IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861. Volume 9, Issue 6 (Sep.- Oct. 2013), PP 64-67
www.iosrjournals.org

Impact of Periodontal Disease on Low Birth Weight and Preterm Birth

Dr. K. Malathi, MDS, PGDHA[1,] Dr. N. S. Nalni[2]
[1]*Head of the department of periodontics, Tamil Nadu Govt. Dental College & Hospital, Chennai.*
[2] *Post Graduate Student, Department of Periodontics, Tamil Nadu Govt. Dental College & Hospital, Chennai.*

Abstract: *Preterm birth represents a major problem in the world because of its increasing frequency and accompanying socioeconomic impact. Globally prematurity is the leading cause of newborn deaths and now the second leading cause of death after pneumonia under age of five. Periodontitis and adverse pregnancy outcomes may be linked through a chronic, systemic inflammatory challenge to the mother and fetus in response to pathogens. Several studies in the past have demonstrated an association between infection and preterm birth. However several other risk factors need to be considered. The principle reasons cited for the continued high rate of preterm and low birth weight is poor understanding of the risk factors associated. This article explains the association between preterm birth and periodontitis by stating various complications of preterm birth, pathophisiology of the associated risk factors like bacterial infection, viral infection, gene polymorphism, adaptive immune responses, preeclampsia. The early diagnostic predictors in the form of biomarkers and the effect of periodontal therapy in preventing the preterm birth are discussed. As Peridontitis is an important risk factor for preterm birth there is a need to expand preventive measures during pregnancy to avoid this adverse effect.*

Keywords: *adversepregnancyoutcome, lowbirthweight, periodontitis, pretermbirth.*

I. Introduction

Periodontal disease is a chronic destructive disease presenting as a low grade infection dominated by gram negative microaerophilic organism resulting in local and systemic inflammatory and immune response. Periodontal disease is the second most prevalent oral disease. In 19th and early 20th century the theory of focal infection was reported, which stated that the foci of sepsis were responsible for the initiation and progression of a variety of systemic diseases. Periopathogenic organisms and their products may have wide range of effects most likely mediated through stimulation of host cytokine production in target tissue.

Galloway(1931) reported that periodontal disease of pregnant women is associated with adverse pregnancy outcome . Preterm low birth weight babies is most commonly associated with periodontitis. Offenbacher et al(1996) reported an association between periodontitis and Preterm low birth weight(PTLW), stating that maternal periodontal disease could lead to 7 fold increase in risk of preterm delivery. Preterm birth(PTB) (WHO 1992) is defined as delivery before the end of 37wks of gestation(<259d). Less than 32wks is termed as very preterm and less than 28wks is termed as extremely preterm. Low birth weight(LBW) is defined as infants weighing <2500g at birth. Very low birth weight is <1500g and extremely low is <1000g.

PTB represents as a major problem for modern obstetrics because of its increasing frequency and accompanying socioeconomic impact. [(1)]This article mainly focuses on periodontal disease as a risk factor for PTB and LBW by discussing on various mechanisms leading to PTB. The influence of periodontal therapy on PTB, possible means of predicting through biomarkers in pregnant women and a few suggestions in preventing this adverse outcome are also discussed.

II. Health sequences to the Newborn with PTB/LBW[2]

2.1Short term sequences

- Respiratory distress syndrome
- Intraventricular haemorrhage
- Periventricular haemorrhagic infarction
- Necrotising enterocolitis
- Bronchopulmonary dysplasia
- Sepsis
- Patent Ductus Arteriosus

2.2 Long Term Consequenses

- Cerebral Palsy

- Attention deficit disorder
- Retinopathy of prematurity
- Mental retardation
- Cardiovascular malformation

2.3 Effect on oral growth and development.[3]

Generalized enamel hypoplasia, localized enamel hypoplasia, Crown dilacerations, Palatal distortions which are usually associated with traumatic laryngoscopy and prolonged intubation and low rate of dental development particularly before 6yrs of age are reported.

III. Risk Factors of Preterm birth.[4]

Denise M Main(1985) summarized various risk factors which were found to be associated with PTB

3.1 Demographic risk: Maternal age (<19yrs/>40yrs), education, Race (Black are 2 times more prone), Low socioeconamis status, Height of mother(<150cm), weight(<20 pounds).

3.2 Behavioural risk: Cigarette smoking, cocaine, alcohol, coffee, tea, poor nutrition, extensive physical activity.

3.3 Health care risk: Poor Obstetric history of previous PTB was reported to be associated with recurrence risk of 17-40%.

