



## RESEARCH ARTICLE

## Impact of Maternal Periodontal Infection on Pregnancy Outcomes: A Review

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ARTICLE INFO	ABSTRACT
Received: Apr 24, 2024 Accepted: Jun 27, 2024 <b>Keywords</b> Low birth weight Periodontitis Pregnancy outcomes Preterm birth	Background: Periodontal disease is a local infection of the tissue surrounding the dentition, but has a systemic impact on human health. During pregnancy, the prevalence of periodontal infection increases. A considerable number of studies evaluate the relationship between periodontal diseases and the outcomes of pregnancy, mainly preterm birth and low weight at birth. The aim of this review is to highlight the present facts about the correlation between pregnancy and periodontitis, as well as the pathogenic mechanisms that underlie this association. Materials and methods: In order to find studies and reviews that have been peer-reviewed, we searched the PubMed and Google Scholar databases using the following keywords: adverse pregnancy outcomes, periodontitis, preterm birth , lowbirth weight , systematic review, meta-analysis. Conclusions: Poor maternal periodontal status may increase the risk of adverse pregnancy outcomes and more study must be carried out to investigate the causal relationship. And although the studies that evaluate the efficacy of non-surgical periodontal treatment in reducing the prevalence of adverse pregnancy outcomes were conflicting, and as long as periodontal therapy is considered safe throughout the second trimester of pregnancy, it is advisable to include periodontal screening and treatment as a standard component of prenatal care for all pregnant women.
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### INTRODUCTION

Periodontitis is known as one of the most prevalent dental infections that begins in gingival tissue, which if left untreated, the inflammation spreads to deeper tissues, disrupting bone homeostasis and resulting in tooth loss (Nazir et al., 2020, Mahmood and Abbas, 2023). The etiological factor responsible for periodontal disease's development is the presence of a diverse bacterial community that colonizes the oral tissues (HajishengallisDarveau and Curtis, 2012, Lamont and Hajishengallis, 2015). Although dental plaque is significant in the development and progression of periodontitis, it is the inflammatory response of the host that causes irreversible damage to the tissues around the teeth, resulting in tooth loss in some instances (Gaffen and Hajishengallis, 2008, Abdulkareem et al., 2023). This host response, together with local and systemic factors such as plaque, calculus,

hereditary and environmental factors, the patient's systemic-health, lifestyle choices, and many social determinants, affects the course of the disease (Bartold and Van Dyke, 2013; Jam et al., 2018).

Significant progress has been made in looking for particular periodontal infections, including the identification of many candidates, most of which are gram negative anaerobic species that establish in the subgingival area (Abdulkareem et al., 2018). The primary members of this collection consist of three species collectively known as the red complex. These species are commonly seen in conjunction and have a strong correlation with pathological areas within the oral cavity. *Porphyromonas-gingivalis*, *Treponema-denticola*, and *Tannerella-forsythia* (HajishengallisDarveau and Curtis, 2012).

### **Preterm birth and low birth weight**

Prematurity and low birth weight are among the primary leading causes of neonatal mortality in developing countries (Hussein et al., 2014). The World Health Organization (WHO), recognizes preterm birth as a worldwide epidemic with a global incidence of approximately 15 million per year (Organization, 2017). It is characterized by the occurrence of delivery before the completion of 37 weeks of gestational age (Organization, 2017), due to the failure of a pregnancy to reach a specified amount of time, rather than by the existence of specific signs or symptoms (Kramer et al., 2012). In 2007, approximately 10% of newborns born in the United States were preterm (Birth, 2007). According to the consensus report of the joint of European Federation of Periodontology and the American Academy of Periodontology (EFP/AAP) workshop on periodontitis and systemic diseases, the worldwide prevalence of preterm birth is 9.6%, corresponding to a total of 12.9 million babies born prematurely (SanzKornman and Workshop, 2013). Currently, preterm birth is the second-leading cause of death in children under the age of 5, after pneumonia. Annually, one million neonates die prematurely. (SanzKornman and Workshop, 2013). According to the WHO, 45% to 50% of preterm births are idiopathic, 30% are due to preterm membrane rupture, and 5% are the result of medical advice. (Soon, 2012).

low birth weight Infants are defined as those who are delivered with a weight under 2500 g, which can be further classified into: very low birth weight infants with a birth weight below 1500 grammes. And extremely low birth weight, with a birth weight below 1000 grammes) (Raju and Berens, 2021). In the United States, in 2022, around 8.24% of babies were delivered have a low birth-weight, while almost 1.34% were delivered with a very low birth-weight (Osterman et al., 2022; Kanval et al., 2024; Rashid et al., 2023). Several reasons were found to be related with increasing the risk of LBW newborns, including maternal weight, weight gain during pregnancy, age, insufficient pre-natal care, poor socioeconomical status, and history of past stillbirth; however, a significant number of cases are with an unknown origin (Chen et al., 2018, WangLiou and Pan, 2013).

