Pregnancy - Part 1: Physiological and pharmacokinetic changes during pregnancy and its impact on oral health care

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Executive summary

Clinical significance/ Importance:

- Oral health during pregnancy is key to maternal and infant overall health and well-being.
- Pregnancy induces complex physiological and pharmacokinetic changes that have important implications for oral health and the safe delivery of dental care.
- A sound understanding of these changes and their implications is essential for recognising pregnancy-associated oral manifestations, assessing individual risks to both mother and baby, selecting appropriate medications, and determining the appropriate timing and nature of oral health care interventions.
- **Part 1** of this series examines the principal physiological and pharmacokinetic changes occurring during pregnancy and their implications for oral health and safe clinical practice.

Key mesages

- Physiological changes support fetal development but may also influence maternal oral health, susceptibility to oral disease and tolerance to dental procedures.
- Hormonal shifts in pregnancy increase susceptibility to periodontal disease.
- Physiological and pharmacokinetic changes during pregnancy impact oral health and how we deliver care.
- Pregnancy is a physiological state requiring adaptation of dental care, not avoidance of dental care.
- Pregnancy changes how care is delivered—not whether necessary care can be delivered.

Practice implications

- Pregnancy represents an important opportunity for preventive counselling, behaviour change and coordinated medical–dental care.
- Recognise pregnancy-related changes and identify risks.
- Benefits and risks of treatment and medication prescribing decisions must be weighed to safeguard both mother and foetus.

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- Share patient information with dental and prenatal health care providers.
- Work collaboratively with the patient and interprofessional care team.
- Optimize prevention and treatment using evidence-based and personalized strategies.
- Greater emphasis should be placed on pharmacovigilance, interprofessional collaboration, personalized care, and the use of evidence-based resources to guide clinical decision-making.

Introduction

Pregnancy is a unique period during a women's life, characterized by complex physiological changes involving the endocrine, cardiovascular, respiratory, gastrointestinal, metabolic and renal systems which may adversely affect oral health and delivery of care.[1-10] These changes support fetal development but may also influence maternal oral health, susceptibility to oral disease and tolerance of dental procedures.[11] Concurrently, alterations in drug absorption, distribution, metabolism and excretion may affect pharmacological responses, therapeutic efficacy and potential fetal exposure to prescribed medicines.[12] At the same time, oral health during pregnancy is key to maternal and infant overall health and well-being[13,14], yet a frequently neglected, component of antenatal (prenatal) care.[14,15]

For dental practitioners and oral hygienists, these physiological and pharmacokinetic changes present important clinical implications and challenges.[15] A sound understanding of these changes and their implications is essential for recognising pregnancy-associated oral manifestations, assessing individual risks to both mother and baby, selecting appropriate medications, and determining the timing and nature of oral health care interventions.[5,16] Inadequate understanding may contribute to inappropriate prescribing, unnecessary postponement of essential treatment or missed opportunities for preventive care.

Part 1 of this series examines the principal physiological and pharmacokinetic changes occurring during pregnancy and their implications for oral health and clinical practice. Part 2 of this series examines the current evidence-based knowledge and provides clinical recommendations on how to optimize safe oral health care and appropriate scheduling trimester-by trimester, and considers timely preventive strategies during pregnancy. The purpose of this two part series is to support appropriate, safe and ethically responsible oral healthcare through individualized risk assessment, interprofessional collaboration, shared and informed clinical judgement, prudent pharmacotherapy and effective disease prevention.

Physiologic changes during pregnancy and its impact on oral health care

Pregnancy is a dynamic state inducing several anatomical, physiological, biochemical, and endocrine changes that are essential for fetal development and support. At the same time pregnancy also affects multiple organs and systems in the body, including the cardiovascular, hematologic, respiratory, renal, gastrointestinal, endocrine, and genitourinary systems which may impacts on oral health and safe delivery of care. (**Table 1**) (**Figure 1**) [1-11,17-19] During pregnancy women also experience notable psychological and behavioural shifts that directly influence their oral health care and safety in the dental practice setting.[7,9,20] Physiological changes can influence both oral disease expression and the patient's tolerance of dental treatment.[11] In addition, these collective changes has a large impact on the pregnant patients' oral health, and how oral health care is delivered. It is therefore critical that dental practitioners understand the complexities of physiological changes and its impact on oral health and service delivery to be able to make treatment and rational medication prescribing decisions to safeguard both mother and fetus.[12,20]

