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ROLE OF PERIODONTAL DISEASE IN PRE-TERM LABOUR- A REVIEW

Dental Science

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ABSTRACT

The purpose of this article is to update the dental clinician how periodontal disease can lead to complication in new born baby. Pregnancy leads to many physiologic changes in the body which is hormone mediated and influences the treatment modalities. In pregnancy various organism and inlammatory mediators are involved in pre-term labour pain. Information about micro-organisms and inflammatory mediators is provided in this article.

KEYWORDS

Pregnant Patient, Physiology, Micro-organisms, Inflammatory Mediators

INTRODUCTION

Pregnancy is a beautifull time and every thing should be done to ensure healthy nine months which includes good thoughts, pre-natal care, maintaining healthy diet, exercising and oral health.Pregnancy leads to many physiological changes in the female body and can lead to severe complication if proper precautions are not taken.Physiological changes occuring in oro-facial system, respiratory, cardiovascular, hematologic, endocrine, gastrointestinal, genitourinary, occur because of increasing maternal and fetal requirement for the growth of fetus and mother.

Apart from these physiological changes ,there are many changes which are seen in the oral cavity which can lead to adverse pregnancy outcomes like pre-term birth. These changes pose various challenges in providing dental care for pregnant patients[1].

Physiologic Changes During Pregnancy

1) Cardiovascular Changes
a) Peak value of increased blood volume occurs at 32 week of gestation.
b) Maternal blood volume increases by 25% to 52% with 20% in RBC.
c) Lowest blood presure occurs at 28 week of gestation
d) Highest heart rate volume in standing position
e) Increased risk of deep vein thrombosis
f) Extra heart sound/systolic S3 murmur
g) Increased uterine mass [2,3]

2) Respiratory Changes
a) Increase in oxygen consumption by 21%.
b) Progestrone induced hyperventilation
c) Decrease PaO2 while supine leads to increased risk of hypoxia
d) Decreased functional residual capacity[4,5]

3) Gastro-intestinal Changes
a) Increased intra-gastric pressure
b) Decreased gastric motility
c) Loss of lower esophageal sphincter tone leads to increased risk of reflux disease
d) HELLP syndrome (hemolysis, elevated liver enzyme,low platelets)

4) Genitourinary Changes
a) Increased glomerular filtration rate
b) Urinary stasis leads to increased risk of urinary tract infection.
c) Loss of intravascular protein leads to decreased oncotic presuure further leading to perpheral edema[8,9]

5) Endocrine change
a) Elevated estrogen,progestrone, thyroxine, steroids, insulin and increae in circulating 1,25,dihydroxy-cholecalciferol[10].

Preterm birth (PTB)

They are defined as the babies born 3 weeks before the gestational period and the gestational weeks normaly last for 40 weeks. It is estimated that about 15 million babies are born PTB each year globally, which accounts for more than one in 10 babies. Inspite of significant advances in medicine and improvement in prenatal care utilization PTB appears to rise in developed countries.Causes for PTB are not so clear but several factors which can increase the risk of PTB are stress, physical or emtional violence maternal weight, trauma,respiratory problems etc.

Globally, incidence of PTB is around 9.6% of all birth representing 12.9 million births. In USA, PTB prevalence increased from 9.5% (1981) to 12.7% (2005). Women classified as black, Afro-Caribbean and Afro-American, are reported to be at higher risk of PTB. PTB rates are in the range of 16–18% in black women compared with 5–9% for white women in USA[11,12].

In India, the incidence of PTB has been reported to be 14.5%[13]. Gopichandran *et al*. in 2010 reported in a study conducted in rural South India that maternal stress due to pregnancy-related anxiety, stressful life events, death of a spouse, depression during pregnancy and poor self-esteem are risk factors for preterm labor. Pre-term leads to breathing difficulties, under developed organs, vision problems, cerebral palsy, learning disabilities etc in the baby[14].