### **Periodontitis and pregnancy outcomes**

Destructive periodontal disease has been seen to impact approximately 15% of women within the reproductive age range. Notably, a significant number of pregnant women exhibit varying degrees of periodontal disease (Moore et al., 2001, Mirza and Salman, 2010). Previous studies have documented an increasing prevalence and intensity of periodontal inflammation during pregnancy (Leka'a and Ibrahim, 2014, Al Najjar and Hussein, 2019). The hormonal fluctuations that occur during pregnancy, which characterized by a significant rise in progesterone and oestrogen levels, reaching approximately 10 to 30 times the average level (Newman et al., 2018), along with inflammatory mediators, can stimulate alterations in vascular responses and connective tissue remodeling in the periodontium. This correlation could explain the increased incidence of inflammation during episodes of hormonal fluctuation at pregnancy (Daalderop et al., 2018, Uwitonze et al., 2018, Lang and Lindhe, 2015).

Over the course of several years, extensive research has been conducted on periodontal disease as a plausible cause of infection and systemic inflammation, hence, mechanistic studies have provided

strong evidence about the ability of periodontal pathogens to migrate from the infected periodontium to the fetoplacental unit and induce a disseminated infection (Boggess and Committee, 2008, Raju and Berens, 2021). Offenbacher, in a case-control study, was the first to report a potential correlation between preterm birth and periodontal disease (Offenbacher et al., 1996). The researchers found that mothers with periodontal infection had a risk of delivering a preterm low birth weight (PLBW) newborn that was more than 7 times higher than mothers without the infection. In addition, Offenbacher conducted case-control research on the concentrations of IL1 and PGE2 in gingival crevicular fluid (GCF) and the presence of periodontal related pathogens (*B.forsythus*, *P.gingivalis*, *A.actinomycescomitans*, and *T.denticola*) in 48 mothers of PLBW infants using microbe-specific DNA probes. GCF levels of PGE2 were considerably greater in mothers of infants with PLBW compared to mothers of normal birth weight infants. Additionally, mothers of PLBW infants had considerably higher levels of the 4 periodontopathogens (Offenbacher et al., 1998). A systematic review has shown that 10 studies estimated that periodontal disease contributes 6 to 41% of low birth weight worldwide, and they discovered a positive correlation between periodontal infection and low birth weight (2.1 to 5.3 odds ratios). A meta-analysis that obtained the highest evaluation score across various systematic reviews, demonstrated a statistically significant correlation between low birth weight and periodontal disease, the relative risk was 1.65 (95% CI: 1.27-2.14) (Corbella et al., 2016).

A review of studies conducted to evaluate the association between periodontal disease and adverse pregnancy outcomes is seen in (Table 1.2)

**Table 1.2: A review of studies assesses the association between periodontal disease and adverse pregnancy outcomes.**

<b>Authors\ Year</b>	<b>Study design</b>	<b>Findings</b>
(Teshome and Yitayeh, 2016)	systematic review	Periodontal disease was found to increase the risk of preterm birth and low birth weight in 9 of the 10 studies reviewed, with 2.04 to 4.19 odds ratios (OR). This association was only mentioned in one article
(Corbella et al., 2016)	systematic review & meta-analysis	identified periodontal disease as a potential determinant of adverse pregnancy outcomes
(Vivares-Builes et al., 2018)	Umbrella review	discovered that a strong positive correlation was observed between preterm birth, low birthweight, and pre-eclampsia with periodontitis in at least six systematic reviews with meta analyses

(Daalderop et al., 2018)	Umbrella review of 23 systematic reviews of observational studies	There is a positive correlation between periodontal disease and premature delivery. LBW, preterm low birth weight, and preeclampsia.
(Ide and Papapanou, 2013)	Systematic review	found a clear and independent correlation between maternal periodontal infection and preterm birth/low birth weight. This conclusion was based on cross-sectional and case-control studies.
(Al-Rawi et al., 2021)	Cross sectional survey	proposed that pregnant women displaying severe periodontitis has the potential to be susceptible to PTB. And demonstrated a substantial association between PTB and a greater depth of PPD.
(Lohana et al., 2017)	Prospective Cohort Study	Significant correlations were found between periodontal disease severity in pregnant women and birth weight, gestational age. Higher periodontal disease severity correlates with elevated rates of preterm and low birth weight babies
(Souza et al., 2016)	Case-control study	the study indicates that there is no link between maternal periodontal disease and low birth weight, even when accounting for other factors that could influence the results.
)Al-Rawi et al., 2021(	Cross section study	Pregnant women with severe periodontitis are at a higher risk of preterm birth (PTB).