Pharmacokinetic changes and its impact on pharmacotherapy

Medication use during pregnancy presents unique clinical challenges due to profound physiological changes of the maternal body and the potential risks to fetal and neonatal health.[21] Physiological and physical changes during pregnancy impacts significantly on absorption, distribution, metabolism, and excretion of medications prescribed to pregnant patients.[12,20,21] Furthermore, the increase in oestrogen and progesterone can impact the renal system, leading to increased kidney size, renal blood flow, and glomerular filtration rate, which alters drug elimination[21], while the decreased production of hydrochloric acid (HCl) by the gastrointestinal system has consequences on drug absorption and bioavailability.[20] Liver enzyme production (i.e., cytochrome CYP2D6) is increased during pregnancy, can alter the process of absorption, metabolism and offset.[23] Codeine, which is converted into morphine by the cytochrome enzyme, whose activity is increased during pregnancy, brings rapid relief for the pregnant mother, but is also accompanied by potentially higher toxicity to the foetus.[24]

Table 1: Summary of key physiological changes in various body systems during pregnancy, associated risks and impact on oral health care

System	Physiological changes	Risks & Impact on oral health care
Endocrine (Hormonal)	• Increased levels of estrogen, progesterone, thyroxine, steroids, insulin and circulating 1,25,dihydroxy-cholecalciferol; • Oestrogen and progesterone increase blood vessel permeability, modifies neutrophil efficiency, alters bacterial composition and diversity in the microbiome, and reduced salivary flow; • Oestrogen and progesterone are insulin antagonists and the increased levels of these hormones lead to insulin resistance, thus insulin levels are elevated predisposing to development of gestational diabetes; • Due to increase in salivary oestrogen, the proliferation and desquamation of the • oral mucosal cells provide a suitable environment for bacterial growth (dysbiosis) which predisposes the pregnant woman to dental caries and periodontal disease; • Cortisol suppresses local inflammatory response and influences oral microbial growth.	• Reduced salivary flow, pH and buffering capacity • Changes in the oral microbiome balance (dysbiosis); • Alters gingival vascularity and immune responsiveness; • Increased erythema, oedema and gingival bleeding; • Predisposes to hormone-mediated inflammatory oral changes; • Increased risk of gingivitis, gingival hyperplasia, periodontitis and oral infections; • Periodontal disease and systemic inflammation linked to risk of pre-term birth and low birth weight; • Optimal timing - the 2nd trimester is the safest window for routine and elective treatments.
Cardio-vascular	• Increased cardiac output driven by higher • stroke volume and heart rate; • Decreased venous return to the heart due • to compression of the inferior vena cava • (IVC) by the gravid uterus; • During the second and third trimesters, a decrease in blood pressure and cardiac output can occur while the patient is in a supine position; • Increased uterine mass causes compression of IVC leading to venous stasis, and increased risk of deep venous thrombosis.	• Supine hypotensive syndrome due to compression of the gravid uterus on the IVC during 2nd and 3rd trimesters – resulting in sudden drops in blood pressure, dizziness and fainting;
Hematologic	• Haemodilution (also referred to as physiological anaemia) due to increase in plasma expansion (40-50%) and increase in red blood cell mass (15-25%); • Hyper-coagulable state – increase in clotting factors and decreased fibrinolytic activity to protect against haemorrhage during delivery; • Thrombocytopenia due to increased platelet turnover and haemodilution; • Compression of the gravid uterus on the IVC and aorta reducing venous return and cardiac output; • Gestational thrombocytopenia and hyper-coagulable state leads to increased risk for thrombosis / embolism; • Leucocytosis (Elevated white blood cell count).	• Bleeding precaution and management • Directly affects periodontal tissues • Increased oedema and gingival bleeding – worsens pregnancy gingivitis; • Increased prevalence of pregnancy tumours (pyogenic granulomas); • Thromboembolic awareness – prolonged immobility during long dental procedures in a hyper-coagulable patient can elevate risk of deep vein thrombosis (DVT); • Anaemia-related manifestations (Pallor of the oral mucosa and atrophic glossitis); • Supine hypotensive syndrome – drop in BP, bradycardia, and severe dizziness specifically during the 3rd trimester; • Leucocytosis is marker for active systemic or oral inflammation; • Dental chair position (semi-supine position) ; • Timing of routine and elective procedures preferably during 2nd trimester; • Increased oxygen demand and sensitivity increases minute ventilation and heightened gag reflex that make long procedures uncomfortable.

