce\*1, Lori Rainchuso2

<sup>1</sup>Director of Quality Assurance, New England Family Dentistry and Co, USA

<sup>2</sup>Graduate Program Director, Forsyth School of Dental Hygiene Associate Professor

Corresponding Author: Erin A. Kierce, Director of Quality Assurance, New England Family Dentistry and Co, USA.

Email: erin@dentistryandbraces.com

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Optimal maternal 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. However, oral health is often overlooked in the scope of comprehensive prenatal care. Maternal periodontal disease has been associated with preterm birth, the development of preeclampsia and gestational diabetes, and the delivery of a low birth weight (LBW) infant, while the maternal oral bacteria transmitted to the newborn infant can also predispose the baby to the development of dental caries. This literature review will assess the relationship between maternal periodontal diseases on adverse birth outcomes as well as document the importance and safety of maintaining oral health care during pregnancy.

Keywords: Periodontitis, Pregnancy, Preterm Birth, Low Birth Weight, Obstetrical Care

### **Learning Objectives**

- 1. Define periodontitis.
- 2. Discuss the relationship between oral health and systemic health.
- 3. Define adverse birth outcomes and identify risk factors.
- 4. Discuss the relationship between maternal periodontitis and adverse birth outcomes.
- 5. Discuss the safety and importance of dental treatment during pregnancy.

#### Introduction

Optimal maternal oral health is a critical component in the overall health of the mother as well as in the success of a pregnancy and health of the child. Untreated maternal oral conditions can be a major determinant of or risk factor for health complications in the developing fetus or newborn infant. 1,2 However, within the scope of comprehensive prenatal care, the oral health of the woman is often overlooked.3 It is estimated that only 22 to 34% of women in the United States seek treatment or preventive care from a dentist during pregnancy.<sup>3,4</sup>

Maternal periodontal disease has been associated with preterm birth, the development of preeclampsia and gestational diabetes, and the delivery of a low birth weight (LBW) infant, while the maternal oral bacteria transmitted to the newborn infant can also predispose the baby to the development of dental caries.<sup>4,5</sup> Both periodontal disease and dental caries are highly prevalent in women of child-bearing age, particularly among low-income women and members of certain racial and ethnic minority groups.<sup>4,5</sup> According to research, 38.4% of US women aged 30 years and older, have some form periodontal disease, with 65.4% are living below the federal poverty level (FPL).6 One recent

study conducted by Chinese researchers identified a 73.9% prevalence of periodontal disease among women pre-conception aged 18-40.7 In 2012, 25.9% of women between 20 and 44 years of age had untreated dental caries, an increase of 4.1% since 2008. Of the 25.9%, 41.4% were African American and 35.7% were Hispanic.8 Consequently, it is pertinent that dental as well as prenatal providers emphasize the importance of pregnant women receiving comprehensive oral health care during pregnancy as well as communicate preventive oral health education, in order to promote optimal overall health of both mother and child. 1,2,4,5,9-13 However, an emphasis on oral health is not an established component of routine obstetrical care, increasing the potential risk of systemic complications including preterm births and/or low birth weight infants.<sup>3,12,13</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

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health.<sup>13</sup> Preterm birth, LBW infants, and periodontal disease all have biological, social, and behavioral determinants that can increase the likelihood of occurrence.<sup>2,14</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>14</sup> However, what is known is that the status of an individual's oral condition does affect their systemic health and possibly the success of a pregnancy and health of their infant.

#### **Adverse Birth Outcomes**

The incidence of preterm births and LBW infants is a major cause of infant mortality and morbidity both in the US and around the world and continues to be a significant public health issue despite many attempts by multiple public health entities to reduce the prevalence. 15-18 In 2012, there were 450,000 babies born preterm in the US, accounting for 35% of all infant deaths.<sup>19</sup> In 2015, 8% of all infants born in the United States were LBW. The prevalence of LBW is higher among non-Hispanic black infants (13.2%) and Puerto Rican infants (9.5%) than among infants of any other racial or ethnic group.8 The World Health Organization (WHO) estimates that 15 million babies are born preterm every year around the globe and this adverse birth outcome is the leading cause of death among children younger than five years of age.20 Approximately 7 out of 10 LBW babies are born prematurely.<sup>21</sup> Preterm birth is the birth of an infant before 37 weeks of pregnancy19 and LBW is defined as birth weight less than 2500 grams (5.5 pounds).21

