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Maternal Periodontitis, Preeclampsia and Adverse Pregnancy Outcomes

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ABSTRACT

Background & aim: Preeclampsia is a considerable problem of pregnancy. Endothelial dysfunction and placental hypoxia are the current hypotheses for the pathogenesis of preeclampsia. Chronic inflammation, including periodontitis may provoke systemic maternal and placental pro-inflammatory endothelial dysfunction, which represent a significant risk factor for diseases of vascular origin. So this study was carried out to evaluate the possible relationship between periodontitis and preeclampsia.

Methods: A total of 360 pregnant women were included, (180 pregnant women with mild or sever periodontitis in one group and 180 pregnant women with healthy periodontal status in the other group). Periodontitis was determined by the sum of all pockets with pocket probing depth (PPD) ≥ 4mm and bleeding on probing. Healthy periodontal status was defined as the absence of PPD≥ 4mm. Then two groups evaluated to determine the presence of preeclampsia. After delivery, weight birth and gestational age was also recorded. Chi square and t test were used to analyze the data.

Results: There was statistically significant difference between two groups in terms of preeclampsia development (P=0.003). Women who had a worse periodontal condition were at higher risk for preeclampsia. In addition, birth weight and gestational age was statistically lower in the case group than the control group (P<0.001).

Conclusion: The results indicate that the development and severity of peridontitis increase the risk for occurrence of preeclampsia and adverse pregnancy outcomes.

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Introduction

Preeclampsia is defined as elevated blood pressure plus proteinuria with or without pathologic edema after 20 weeks of gestation. The global incidence of preeclampsia has been estimated at 5-14% of all pregnancies and is still a major cause of maternal and prenatal mortality and morbidity (1). Several factors are associated with preeclampsia but some are not clearly proved. Current theories for the pathogenesis of preeclampsia include abnormal placentation, cardiovascular maladaptation to pregnancy, genetic and immune mechanisms, enhanced systemic inflammatory responses, nutritional, hormonal and angiogenic factors (1-4). The initiating event in preeclampsia is generally regarded to be placental ischemia-hypoxia. Alternatively, the preeclampsia syndrome may also be evidenced as decreased formation of vasodilators such as nitric oxide and prostacyclin. Moreover, the quantitative importance of the various endothelial and hormonal factors that mediate vasoconstriction and elevation of arterial pressure during preeclampsia remains to be elucidated (5-7).

Periodontal disease can refer to any condition that affects gums and other structures

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supporting the teeth (8). Pregnancy status most often combined with gag reflex that makes brushing teeth more difficult for pregnant women. In addition due to hormonal changes the majority of pregnant women develop "pregnancy gingivitis" (9-11). Periodontal pathogens have been found not only in supra- and subgingival plaque, gingivo-crevicular fluid, and periodontal tissues, but also dispersed systemically in maternal serum and plasma, vagina, placenta, amniotic fluid, and umbilical cord (5,12-14). It is hypothesized that if lipopolysaccharides (i.e. endotoxins) from periodontopathogens gain access to the placenta, they could stimulate IL-1β and PGE2 production in chorioamniotic and trophoblastic cells, leading to preterm labor (13-15). In addition, Low birth weight child (weight of infant at birth less than 2,500 g or 5.5 pounds) and preterm birth (birth occur before 37 weeks of gestation) seems to be the following adverse consequent of that. Gestational age, measured in weeks or full days, is defined as the time that has elapsed since the first day of the last normal menstrual period (LMP) (16). Along with weight at birth, this measurement is an important indicator of neonatal health (17).

Some of recent reports have shown the effect of periodontal pathogens on maternal and fetal immuno-inflammatory response (5,7,12). Some studies have suggested that periodontal disease is more prevalent in preeclampsia (15,18). However, other studies have found no relationship between periodontal health and adverse pregnancy outcomes (9,17,19). Thus the body of evidence for such association is still limited and a gap in the knowledge necessary to direct therapeutic strategies has been remained. We therefore conducted this study in one of the main obstetric centers in Ahvaz between September 2011 and Jun 2012 to determine whether periodontitis in pregnant women is associated with an increased development of preeclampsia and also to evaluate the influence of severity of periodontal parameters including on probing (BOP) and periodontal pocket depth (PPD) in association with adverse pregnancy outcomes.

Materials and Methods

This study was carried out on a group of singleton pregnant women from south of Iran who were admitted to the obstetrics department of Bahman Hospital, Ahvaz for their pregnancy routine visit between September 2011 and June 2012. According to a priori power calculation for achieving a power of 80%, p value of 0.05 and selection ratio of 1:1, the sample size was estimated to be 342 which later increased up to 360 participants, 180 with periodontal disease and 180 without it. A clinical record regarding personal information, marital status, educational level, household income and also height and weight before pregnancy for calculating body-mass index before pregnancy (weight (kg)/height^2 (m^2), number of pregnancies, and medical examinations completed for all patients by a trained midwife. With very young (<18) or old (>37) age, with preexisting hypertension (blood pressure before 20 weeks of gestation ≥ *140/90* mmHg) or using antihypertensive medication or with a history of diabetes mellitus, renal disease, cardiovascular disease in themselves and/ or in their families and any systemic illness, smoking and also periodontal treatment within the last 6 months or any antibiotic medication during pregnancy and any recent infections were also excluded from the study. Gestational age of all participants was between 20 to 28 weeks.

