

Maternal Periodontal Disease as a Potential Risk Factor for Preterm Birth and Low Birth Weight

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Abstract

Background and Aim: Periodontal disease may cause adverse pregnancy outcomes such as low birth weight (LBW) or preterm birth (PTB). In the present study, mothers with one of these two delivery complications were analyzed regarding presence/absence of periodontal disease as a possible risk factor in comparison with related medical risk factors.

Materials and Methods: In this cross-sectional study, the sample included 50 women admitted to Afzalipour Hospital in Kerman. All mothers had a history of PTB or LBW in their recent delivery. Medical risk factors including intra-uterine growth restriction (IUGR), premature rupture of the amniotic membrane (PROM) and vaginal bleeding in addition to periodontal parameters including bleeding on probing (BOP), plaque index (PI) and attachment loss were recorded. Descriptive indices, Spearman's coefficient, logistic regression model, and receiver-operating characteristic (ROC) curve were used for data analysis.

Results: All patients had various forms of periodontal involvement; 86% had periodontitis. The frequency of periodontitis was significantly higher than medical risk factors ($P=0.024$). The area under the curve (AUC) demonstrated higher discriminating power for maternal periodontal parameters in comparison with medical risk factors.

Conclusion: Maternal periodontal disease appears to be an independent risk factor for PTB and LBW.

Key Words: Infant, Low Birth Weight; Periodontal Diseases; Pregnancy; Premature Birth

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Introduction

Periodontal disease adversely affects the tooth-supporting structures, and is associated with accumulation of bacteria and their products as well as the release of inflammatory mediators that can adversely affect the placenta [1].

Maternal periodontal disease is an important infectious condition that is believed to increase the risk of pre-eclampsia, intrauterine growth restriction (IUGR), preterm birth (PTB) and low birthweight (LBW) of infants [2]. The level of female sex hormones increases by the end of the 3rd

trimester in pregnancy. Progesterone and estrogen reach peak plasma levels that are 10 and 30 times higher than their level in menstrual cycles, respectively. The progesterone and estrogen hormone receptors have been found in different periodontal cell subsets, considering periodontal tissue as a possible target. During pregnancy, the raised hormonal levels increase the vascular permeability, which in combination with gingival inflammation and bleeding induced by periodontal infection may enhance the leakage of periodontal pathogens into the bloodstream. The hematogenous dissemination of commensal and pathogenic microorganisms could then enable the establishment of a metastatic infection in the fetoplacental unit [3]. Many studies have detected *Bergeyella* spp., *Eikenella corrodens*, *Capnocytophaga* spp., *Parvimonas micra*, *Tannerella forsythia*, *Porphyromonas gingivalis* and/or *Treponema denticola* in certain women with PTB/LBW [3-6]. In addition, the results of an animal study showed that inoculation of *Fusobacterium nucleatum* resulted in selective localization of this microorganism in the placental blood vessels; the resultant infection might lead to premature birth after penetration through the endothelium and the amniotic fluid [7]. Translocation of *Porphyromonas gingivalis* and *Campylobacter rectus* to placental tissues can limit the fetal growth, as contamination with periodontal pathogens increases the inflammatory response in the fetoplacental unit. *Porphyromonas gingivalis* infection can cause an approximately 2-fold rise in the level of circulating pro-inflammatory cytokines [3, 8]. *Porphyromonas gingivalis* is believed to be involved in several pregnancy disorders that include impaired spiral artery remodeling with or without IUGR [9]. Also, Streptococcaceae and Mycoplasmataceae families have shown to be correlated with both periodontitis and adverse pregnancy outcomes [10]. Periodontal therapy can decrease the hazards of PTB in

mothers with periodontitis [11]. Some experimental interventional studies showed that the risk of PTB/LBW decreased after periodontal treatment during pregnancy [12-15]. However, some others did not confirm the hypothesis that periodontal therapy decreases the risk of PTB or LBW [16-18]. Therefore, such an effect has not been definitively proven. The available studies on this topic mainly have a case-control design, and periodontal parameters in mothers with PTB/LBW infants were compared with mothers with full-term infants with normal birth weight [2,13]. However, due to the role of various possible factors in the incidence of LBW/PTW, it is necessary to determine the role of periodontal disease, among other possible risk factors, in this respect.

