

KEYNOTES AND RESOURCES

Episode 110 – Pregnancy and Oral Health: Part 3 June 7, 2024

Introduction

Pregnancy is accompanied by a variety of physiologic, anatomic, and hormonal changes that can affect oral health and oral healthcare. Preventive, diagnostic, and restorative oral healthcare is safe throughout pregnancy. Oral disease may contribute to adverse pregnancy outcomes, such as preterm birth, low birth weight, and preeclampsia. [1] [2]

Globally, preterm birth (<37 weeks of gestation) affects almost 11% of all pregnancies, low birth weight (<2.5 kg) affects about 23%, and preeclampsia almost 5%. Pregnancy complications represent a significant cause of fetal, neonatal, and maternal morbidity and mortality. [3] [4]

Preterm and low birth weight infants are at higher risk of multiple lifelong challenges, such as respiratory distress, impaired motor skills, cognitive and intellectual impairment, learning difficulties, and cardiovascular and metabolic disorders. [3]

Pregnancy complications can also have long-term effects on the pregnant person. A review by <u>Hauspurg et al. (2018)</u> found after certain pregnancy complications (e.g., hypertensive disorders of pregnancy, gestational diabetes, or delivering an infant who is preterm or low birth weight) the person's cardiovascular disease³ risk increases. [5]

A cohort study by <u>Crump et al (2024)</u>, involving almost 2.2 million participants, found pregnant individuals who experienced adverse pregnancy outcomes had up to a 50% increased risk of dying from any cause up to 46 years after giving birth. Cardiovascular and respiratory diseases, cancer, and diabetes were the major specific causes of death linked to adverse pregnancy outcomes. Participants had increased mortality risks with any of five major adverse pregnancy outcomes: preterm delivery, low birth weight, preeclampsia, other hypertensive disorders, and gestational diabetes. These findings were not explained by shared familial factors. The results suggest individuals with pregnancy complications need early preventive evaluation and long-term clinical follow-up to detect and treat chronic disorders. [6]

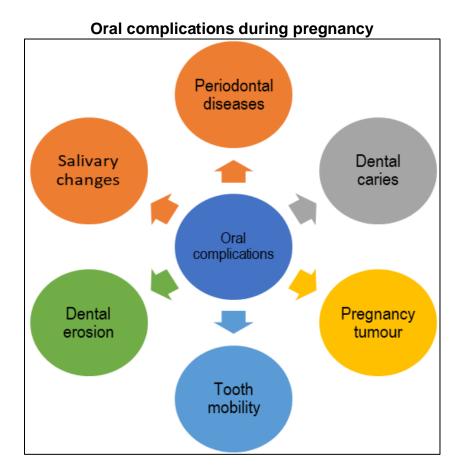
¹ Refer to Episode 108 for discussion on physiologic changes and pathologic conditions during pregnancy and their impact on oral health and oral healthcare.

² Refer to Episode 109 for discussion on medication and substance use in pregnancy and their effect on oral and systemic, as well as providing safe oral healthcare to pregnant clients, including the use of local and topical anesthetics, chlorhexidine, and dental radiographs.

³ Refer to Episodes 79, 80, and 81 for additional information on cardiovascular diseases.

Oral complications during pregnancy

Pregnant individuals may experience increased risk of developing periodontal diseases, dental caries, pregnancy tumours, tooth mobility, dental erosion, and salivary changes. [7] [8]



Periodontal disease

Pregnancy does not cause periodontal disease, but it may modify or worsen preexisting disease. Evidence demonstrates scaling and root planning are safe during pregnancy and are beneficial for oral and systemic health. Those who are pregnant or planning to become pregnant should undergo a periodontal examination and any necessary treatment, as early detection and treatment of periodontal disease is essential. [8] [9] [10] [11]

A systematic review and meta-analysis by <u>Chen et al. (2022)</u> compiled data from 20 studies to examine the risk and prevalence of periodontal disease in pregnant individuals. The prevalence rates in pregnancy were:

- 40% for periodontitis.
- 67% for bleeding on probing,
- 42% for pocket depths ≥4 mm, and
- 24% for clinical attachment loss ≥4 mm.