The gestational age of an infant is the most important predictor of his or her subsequent health and survival.<sup>22</sup> Premature infants have a greater risk of feeding difficulties, respiratory distress, and delayed brain development as well as lifelong complications in health, including visual problems, developmental delays, deafness, and poor motor skills.<sup>2,4,5,17,22-24</sup> Babies born at a LBW may be more likely than babies born at a normal weight to have certain health conditions later in life, including diabetes, heart disease, and high blood pressure.<sup>21</sup>

There are multiple causes for adverse pregnancy outcomes. In many cases, preterm births can be attributed to infection or other chronic systemic conditions (diabetes and/or high blood pressure). However, it is estimated that in 50% of preterm births, the direct cause is not immediately known. 13 Research has discovered that there are multiple factors responsible for the occurrence of preterm births and LBW babies. Some of these documented factors include a history of premature baby, chronic health conditions (high blood pressure, preeclampsia, diabetes), insufficient maternal weight gain during pregnancy, smoking, alcohol consumption, and taking street drugs/abusing prescription drugs, stress, and being of a certain racial/ethnic group (African-American). 13,25-27

The prevalence of preterm births and LBW infants signify a necessity to focus prenatal care on reducing or eliminating any and all risk factors that may contribute to its occurrence. This includes acknowledging the possible relationship of these adverse pregnancy outcomes with untreated maternal periodontal disease and incorporating oral health practice guidelines into all routine obstetrical care.

## How the Mechanism of Periodontitis May Contribute to Adverse Birth Outcomes

During pregnancy, changes in hormone levels promote an inflammatory response that increases the risk of developing gingivitis and periodontitis. <sup>5,13</sup> In pregnancy gingivitis, the most common oral disease in pregnancy, clinical manifestations include gingival inflammation, erythema, and bleeding, whether spontaneous or after manipulation. <sup>1</sup> It is estimated that the majority of pregnant women experience gingivitis resulting from pregnancy-related hormonal changes. <sup>3,13,28</sup> Various studies have identified a large range regarding the prevalence of pregnancy gingivitis, from 36% in one study to 100% in another. <sup>3,13,28</sup> Differences in study design and demographics of study participants may account for these considerable variations.

Periodontitis, an inflammatory disease of the periodontal tissues, is the advanced stage of gingival disease, involving inflammation and destruction of the supporting structures of the teeth. <sup>13,29</sup> The destructive process of this disease involves both direct tissue damage resulting from the presence of bacterial products surrounding the tooth and its adjacent structures as well as indirect damage through the inflammatory response of the host in response to the bacteria <sup>13,15,17,30</sup>

According to research, the systemic inflammation due to periodontal infection and bacterial colonization in the oral cavity may have a role in the incidence of adverse pregnancy outcomes.31 Researchers hypothesize that periodontal pathogens (inflammatory mediators) reach the maternal reproductive system through the bloodstream and cause an inflammatory cascade triggering a second round of inflammatory responses. 13-15,29,31-33 Eventually, the bacteria, virulence factors, and inflammatory cytokines reach the placenta and create a new bacterial infection, initiating a new inflammatory response at the fetal-placental interface. 13,30,34,35 As more inflammatory cytokines are produced, tissue destruction can occur, affecting the structural integrity of the placenta. 13,30,32,35 These cytokines are related to the onset of labor, inducing a tenderness of the uterine muscles, stimulating uterine contractions and cervical dilation, and consequently, triggering preterm birth. 13,30,35 In some cases of preterm birth, elevated levels of these cytokines have been found in the amniotic fluid.<sup>30</sup> One study discovered P. gingivalis, a pathogen observed in periodontitis, in the amniotic fluid of women with threatened premature labor.<sup>36</sup> Researchers found that the P. gingivalis antigens were numerous in the placental tissues, strengthening the theory of bacterial migration from oral cavity to the fetus.<sup>36</sup> Other studies have successfully isolated the anaerobic microbe F. nucleatum from the amniotic fluid, placenta, and chorio-amnionic membranes of women delivering prematurely. 14,31,35-40 Another study identified P. gingivalis and A. actinomycetemcomitans in the amniotic fluid of women with active periodontitis.<sup>14</sup> Studies performed by Moliterno et al. (2005), Lopez, Smith, and Gutierrez (2002), Tellapragada et al. (2016), Reza-Karimi et al. (2015), Heimonen et al. (2009), Mathew et at. (2014), and Govindaraju et al. (2015) have all discovered a statistically significant relationship between the presence of active maternal periodontal disease and premature birth and/or LBW. 2,18,28,41-4344,45