Role Of Periodontal Diseases In Pregnancy

Periodontal disease begins with gingi-vitis, the localized inflammation of the gingiva that is initiated by bacteria in the dental plaque, which is a microbial biofilm that forms on the teeth and gingiva Periodontal disease begins with gingi-vitis, the localized inflammation of the gingiva that is initiated by bacteria in the dental plaque, which is a microbial biofilm that forms on the teeth and gingiva Periodontal disease begins with gingi-vitis, the localized inflammation of the gingiva that is initiated by bacteria in the dental plaque, which is a microbial biofilm that forms on the teeth and gingiva Periodontal disease begins with gingi-vitis, the localized inflammation of the gingiva that is initiated by bacteria in the dental plaque, which is a microbial biofilm that forms on the teeth and gingiva Periodontal disease begins with gingi-vitis, the localized inflammation of the gingiva that is initiated by bacteria in the dental plaque, which is a microbial biofilm that forms on the teeth and gingiva Periodontal disease starts with gingivitis, which is the localized inflammation of the gingiva that is initiated by bacterias in the dental plaque. In the absence of adequate oral hygiene, periodontal bacteria start accumulating in gingival crevice of teeth. Periodontal diseases are the infectious disease affecting more than 23% of women between the ages group of 30 and 54 years[15]. In diseased state,pregnancy has shown to exacerbate existing oral disease even in absence of increasing oral plaque[16]. In normal pregnancy, susceptibilty to pregnancy induced gingivitis usually occurs between 12 to 28 weeks of pregnancy[17]. Sex

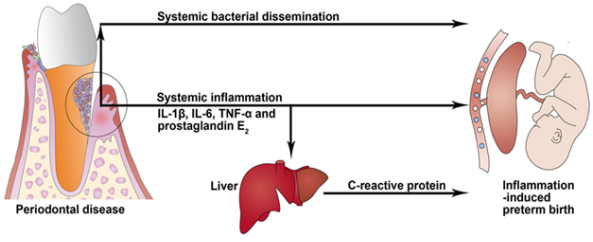
hormones are reported to increase vascular permeability and proliferation while inhibiting oral mucosal tissue repair, suggesting that sex hormone associated gingivitis (e.g. puberty, menstruation, pregnancy) alters the effectiveness of the epithelial barrier to the oral microbiota[18,19]. The first experiment to suggest a possible associaton of periodontitis with adverse effects on pregnancy was done by Collins and colleagues in which they injected periodontal pathogen porphyromonas gingivalis and found that infection leads to reduction in size of the fetus (20% decreased weight) and increase in inflammtory mediators (TNF-alpha, PGE_2) at the site of infection and in amniotic fluid[20,21].

There are different type of T-cells (Th, Tc, Treg) which play a important role in immune response. The balance of TH17 cells relative to Treg cells is a central component to balance the immune response. Pregnancy requires to fix this balance to protect the mother from infection while accepting a semi-allogenic fetus but this balance gets disturbed if the mother has periodontitis. Figueiredo reviewed that an excess of TH17 with a reduced Treg cell level can lead to adverse pregnancy outcomes[22].

Periodontal diseases can lead pre-term labour in 2 ways –
1)Direct pathway (micro-organisms)
2)Indirect pathway (Inflammatory mediators)

P. Gingivalis And Pre-term Labour (direct Pathway)

It has been accepted that different of bacteria and not a single microorganism, are involved in periodontal diseases. Initially, periodontal tissue inflammation is triggered by the colonization of the both gram positive and gram negative bacteria in subgingival region. Over time, Gram-negative anaerobes become more established[23]. Among many periodontal pathogens, *P. gingivalis* is one of the main etiological agents in the pathogenesis and progression of the inflammatory events of periodontal disease.A interactive association develops between P. gingivalis and the epithelial cells that line the gingival crevice and comprise a barrier to oral microbial intrusion[24].



Intracellular P. gingivalis cells remain viable and capable of spreading between host cells and epithelial cells can survive for up to 8 days after infection with P. gingivalis[25]. Epithelial cells recovered from the oral cavity show high levels of intracellular P. gingivalis[26]. Porphyromonas gingivalis has been shown to modulate apoptotic cell death in many kinds of cells, including immune cells, fibroblasts, epithelial cells and endothelial cells, resulting in both pro- and anti-apoptotic outcomes[27]. In primary and transformed epithelial cells derived from the gingiva, metabolically active P. gingivalis do not induce apoptosis and, moreover, inhibit chemically induced apoptotic cell death[28]. All of these properties could potentially disrupt homeostasis in the placental tissues. It is also potentially important that, during the first 10-12 wks of gestation, the placenta is in a state of physiological hypoxia and this hypoxic environment favours the growth of P.gingivalis[29]. Acc to a study by J.katz concluded that periodontal pathogens such as *P. gingivalis* can lead to pregnancy complications, including preterm delivery[30]. Barak also showed that *P. gingivalis* antigens can be present in the normal asymptomatic human placenta[31].

