REVIEW ARTICLE KERALA MEDICAL JOURNAL

Periodontal Diseases and Adverse Pregnancy Outcome: Revisiting the Myth Truth Saga

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ABSTRACT

Published on 27th March 2017

The possibility that pathogenic microorganisms and their products from infectious foci including those in the mouth can spread to other parts of the body and trigger different diseases was first suggested by Hunter in 1910, in his "focal infection theory". Periodontal Medicine emerged as a branch which focused on this oral systemic connection. More than 45 systemic diseases were found to have a link with periodontal diseases. Among them diabetes is having the strongest association in the form of two way relationship. Periodontal diseases in the pregnant mother can lead to adverse pregnancy outcomes which can lead to preterm low birth weight babies. This article gives an insight into the general aspects of the pathophysiology and the current evidence in literature both supporting and contradictory and the relevance of this connection.

Keywords: Periodontal diseases, Preterm low birth weight babies, Bacterial vaginosis, Pre eclampsia, Premature membrane rupture

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INTRODUCTION

Periodontitis is a local inflammatory process mediating the destruction of periodontal tissues. Advances in science and technology over the last century have greatly expanded our knowledge of pathogenesis of periodontal diseases.[1]

Periodontal disease is an infectious disease but environmental, physical, social and host stresses may effect and modify disease expression. Certain systemic conditions clearly may affect the initiation and progression of gingivitis and periodontitis. Systemic disorders and conditions alter host tissue and physiology, which may impair host barrier integrity and host defences to periodontal infection, resulting in more destructive disease. These systemic disorders affecting neutrophil, monocyte/macrophage and lymphocyte function result in altered production or activity of the host inflammatory mediators. These alterations may manifest clinically as early onset of periodontal destruction or a more rapid rate of destruction than would occur in the absence of such disorders. Inflamed periodontal tissues serve as reservoirs for periodontal pathogens, endotoxins, and inflammatory mediators.[2] The detection of oral pathogens in amniotic fluids by polymerase chain reaction tests suggests a possible hematogenous spread of these infections.[3] Although the role of periodontal disease in PTB has been investigated extensively, the results have been inconclusive; a number of studies found an association, whereas other studies did not.

Preterm birth (PTB), defined as birth before 37 weeks of gestation, accounts for 75% of perinatal mortality and more than half of long-term morbidity.[4] A history of spontaneous preterm delivery has been identified as the most significant risk factor; other risk factors include preeclampsia, thrombophilia, low socioeconomic status, very young or old maternal age, multiparity, inadequate prenatal care, and the use of alcohol and tobacco. Despite extensive literature on the subject and improved antenatal care, there has been no significant decrease in the incidence of PTB in developed societies.[5] This has led to the belief that other factors may contribute to PTB. Hence, the search for relevant risk factors must continue.[2] Maternal infections may threaten the welfare of the fetus and lead to PTB through the activation of the innate immune system, leading to an increased expression of prostaglandins and inflammatory cytokines.[1] Intrauterine infections can result in spontaneous preterm delivery by stimulating uterine contractions or membrane rupture.[1] Systemic infections, such as pneumonia,[5] and genitourinary tract infections, like bacterial vaginosis,

Cite this article as: Manikandan GR, Ajithkumar KC. Periodontal Diseases and Adverse Pregnancy Outcome: Revisiting the Myth Truth Saga. Kerala Medical Journal. 2017 Mar 27;10(1):29–38.

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Chlamydia trachomatis, and syphilis, are also associated with PTB.[6,7]

Periodontitis associated pregnancy complications

Adverse pregnancy outcomes include

1. Preterm Birth
2. Low birth weight
3. Preeclampsia
4. Bacterial vaginosis
5. Pre mature rupture of membranes
6. Small for gestational baby

Preterm birth:[8]

Normal gestation: 40 weeks

Preterm birth: < 37 weeks of gestational age

Late Preterm birth: 34-36 weeks of gestational age

Very Preterm birth: Birth < 32 weeks of gestational age

Extremely Preterm birth: Birth <28 weeks of gestational age

Low Birth Weight:[8]

The international definition of low birth weight adopted by 29th world Assembly in 1976

Low birth weight (LBW):<2500 gm (upto and including 2499 gm)

Very Low birth weight (VLBW):<1500 gm (upto and including 1499 gm)

Extremely Low birth weight (ELBW):<1000 gm (upto and including 999 gm)

Risk factors for adverse pregnancy outcomes

The main causes of adverse pregnancy outcomes are reported to be maternal infection and placental or fetal or uterine pathosis. Increasingly very pre term birth occurs with multiple pregnancies and is often a result of assisted reproductive technology. Prominent risk factors for preterm birth includes history of previous preterm birth, demographic characteristic periodontal disease, behavioural factors like alcohol and tobacco use, young maternal age, low social economic status, stressful life situation, genetic background and genitor urinary tract infections. A higher risk of spontaneous preterm delivery has been associated with genetically driven excessive amniotic fluid IL-β or with a disturbance of bioavailability and/or bio response of cytokine which is central to proinflammatory reaction to infectious stimulus.[8]

Genetic risk factor, demographic and psychosocial risk factor, obstetric risk factor, nutritional risk factor, infection, toxic exposure and antenatal care are the various risk factors for adverse pregnancy outcomes **(figure 1).**