All of subjects received information about the purpose of the study and provided informed consent at the first interview. This study was approved by the Committee of the Ethics, Ahvaz Jundishapour University of Medical Sciences (protocol no. 249). All recruited women underwent a full-periodontal examination by one periodontist and co-incidentally fell into two groups in a 50/50 ratio, one with periodontal disease and the other without it. The examination was conducted within the subject supine position in the hospital bed. An external head lamp was used to facilitate a calibrated periodontal examination.

Clinical measures of periodontal health were determined in all subjects including pocket probing depth (PPD), and bleeding on probing (BOP). Gingival Pocket depth (sulcus) was measured in millimeters with a williams UNC-15 periodontal probe with 1 to 15 mm markings at six sites per tooth as the distance from gingival margin to periodontal attachment. Gingival

recession was determined by measuring the distance from the cemento-enamel junction to the gingival margin in millimeters and rounded down to the next millimeter. BOP was expressed as the percentage of sites showing bleeding within 15 seconds after probing. The periodontal condition was further classified for its severity according to the criteria used by Boggess *et al*. (2003) (20). Periodontal health was defined as the absence of PPD≥ 4 mm. Mild periodontal disease was defined as one to 15 tooth sites with PD≥ 4mm and BOP. Severe periodontal disease was defined as ≥15 tooth sites with≥ 4mm PPD and BOP (20).

All women received prenatal by care midwives or the other members of health team.

Preeclampsia was defined according to the report of the National High Blood Pressure Education Program (1,21): the appearance of a blood pressure ≥ *140/90* mm Hg observed at least on two occasions 4-6 h apart, with the patients resting in bed in combination with proteinuria
(≥ 300mg. 24 h or 1+dipstick in at least two random clean catch samples), developing after a gestational age of 20 weeks in a previously normotensive women.

After delivery information about occurrence of preeclampsia was collected from the women's files. Also, gestational age at delivery (weeks) and child weight at birth (g) were recorded.

The gestational age was calculated in full months, according to the recommendation of World Health Organization (WHO) (17). A gestational calendar was used to calculate the gestational age according to LMP and ultrasound. The LMP method was used for those mothers with a regular menstrual cycle (between 25 and 31 days) and date (day and month) as of the last menstrual period (17). The following ultrasound examinations were included in the study: examinations carried out before the 10th week of gestation in which gestational age was evaluated by measuring the length from head to buttocks, or those carried out between the 11th and 20th week, where the gestational age had been evaluated by measuring the length of the femur or the biparietal diameter (17,22). The newborns were weighted using the routine procedures, which consisted of weighing the newborn immediately after birth, unclothed, with the umbilical clamp. An electronic scale with a capacity of 15 kg, that sensitivity it's calibrated at 5 g and reset for each was used for weighing. All statistical analyzes were performed using SPSS for Windows 15.0 (SPSS Inc., Chicago, Illinois). Univariate association between preeclampsia occurrence, low birthweight and preterm birth child in pregnant women with periodontal disease was assessed using the chi-square test. Differences between two groups were in case of normally distributed continuous data analyzed by student't–test. Statically significant was estimated as $P< 0.05$.

Results

A total of 360 pregnant women were included 180 pregnant women with mild or sever periodontitis in one group and 180 pregnant woman with healthy periodontal status in the other group. Table 1 shows the demographic and pregnancy-related characteristics of the participants. None of the pregnant women drank alcohol and all were married. There were no significant differences between two groups in age mean, gravidity mean, and body mass index mean ($P> 0.05$) with exception

Table 1. Demographic and pregnancy- related characteristics of study groups

	Periodontitis group	Control group	P-value (N=180)
Age (M±SD)	28.53±4.67	26.07±3.98	0.075
Gravidity (M±SD)	2.31±1.35	2.17±1.28	0.307
Number of Prenatal visits (%)	4(37.2%)	6(41.8%)	0.010
Education level N (%)			
Very low (elementary school)	30(17%)	31(17.2%)	0.030*
Low (secondary school)	77(43%)	57(31.7%)	
Moderate (university degree)	48(26%)	56(31.1%)	
High (≥Master degree)	25(14%)	36(20%)	
Household income (M±SD)	302.1±83.7	415.4±72.5	0.009
Body mass index (kg.m^2) (M±SD)	26.8±5.8	24.1±3.7	0.051

P values refer to comparison between each case and control group

Table 2. Presence and severity of periodontitis and obstetric variables

	Periodontitis groups		Control group	P-value
	Mild (N=145)	Sever (N=35)	(N=180)	
Preeclampsia N (%)	2 (12.5%)	14 (87.5%)	3 (1.7%)	0.003*
Gestational age at delivery (weeks)	39.34±2.49	36.61±4.30	39.92±1.52	0.009*
Birthweight (g)	3258±539.83	457±913.99	3356±401.49	0.001*

Values are expressed as means (SD) or number (%).* P-values refer to the χ^2 test results for comparison between each case and control group

of education level, number of prenatal visits and household income means that were higher in the control group (P<0.05). The results of the periodontal condition and obstetric variables are presented in Table 2.