The purpose of the present study was to assess the role of maternal periodontal disease in the incidence of LBW/PTB in comparison with other possible risk factors.

Materials and Methods

This study was carried out on mothers selected by convenience sampling. The sample size was determined to be 50 based on similar studies [2,19]. The participants consisted of volunteered women who had LBW or PTB in their recent delivery in Afzalipour Hospital in Kerman. The inclusion criteria consisted of an age range of 20-40 years for mothers, and general health with no systemic conditions such as diabetes mellitus, cardiovascular disease, HIV, etc. The exclusion criteria consisted of infants with deficiencies other than LBW, including congenital malformations, infections, complications for mothers during pregnancy such as preeclampsia, mothers who were edentulous in one or both quadrants of the mandible or maxilla, mothers using tobacco or alcoholic drinks, mothers with gingival hyperplasia, and mothers with twins or triplets [2,19]. The examiner was a senior dental student, who was adequately trained before

the study on how to measure periodontal parameters. The student then recorded the periodontal parameters of 10 patients referring to the Department of Periodontics, Faculty of Dentistry and her eligibility for clinical examination of patients was confirmed by a periodontist. Periodontal examinations were carried out in the Obstetrics Department of Afzalipour Educational Center, Kerman University of Medical Sciences, on a chair under adequate lighting, using sterile intraoral examination instruments, including a disposable dental mirror (No.4; Fatah Teb, Sari, Iran), a dental explorer (Fatah Teb, Sari, Iran), a Williams periodontal probe (R&S; Premium Instruments Company, New York, USA), within 3 days after parturition.

Bleeding on probing (BOP), plaque index (PI) and attachment loss were recorded as clinical periodontal parameters. The following classification system was used:

- Gingivitis: No attachment loss
- Mild periodontitis: Attachment loss by 1-2 mm
- Moderate periodontitis: Attachment loss by 3-4 mm
- Severe periodontitis: Attachment loss by ≥ 5 mm

The following non-periodontal parameters at the time of birth were also recorded, using the mothers' hospital records:

Intrauterine growth restriction (IUGR): Ultrasound biometry is the gold standard for evaluation of fetal size and the volume of amniotic fluid. The growth retardation of the fetus was determined by assessing the size of the uterus. Methods such as sequential evaluation of the uterine fundus can help monitor growth continuation. These evaluations were performed by an obstetrician. The size of the uterus was evaluated at every prenatal appointment. A tape measure was used to measure the distance from the top of the pubic symphysis to the dome of the uterine fundus for the gestational age (in weeks)

with standard values [20].

Premature rupture of the amniotic membrane (PROM): PROM was diagnosed with the use of ultrasonic technique by determining the amount of fluid around the fetus through examination by an obstetrician; evidence of diminished amniotic fluid volume may suggest PROM in an appropriate clinical setting, and also by observing leakage of fluid from the uterus, and by collecting fluid and noticing its color change. The alkaline pH of the cervico-vaginal discharge is usually confirmed by observing whether the discharge changes the color of yellow nitrazine paper to blue (nitrazine test) [21].

Vaginal bleeding: Vaginal bleeding was detected by taking history, mothers' reports or noticing by an obstetrician during clinical examination.