The prevalence rates of bleeding on probing and probing depth gradually increased throughout pregnancy, and the highest prevalence rate of clinical attachment loss occurred in the second trimester. These results demonstrate the high prevalence of periodontal disease during pregnancy. [12]

The potential link between periodontal diseases and negative pregnancy outcomes has been researched for several decades. Reviews on observational, intervention, and mechanistic studies provide valuable insights into this subject. However, these investigations are limited by methodologic limitations, making it difficult to reach definitive conclusions. [3]

For example, a comprehensive overview of 23 systematic reviews by <u>Daalderop et al.</u> (2017) found a strong association between periodontal disease and various adverse pregnancy outcomes, such as preeclampsia and delivering a preterm birth and/or low birth weight infant. Research has also demonstrated a significant association between periodontitis and gestational diabetes. [2] [13] [14]

A systematic review and meta-analysis by <u>Karimi et al. (2023)</u> found periodontal disease may be a potential factor in increasing the risk of adverse neonatal and maternal outcomes. [15]

A systematic review and meta-analysis by <u>Castaño-Suárez (2024)</u> analyzed 35 studies involving 2,510,556 participants. The authors concluded the low-quality evidence available suggests periodontitis is moderately associated with low birth weight and weakly associated with preterm delivery. These findings need to be interpreted cautiously due to potential biases and heterogeneity in the studies. Further high-quality research is required to show a definite causal association between periodontitis and pregnancy outcomes. However, healthcare providers should emphasize the importance of oral health during pregnancy and include periodontal examinations and appropriate therapies in prenatal care to help improve maternal and fetal health outcomes. [16]

Potential mechanisms explaining the relationship

Adverse pregnancy outcomes are associated with elevated local intrauterine and systemic inflammatory responses, as well as intrauterine infections. Periodontal diseases are infectious inflammatory diseases with systemic effects, such as:

- Inducing transient bacteremia when periodontal pathogens enter the bloodstream.
- Initiating a chronic low-grade systemic inflammatory response when periodontal pathogens, their by-products, and inflammatory mediators produced by the gingiva enter the circulation. [3]

Hypothetical direct and indirect biological pathways have been proposed to explain the possible link between periodontal diseases and adverse pregnancy outcomes.

In the direct pathway, periodontal pathogens and/or their pathogenic by-products reach and invade the fetal-placental tissues and establish an ectopic site of infection. Their presence triggers a local inflammatory response (e.g., inflammatory cytokines and mediators) that results in tissue damage, leading to pregnancy complications.

Research helps to support this hypothesis. For example, *Porphyromonas gingivalis* and *Fusobacterium nucleatum* have been found in some samples of amniotic fluid or placenta taken from people with periodontitis who had a premature birth, and specimens of *P. gingivalis* and *Aggregatibacter actinomycetemcomitans* were detected in the amniotic fluid of pregnant individuals with periodontal disease. [17]

In the indirect pathway, inflammatory cytokines and mediators produced at the gingival level in response to periodontal pathogens, as well as acute-phase reactants from the maternal liver induced by the systemic inflammatory response to periodontal infection accumulate in the intrauterine compartment, which exacerbates intrauterine inflammation and contributes to pregnancy complications. [3] [18]

Influence of host immune response

When periodontal pathogens enter the placenta, they can activate the maternal adaptive immune response and prompt the production of bacterial-specific antibodies with bacterial-IgM antibodies formed first. Elevated IgM antibodies in fetal umbilical cord blood may be a risk factor for adverse pregnancy outcomes. Concentrations of IgM antibodies against red and orange complex bacteria were significantly increased in cord blood of preterm infants compared with term infants. [19]

Nonsurgical periodontal therapy and pregnancy outcomes

Most of the systematic reviews that analyzed the high-quality randomized controlled trials reveal nonsurgical periodontal therapy during the second trimester of gestation is safe and does not affect pregnancy outcomes. Whether this lack of effect implies periodontal diseases do not contribute to adverse pregnancy outcomes remains to be elucidated. [3]

A <u>2017 Cochrane review</u> assessed whether treating periodontal disease during pregnancy could prevent adverse birth outcomes. Fifteen randomized controlled trials (RCTs), with 7,161 participants, met the inclusion criteria. The authors found no clear evidence that periodontal treatment during pregnancy reduces preterm birth. There is some evidence it may reduce the incidence of low birth weight. There is insufficient evidence to determine which periodontal treatment is better in preventing any adverse pregnancy outcome. The authors noted the quality of the evidence was low to very low because of high bias risk, imprecision, or serious inconsistency. Thus, further research is likely to change the confidence of the effect and the estimate. [20]