Two groups of study were statistically different in preeclampsia, gestational age and birth weight (P< 0.05). Preeclampsia was found in 16 of 180 (8.9%) participants of case group and in 3 of 180 (1.7%) of the controls. Sever periodontal disease was found in 14 of the 19 (87.5%) preeclamtic women (P=0.003). Birthweight (2457±913.99 versus 3356±401.49; P<0.05) and gestational age at delivery (36.61±4.30 versus 39.92±1.52) was statistically lower in preeclamptic women with sever periodontitis than in the other group (P<0.05). After adjusting for body mass index, number of prenatal visits, socioeconomic status and age by multivariate logistic regression analysis, the odds ratio was calculated 8.2 (with 95% confidence interval: 2.2-33.1).

Discussion

Although in this study we found a higher occurrence of preeclampsia and adverse pregnancy outcomes in women with periodontal disease but the cause seems to be multifactorial.

A relation between preeclampsia and hypertension, collagen vascular disease, obesity, black race, insulin resistance diabetes, increased circulating testosterone and thrombophillias has been noted (1,3,4) In the present study, effect of the other known risk factors or medical conflictions for preeclampsia was excluded in order to minimize confounding of the primary association with age, gravidity, BMI, preexisting hypertension or using antihypertensive medication, diabetes mellitus, renal disease, cardiovascular or any systemic illness, antibiotic medication, smoking and history of periodontal treatment. Adjusted odds ratios for preeclampsia such as low socioeconomic status and number of prenatal visits were calculated using multivariate logistic regression analysis. Since racial diversity can increase the risk of preeclampsia-black women as a case in point (1), this variable was not a confounder in our study, because all the participants were white Iranians, but still we cannot rule out other risk factors such as genetic.

On account of these criteria, it can be claimed, as already shown in some other studies (20,23-27), that periodontal disease may be a risk factor for preeclampsia. Although, our study confirmed findings from previous study carried out in Iran by Zadeh-Modarres *et al*. (2007) to assess the association between periodontal health and preterm labor in Iranian female population (28). But the accuracy of preeclampsia did not evaluate in their study. This study found the same association between maternal periodontitis, low birth weight Childs and gestational age. In contrast to our findings, preeclampsia was found not to be associated with periodontal disease in a large prospective cohort study in which about 6% of the participants developed preeclampsia (29). Another investigative group (30) applied six different periodontal case definitions in their analysis of data from a case-control study and found no evidence of an association between periodontal disease and preeclampsia. The difference in these results can be explained by different definitions of periodontitis, various methods used, and population study, which is one of the most important reasons (31,32). In our study, probing depth was the most important index for periodontal health (33) and preeclampsia was more prevalent in periodontitis group. Not only the presence of disease but also its severity seems to be

important to increase the risk of preeclampsia. We tried to apply classifying periodontal disease on PPD≥4 mm according to the definitions used by Boggess *et al*. (2003) that was enough to measure periodontal disease and the severity of it (20).

This study shows that in nonsmoking and nondrinking women in south of Iran, a worse periodontal condition is associated with an increased risk for preeclampsia. In addition, our findings showed lower birth weight and gestational age in the periodontitis group than the periodontal health group, which was consistent with previous reports (33-35), but it was in contrast with some other studies that rejected the hypothesis that periodontal disease is a risk factor for undesirable pregnancy outcomes (9,36). One possible explanation for their negative findings is poor control for potential confounders. Classification bias is the most common systematic error compromising validity of case-control studies. In this study, gestational age was estimated through the LMP, the gold standard method for gestational age assessment in epidemiological studies (20,37). In the absence of LMP such as cases of irregular menstrual cycles, bleeding after conception, and failure to remember LMP, ultrasound examinations carried out to determine gestational age, the most commonly recommended method (17). Although Capurro somatic method widely used in previous studies (9,36,38,39), but it could under or overestimates gestational age compared with LMP and ultrasound (40-42) and may affect their results. There is a clear need for methodologically rigorous observational studies with sufficiently large sample sizes and control for confounders and also developing a more universally accepted research definition and criteria for periodontal health.

Conclusion

Although associations between periodontal disease and risk of preeclampsia and adverse pregnancy outcomes are relatively consistent in this study, however, unambiguous evidence from large-scale randomized clinical trials to support recommending routine periodontal care as an effective strategy to prevent adverse pregnancy outcomes is lacking. It seems prudent for all caregivers to attempt to ensure pregnant women have their oral health status evaluated and receive non-surgical periodontal treatment as needed.

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Conflict of Interest

The authors declare no conflicts of interest.

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