3.4 Selected medical and surgical disease: Sickle cell trait, uterine malformation, heart disease, diabetes mellitus, hypothyroidism, hyperthyroidism, nephritis, urinary tract infection.

3.5 Current pregnancy complications: Multiple gestation, placental pathology, abnormalities in amniotic fluid volume, fetal abnormalities.

3.6 Infections: Genitourinary infection[5], bacterial vaginosis, Periodontal disease as an important and independent risk factor[6].

IV. Pathophysiological mechanisms and factors associated with periodontal disease leading to PTB/LBW

4.1 Pathogenic Microflora contributing to PTB/LBW : It is suggested that oral infection may contribute upto 50% of PTB's. This may include systemic infections (Pneumania, Genitourinary tract infections, bacterial vaginosis, Chlamydia trachomatis, Syphilis)[7] and oral inflammatory diseases like Mucositis, Gingivitis and Periodontal infection[8].

4.1.1 Specific Bacterial Colonization

Some of the suggested organisms in studies favouring PTB are P.Gingivalis, T.Forsythia, T.Denticola, F.Nucleatum[9]. Chronic periodontitis is strongly associated with preterm labor, PTB and LBW. The presence of periodontal pockets, clinical attachment loss and gingival bleeding are shown to be important factors[10] .P.Gingivalis is a gram negative anaerobic bacteria and has bio active components including lipopolysaccharide capsule and fimbriae on cell surface.

Delivery is started in the late stage of gestation by events including changes of various hormones and stimulation of biomechanical molecules by fully grown fetus. The initial signals enhance the production of proinflammatory molecules including IL-6, IL-8, IL-1b. These factors lead to uterine contration, cervical ripening, directly or indirectly which leads to parturition.

Two possible mechanisms linking periodontal disease and PTLBW are

- The bacteria in periodontal lesions migrate to the materno-fetal unit via the blood and directly cause adverse pregnancy outcomes[11,7].-Lopez etal(1987), Romero etal(1982), Gibbs RS(1992).
- Proinflammatory molecules produced by the periodontal organisms before the later stages of gestation cause parturition.

Cytokines which are capable of eliciting the acute phase response, are a component of this inflammatory response and are classified as

1.Proinflammatory molecules, which initiate or enhance a cascade of events. Example TNFα(Tumour necrosis factor-α) and IL-1(interlukin).

2.Those which propagate many of the systemic manifestation of acute phase response.Example IL-6,IL-11.
3.Anti inflammatory which down regulate the acute phase response. Example IL-10,TGF-β(transforming growth factor-β)[12].

P.Gingivalis lipopolysaccharide induces IL-6, 8 production via both TLR-2 and TLR-4 in chorion derived cell. [13].Increased systemic levels of pathogenic microorganisms , their endotoxin or directly via inflammatory mediators especially Prostaglandin E2($PGE_{2)}$ contribute to PTB/LBW.[14] The actions of prostaglandin are effected through specific receptors. PGE2 induces myometrial contractions by binding to EP-1 and EP-3 receptors, which mediate contractions through mechanisms that lead to increased calcium mobilization and reduced levels of production of inhibition of intracellular cAMP. Prostaglandins also enhance the production of matrix metalloproteinases (MMP) in the cervix and decidua to promote cervical ripening and decidual and fetal membrane activation. PGF2α binds to FP receptors to induce myometrial contractions. In contrast, in the lower uterine segment PGE2 induces myometrial relaxation by binding to EP-2 and EP-4 receptors that increase the level of cAMP formation.

Prostaglandins are formed from arachidonic acid by PGHS(prostaglandin H2 synthetase). In turn, prostaglandins are metabolized to inactive forms by the actions of PGDH. Cortisol, CRH(corticotropic releasing hormone), and estrogens stimulate PGHS activity and cortisone and CRH also inhibit PGDH expression. Thus, increases in fetal steroid hormone production following fetal HPA(Hypothalamic pituitary axis) activation leads to a net increase in prostaglandin levels. Similarly, proinflammatory cytokines such as IL-1 and
tumor necrosis factor alpha (TNF-α) up-regulate PGHS expression and down-regulate PGDH expression leading to prostaglandin synthesis associated with preterm delivery in the setting of infection[15]

Systemic antibody Responses to selected periodontal Bacteria[16].

Oral bacteria trigger local and systemic adaptive immune responses in healthy adults and childre.PTB is associated with low levels of IgG antibody to periodontal pathogens in women with periodontitis.Madionos et al, found that elevated IgG antibody to certain oral bacteria in mothers serum was related to decreased rate of PTB and increased birth weight .Decreased levels of antibody to P.Gingivalis are reported in women during second trimester, who delivered at preterm. Increased levels of serum antibody to F.Nucleatum were elevated in women who suffered fetal loss.