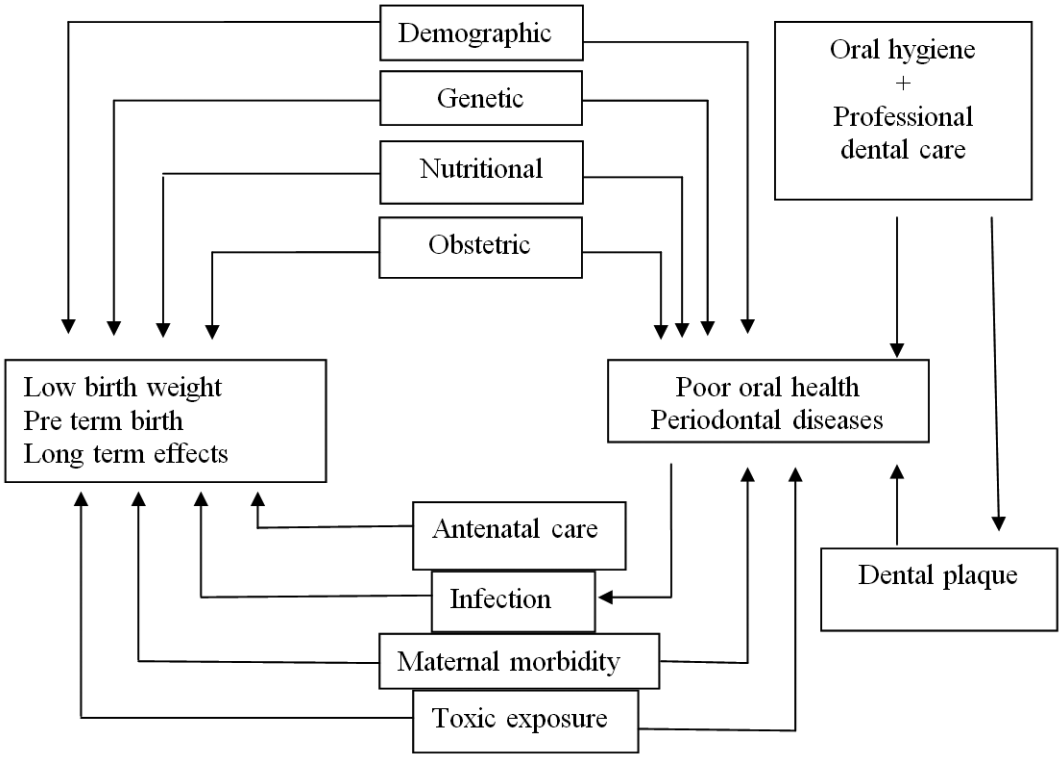

Figure 1. **Interactions between risk factors and adverse pregnancy outcomes**

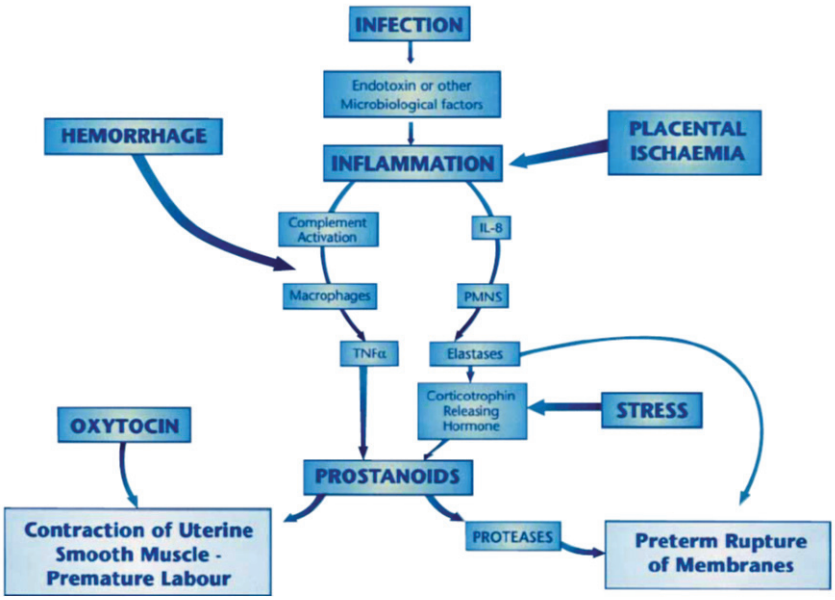

Figure 2. **Mechanisms involved in preterm labour**

It is clear that the causes of preterm low birth weight are complex and multifactorial, but there may be common pathways in the mechanisms involved. Infection is an important risk factor, and the process of understanding how infections including the periodontal diseases could be involved may be facilitated by the examination of the putative mechanisms linking known risk factors to preterm low birth weight.

Interactions between risk factors and low birthweight:[9]

Mechanisms involved in preterm labour:[9]

The possible mechanisms involved with preterm labour includes **(figure 2)**

1. Normal physiologic process happening early
2. Infection
3. Inflammation
4. Hemorrhage
5. Placental ischemia
6. Stress.