A systematic review and meta-analysis by <u>Le et al. (2021)</u> investigated whether treating gingivitis in pregnancy affects pregnancy outcomes. Three clinical trials with 1,031 participants were included in the review. The results showed treating gingivitis may improve pregnancy outcomes, including reduced risk of preterm birth and low birth weight in infants. Future trials are needed to validate the results. [4]

A small randomized controlled trial by <u>Caneiro-Queija et al. (2019)</u> included 40 pregnant participants with stage II grade B periodontitis. Participants were randomly allocated to control and intervention groups. During the second trimester, the control group received only oral hygiene instructions and professional supragingival dental biofilm control,

whereas the intervention group also received subgingival instrumentation. The study found a statistically significant reduction in all clinical and microbiological parameters after periodontal treatment in the intervention group. However, there were no significant differences observed in the risk for preterm birth or low birth weight. [3] [21]

A review by <u>Bobetsis et al. (2020)</u> reported most high-quality randomized controlled trials indicate nonsurgical periodontal therapy during the second trimester does not improve pregnancy outcomes. A partial explanation might be that therapy delivered at the fourth to sixth months of pregnancy is too late to prevent placental colonization by periodontal pathogens and consequently incapable of affecting pathogen-induced injury at the fetoplacental unit. Therefore, nonsurgical interventions may be more significant preconception or early in pregnancy, considering the potential association between periodontal disease and adverse pregnancy outcomes. Although there is not enough evidence that periodontal therapy alters pregnancy outcomes, it improves oral health and health-promoting behaviour, which advances general health of the pregnant person. [22] [23]

Gingivitis is the most prevalent oral complication associated with pregnancy, reported to occur in 60% to 75% of all pregnant people. Gingival changes are usually associated with poor oral hygiene and local irritants, especially dental plaque. However, hormonal and vascular changes during pregnancy often exaggerate the inflammatory response to these local irritants. [24]

Inflamed gingiva during pregnancy is characterized by fiery red marginal gingiva and interdental papillae. The tissue is edematous, with a smooth, shiny surface, loss of resiliency and a tendency to bleed easily. There may also be increased pocket depth with minimal attachment loss (i.e., pseudopocket). Gingival changes are most noticeable from the second month of gestation, reaching a maximum in the eighth month. These changes occur earlier and more frequently anteriorly than in posterior areas. The severity of gingival disease reduces after childbirth, but the gingiva does not necessarily return to its prepregnancy condition. [24]

Elevations in sex steroid hormones during pregnancy may modify the gingival inflammatory response and result in an exaggerated gingival inflammation in the presence of even relatively small amounts of plaque. Thus, as per the AAP classification of periodontal diseases, pregnancy is considered a potential systemic modifying factor for plaque-induced gingivitis. [25]

Management strategies may include regular oral health appointments, dental scaling, thorough daily tooth brushing, and interdental cleaning. Mild saline mouthrinses may help ease gingival irritation. Chlorhexidine mouthrinse use may be considered for severe gingivitis. [8] [11] [26]

Mouthrinses⁴

There is limited evidence for appropriate over-the-counter mouthrinse use during pregnancy. Chlorhexidine use is not contraindicated during pregnancy and can be used when the benefits outweigh the risks. There is limited evidence of the concurrent use of chlorhexidine mouthrinse with periodontal therapy in pregnancy. A systematic review and meta-analysis by Merchant et al. (2022) reported that for pregnant clients with periodontal disease, using chlorhexidine with conventional periodontal treatment (i.e., scaling and root planing) reduced risks of preterm birth and low birth weight. However, there were significant biases in the studies analyzed in this research. Further well-conducted randomized controlled trials are needed to ascertain this potential benefit. [27] [28]

Dental caries⁵

Pregnant individuals may be at risk for dental caries due to:

- Changes in eating habits, such as snacking due to cravings or nausea.
- Dry mouth
- Increased acidity due to vomiting.
- Decreased attention to or inability to perform oral hygiene, which may result from nausea and vomiting. [29]