Role Of Periodontal Inflammatory Mediator In Pre –term Labour (indirect Pathway)

Periodontal disease are one of the most frequent occuring diseases in the world. The milder reversible form gingivitis results in inflamation of gingiva but in disease susceptible indivduals may lead to periodontitis which further causes destruction of connective tissue and alveolar bone[32]. Periodontitis is a complex interaction between the microbes and the host, which alters connective tissue and bone metabolism further leading to periodontal damage. The host response to the bacterias includes the action and stimulation of various inflammatory cell types[33].

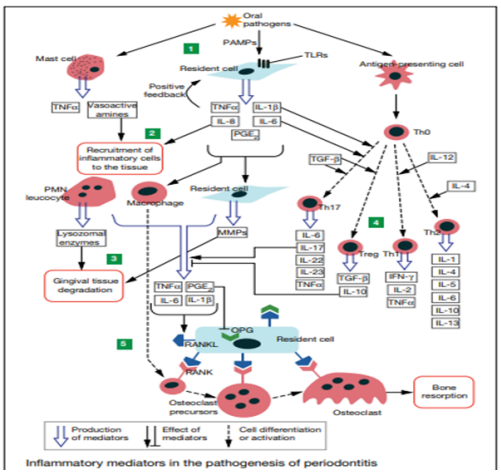


Figure 1 Inflammatory mediators in the pathogenesis of periodontitis Tülay Yucel-Lindberg* and Tove Båge

(1) In innate immunity, components of the pathogens present in the oral biofilm, such as LPS, stimulate mast cells to release vasoactive amines and preformed TNFα and cause a release of inflammatory mediators in resident cells of the gingival tissue. (2)Through the action of the released mediators, inflammatory cells are recruited into the tissue. (3) PMN leucocytes release lysosomal enzymes, and in response to the milieu of inflammatory mediators, MMP levels increase. MMPs and lysosomal enzymes contribute to degradation of the gingival tissue. (4) Lymphocytes and macrophages invade the tissue. Antigen-presenting cells activate Th0 cells. T-cellproduced cytokines can increase or inhibit the production of inflammatory mediators. (5) Cytokines and PGE2 affect RANKL and OPG expression, resulting in the formation and activation of osteoclasts capable of alveolar bone degradation. IFN-γ, interferon-γ; IL, interleukin; LPS, Lipopolysaccharide; MMP, matrix metalloproteinase; OPG, osteoprotegerin; PAMPs, pathogen-associated molecular patterns; PGE2, prostaglandin E2; PMN, polymorphonuclear leukocytes; RANK, receptor activator of nuclear factor-κB; RANKL, receptor activator of nuclear factor-κB ligand; TGF-β, transforming growth factor β; TLRs, toll-like receptors; TNFα, tumour necrosis factor α; and Treg, regulatory T cel.

Many literatures have shown that during pregnancy, periodontal disease have shown corelation between pathogenic bacteria with moderate or severe periodontitis.Periodontal pathogens generate virulence factors through the production of lipopolysaccharides (LPSs) and increased cytokines such as tumor necrosis factor- (TNF-) α, interleukin- (IL-) 1, IL2, and IL-6 as well as inflammatory mediators such as prostaglandin E2 (PGE_2)[34].

In a normal pregnancy, prostaglandins are synthesized in the fetal membranes: the decidua, the myometrium, and the placenta. The amnion and chorion primarily produce PGE_2; the decidua synthesizes PGE_2 and PGF_2; and the myometrium secretes PGI_2. Larger amount of PGI_2 is released from placenta that protects against thrombosis during low pressure in the intervillous space. Further production of these substances is proportional to gestational age and hence more PGs are present at the end of pregnancy than during the first trimester and Inhibition decreases over time. Prostaglandins also increase the number of myometrium receptors for oxytocin[35].