Bacterial vaginosis

Bacterial vaginosis (BV) is a Gram negative, predominantly anaerobic infection of the vagina, usually diagnosed from clinical signs and symptoms. It is associated with a decrease in the normal lactobacillus dominated flora and an increase in anaerobes and facultative species including Gardnerella vaginalis, Mobiluncus curtsii, Prevotella bivia and Bacteroides ureolyticus. Bacterial vaginosis is a relatively common condition that occurs in about 10% of all pregnancies. It may ascend from the vagina to the cervix and even result in inflammation of the maternal fetal membranes, (chorioamnionitis). Extending beyond the membranes, the organisms may appear in the amniotic fluid compartment that is shared with the fetal lungs and/or may involve placental tissues and result in exposure to the fetus via the bloodstream. Despite the observed epidemiological linkage of bacterial vaginosis with preterm birth, the results from randomized clinical trials to determine the effects of treating bacterial vaginosis with systemic antibiotics on incident preterm birth are equivocal. Still, there are compelling data linking maternal infection and the subsequent inflammation to preterm birth. It appears that inflammation of the uterus and membranes represents a common effect or mechanism that results in preterm birth, and thus, either clinical infection or subclinical infection is a likely stimulus for increased inflammation.

Role of inflammatory mediators in pregnancy outcome[10]

The role of prostaglandins in regulating the normal physiology of pregnancy has been well documented. The evidence supporting the role of prostaglandins in human labour is as follows:

1) The administration of prostaglandins results in abortion or labour.
2) Treatment with prostaglandin inhibitors delays the process of mid trimester abortion and the onset of labour and can arrest preterm labour.
3) Parturition at term is associated with elevated amniotic fluid and maternal plasma concentrations of prostaglandins.
4) Arachidonic acid (prostaglandin precursor) concentrations in the amniotic fluid increase during labour.
5) Intraamniotic administration of arachidonic acid results in labour.

Mazor et al[11] (1990) demonstrated that women with preterm labour and intraamniotic infection had significantly higher amniotic fluid concentrations of PGE2 and PGF2α than women with preterm labour but without infection. This may be explained by the fact that amnion from women with preterm labour and

histologic chorioamnionitis produced more PGE than amnion from women without placental inflammation.

Tamatani et al[12] (1988) have shown that IL-1β is present in normal amniotic fluid and IL-1β has been produced by human placental macrophages. The small amount of IL-1β detected in the second trimester amniotic fluid has been shown to exhibit a 3 fold increase with the onset of labour.

Kent et al[13] (1993) in a study on the effects of IL-1 on prostaglandin production by cultured human fetal membranes have demonstrated that IL-1β is a potent stimulator of the synthesis of prostaglandins by decidua and amnion.

IL-1 was the first cytokine implicated in the onset of labour in the presence of infection. The key data are summarized as follows:

1) IL-1 is produced in vitro by human decidua in response to bacterial products.

2) In patients with preterm labour and bacteria in the amniotic cavity, amniotic fluid IL-1 bioactivity and concentrations are elevated.

3) **Romero et al[14] (1989)** have also demonstrated elevated amniotic fluid IL-1β bioactivity and concentrations in patients with premature rupture of membranes (PROM) and bacteria in the amniotic cavity with labour, compared to those without labour.

4) IL-1β stimulates prostaglandin production by amnion and decidua in vitro.

Role of periodontitis

In the early 1990s, studies have hypothesized that oral infections, such as periodontitis, could represent a significant source of both infection and inflammation during pregnancy. Studies stated that periodontal disease is a Gram-negative anaerobic infection with the potential to cause Gram negative bacteremias in persons with periodontal disease. They hypothesized that periodontal infections, which serve as reservoirs for Gram negative anaerobic organisms, lipopolysaccharide (LPS, endotoxin) and inflammatory mediators including PGE2 and TNF-α may be a potential threat to the fetal-placental unit.

Women having LBW infants have higher levels of Actinobacillus actinomycetemcomitans, Tannerella forsythia, Porphyromonas gingivalis and Treponema denticola in their subgingival plaque. Women having LBW infants have higher levels of gingival crevicular fluid (GCF) PGE_2 and IL-1. GCF levels of IL-1 and PGE_2 have been shown to correlate highly with intraamniotic IL-1 and PGE_2 levels. Thus women having LBW infants have a higher prevalence and severity of periodontitis, more gingival inflammation, higher levels of putative periodontal pathogens and an elevated subgingival inflammatory response compared with women having normal birth weight infants.[1]

Dasanayake[15] (1998) evaluated the hypothesis that poor oral health of the pregnant women is a risk factor for LBW. The effect of periodontal status of the women at the time of delivery on the birth weight of the infant was evaluated by using conditional logistic regression analyses, while controlling for known risk factors for low birth weight (LBW). The author concluded that poor periodontal health of the mother is a potential risk factor for LBW.

Jeffcoat et al[16] (2003) conducted a study to determine the feasibility of conducting a trial to determine whether treatment of periodontitis reduces the risk of spontaneous preterm birth. The treatment groups consisted of 1) dental prophylaxis plus placebo capsule 2) scaling and Root planing plus placebo capsule and 3) SRP plus metronidazole capsule. The author concluded that performing SRP in pregnant women with periodontitis may reduce preterm birth in this population compared with other groups.

Lopez et al[17] (2005) conducted a study to determine the effect of routine plaque control and scaling on pregnancy outcomes in women with gingivitis. Periodontal therapy consisted of plaque control, scaling, and daily rinsing with 0.12% chlorhexidine. The author concluded that periodontal treatment significantly reduced the preterm or low birth weight rate in the population of women with pregnancy associated with gingivitis.

Noack et al[18] (2005) conducted a study to investigate the link between periodontal health status of pregnant women and preterm low birth weight in a German Caucasian population. The author concluded that in this population, periodontitis was not a detectable risk factor for preterm low birth weight in pregnant women.