Table 1 (contd): Summary of key physiological changes in various body systems during pregnancy, associated risks and impact on oral health care

System	Physiological changes	Risks & Impact on oral health care
Gastrointestinal	• Heart burn and acidity; • Anatomical displacement of the growing uterus pushes the stomach upwards and increases intra-abdominal pressure; • Increased gastric reflux – High progesterone levels dilates the lower oesophageal sphincter, letting stomach acids enter the mouth; • Morning sickness, nausea and vomiting (hyperemesis) particularly during the 1st trimester; • Hepatic dysfunction and Iron deficiency causes nausea and vomiting.	• Increased acidic environment in oral cavity; • Reduced saliva pH and buffering capacity; • Changes in the oral microbiome balance (dysbiosis); • Increases risk of enamel erosion, dental caries and periodontal disease; • Aspiration risk when patient is reclined or nauseated in the chair; • Aversive triggers: strong smells, dental impressions, or in reclined position can easily trigger sever gag reflex or a vomiting episode; • Modified guidelines: Patient positioning in the chair - patients should be seated in a semi supine or comfortable position; • Time scheduling – avoid morning appointments – preferably short appointments during the 3rd trimester; • The procedure should be stopped immediately if patient experiences nausea and the chair should be repositioned upright; • Rinse mouth with baking soda rinse to neutralise gastric acids..
Respiratory	• Diaphragm elevation – the enlarging uterus pushes the diaphragm upward increasing intra-thoracic pressure and decreasing expiratory reserve lung volume; • Upper airway oedema – elevated estrogen cause capillary engorgement, increased mucosal fragility and oedema in the upper respiratory tract, increasing risk of rhinitis, nose bleeds (epistaxis), and mid-airway resistance (dyspnoea).	• Increased risk of hypoxia while in supine position and during sedation or prolonged procedures; • Supine hypotension can quickly trigger respiratory distress (dyspnoea) in the dental chair; • Upper airway vulnerability – Mucosal congestion, swelling, oedema, make pregnant patients more sensitive to airway restriction if throat packs, rubber dams, or awkward head positions are used; • Anxiety induced hyperventilation - Stress or pain can easily exacerbate the already elevated baseline respiratory drive, leading to panic; • Dental chair management strategies - • Use semi-reclined position and elevate the patients right hip with a cushion to relieve vascular and diaphragm pressure; • Stick to shorter appointments to minimize fatigue and breathing discomfort; • Allow frequent breaks – allow the patient to sit upright periodically to ease chest compression and improve ventilation; • Use careful airway management techniques – Avoid placing restrictive materials, impressions, devices, deep in the oral cavity that could obstruct an already compromised upper airwa

In pregnant patients, body mass, and volume increases, and therefore , there is a greater distribution volume and clearance of medications making it difficult to predict the half-life of drugs.[25,26] Such dynamics contribute to easy access of medications through the placenta, therefore compromising the health of the foetus, especially during the first trimester when organogenesis is taking place. In addition, medications may result in adverse effects such as low birth weight and teratogenicity leading to miscarriage.[12,21]

Furthermore, all local anaesthetics can cross the placental barrier, with the possibility of producing effects on the foetus. These drugs can cause cardiovascular and neurological toxicity.[20] Vasoconstrictors, such as epinephrine, are often added to increase the duration of its effect and to reduce toxicity. Epinephrineinduced vasoconstriction delays the absorption of the anaesthetic and, therefore, the level of local anaesthetic in the blood increases gradually and without peaks.[20] The anaesthetic is transferred to the foetus