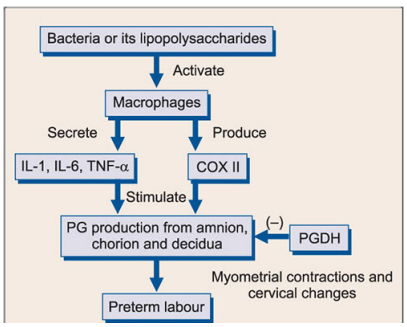


Figure 2 https :// d 45jl3 w9 libvn. cloudfront. net/jaypee/ static/ books/ 9788180619113/Chapters/images/417-1.jpg

At the end of a normal term pregnancy (more than 37 weeks) the levels of PGE_2, TNF-α, and IL-1β are increased until they reach critical levels, which initiates uterine contractions and produces birth. However, during pregnancy and before the end of term, the proinflammatory immune response must be strictly regulated within the uterus to avoid the immune rejection of the fetus. A local increase in proinflammatory mediators (figure 2) can interrupt this delicate balance; therefore, an inflammatory response stimulated by a local infection (e.g., periodontal disease) under this mechanism would contribute to the premature rupture of membranes and uterine contraction, thereby triggering preterm delivery[36].

Different studies showing association between periodontal disease and pre-term delivery-

STUDIES	CONCLUSION
1)Catalina latorre uriza (2018)[37]	Increased levels of cytokines were seen in pregnant women with periodontal disease
2)Zadeh (1999) and Van dyke (2013)[38,39]	Periodontal infection triggers increase in cytokine and TNF-alpha levels.
3) Perunovik et al. (2016)[40]	Found that women with preterm delivery exhibited significantly more periodontitis and showed an increase in the levels of IL-6 and PGE_2 in the crevicular fluid.
4) Arntzen et al. (1998)[41]	Found an association between increases in TNF-α, IL-1, and IL-6 levels and preterm delivery.
5) Corbella et al. (2016)[42]	Concluded that an association exists, albeit low, between periodontitis and adverse pregnancy outcomes

COX2 is expressed at low-to-undetectable ranges in the uterus during most of pregnancy, and it is highly regulated by proinflammatory cytokines and PGE_2; COX2 catalyzes the production of prostaglandins in the amnion and plays a crucial physiological role in the initiation of labor by functioning as a potent activator of uterine contractions. PGE_2 is positively regulated during preterm delivery; in turn, it is induced by an inflammatory response that promotes the contraction of the uterine smooth muscle[43].

Effect Of Periodontal Therapy On Pregnancy Outcomes

Although many studies have shown association between periodontal disease and pregnancy but also many literatures have shown that periodontal treatment during pregnancy can help in reducing adverse pregnancy outcomes. Most healthcare workers (dentist and physician) have rated that pre-natal dental screenning is important and also that pregnant ladies could safely undergo dental cleaning[44]. Interventions to reduce the morbidity and mortality associated with pre-term birth can be classified as primary, secondary and tertiary. Primary interventions are administered to all women before and during pregnancy to prevent or reduce risk. Secondary interventions are aimed at eliminating or reducing risk in women with known risk factors. Tertiary interventions are started at or near parturition (i.e. around the time of labor and delivery) in order to delay delivery or to promote the health of pre-term infants[45].

In most population with periodontal disease, oral hygiene instructions plus scaling and root planing are very effective in dramatically reducing the clinical signs of periodontal infection / inflammation. There ia a possibility that modifications in innate and adaptive immune responses during pregnancy make it more difficult to control periodontal infections by routine therapeutic interventions and it should not be assumed that only periodontal therapy is effective in reducing periodontal infection during pregnancy[52].

CONCLUSION

During pregnancy, there are many changes in innate and adaptive immunity that have an impact on the number of infectious diseases, including those affecting periodontal tissues. Inflammation of periodontal tissues increases dramatically in extent and severity during the course of a normal pregnancy.All the above mentioned studies suggest that performing periodontal treatment during the second trimester would decrease the risk of development of adverse pregnancy outcomes, especially preterm birth and/or low birth weight. Finally, it should not be forgotten that there are many factors like smoking,stress,air pollution etc which can lead to adverse pregnancy outcome and control of periodontal infections is a large part of providing a healthy mouth that is comfortable, functional and esthetically pleasing.

STUDIES	TREATMENT OUTCOME
1) Silness j (1964), Yalcin F (2002)46,47	non-surgical periodontal therapy is effective in reducing the increased amount of periodontal inflammation associated with pregnancy
2) Newnham JP(2009), Offenbacher S(2009)48,49	non surgical periodontal tharapy is safe and does not trigger increase in adverse pregnancy outcome.
3) Lo´pez NJ(2002)50,51	non-surgical periodontal therapy in pregnant women with slight to moderate chronic periodontitis reduced the rates of pre-term low-birthweight babies.

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