Khader et al[19] (2005) conducted metaanalysis of periodontal disease in relation to the risk of preterm birth/ low birth weight based on two case control studies and three prospective cohort studies. The findings indicate that periodontal disease in the pregnant mother significantly increases the risk of subsequent preterm birth or low birth weight. Periodontal infection increases

the proinflammatory cytokines that affect the placental viability leading to low birth weight and initiate contractions of the uterus prematurely leading to premature birth.

Offenbacher et al[20] (2006) examined the effects of periodontal therapy during pregnancy on periodontal status, biologic parameters and pregnancy outcomes. Author concluded that there was improved periodontal health and prevented periodontal disease progression. There was 3.8 fold reduction in the rate of preterm delivery, a decrease in the periodontal pathogen load and a decrease in both GCF-IL-1β and serum markers of IL-6 response.

Gazolla et al[21] (2007) evaluated the incidence of preterm low birth weight in patients undergoing periodontal therapy. The pregnant women who engaged in the study were considered healthy; they did not have any systemic alterations, had healthy habits and were in good gynaecological and obstetric conditions. Periodontal condition was related significantly to preterm low birth weight. The data showed that even when other relevant aspects were adjusted, women with non treated periodontal disease had a greater risk for preterm delivery. They suggested that periodontal treatment should be included in prenatal care programs.

Leon et al[22] (2007) conducted a study to determine the presence of microbial invasion of the amniotic cavity by periodontal bacteria and detection of Porphyromonas gingivalis in the amniotic fluid in pregnant women with a diagnosis of threatened premature labour. In the study Porphyromonas gingivalis was identified primarily by colony morphology under stereoscopic microscope and rapid biochemical tests. Amniotic fluid or plaque samples were homogenized, DNA was extracted and polymerase chain reaction amplification of 16S rRNA with specific and universal primers was carried out. The author concluded that the presence of microbial invasion of the amniotic cavity by P. gingivalis could indicate a role for periodontal pathogenic bacteria in pregnant women with a diagnosis of threatened premature labour.

Toygar et al[23] (2007) correlated the association between periodontal health and adverse pregnancy outcome in 3,576 Turkish women. The results provided strong evidence that maternal periodontal disease is an independent risk factor for an adverse outcome of pregnancy.

Tarannum et al[24] (2007) determined the effect of non surgical periodontal therapy on pregnancy outcome in women affected by periodontitis. Periodontal therapy in the study included plaque control instructions and scaling and root planing performed under local anaesthesia. The outcome measures assessed were gestational age and birth weight of the infant. Preterm birth was recorded when delivery occurred at< 37 weeks of gestation and low birth weight was recorded when the infant weighed <2500 gm. The author concluded that non-surgical periodontal therapy can reduce the risk for preterm births in mothers who are affected by periodontitis. The author also concluded that periodontitis can influence pregnancy outcomes adversely. Non surgical periodontal therapy aimed at reducing the microbial load and thereby decreasing the inflammatory response, may help to reduce the risk of adverse pregnancy outcomes.

Siqueira et al[25] (2007) conducted a study to determine the association between maternal periodontitis and preterm birth, low birth weight and intrauterine growth restriction. The study showed a risk association between maternal periodontitis and adverse pregnancy outcomes. Results emphasized the importance of periodontal care in prenatal health programs.

Horton et al[26] (2008) conducted a study to determine whether maternal periodontal disease in early pregnancy is associated with elevated serum C-reactive protein (CRP) levels and whether maternal race influences the relationship between maternal periodontal disease and systemic inflammatory responses among African American women. The author found that maternal periodontitis was associated with maternal inflammation as measured by CRP, among African American women but not white women. The reasons for these findings were unclear but were explained by racial differences in oral microbiology, maternal genetic predisposition to proinflammatory responses to microbial challenges, or maternal behavioural differences that predispose to oral infection and subsequent inflammation.

Novak et al[27] (2008) evaluated seven target bacteria, Aggregatibacter actinomycetem- comitans, Porphyromonas gingivalis, Treponema denticola, Tannerella forsythia, Prevotella intermedia, Campylobacter rectus and Fusobacterium nucleatum in subgingival dental plaque of pregnant women in the Obstetrics and Periodontal therapy(OPT) study and their association with birth outcomes. The results of the study indicated that the baseline subgingival bacterial profiles obtained in the second trimester of pregnancy do not differ significantly between women who eventually deliver either preterm or full term infants; periodontal intervention during the second and third trimesters of pregnancy significantly reduced the numbers and proportions of

subgingival periodontal pathogens as well as the total bacterial load. The author concluded that in pregnant women with periodontitis, non surgical periodontal therapy significantly reduced levels of periodontal pathogens. Changes in the bacteria resulting from therapy were not associated with preterm birth.

Agueda et al[28] (2008) conducted a study to determine the association between periodontitis and the incidence of preterm birth (PB), low birth weight (LBW) and preterm low birth weight (PLBW). In this study no relationship was found between socioeconomic status and adverse pregnancy outcomes and all participants had free access to medical and prenatal medical care. The author concluded that there is a modest association between periodontitis and PB but not between periodontitis and LBW or PLBW.

Ebersole et al[29] (2009) described the systemic immune responses in pregnancy and periodontitis and conducted a study to determine if serum levels of IgG measured at baseline and during pregnancy to A. actinomycetemcomitans, campylobacter rectus, Fusobacterium nucleatum, P gingivalis, P intermedia, Tannerella forsythia and T denticola were related to adverse pregnancy outcomes. The author concluded that live pre term birth is associated with decreased levels of IgG antibody to periodontal pathogens in women with periodontitis when assessed during the second trimester. Changes in IgG antibody during pregnancy are not associated with birth outcomes.