Management strategies may include nutritional guidance (e.g., limiting refined carbohydrate snacks), oral self-care⁶ instruction (e.g., brushing regularly with fluoridated⁷ toothpaste, daily interdental cleaning, using over-the-counter fluoride mouthrinses), utilizing xylitol-containing gum or mints, regular oral health appointments, and receiving professionally applied topical fluoride varnish. Clients with untreated caries and associated complications should receive dental treatment. [8] [11] [30]

Pregnancy tumour

Pregnancy may cause single, tumour-like growths, referred to as a pregnancy tumour, epulis gravidarum, or pregnancy granuloma. The histologic appearance is a pyogenic granuloma. Pregnancy tumours may occur in up to 10% of pregnant people. The lesion usually develops on the interdental papillae or other areas of frequent irritation, most frequently on the labial aspect of the maxillary anterior region during the second trimester. It often grows rapidly and seldom becomes larger than 2 cm in diameter. A pregnancy tumour classically starts to develop in an area of inflammation. Poor oral hygiene is usually present, with plaque or calculus deposits on the teeth adjacent to the lesion. Pregnancy tumours are sessile or pedunculated and usually painless. The colour varies from purplish red to deep blue, depending on the lesion's vascularity and degree of venous stasis. The surface may be ulcerated and covered by yellowish exudate, and

⁴ Refer to Episode 103 for additional information on the role of mouthrinses in oral care.

⁵ Refer to Episodes 86 and 87 for additional information on dental caries.

⁶ Refer to Episode 89 for additional information on oral self-care.

⁷ A 2017 Cochrane review evaluated the effects of pregnant individuals taking fluoride supplements (tablets, drops, lozenges, or chewing gum) compared with no fluoride supplementation to prevent dental caries in the primary teeth of their children. The authors concluded there is no evidence fluoride supplements taken during pregnancy effectively prevent dental caries in offspring. [50]

gentle manipulation of the mass induces hemorrhage. Bone destruction is rare around pregnancy tumours.

Generally, the lesion will regress postpartum. However, complete resolution often requires surgical excision. Before birth, scaling, root planing, and oral hygiene instruction may be needed to reduce plaque retention. If the pregnancy tumour affects function, causes discomfort, disrupts tooth alignment, or bleeds easily on mastication, it may need to be excised. Pregnancy tumours excised before delivery may recur. Thus, the client should be informed that further surgery may be required postpartum. [24]

Tooth mobility

Although uncommon, tooth mobility may occur during a late pregnancy due to increased levels of progesterone and estrogen affecting the periodontium. The increased mobility is probably related to changes in the lamina dura and attachment apparatus. Underlying pathology (e.g., periodontitis) unrelated to the pregnancy may cause tooth mobility. This condition typically resolves postpartum. Any underlying pathology needs appropriate treatment and referral if necessary. [24] [31]

Dental erosion

Gastrointestinal changes during pregnancy may lead to vomiting (e.g., morning sickness) and gastroesophageal reflux,⁸ increasing the risk of dental erosion.⁹ [32]

Strategies to help mitigate dental erosion include:

- Rinsing the mouth with water, a sodium bicarbonate rinse, or an alcohol-free fluoride mouthrinse after vomiting.
- Brushing should be delayed for at least an hour after vomiting.
- Using a tongue cleaner to remove acid residue as soon as possible after vomiting.
- Professionally applied topical fluoride varnish. [33] [34] [35] [36]

Xerostomia

Some pregnant individuals experience dry mouth, possibly associated with hormonal alterations. Also, increased estrogen production results in edema of the nasal tissues, leading to nasal congestion and an increased tendency to epistaxis (nosebleeds). As nasal breathing becomes more difficult, there is a tendency to mouth breathe, especially at night, contributing to dry mouth. Xerostomia can increase the risk of dental caries, periodontal diseases, and halitosis.¹⁰

Management strategies to alleviate dry mouth may include:

- Staying hydrated,
- Using sugarless candy and gum (e.g., xylitol-sweetened),
- Avoiding caffeine, tobacco, and alcohol, and
- Nighttime use of a humidifier. [9] [24] [37]

⁸ Refer to Episode 108 for strategies to manage pregnancy-induced vomiting and gastroesophageal reflux.