In 2016, Corbella et al. published a systematic review that aimed to measure the potential association between adverse birth outcomes and periodontitis. The authors examined and analyzed case-control and prospective cohort studies (n=22).15 Upon investigating the studies' characteristics (total number of subjects, mean age of subjects, and definition of periodontal disease), control of possible confounders, and risk of bias, the researchers concluded that periodontitis may be a risk factor for preterm birth (95% CI: 1.61 (1.33-1.95)), LBW (95% CI: 1.65 (1.27-2.14)), and preterm low birth weight (95% CI: 3.44 (1.34-8.80)), although the association was low.15 The authors conclude that while a low association between periodontitis and adverse birth outcomes had been identified with this systematic review, more research is needed to identify a more definitive causal relationship as well as measure the effect of nonsurgical periodontal therapy and the reduction in adverse birth outcomes.15

However, other studies and systematic reviews have revealed contradictory results. 16,44,46-50 Vettore, Leal, Leao, da Silva, Lamarca, and Sheiham (2008) performed a case-control study among post-partum women (n= 542) to compare periodontal health status with birth outcomes. They concluded that periodontal disease did not increase the risk of preterm LBW according to 15 measures of periodontal disease.<sup>50</sup> Another study by Ali and Abidin (2012) also assessed whether the presence of periodontitis impacted adverse birth outcomes. They conducted a prospective cohort study on pregnant women (n=73) who were between 28 to 36 weeks gestation. Among this study population, periodontitis was not shown to be a risk factor for preterm delivery or a LBW infant.51 Probable reasons for the discrepancies in research could be the differences in study definitions and methods of diagnosis for preterm birth, preterm LBW, or periodontal disease, as well as disparities in confounder controls, study participant demographics, and numbers. 13,17

Studies performed on the effect of non-surgical treatment of periodontitis in pregnant women and its impact on reducing rates of preterm births or LBW infants have revealed different results. Fiorini et al. (2013) and Kaur et al. (2014) documented that while periodontal treatment improved clinical oral conditions and decreased inflammatory markers, there was no significant decrease in the incidence of adverse birth outcomes. 13,52,53 Studies conducted by López et al. (2005), Offenbacher et al. (2006), Jeffcoat et al. (2011), and Offenbacher et al. (2011), all detailed results indicating a reduced prevalence of preterm births after treating severe periodontitis in pregnant women. 13,54-57 However, studies performed by Michalowicz et al. (2006), Horton et al. (2012), Xiong et al. (2011), and Han (2011), observed no positive effect of periodontal treatment on reducing adverse birth outcomes. 58-60 Similar to the lack of definitive research concerning the causal relationship between periodontitis and preterm births/LBW infants, researchers hypothesize that that conflicting data regarding the treatment of periodontitis in pregnant women, is also due to the inconsistent study definitions used to classify disease and the possible lack of control in the studies for other factors, such as smoking, maternal age, and ethnicity.13

#### **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. 61,62-64

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. <sup>12,62</sup> 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>12,62-64</sup>

#### **Necessity of Future Research**

This literature review indicates that periodontitis is an oral disease that may have an adverse effect on birth outcomes, including preterm births and LBW infants. Although there is inconclusive research relating to the treatment of periodontitis and its effect on improving birth outcomes, the maintenance of oral health during pregnancy significantly decreases the maternal bacterial load in the oral cavity, improving overall health.<sup>13</sup> Also, while the link between oral pathogens and systemic health has been documented, <sup>13,14,31,35-40,65</sup> there is still further need to definitively link periodontal disease with adverse birth outcomes in order to more successfully manage chronic disease as well as promote maternal and child health.

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