Preeclampsia

It is the development of hypertension with proteinuria or edema or both due to pregnancy or the influence of a recent pregnancy. Usually occurs after the 20th week of gestation. Termination of pregnancy results in resolution of signs and symptoms.

Risk factors:

Primiparity (first birth), nulligravidity (no previous pregnancy), first pregnancy with a newer partner, preeclampsia in previous pregnancies, age <20yrs or >35yrs, pre-existing hypertension, renal diseases and diabetes, familial history of preeclampsia or eclampsia, uterine malformation, obesity, multiple pregnancy, couples conceiving shortly after beginning of their sexual relationship (less than 4 months), hydatidiform mole (rapidly growing placenta but no fetus) and fetal hydrops (edema).[30]

Signs and symptoms

Systolic Blood pressure (B.P) of 140mmHg or more or a rise of 30 mmHg or more above the women's usual systolic B.P, diastolic B.P of 90mmHg or more or a rise of 15mmHg or more above the women's usual diastolic B.P recorded on 2 occasions 6 hrs apart with the women at bed rest. The hypertension associated with preeclampsia results in a unique renal lesion, glomerular endotheliosis. It is characterized by hypertrophy of the intracapillary cells and enlarged and swollen glomerular capillary endothelial cells. More severe manifestations of preeclampsia may include coagulation disorders, renal lesions, liver dysfunction and abnormalities of the central nervous system, even leading to the convulsive characteristic of eclampsia.[30]

Pathophysiology

Extensive cardiovascular changes occur in pregnancy in order to meet the metabolic needs of the fetus. In the early stages of pregnancy the total blood volume is increased to help serve the added needs of the uterus and placenta, among other functions. Blood pressure declines during the second trimester, and then resumes the first trimester levels. Prostaglandin formation is increased and the ratio of the vasodilatory prostanoid PGI_2 to the vasoconstrictor thromboxane A_2 (TXA_2) is increased, leading to generalized systemic vasodilation. In preeclampsia peripheral vascular adaptation to pregnancy is inadequate leading to a lack of increase in total plasma volume and sensitization to vasoconstrictor agonists. A stressed placenta and TXA_2 over production from platelets lead to a prostacyclin / TXA_2 imbalance, promoting peripheral vasoconstriction and associated hypertension. Preeclampsia is also associated with activation of the coagulation cascade especially involving platelets which may lead to the formation of micro thrombi and the reduction of organ perfusion.

Abnormal placentation is another important characteristic of preeclampsia. Normal placentation involves the transformation of the terminal branches of the maternal uterine arteries (the spiral arterioles) from thick walled, muscular arteries into dilated flaccid vessels that permit delivery of greater volumes of blood to the uteroplacental unit. The spiral arterioles are invaded by placental cytotrophoblast cells which replace the endothelium and muscular wall and convert them into thin walled, low resistance vessels during the first trimester. Successful trophoblastic invasion allows the fetus to receive adequate supplies of oxygen and nutrients. In preeclampsia trophoblastic invasion of the spiral arteries is impaired and at least 1/3rd escape trophoblastic invasion. They remain thick walled and muscular leading to reduced placental perfusion and ischemia. Local vessel pathology may be due to TNF-α production by activated decidual leukocytes or to the

altered production of growth factors such as VEGF. The pathology has been described as the formation of atherosclerotic-like lesion of the spiral arteries and termed atherosis.[31]

One of the commonly proposed mechanisms is that the endothelial dysfunction associated with preeclampsia may result from a generalized maternal intravascular hyper inflammatory state. Cytokines including TNF-α and interleukins may contribute to the associated oxidative stress. Oxygen free radicals may lead to the formation of self propagating lipid peroxides that propagate highly toxic radicals, which in turn injure endothelial cells. Such injury modifies endothelial cell production of nitric oxide and interferes with prostaglandin balance. Other consequences of oxidative stress include activation of microvascular coagulation, increased capillary permeability and the production of lipid laden foam cells which are the characteristic feature of atherosis. Acute atherosis, the placental lesion of preeclampsia share with atherosclerosis a similar pathology, pathogenesis (inflammation) and clinical setting (endothelial cell damage). It is also characterized by focal endothelial disruption, fibrinoid necrosis of the arterial wall, infiltration of the perivascular spaces by mononuclear cells, an accumulation of lipid laden macrophages and lipoprotein deposition.[32]

There is increasing evidence connecting chronic infection and the initiation of atherosclerosis. Reports have shown a correlation between the occurrence of atherosclerosis and the presence of at least two types of microorganisms- Herpes viruses and Chlamydia pneumoniae. Periodontal pathogens such as Bacteroides forsythus have been detected in atherosclerotic plaques. There are studies suggesting an association between specific chronic infection such as periodontitis and an increased risk for coronary vascular disease and stroke. The chronic inflammatory burden of periodontal infection, together with evidence linking periodontitis with atherosclerosis and generalized hyper inflammatory state, provide the basis of the hypothesis concerning a possible association between periodontal disease and preeclampsia.

Riche et al[30] (2002) conducted a study to determine whether maternal periodontal disease increases the risk for preterm delivery among preeclamptic women. Women were enrolled prior to their 26 week of gestation. Periodontal status was assessed at baseline and at delivery. The author concluded that mothers with preeclampsia may be at greater risk for preterm delivery if periodontal disease is present early in pregnancy or progress during pregnancy.