⁹ Refer to Episode 82 for additional information on dental erosion.

¹⁰ For additional information on halitosis refer to Episode 67.

Excess saliva

A relatively rare finding among pregnant people is excessive secretion of saliva, known as sialorrhea or ptyalism. It usually begins at two to three weeks of gestation and may abate at the end of the first trimester. In some instances, it continues until delivery. Occasionally, those with morning sickness have excess saliva. [24] [38]

Oral cancer¹¹

Oral cancers in pregnancy are rare. However, cancer diagnosis complicates both cancer treatment and pregnancy outcomes. Cancer is the second leading cause of death in females of reproductive age. Nearly one in 118 females with cancer are diagnosed during their pregnancy, with the most common being cervical cancer, breast cancer, ovarian cancer, lymphoma, melanoma, brain cancer, and leukemia. Oral cancer accounts for 2% of all the cancers in pregnancy. This low incidence is might be because oral cancers are less common in young people and occur more commonly in males. Nevertheless, the incidence of oral cancers during pregnancy may increase because of the trend toward later child-bearing and the increase of oropharyngeal cancer in younger individuals related to HPV infection. This highlights the importance of screening all pregnant clients for oral cancer during oral health appointments. [39] [40]

Unfavourable oral health beliefs

Certain oral conditions are associated with adverse pregnancy outcomes, such as preeclampsia, preterm birth and low birth weight. Unfavourable beliefs about oral health can negatively influence oral health behaviours, including hesitation to access preventative oral care and treatment. Factors associated with a higher likelihood of believing health-related misinformation include lower education levels and healthcare knowledge, cultural customs and traditions, distrust in the healthcare system, and pre-existing false beliefs. Several health-related unfavourable beliefs associated with pregnancy have perpetuated over centuries, some of which are still common, including some related to oral health during pregnancy. Consequently, some oral health conditions during pregnancy are considered 'normal' (e.g., oral pain, gingivitis, periodontitis, dental caries, and tooth loss).

A systematic review by <u>Kamalabadi et al. (2023)</u> examined commonly held unfavourable beliefs about oral health and oral treatment during pregnancy. A total of 39 quantitative and six qualitative studies met the inclusion criteria. Commonly cited beliefs included:

- Pregnancy causes tooth loss (e.g., a tooth per child).
- Periodontal diseases and dental caries are normal during pregnancy, and pregnancy causes these oral diseases.
- Oral care (e.g., dental radiography, periodontal treatment, restorative treatment) is not safe and harms the fetus.
- Calcium is absorbed from the pregnant person's teeth by the developing fetus.
- Tooth brushing should be avoided during and after pregnancy.

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¹¹ Refer to Episodes 76, 77, and 78 for additional information on oral cancer.

¹² Refer to Episode 7 for information on HPV and oral cancer.

The review identified that oral health literacy was directly associated with myths and unfavourable beliefs. Furthermore, studies have shown that healthcare professionals may be a source of oral health misinformation.

The results highlight the importance of:

- Engaging pregnant clients and healthcare providers in evidence-based oral health education and
- Integrating preventative and primary oral care services in routine prenatal care. [42]

Fertility

A systematic review by <u>Ricci et al. (2022)</u> evaluated the potential association between oral health and the chance of clinical pregnancy (spontaneous or *in vitro* fertilization [IVF]). In all the studies, the chance of conception was significantly lower in females with periodontal disease, except for a single study that only included females with different grades of gingivitis. The authors note findings from this systematic review are based on a limited number of studies; thus, the results should be considered cautiously.

The mechanisms of these findings are not clear. Smoking and diabetes increase the risk of periodontal disease and may also be associated with infertility and/or the time taken to conceive. Smoking was a confounding factor in two of the studies. There is some evidence that periodontal disease is associated with endometriosis, which is associated with fertility problems. [43]

It is recognized systemic inflammation may affect reproduction, and periodontal disease is associated with inflammation. Therefore, inflammation may be the linking factor between fertility and periodontal disease. A systematic review by Kellesarian et al. (2018) showed periodontal disease reduces the quality of semen parameters. [44] Thus, factors in males may partially explain the observed association. Overall, this review is preliminary as more articles would be necessary to draw a definite conclusion. [43]