4.I.2 Human Immuno deficiency virus-a factor for PTB[17]

There is a positive risk of having adverse neonatal outcomes in HIV infected women who had moderate periodontitis .In the of (HAART) Highly active anti retroviral therapy, a combination of anti retroviral medications administered during preconception period increased of PTB/LBW.

II. Gene polymorphism as a factor to cause PTB[18]

FCγR11b(CD32B) is a human type 2 low infinity receptor of IgG .This receptor is encoded by three highly homologous genes-FCRY11a,FCYR11b,FCYR11c, that are clustered on chromosome Iq23.One of the polymorphism,FCγR11b-1232T, in patient with periodontitis was associated with increase in serum specific I_gG_2 levels against the outer membrane protein from P.Gingivalis.Thus FCYR11b gene polymorphism may mediate the relationship between periodontitis and PTB. FCγR11b-nt645+25AA carriers are more likely to experience preterm birth than FCγR11b-nt645+25AG and GG carriers. Also women with FCγR11b-nt645+25AG exhibited a greater tendency to have periodontitis than those with FCγR11b-nt645+25A.

4.3 Pre-eclampsia poses a risk factor of PTB[19]

Pre-eclampsia is usually defined as maternal systolic pressure>/= 140mmHg or diastolic pressure>/=90mmHg with proteinuria. The syndrome is characterized by inappropriate inflammatory and abnormal vascular response to placentation which causes endothelial dysfunction resulting in maternal hypertention during pregnancy(Sibbas et al).The hypothetical mechanism is that inflamed periodontal tissue release elevated levels of C-Reactive protein and other inflammatory mediators(PGE_2) which enter the systemic circulation and induces inflammation that damages the placenta and causes pre-eclampsia

V. Early Prediction and Possible Prevention of PTB

Periodontal disease is a source of persistent infection and raises the plasma levels of CRP(C reactive protien) by 14wks of gestation(Pitiphat et al)[20].Depending on the source of the sample(maternal serum,amniotic fluid, vaginal swabs) many diagnostic markers can predict the PTB before 21wks of gestation.Ex: wbc count, IL-1b, IL-6, IL-8 , alkaline phosphatase in serum [21] and fibronectin in cervical /vaginal secretions indicates the border between the chorion and deciduos has been destructed.

BANA Test[22] :P.Gingivalis, T.Forsythia, T.Denticola, posses a trypsin like enzyme that can hydrolyse the synthetic trypsin substrate- Benzoyl-DL arginine-Naphthylamide(BANA).The presence of these organisms

in the sub gingival plaque hydrolyse BANA using a 5minute chais side assay. The third trimester bacterial status of subgingival plaque may be an important predictor of PTBs.

VI. Non-Surgical Periodontal therapy in pregnant mothers.

Non-Surgical Periodontal Therapy which includes Scaling, root planning, plaque control decreases the levels of inflammatory cytokines[23].This serves as a protective factor promoting the birth of children with normal weight.

VII. Conclusion

PTB / LBW and thus the prematurity is responsible for 70% of perinatal deaths(Goldenberg et al).It occurs in about 10% of pregnancies and is responsible for 50% of neurological disorders in the new born(McCornick1985). Periodontal disease is an independent risk factor for adverse outcome of pregnancy.Non-Surgical periodontal therapy significantly reduces the rate of PTLBW and improved the general health of women with periodontal disease.The various biomarkers suggested may be used as tools to predict the risk associated and early intervention may be done to prevent the adverse outcome. In HIV associated periodontitis the pathophysiological mechanism that relates the viral load and preterm birth requires further conformational studies. The earliest biomarker of PTB associated with periodontitis and periodontal therapy to completely avoid this adverse outcome may challenge the scope for further research.

References

[1] WHO-International statistical of diseases and related health problems.*Tenth vision*. Geneva: WHO 1992.

[2] Bryan S.Michalowtz and Robert Dwand,Maternal periodontal disease and spontaneous preterm birth*, Periodontology 2000,44*, 2007,103-112.

[3] W.Kim Seow MDSc, DDSc, Phd, FRACDS, Effect of preterm birth on oral growth and development, *Australian dental journal*, *42(2)* ,1997,85-91.

[4] AN Guimaraes, AS Mato, LO Miranda Cota, FM Siqueira and FO corta, Maternal periodontal disease and preterm or extreme preterm birth: An ordinal logistic regression analysis, *Journal of Periodontology, 81(3*), 2010, 350-358.