Barak et al [31] (2005) conducted a study to investigate a possible link between preeclampsia and chronic periodontal infection. 30 primigravidas, 15 suffering from preeclampsia, had full mouth periodontal examinations. GCF samples were taken for immunological assessment. Similar examinations and sampling were performed in 15 age and maternal status matched controls. The results of the study suggest a possible role for periodontal inflammation in the pathogenesis of preeclampsia. Among the preeclampsia patients the periodontal disease was more severe. Levels of proinflammatory mediators IL-1β, TNF-α and PGE_2 were also higher in the preeclampsia group.

Contreras A et al[32] (2006) conducted a study to determine the effect of periodontitis and the subgingival microbial composition on preeclampsia. Preeclampsia was defined as blood pressure ≥140/90 mm Hg and ≥2+ proteinuria, confirmed by 0.3g proteinuria / 24 hours urine specimens. The author concluded that chronic periodontal infection increases the risk of developing preeclampsia in pregnant women. They stated that maternal chronic periodontal disease is a risk factor for children with low birth weight among preeclamptic women compared to non- preeclamptic women.

Pitiphat W et al[33] (2006) conducted a study to examine the relationship between periodontitis and plasma CRP levels among pregnant women .The author found 65% higher CRP levels among pregnant women with periodontitis compared to periodontally healthy women. The author concluded that periodontitis is associated with increased plasma CRP levels in early pregnancy and raise the possibility that CRP may mediate the association of periodontitis with adverse pregnancy outcomes.

Khader YS et al[34] (2006) conducted a study to determine the association between periodontal parameters and preeclampsia among women in the north of Jordan. The author concluded that apart from the general variables that are well known to be associated with preeclampsia, the only dental parameter that was significantly associated was the number of decayed surfaces. There was no association found between any periodontal parameter and preeclampsia in this study.

Cota Lom et al[35] (2006) conducted a study to determine whether periodontitis is associated with an increased risk of preeclampsia. Preeclampsia was defined as blood pressure > 140/90 mm Hg and ≥1+ proteinuria after 20 weeks of gestation. The author concluded that maternal periodontitis is associated with an increased risk of preeclampsia. The study emphasized that

primary health care services must be able to diagnose and control periodontal disease during pregnancy and managing periodontal disease may represent a novel strategy to reduce the incidence and/or complications from this pregnancy hypertensive disorder.

Xiong et al[36] (2006) had done a systematic review to examine the existing evidence on the relationship between periodontal disease and adverse pregnancy outcomes. Twenty-five studies were identified. Of the chosen studies, 18 suggested an association between periodontal disease and increased risk of adverse pregnancy outcome and 7 found no evidence of an association. The authors concluded that periodontal disease may be associated with an increased risk of adverse pregnancy outcome.

Vettore et al[37] (2006) had done a systematic review of epidemiological studies on periodontal infection and pregnancy outcomes. Out of 36 analytical studies in the study 26 studies reported the association between periodontal disease and adverse pregnancy outcomes.

Barak S et al[38] (2007) conducted a study with a purpose to explore the possibility that periopathogenic bacteria may translocate into the placental tissues of women with preeclampsia. In this study polymerase chain reaction (PCR) was used to detect A. actinomycetemcomitans, F. nucleatum ssp, P. gingivalis, P. intermedia, T. forsythensis and T. denticola. Bacterial counts were statistically significantly higher in the preeclampsia group for the entire periopathogenic bacteria examined. The author concluded that the significant presence of periopathogenic microorganisms or their products in human placentas of women with preeclampsia may suggest a possible contribution of periopathogenic bacteria to the pathogenesis of this syndrome.

Horton AL et al[39] (2009) conducted a study to examine the relationship between maternal periodontal disease and plasma angiogenic factor expression of soluble fms-like tyrosine kinase (sFlt)-1. Maternal plasma was collected at delivery. sFlt-1 was measured with an immunoradiometric assay. The author concluded that fetal exposure to oral pathogens has increased plasma levels of sFlt-1.

Srinivas et al[40] (2009) have studied on 786 women with and without periodontitis to compare the risk of a composite of adverse pregnancy outcomes and single pregnancy outcomes of preterm birth, preeclampsia, fetal growth restriction or perinatal death. In this study after adjusting for the confounding variables no association was found between periodontal disease and the composite outcomes and individual outcomes of preeclampsia or preterm birth.

Cruz et al[41] (2010) studied to evaluate whether periodontal therapy among pregnant women would reduce the incidence of low birth weight. They stated that frequency of low birth weight among the women with treated periodontitis was 9.22%, while it was 13.10%with untreated group. The author concluded that periodontal therapy is a protective factor for birth weight.

Kunnen et al[42] (2010) reviewed the possible relationship between periodontal disease and preeclampsia, a major pregnancy complication. 12 observational studies and 3 randomized control trials were included in the review. 8 observational studies reported association while 4 studies showed no association. None of the randomized control trials reported reductions in preeclamptic rates after periodontal therapy.

Fogacci et al[43] (2011) reviewed the randomized controlled trials that evaluated the effect of periodontal therapy on preterm birth and low birth weight (LBW). Results of metaanalysis did not support the hypothesis that periodontal therapy reduces preterm birth and LBW indices.