Table 1 (contd): Summary of key physiological changes in various body systems during pregnancy, associated risks and impact on oral health care

System	Physiological changes	Risks & Impact on oral health care
Genitourinary	• Increased glomerular filtration rate (GFR), renal blood flow; • Gravid uterus cause anatomical compression on the bladder reducing its capacity; • Urinary stasis and altered urine biochemistry – Dysuria; • Increase size of the gravid uterus and compression on the inferior vena cava (IVC) causes drop in blood pressure.	• Significantly accelerates clearance and urinary excretion of medications - Collaborate with patients' obstetrician for optimal therapeutic medication dosage; • Frequent urination and discomfort; Ask the patient to empty the bladder just prior to starting the dental procedure; • Avoid long extended appointments; Allow frequent bathroom breaks; Schedule shorter flexible appointments; Anticipate multiple interruptions during a procedure; • Supine hypertensive syndrome – modify patient positioning in the dental chair , especially during 3rd trimester; Keep chair semi-reclined; Tilt patient onto her left side using a pillow under the right hip.
Psychological & Behavioural	• Anxiety and stress about fetal safety; • Depression and self-efficacy; • Misconceptions – unfavourable cultural beliefs preventing women from receiving timely treatment; • Behavioural habits and nutritional demands – dietary changes.	• Increased anxiety and pain perception; • Oral parafunction (bruxism) – tooth wear; dry mouth and heightened gag reflex; • Neglect of oral hygiene practices – gingivitis and dental decay; • Sugar cravings, frequent snacking – enamel erosion and decay; • Reduced saliva pH and buffering capacity; • Changes in the oral microbiome balance (dysbiosis); • Increased susceptibility to dental caries and periodontal disease.

just as slowly, with a wider safety margin.

Medication use in pregnancy is ubiquitous, with off-label prescribing and over the counter medications (OTC) very common.[12] Furthermore limitations exist in our body of evidence regarding the safety and efficacy of both OTC and prescription medications in pregnancy, posing a challenge when attempting to weigh risks and benefits of a particular medication that may, for instance, have known maternal benefit but unknown fetal risk.[12] In such cases it is suggested that clinicians consult a patients' prenatal care provider and consider contraindications before prescribing medications.[5]

Thus, considering the unique challenges and risks associated with medication use in pregnant patients, it is recommended that greater emphasis should be placed on pharmacovigilance, personalized care, and the use of evidence-based resources to guide clinical decision-making.[21]

Key oral manifestations in women during pregnancy

Physiological changes in women during pregnancy increases susceptibility to development of oral conditions such as: dental erosion, dental caries, gingivitis, periodontal disease, gingival hyperplasia, pyogenic granuloma (granuloma gravidarum) and candidiasis.[1,3,11,27,28] Collectively, physiological changes in pregnant women directly and indirectly modifies saliva, including a decrease in pH and buffering capacity9, disrupts oral microbiome balance[10,38], alters immune inflammatory responsiveness[10,29], and tissue response promoting increased vascular permeability.[19,28,29] A recent study indicated a lower salivary pH in the first and second trimesters and higher salivary cortisol levels throughout pregnancy compared to the control group, suggesting salivary modifications as key findings.[28] A decrease in salivary pH and buffer effect, along with an increase in certain salivary cariogenic microorganisms, temporarily predisposes a woman to dental caries and erosion. Pregnancy-related physiological changes, such as increases in acidic environment in the oral cavity due to nausea and vomiting, dietary modifications such as increased sugar consumption, and changes in oral hygiene habits, may also contribute towards dental erosion and enamel demineralization.[28] Erosion/ Enamel loss – Induced by nausea and vomiting (hyperemesis gravidarum) are very common in pregnant women: 70% to 85% of women experience these symptoms, which tend to disappear after the first trimester.[30]



Figure 1: Physiological changes during pregnancy and its impact on oral health care