A case-control study by <u>Tao et al. (2020)</u> compared the differences in periodontal health status between males with abnormal semen parameters (case group) and males with normal parameters (control group). The study found a significantly higher proportion of participants in the case group had moderate or severe periodontitis and abnormalities in sperm progressive motility. The odds ratio of having semen abnormality was 3.4 times higher for participants with moderate/severe periodontitis than for those in periodontal health. The authors concluded periodontal disease is associated with semen abnormalities and sperm motility. [45]

A literature review by <u>Ludovichetti et al. (2021)</u> analyzed the available literature to determine if periodontal disease affects conception. The study findings were insufficient to establish with certainty the presence of a link between periodontitis and female and male infertility. [17]

However, a study by <u>Bond et al. (2021)</u>, not included in the 2021 literature review, found females with a history of periodontitis (measured by three different self-reported measures) took longer to become pregnant than those without a history of periodontitis.

While these findings indicate periodontitis may be associated with a reduced ability to conceive, the authors caution against interpreting causality given the limitations of self-reported data. However, considering the high prevalence of periodontitis in the general population and periodontal disease can often be mitigated with treatment, periodontitis warrants careful evaluation as a potential modifiable risk factor for reduced fertility. [46]

Novel research

Xylitol chewing gum

Preterm birth is one of the main risk factors for neonatal mortality and is associated with short-term and long-term effects. Globally, there are over 13 million preterm births annually, and low-resourced countries are disproportionately affected. [47]

Xylitol chewing gum reduces dental caries, but its effect on improving periodontal health and reducing preterm birth is unknown. <u>Aagaard et al. (2022)</u> hypothesized daily xylitol gum use starting periconception would reduce periodontitis and preterm birth. The researchers conducted a cluster randomized trial in Malawi, the country with the highest known preterm birth rate (22%). A total of 10,069 participants enrolled in the trial (4,549 intervention and 5,520 control), and 9,670 outcomes were available at follow-up.

The cluster randomized trial was conducted across eight centres in Malawi over six years. Participants were followed for 28 days postpartum. Four centres were randomized to perinatal and oral health education plus daily xylitol chewing gum use (intervention group), and the other four centres were randomized to education only (control group). The authors compared rates of preterm birth, low birth weight (<2.5 kg), and oral health outcomes between the two groups.

The researchers found perinatal xylitol chewing gum use (two times a day) reduced the incidence of preterm birth by 24%. It also resulted in fewer low birth weight infants and a significant reduction in periodontitis. Xylitol chewing gum may be a cost-effective strategy to reduce preterm birth rates in this population. [48]

Artificial intelligence and preterm birth

Many machine learning techniques¹³ have been applied to predict preterm birth using health records, inflammatory markers, and vaginal microbiome data. However, the role of the prenatal oral microbiome remains unclear. <u>Hong et al. (2023)</u> aimed to compare oral microbiome compositions between a preterm and a full-term birth group, identify the oral microbiome associated with preterm birth, and develop a preterm birth prediction model using machine learning of oral microbiome compositions.

Participants were divided into a preterm and a full-term birth group based on pregnancy outcomes. Oral microbiome samples were collected using mouthwash within 24 hours before delivery, and 16S ribosomal RNA sequencing was performed to analyze taxonomy.

¹³ Refer to Episode 85 for additional information on artificial intelligence and oral health.

The study identified 25 differentially abundant taxa that could differentiate preterm and full-term birth groups. A preterm birth prediction model was developed using machine learning of oral microbiome compositions in mouthwash samples. The findings of this study suggest the potential of using oral microbiome for predicting preterm birth. Larger multi-centre studies are required to validate the results before clinical applications. [49]

Take home messages

- Regular oral health appointments, preventive oral care, and treating oral conditions are safe and an essential part of pregnancy care.
- Oral health professionals should educate clients on the possible link between oral health and pregnancy outcomes and the importance of good oral health preconception and during pregnancy.
- Pregnant clients should be counselled on the safety and benefits of prenatal oral care and encouraged to maintain good oral self-care, including brushing twice daily with fluoridated toothpaste and cleaning interdentally to promote oral health.
- Pregnant clients should be encouraged to consume noncariogenic, nutrient-dense foods to promote their general and oral health and the health of the developing fetus.

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