However, clinical trials investigating the impact of periodontal therapy on adverse pregnancy outcomes have yielded conflicting findings (LopezUribe and Martinez, 2015). In a 2001 study by Mitchell Lewis, 74 young pregnant women were given oral hygiene instructions and professional scaling/root planning (SRP), while 90 subjects as controls did not receive any periodontal intervention. PLBW was observed in 18.9% of women who did not get periodontal therapy and 13.5% of those who did (Mitchell-Lewis et al., 2001). (Raju and Berens, 2021) found that eight of the 17 systematic reviews/meta-analyses conducted between 2006-2020 of randomized controlled trials RCTs on how periodontal disease treatment affects the outcomes of pregnancy failed to find a causal relationship, while nine, had a statistically significant improvement following non-surgical periodontal treatment. In 2017, an analysis of 15 randomised controlled studies examining the influence of periodontal therapy on the prevention/reduction of perinatal morbidity and mortality revealed that the evidence about the impact of periodontal therapy on pre term delivery, perinatal death, and pre-eclampsia was conflicting (Iheozor-Ejiofor et al., 2017).

The consensus report from the joint (EFP/AAP) workshop on periodontitis and systemic illnesses found two primary pathways related to the biological processes underlying adverse pregnancy outcomes (SanzKornman and Workshop, 2013):

**Direct-pathway:** Bacteria from the oral cavity and/or their components get transmitted to the fetoplacental unit via the bloodstream (FiguroHan and Furuichi, 2020). The infiltration of oral bacteria into amniotic fluid can lead to amniochorionic infection (HuckTenenbaum and Davideau, 2011), which is a significant contributing factor to preterm birth (Horvath et al., 2014).

**Indirect-pathway:** maternal periodontitis is considered a nongenital source of infection (Puertas et al., 2018). The inflamed periodontal tissues release substantial quantities of pro-inflammatory cytokines, including interleukin 1 (IL-1b), IL-6, prostaglandin E2, and tumour necrosis factor alpha (TNF-a), that upon reaching the fetoplacental unit, cause premature contractions, early rupture of membrane, and preterm birth (Green and Arck, 2020, Lohana et al., 2017, Raju and Berens, 2021).

### **Prediction of adverse pregnancy outcomes**

Numerous studies evaluate the ability to predict the outcome of pregnancy depending on the maternal periodontal status. In one study performed by (Al Habashneh et al., 2013), the researchers employed receiver-operating characteristic (ROC) analysis to comparatively assess maternal periodontal parameters in order to predict preterm (PB) birth and low birth weight (LBW) delivery among women. Because it has the greatest AUC, average CAL (with an AUC ranging from 0.84 to 0.87), performed the best in predicting the unfavorable pregnancy outcomes that were evaluated. Consequently, negative pregnancy outcomes could be predicted depending on the extent and intensity of periodontal disease as measured by CAL. Whereas in a retrospective cohort study performed by (HeoAhn and Park, 2020), the diagnosis of the severity of maternal periodontitis was determined using radiographical screening rather than the commonly employed method of periodontal probing, giving an entirely novel suggestion regarding the value of using radiographic screening of periodontitis in the mother to predict adverse pregnancy outcomes. (TarannumFaizuddin and Madaiah, 2011) screened the level of prostaglandin E2 in gingival crevicular fluidGCF and serum throughout pregnancy and postpartum period. And investigate the utilization of GCF-PGE2 levels as a risk indicator for preterm/low birth weight (PLBW). They observed a significant association between birth outcomes and serum PGE2 levels. Statistical significance was observed for both the weight of the newborn at birth and the duration of the pregnancy.

### **CONCLUSIONS**

Periodontal disease has a negative impact on the health of both the mother and her growing fetus. Poor maternal periodontal status may increase the risk of adverse pregnancy outcomes and more

study must be carried out to investigate the causal relationship. And although the studies that evaluate the efficacy of non-surgical periodontal treatment in reducing the prevalence of adverse pregnancy outcomes were conflicting, and as long as periodontal therapy is considered safe throughout the second trimester of pregnancy, it is advisable to include periodontal screening and treatment as a standard component of prenatal care for all pregnant women.

### **ETHICAL CONSIDERATION**

Not applicable.

### **FINANCIAL SUPPORT AND SPONSORSHIP**

Not applicable.

### **CONFLICTS OF INTEREST**

There are no conflicts of interest.

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