Data were analyzed with SPSS version 23 using descriptive statistics, Spearman's correlation coefficient for initial evaluation of the relationship between etiologic variables such as periodontal disease and the incidence of LBW/PTB, a logistic regression model for assessment of the effects of these variables on the incidence of the two abovementioned complications, and receiver-operating characteristic (ROC) curve to investigate the discriminating power of factors involved in the incidence of PTB/LBW. The area under the curve (AUC) was explained as:

- 90-100%: Excellent
- 70-80%: Good
- 60-70%: Poor
- <60%: Very poor

A larger AUC indicated a higher discriminating power for predicting the outcome in question. All the subjects participated in the study after signing informed consent forms, and their demographic data were kept confidential throughout the study. The study was approved by the Ethics Committee of Kerman University of Medical Sciences under the code IR.KMU.REC.1394.518.

Results

In the present study, 50 mothers whose pregnancies had ended up in birth of infants with PTB/LBW were evaluated. The mean age of the subjects was 28.8 ± 4.91 years (range 20-39 years). Most of the women were housewives (92%) and regarding their level of education, 42% and 18% had high school diploma and bachelor's degree, respectively. The mean values of BOP and PI (both determined at four tooth surfaces) were 62.96 ± 22.87 and 89.84 ± 15.18 , respectively. The Pearson's correlation coefficient was 0.32, which showed a significant relationship between these two indices ($P=0.024$).

Table 1 presents the frequency of the most significant risk factors for the incidence of PTB/LBW in the subjects. As shown in Table 1, although PROM had the highest frequency, there were no cases of IUGR. All 50 subjects exhibited some degrees of periodontal disease, and 86% had different forms of periodontitis.

Table 1. Frequency distribution of possible medical and periodontal contributing risk factors to PTB/LBW

Risk Factors	Frequency	Percentage
IUGR	0	0
PROM	22	44
Vaginal bleeding	12	24
Gingivitis	7	14
Mild	1	2
Periodontitis		
Moderate	34	68
Severe	8	16
Total	50	100

Figure 1 shows the ROC curve. As depicted in the graph, the AUC was moderate for periodontal indices (BOP: 75% and PI: 67%) and very poor for medical indices (PROM: 39% and vaginal bleeding: 49%). Therefore, periodontal indices exhibited higher discriminating power for the prediction of

these two complications compared with medical indices. With the use of a logistic regression model in two series, gingivitis and periodontitis variables were considered dependent, and in each series, the relationship between these variables and independent variables such as age, occupation, vaginal bleeding and PROM was evaluated; the results showed no significant relationship ($P>0.05$).

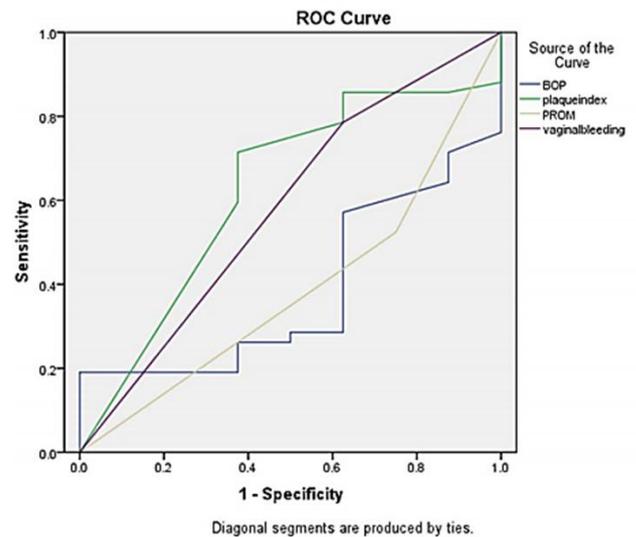


Figure 1. ROC curve for determination of the distinction between possible medical and periodontal contributing risk factors to PTB/LBW

Discussion

The present study assessed the effect of maternal periodontal disease, in comparison with other possible risk factors, on birth of neonates with PTB/LBW. The results showed a significantly higher frequency of periodontitis compared with other risk factors with a role in PTB/LBW. The age range of the subjects in the present study was 20-40 years, and mothers who used tobacco or alcoholic drinks were excluded. The mean age of the subjects in a study by Haerian-Ardakani et al. [22] (24 years) was almost similar to that in the present study (28 years). They also excluded mothers who used tobacco or alcoholic drinks from their study [22]. However, Muwazi et al. [23] evaluated patients between 18-45 years.