[5] LA.Schieve, A.Handler, R.Hershow, V.Persky, F.Davis, Urinary tract infection during pregnancy, its association with maternal morbidity and perinatal outcome, *American journal of publichealth, 84(3*), 1994, 405-410.

[6] J.K.Baskaradoss, A.Geevarghese, V.R.Kutty,Maternal Periodontal status and preterm delivery a hospital based case control study, *Journal of periodontal research, 46(5*), 2011, 542-549.

[7] Lorief. Cram, Maria-Isabel Zapata, Eugene C. Toy, and Benton Baker *Am Fam Physician*. 2002 Jan 15;65(2):241-249.,.

[8] Auro Heimonen, Sok-ja-Janket, Risto Kajaa, Leland K Ackerson, Preetika Muthukrishnan, Jukka H.mausman, Oral inflammatory burden and preterm birth, *Journal of Periodontology, 80(6),*2009, 884-891.

[9] Hui-chen chan, Chen-trai Wu, Kathleen B.Welch, and Watter J.Loeshe, Periodontal disease activity measured by the Benzoyl-DL-Arginine Naphthilamide test is associated with preterm births, *Journal of Periodontology, 81(7),* 2010, 982-991.

[10] SA.Santos Pareira, Gealdo.PC, Eduardo Saba, RLG Amaral, SS Morais, AM Gonlalalics, Chronic Periodontitis and preterm labour on Brazilian pregnant women : an association to be analyzed. *Journal of clinical Periodontology, 34(3*), 2007, 208-213.

[11] Bryan.S.Michalowicz, M.John Novak, James s. Hodger, Antony Di Angels, William Buchanan, Panos N.Papanou etal, Serum inflammatory mediators in pregnancy, changes after periodontal treatment and association with pregnancy outcomes, Journal of *Periodontology, 80(11*), 2009, 1731-1741.

[12] K.Hasegawa Nakamura, F.Jateishi, T.Nakamura, Y.Nakajima, k.kawamata , T.Douchi etal, The possible mechanism of preterm associated with periodontopathic P.Gingivalis*, Journal of periodontal research,46(4*), 2011, 497-504.

[13] Romero R, HObbins JC, Mitchell MD, Endotoxin stimulates PGE_2 production by human amnion, *Journal of Obstetrics Gynynecology,71*,1989,211-218.

[14] Offenbacher S, Jared HL, Reilly PG etal, Potential Pathogenic mechanism of periodontal associated pregnancy complications, *Ann Periodontology,3(1),* 1998, 233-250.

[15] Behrman RE, Butler AS, Institute of medicine(us) Committee on understanding premature birth and assessing healthy outcomes (Ed), Biological Pathways leading to Preterm birth, (*Washington DC National Academis Press(US):2007*).

[16] Jeffrey L.Eberson, M.John Novah, Bryan SM, James S. Hodger, Mitchelle J.Steffen, James E Fergusson etal,Systemic Immune Responses in pregnancy and Periodontitis.Relationship to pregnancy outcomes in obstetrics and periodontal therapy(OPT) study,*Journal of Periodontology, 80(6*), 2009,

[17] Pakkaporn Pattrapornan, Timothy A. Deroven, Yupin Songpaissan, Increased risks of preterm birth and a low birth weight baby in Thai Human immunodeficiency Virus-Positive pregnant women with periodontitis, *Journal of Periodontology,83(11),* 2012,1372-1381.

[18] R.Iwanga, N.Sugita, E.hirano, J.Sasahara, A.Kikuchi, K.Tanaka, etal, FCγR11B ppolymorphisms, periodontitis and preterm birth in Japanese pregnant women, *Journal of periodontal research, 46(3*), 2011,292-302.

[19] C.Nabet, N.Lelong, ML Colombrie, M Sixon, AM Goffinet, F Kamineh M etal, Maternal periodontitis and cause of preterm birth, case control epipap study, *Journal of Periodontology,37(1*), 2010, 37-45.

[20] Waranuch Pitiphat, Mathew W .Gilman, Kaumudi J.Joshipura etal, Plasma C-reactive protein in early pregnancy and preterm delivery, *American Journal of Epidemiology, 162(11*), 2005, 1108-1113.

[21] Stephen W. Looney, Treatment of periodontal disease and risk of preterm birth, *Journal of Periodontology, 79(1*), 2008, 1-2.

[22] Francois Goffinet, Primay predictors of preterm labour, *International journal of Obstetrics and gynecology,112(1*), 2005, 38-47.

[23] Fouzia Tarannum and Mohammed Faizudin, Effect of periodontal therapy on pregnancy outcomes in women affected by periodontitis, *Journal of periodontology,78(11*), 2007.