CONCLUSION

The periodontal diseases share many common risk factors with preterm low birth weight. Examples include age, socioeconomic status and smoking .Studies to date have only shown an association between the two conditions, and this does not indicate a causal relationship. Since the inflammatory mediators that occur in the periodontal diseases also play an important part in the initiation of labour, there are plausible biological mechanisms that could link the two conditions. The challenge for the future is to characterize the nature of the factors that predispose a mother to give birth prematurely to infants less than 2500 g and to assign relative probabilities to each condition. Larger prospective studies and interventional studies will be necessary before periodontitis can be considered as a causal factor for PLBW.

END NOTE

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Conflict of Interest: None declared

Editor's Remarks: This extensive article reviews the causes of adverse pregnancy outcome and discusses the effects of periodontal diseases on pregnancy. Periodontal diseases in the pregnant mother can lead to adverse pregnancy outcome s which can lead to preterm low birth weight babies.

REFERENCES

1. Newman, Takei, Klokkevold, Carranza. Clinical Periodontology. 10th ed. St Louis Missouri; Saunders: 2007.
2. Offenbacher S, Katz V, Fertik G, et al. Periodontal infection as a possible risk factor for preterm low birth weight. J Periodontol 1996; 67:1103-1113.
3. Bearfield C, Davenport ES, Sivapathasundaram V, Allaker RP. Possible association between amniotic fluid micro-organism infection and microflora in the mouth. BJOG 2002; 109:527-33.
4. Goldenberg RL, Culhane JF, Iams JD, Romero R. Preterm birth 1. Epidemiology and causes of preterm birth. Lancet 2008; 371:75-84.
5. Agueda A, Ramo´n JM, Manau C, Guerrero A, Echeverrı´a JJ. Periodontal disease as a risk factor for adverse pregnancy outcomes: A prospective cohort study. J Clin Periodontol 2008; 35:16-22.
6. Karinen L, Pouta A, Bloigu A, et al. Serum C-reactive protein and Chlamydia trachomatis antibodies in preterm delivery. Obstet Gynecol 2005; 106:73-80.
7. Tridapalli E, Capretti MG, Sambri V, et al. Prenatal syphilis infection is a possible cause of preterm delivery among immigrant women from Eastern Europe. Sex Transm Infect 2007; 83:102-105.
8. Wimmer G, Pihlstrom BL. A critical assessment of adverse pregnancy outcome and periodontal disease. J Clin Periodontol 2008; 35(8): 380-397.
9. Williams CECS, Davenport E, Sterne JAC, Sivapathasundaram V, Fearne JM, Curtis MA. Mechanisms of risk in preterm low-birth weight infants. Periodontol 2000; 23:142-150.
10. Offenbacher S, Jared HL, O'Reilly PG, Wells SR, Salvi GE, Lawrence HP, et al. Potential pathogenic mechanisms of periodontitis associated pregnancy complications. Ann Periodontol 1998; 3:233-250.
11. Mazor M, Wiznitzer A, Mlymon E, Leiberman JR, Cohen A. Changes in amniotic fluid concentrations of prostagalandins E2 and F2 in women with preterm labour. Isr J Med Sci 1990; 425-428
12. Tamatani T, Tsunoda H, Iwasaki H, Kaneko M, Hashimoto T, Onozaki K. Existence of both IL-1α and IL-1β in normal amniotic fluid: Unique high molecular weight form of IL-1. Immunology. 1988 Nov; 65(3): 337–42.
13. Kent AS, Sun MY, Sulivan MH, Elder MG. The effects of IL-1α and IL-1β on prostaglandin production by cultured human fetal membranes. Prostaglandins. 1993 Jul;46(1):51-9.
14. Romero R, Brody DT, Oyarzun E. Infection and labour. III. Interleukin-1: A signal for onset of parturition. Am J Obstet Gynecol. 1989 May;160(5 Pt 1):1117-23.
15. Dasanayake AP. Poor periodontal health of the pregnant woman as a risk factor for low birth weight. Ann Periodontol 1998 Jul;3(1):206-12.
16. Jeffcoat MK, Hauth JC, Geurs NC, Reddy MS, Cliver SP, Hodgkins PM, et al. Periodontal disease and preterm birth: Results of a pilot intervention study. J Periodontol 2003; 74: 1214-1218.
17. Lopez NJ, Da Silva I, Ipinza J, Gutierrez J. Periodontal therapy reduces the rate of preterm low birth weight in women with pregnancy associated gingivitis. J Periodontol 2005 Nov;76(11 Suppl):2144-53.
18. Noack B, Klingenberg J, Weigelt J, Hoffmann T. Periodontal status and preterm low birth weight: a case control study. J Periodont Res; 2005 Aug;40(4):339-45.
19. Khader YS, Ta'ani Q. Periodontal diseases and the risk of preterm birth and low birth weight: A metaanalysis. J Periodontol 2005; 76:161-165.
20. Offenbacher S, Lin D, Strauss R, McKaig R, Irving J,Baross SP, Moss K, Baroww DA, Hefti A, Beck JD. Effects of periodontal therapy during pregnancy on periodontal status, biologic parameters, and pregnancy outcomes: A pilot study. J Periodontol 2006; 77:2011-2024.
21. Gazolla CM, Ribeiro A, Moyses MR, Oliveira LAM, Pereira LJ, Sallum AW. Evaluation of the incidence of preterm low birth weight in patients undergoing periodontal therapy. J Periodontol; 2007 May;78(5):842-8.
22. Leon R, Silva N, Ovalle A, Chapparo A, Ahumada A, Gajardo M, et al. Detection of Porphyromonas gingivalis in the amniotic fluid in pregnant women with a diagnosis of threatened premature labour. J Periodontol; 2007 Jul;78(7):1249-55.
23. Toygar HU, Seydaoglu G, Kurklu S, Guzeldemir E, Arpak N. Periodontal health and adverse pregnancy outcome in 3,576 Turkish women. J Periodontol 2007; 78:2081-2094.
24. Tarannum F, Faizuddin M. Effect of periodontal therapy on pregnancy outcomes in women affected by periodontitis. J Periodontol. 2007 Nov;78(11):2095-103.
25. Siqueira FM, Cota LOM, Costa JE, Haddad JPA, Lana AMQ, Costa FO. Intrauterine growth restriction, low birth weight, and preterm birth: adverse pregnancy outcomes and their association with maternal periodontitis. J Periodontol 2007; 2007 Dec;78(12):2266-76.
26. Horton AL, Boggess KA, Moss KL, Jared HL, Beck J, Offenbacher S. Periodontal disease early in pregnancy is associated with maternal systemic inflammation among African American women. J Periodontol. 2008 Jul;79(7):1127-3.
27. Novak MJ, Novak KF, Hodges JS, Kirakodu S, Govindaswami M, Diangelis A, et al. Periodontal bacterial profiles in pregnant women: response to treatment and associations with birth outcomes in the obstetrics and periodontal therapy (OPT) study. J Periodontol. 2008 Oct;79(10):1870-9.
28. Agueda A, Ramon JM, Manau C, Guerrero A, Echeverria JJ. Periodontal disease as a risk factor for adverse pregnancy outcomes: a prospective cohort study. J Clin Periodontol. 2008 Jan;35(1):16-22. Epub 2007 Nov 21
29. Ebersole JL, Novak MJ, Michalowicz BS, Hodges JS, Steffen MJ, Ferguson JE, et al. Systemic immune responses in pregnancy and periodontitis: relationship to pregnancy outcomes in the obstetrics and periodontal therapy (OPT) study. J Periodontol. 2009 Jun;80(6):953-60
30. Riche EL, Boggess KA, Lieff S, Murtha AP, Auten RL, Beck JD, Offenbacher S. Periodontal disease increases the risk of preterm delivery among preeclamptic women. Ann Periodontol. 2002 Dec;7(1):95-101.
31. Barak OO, Barak S, Ohel G, Oettinger M, Kreutzer H, Peled M, et al. Severe pregnancy complication (Preeclampsia) is associated with greater periodontal destruction. J Periodontol 2005; 76:134-137.
32. Contreras A, Herrera JA, Soto JE, Arce RM, Jaramillo A, Botero JE. Periodontitis is associated with preeclampsia in pregnant women. J Periodontol 2006; 77:182-188.