Mathew et al. [24] reported an age range of 18-35 years for their patients, and 9.9% of the subjects in a study by Soroye et al. [25] used alcoholic drinks. In some studies, other possible factors for the incidence of PTB/LBW were evaluated, including PROM, IUGR and vaginal bleeding [26-28]. In addition, in some studies, apart from the above-mentioned factors, other parameters were evaluated, including the height of the uterine fundus, the type of parturition, and premature uterine contractions [29-31].

In the present study, all the pregnant women exhibited some degrees of periodontal disease, and 86% were affected by various forms of periodontitis. Differences in the prevalence of periodontal disease in different communities and differences in oral hygiene of pregnant women lead to results such as those in the present study, making it more difficult to assess the correlation between maternal periodontal disease and incidence of PTB/LBW. Obstetricians are not usually familiar with periodontal disease and do not include it in their counseling list. Rocha et al. [32] believed that obstetricians do not have a positive attitude towards the role of periodontal disease in their field of activity.

Contrary to the results of the present study, Ali Abidin et al. [33] did not consider periodontal disease as a separate risk factor for PTB/LBW in their prospective study. However, the outcomes of a cohort study by Rakoto-Alson et al. [34] showed a strong correlation in this respect. In the present study, the ROC curve showed a higher discriminating power for periodontal parameters used in the present study compared with other known medical risk factors for the incidence of pregnancy outcomes in question. Consistent with the present study, Al-Habashneh et al. [35] evaluated mothers with LBW or PTB in one group and the ROC curve analysis carried out by these researchers showed that the severity and extent of periodontal disease

might be a predictive factor for the incidence of unfavorable pregnancy outcomes.

Conclusion

Considering the present results, it appears that maternal periodontal disease is an independent risk factor for PTB and LBW; however, further case-control and longitudinal studies are required to confirm this hypothesis.

Considering the existing evidence, it is necessary to implement the following practical measures: Educational programs by healthcare centers and mass media regarding pregnancy, cooperation between obstetricians and dentists regarding the referral of pregnant women to dentists for oral examinations and oral hygiene instructions, and emphasizing the potential effect of oral health status on the incidence of unfavorable pregnancy outcomes in the curriculum of obstetrics, including continuing education programs.

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Conflict of interests

The authors declare that there is no conflict of interests.

References

1. Ananth CV, Andrews HF, Papapanou PN, Ward AM, Bruzelius E, Conicella ML, et al. History of periodontal treatment and risk for intrauterine growth restriction (IUGR). *BMC Oral Health*. 2018 Sep 29;18(1):161.
2. Bansal M, Khatri M, Kumar A, Bhatia G. Relationship between maternal periodontal status and preterm low birth weight. *Rev Obstet Gynecol*. 2013;6(3-4):135-40.
3. Bobetsis YA, Graziani F, Gürsoy M, Madianos PN. Periodontal disease and adverse pregnancy outcomes. *Periodontol 2000*. 2020 Jun;83(1):154-74.
4. Mesa F, Pozo E, Blanc V, Puertas A, Bravo M, O'Valle F. Are