Link between periodontal disease and adverse pregnancy outcomes

Periodontal disease, including both gingivitis and periodontitis, occur commonly among pregnant women.[29] Pregnancy induces significant hormonal, immunological, and physiological changes that affect the periodontium. These modifications increase vascular permeability, alter subgingival microbiota, and modulate immune defences, making women more susceptible to gingivitis, epulis, and the progression of pre-existing periodontitis.[29]

Periodontitis, a chronic destructive disease, has been studied as a possible risk factor for adverse pregnancy outcomes (APO's) such as preterm birth, low birth weight, preeclampsia, gestational diabetes, and early pregnancy loss.[31,32] The strongest mechanistic evidence linking periodontal diseases with APO's are systemic inflammation and hematogenous dissemination of periodontopathic bacteria to the fetoplacental unit.[29,33] This highlights the role the oral microbiome as a biologically plausible contributor to adverse maternal and neonatal outcomes.[34,35]

Much has been written in recent years about the relationship between maternal periodontitis and pregnancy outcomes. While findings of individual studies have been mixed, an overview of 23 systematic reviews concluded that associations exist between periodontitis and pre-term birth, low birthweight babies, low birthweight babies born prematurely and the development of pre-eclampsia.[31] Current evidence also supports a significant association between maternal periodontal disease, gestational diabetes mellitus (GDM), and adverse maternal-fetal outcomes.[31] It is suggested that gestational hyperglycaemia may enhance periodontal inflammation and gingival tissue responsiveness.

A recent systematic review suggested that treating periodontal disease during pregnancy may reduce the risk of pre-term birth.36 Abovementioned findings though should be interpreted with caution due to methodological limitations and variability in findings across studies.[29,31,36] Furthermore, association does not establish causality and the causal link between periodontitis and adverse pregnancy outcomes remains largely unknown.

In the absence of conclusive evidence, prevention always remains the best solution. Therefore, achieving optimal periodontal health before conception appears to be a reasonable approach to limit any potential, though still unproven, influence of periodontal disease on adverse pregnancy outcomes.[29] Thus, incorporating periodontal screening into prenatal care may benefit maternal oral and metabolic health. However, further longitudinal and interventional studies are needed to clarify causality between periodontal disease and APO's[31], and to explore

whether periodontal therapy may help reduce risks linked to GDM.[37]

Conclusion

Pregnancy induces complex physiological and pharmacokinetic changes that have important implications for oral health and the safe delivery of dental care. Hormonal fluctuations, increased cardiovascular demands, altered respiratory function, gastrointestinal changes and progressive metabolic adaptations influence maternal oral tissues, systemic homeostasis and treatment tolerance. These changes may increase susceptibility to gingival inflammation and modify responses to existing oral disease, underscoring the importance of individualised risk assessment and preventive care.

Pregnancy also alters drug absorption, distribution, metabolism and excretion. In addition, changes in plasma volume, protein binding, hepatic enzyme activity and renal clearance may influence medication exposure and therapeutic response. Pharmacotherapy therefore requires careful consideration of gestational age, maternal physiology, placental transfer, potential fetal effects, dose requirements and the availability of safer alternatives. Clinicians should prescribe only when indicated, using the most appropriate medicine at the lowest effective dose for the necessary duration, guided by current evidence and authoritative prescribing recommendations.

Common oral manifestations include pregnancy-associated gingivitis, increased gingival bleeding, pregnancy-associated pyogenic granuloma (epulis gravidarum), enamel erosion related to recurrent vomiting, and possible exacerbation of pre-existing periodontal disease or caries risk. Although periodontal disease has been associated with adverse pregnancy outcomes, including preterm birth and low birth weight, association does not establish causation. Current evidence does not demonstrate consistently that periodontal treatment prevents these outcomes. Nevertheless, maintaining periodontal health remains essential for maternal wellbeing and the prevention of oral disease.

Ultimately, pregnancy is not a contraindication to appropriate dental care. Evidence-based prevention, timely diagnosis, judicious pharmacotherapy and coordinated interprofessional care supporting maternal oral health while protecting fetal wellbeing is aligned with safe and appropriate care.

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