33. Pitiphat W, Joshipura KJ, Rich-Edwards JW, Williams PL, Douglass CW, Gillman MW. Periodontitis and plasma C-reactive protein during pregnancy. J Periodontol. 2006 May; 77(5): 821–825.
34. Khader YS, Jibreal M, Al-Omiri M, Amarin Z. Lack of association between periodontal parameters and preeclampsia. J Periodontol. 2006 Oct;77(10):1681-7.
35. Cota LOM, Guimaraes AN, Costa JE, Lorentz TCM, Costa FO. Association between maternal periodontitis and an increased risk of preeclampsia. J Periodontol 2006; 77:2063-2069.
36. Xiong X, Buekens P, Fraser WD, Beck J, Offenbacher S Periodontal disease and adverse pregnancy outcomes: a systematic review. BJOG. 2006; 113(2):135-43.
37. Vettore MV, Lamarca Gde A, Leao AT, Thomaz FB, Sheiham A, Leal Mdo C. Periodontal infection and adverse pregnancy outcomes: a systematic review of epidemiological studies. Cad Saude Publica 2006; 22(10):2041-53.
38. Barak S, Oettinger-Barak O, Machtei EE, Sprecher H, Ohel G. Evidence of periopathogenic microorganisms in placentas of women with preeclampsia. J Periodontol 2007; 78:670-676.
39. Horton AL, Boggess KA, Moss KL, Beck J, Offenbacher S. Maternal periodontal disease and soluble Fms-like Tyrosin kinase-1 expression. J Periodontol. 2009 Sep;80(9):1506-10.
40. Srinivas SK, Sammel MD, Stamilio DM, Clothier B, Jeffcoat MK, Parry S, et al. Periodontal disease and adverse pregnancy outcomes: is there an association? Am J Obstet Gynecol. 2009 May;200(5):497.e1-8.
41. Cruz SS, Costa MCN, Gomes Filho IS, Barreto ML, Santos CST, Martins AG, et al. Periodontal therapy for pregnant women and cases of low birth weight: An intervention study. Pediatr Int. 2010 Feb;52(1):57-64
42. Kunnen A, van Doormaal JJ, Abbas F, Aarnoudse JG, van Pampus MG, Faas MM. Periodontal disease and pre-eclampsia: a systematic review. J Clin Periodontol 2010; 37: 1075–1087.
43. Fogassi MF, Vettore MV, Thome leao AT. The Effect of Periodontal Therapy on Preterm Low Birth Weight: A Meta-Analysis. Obstet Gynecol. 2011 Jan;117(1):153-65