- periodontal bacterial profiles and placental inflammatory infiltrate in pregnancy related to birth outcomes? *J Periodontol.* 2013 Sep;84(9):1327-36.
5. Santa Cruz I, Herrera D, Martin C, Herrero A, Sanz M. Association between periodontal status and pre-term and/or low-birth weight in Spain: clinical and microbiological parameters. *J Periodontol Res.* 2013 Aug;48(4):443-51.
6. Wang X, Buhimschi CS, Temoin S, Bhandari V, Han YW, Buhimschi IA. Comparative microbial analysis of paired amniotic fluid and cord blood from pregnancies complicated by preterm birth and early-onset neonatal sepsis. *PLoS One.* 2013;8(2):e56131.
7. Han YW, Redline RW, Li M, Yin L, Hill GB, McCormick TS. *Fusobacterium nucleatum* induces premature and term stillbirths in pregnant mice: implication of oral bacteria in preterm birth. *Infect Immun.* 2004 Apr;72(4):2272-9.
8. Ao M, Miyauchi M, Furusho H, Inubushi T, Kitagawa M, Nagasaki A, et al. Dental Infection of *Porphyromonas gingivalis* Induces Preterm Birth in Mice. *PLoS One.* 2015 Aug 31;10(8):e0137249.
9. Tavarna T, Phillips PL, Wu XJ, Reyes L. Fetal growth restriction is a host specific response to infection with an impaired spiral artery remodeling-inducing strain of *Porphyromonas gingivalis*. *Sci Rep.* 2020 Sep 3;10(1):14606.
10. Miranda-Rius J, Brunet-Llobet L, Blanc V, Álvarez G, Moncunill-Mira J, Mashala EI, et al. Microbial profile of placentas from Tanzanian mothers with adverse pregnancy outcomes and periodontitis. *Oral Dis.* 2021; 1-14.
11. Tarannum F, Faizuddin M. Effect of periodontal therapy on pregnancy outcome in women affected by periodontitis. *J Periodontol.* 2007 Nov;78(11):2095-103.
12. George A, Shamim S, Johnson M, Ajwani S, Bhole S, Blinkhorn A, et al. Periodontal treatment during pregnancy and birth outcomes: a meta-analysis of randomised trials. *Int J Evid Based Healthc.* 2011 Jun;9(2):122-47.
13. López NJ, Da Silva I, Ipinza J, Gutiérrez J. Periodontal Therapy Reduces the Rate of Preterm Low Birth Weight in Women With Pregnancy-Associated Gingivitis. *J Periodontol.* 2005 Nov;76 Suppl 11S:2144-53.
14. Jeffcoat M, Parry S, Sammel M, Clothier B, Catlin A, Macones G. Periodontal infection and preterm birth: successful periodontal therapy reduces the risk of preterm birth. *BJOG.* 2011 Jan;118(2):250-6.
15. Sant'Ana AC, Campos MR, Passanezi SC, Rezende ML, Greggi SL, Passanezi E. Periodontal treatment during pregnancy decreases the rate of adverse pregnancy outcome: a controlled clinical trial. *J Appl Oral Sci.* 2011 Apr; 19(2):130-6.
16. Chambrone L, Pannuti CM, Guglielmetti MR, Chambrone LA. Evidence grade associating periodontitis with preterm birth and/or low birth weight: II: a systematic review of randomized trials evaluating the effects of periodontal treatment. *J Clin Periodontol.* 2011 Oct;38(10):902-14.
17. Fogacci MF, Vettore MV, Thomé Leão AT. The effect of periodontal therapy on preterm low birth weight: a meta-analysis. *Obstet Gynecol.* 2011 Jan;117(1):153-65.
18. Polyzos NP, Polyzos IP, Zavos A, Valachis A, Mauri D, Papanikolaou EG, et al. Obstetric outcomes after treatment of periodontal disease during pregnancy: systematic review and meta-analysis. *BMJ.* 2010 Dec 29;341:c7017.
19. Bearfield C, Davenport ES, Sivapathasundaram V, Allaker RP. Possible association between amniotic fluid microorganism infection and microflora in the mouth. *BJOG.* 2002 May;109(5):527-33.
20. Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS. *Williams obstetrics, 24e.* New York, NY, USA: Mcgraw-hill; 2014.
21. Di Renzo GC, Roura LC, Facchinetti F, Antsaklis A, Breborowicz G, Gratacos E, et al. Guidelines for the management of spontaneous preterm labor: identification of spontaneous preterm labor, diagnosis of preterm premature rupture of membranes, and preventive tools for preterm birth. *J Matern Fetal Neonatal Med.* 2011 May;24(5):659-67.
22. Haerian-Ardakani A, Eslami Z, Rashidi-Meibodi F, Haerian A, Dallalnejad P, Shekari M, et al. Relationship between maternal periodontal disease and low birth weight babies. *Iran J Reprod Med.* 2013 Aug;11(8):625-30.
23. Muwazi L, Rwenyonyi CM, Nkamba M, Kutesa A, Kagawa M, Mugenyi G, Kwizera G, et al. Periodontal conditions, low birth weight and preterm birth among postpartum mothers in two tertiary health facilities in Uganda. *BMC Oral Health.* 2014 Apr 28;14:42.
24. Mathew RJ, Bose A, Prasad JH, Muliyl JP, Singh D. Maternal periodontal disease as a significant risk factor for low birth weight in pregnant women attending a secondary care hospital in South India: a case-control study. *Indian J Dent Res.* 2014 Nov-Dec;25(6):742-7.
25. Soroye M, Ayanbadejo P, Savage K, Oluwole A. Association between periodontal disease and pregnancy outcomes. *Odontostomatol Trop.* 2015 Dec;38(152):5-16.

26. Goldenberg RL, Nelson KG, Koski JF, Cutter GR. Low birth weight, intrauterine growth retardation, and preterm delivery. *Am J Obstet Gynecol.* 1985 Aug 15;152(8):980-4.
27. Hanke K, Hartz A, Manz M, Bendiks M, Heitmann F, Orlikowsky T, et al. Preterm prelabor rupture of membranes and outcome of very-low-birth-weight infants in the German Neonatal Network. *PLoS One.* 2015 Apr 9;10(4):e0122564.
28. Sun L, Tao F, Hao J, Su P, Liu F, Xu R. First trimester vaginal bleeding and adverse pregnancy outcomes among Chinese women: from a large cohort study in China. *J Matern Fetal Neonatal Med.* 2012 Aug;25(8):1297-301.
29. Ercan E, Eratalay K, Deren O, Gur D, Ozyuncu O, Altun B, et al. Evaluation of periodontal pathogens in amniotic fluid and the role of periodontal disease in pre-term birth and low birth weight. *Acta Odontol Scand.* 2013 May-Jul;71(3-4):553-9.
30. Scannapieco FA, Bush RB, Paju S. Periodontal disease as a risk factor for adverse pregnancy outcomes. A systematic review. *Ann Periodontol.* 2003 Dec;8(1):70-8.
31. Xiong X, Buekens P, Fraser WD, Beck J, Offenbacher S. Periodontal disease and adverse pregnancy outcomes: a systematic review. *BJOG.* 2006 Feb;113(2):135-43.
32. Rocha JM, Chaves VR, Urbanetz AA, Baldissera Rdos S, Rösing CK. Obstetricians' knowledge of periodontal disease as a potential risk factor for preterm delivery and low birth weight. *Braz Oral Res.* 2011 May-Jun;25(3):248-54.
33. Ali TB, Abidin KZ. Relationship of periodontal disease to pre-term low birth weight infants in a selected population--a prospective study. *Community Dent Health.* 2012 Mar; 29(1):100-5.
34. Rakoto-Alson S, Tenenbaum H, Davideau JL. Periodontal diseases, preterm births, and low birth weight: findings from a homogeneous cohort of women in Madagascar. *J Periodontol.* 2010 Feb;81(2):205-13.
35. Al Habashneh R, Khader YS, Jabali OA, Alchalabi H. Prediction of preterm and low birth weight delivery by maternal periodontal parameters: receiver operating characteristic (ROC) curve analysis. *Matern Child Health J.* 2013 Feb;17(2):299-306.