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Is there a relationship between maternal periodontitis and pre-term birth? A prospective hospital-based case-control study

GULCIN BULUT[1], OZGUR OLUKMAN[2] & SEBNEM CALKAVUR[2]

[1]*Department of Paediatric Dentistry, and* [2]*Neonatal Intensive Care Unit, Dr. Behcet Uz Children's Hospital, Izmir, Turkey*

Abstract

Objective. The aim of this study is to verify the existence of an association between maternal periodontal disease and pre-term delivery in an unselected population of post-partum Turkish women. ***Materials and methods.*** This case-control study was conducted on 100 women who gave birth in either a special or a government maternity hospital. The case group consisted of 50 mothers who had delivered an infant before 37 weeks' gestation and weighed under 2500 g. The control group included 50 mothers who had given birth to an infant with a birth weight of more than 2500 g and a gestational age of ≥37 weeks. Data of mothers and infants were collected using medical registers and questionnaires. Clinical periodontal examinations were carried out in six sites on every tooth in the mother's mouth. A participant who presented at least four teeth with one or more sites with a PPD ≥4 mm and CAL ≥3 mm at the same site was considered to have periodontal disease. Statistical methods included parametric and non-parametric tests and multiple logistic regression analysis. ***Results.*** There were no statistically significant differences between the cases and controls with regard to periodontal disease and pre-term delivery (OR = 1.48; 95% CI = 0.54–4.06). ***Conclusion.*** The findings indicated that maternal periodontitis was not a possible risk factor for pre-term delivery. Further studies with additional clinical trials are needed to explore the possible relationship between periodontal disease and pre-term birth.

Key Words: *low birth weight, periodontitis, pre-term birth, risk factors*

Introduction

Pre-term birth is a significant public health problem that remains a leading cause of perinatal morbidity and mortality for years worldwide, accounting for 60–80% of deaths of infants without congenital anomalies. A pre-term delivery, as defined by the World Health Organization, is one that occurs at less than 37 and more than 20 gestational weeks. Low birth weight is defined as being less than 2500 g [1].

The frequency of pre-term births is ~ 12–13% in the US and 5–9% in many other developed countries. It has been reported that, in developed countries, there has been a drop in mortality rate of premature infants due to recent advances in obstetric care and neonatal intensive care. However, the rate of prematurity has not changed over the past 4 decades and may actually have increased slightly because of increasing indicated pre-term births [2,3].

Risk factors of pre-term low birth weight (PLBW) are categorized as epidemiologic, clinical and environmental factors which include alcoholism, tobacco consumption, use of illegal drugs, young maternal age, low maternal weight gain, low pre-gravid weight, multiple gestations, genitourinary infections, gestational diabetes, arterial hypertension and lack of pre-natal care, while previous pre-term delivery is a strong predictive marker of future pre-term labor [4,5].

Despite all these risk factors, the pathogenesis of pre-term labor is not well understood. It is estimated that 50% of pre-term births are idiopathic and it is still unclear whether pre-term labor represents an idiopathic activation of the normal labor process or results from a different pathologic mechanism [6].

Recently it has been suggested that maternal infections leading to alterations in the normal cytokine and hormone-regulated gestation may result in pre-term

Correspondence: Gulcin Bulut, Talatpasa Bulvari, No:16/5 Palmiye Apt, Alsancak, Izmir, Turkey. Tel: +90 232 4116298. Fax: +90 232 4892315. E-mail: gulcinbulut@yahoo.com

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labor, premature rupture of membranes and pre-term birth [7]. Colonization or infection of the genital tract with Gram-negative bacteria which release endotoxins named lipopolysaccharides (LPS), induce the production of several inflammatory mediators such as prostaglandins (PGE_2 and $PGF_{2\alpha}$), interleukin (IL)-6, IL-1β and tumor necrosis factor-α (TNF-α) initiating a cascade of events resulting in local inflammation, disruption of the choriodecidual interface and ultimately causing rupture of membranes and cervical ripening [8].

Micro-organisms themselves or microbial toxins such as endotoxins can also gain access to the intra-uterine cavity by the blood borne route from a non-genital focus. Recently, it has been postulated that distant focal infections like periodontitis may be associated with pre-term labor through similar mechanisms as other maternal infections [9].

Periodontal diseases are a group of infectious diseases caused by Gram-negative, anaerobic and microaerophilic bacteria that can act as a reservoir for microbial products and inflammatory mediators. Today it is well known that there is an increase in gingival inflammation during pregnancy and periodontal bacteria frequently enter the maternal circulation during routine daily feeding activity or dental care [10,11]. Increased levels of both local and systemic PGE_2, IL-1β, IL-6 and TNF-α have been shown in patients with periodontal disease [12]. High concentrations of these cytokines in pregnant women have been proposed to be responsible for the rupture of the uterine membranes resulting in pre-term labor [13].

In 1996, Offenbacher et al. [14] first reported a positive association between maternal periodontitis and pre-term birth and several authors supported this opinion [15–19]. On the other hand, some recent studies have not found any relationship between these two health problems [20–23].

Despite the studies undertaken, the relationship between periodontitis and pre-term labor still remains unclear. Thus, this study was conducted to verify the existence of an association between maternal periodontal disease and pre-term delivery in an unselected population of post-partum Turkish women.

Materials and methods

Setting and study population

This case-control study was conducted on 100 women between the ages of 18–40 years who gave birth in either a special or a government maternity hospital and whose newborn infants were hospitalized at the neonatal intensive care unit of Dr Behcet Uz Children's Hospital, Izmir, Turkey between September 2010 and December 2011.

The case group consisted of 50 mothers who had delivered an infant before 37 weeks' gestation and weighed under 2500 g. The control group included 50 mothers who had given birth to an infant with a birth weight of more than 2500 g and a gestational age of ≥37 weeks, in accordance with World Health Organization criteria [24]. Only mothers with a singleton gestation were included in the study.

Exclusion criteria

Exclusion criteria included systemic medical conditions like chronic hepatic, renal or cardiovascular disorders, type 1 or type 2 diabetes mellitus, severe anemia, coagulation abnormalities, essential hypertension associated premature birth or intra-uterine growth delay. In addition, mothers who had a medically indicated pre-term delivery that followed pregnancies complicated by maternal obstetric disorders such as pre-eclampsia/eclampsia, placenta previa, abruptio placenta, poly/oligohydramnios, uterine or cervical malformations, gestational diabetes, pregnancy induced hypertension or mothers whose infants were stillborn or had fetal anomalies, who received systemic antibiotics during pregnancy, who had multiple gestation and who received inadequate number of pre-natal consultations (<6) were also excluded from the study.

Data collection

Demographical features and daily habits such as age, educational level, occupation, family income, number of people living in the same house, smoking, alcohol consumption and frequency of tooth brushing were collected by means of a questionnaire. Obstetric information including gestational age (GA), birth weight, gender, size classification (small for GA-SGA, adequate for GA-AGA, large for GA-LGA), type of delivery, total number of pregnancies, total number of births, number of previous spontaneous abortions, history of prior pre-term delivery, body mass index before pregnancy and weight gain during pregnancy and use of any medication during pregnancy was obtained from the medical records.

Examiner and definition of periodontitis

This research was designed as a blind study. Data of mothers and infants were collected by the pediatricians using medical registers and questionnaires as mentioned above. Intra-oral examination was carried out with only one dentist blinded to the case and control status at the dental clinic of the study hospital. Periodontal condition such as probing pocket depth (PPD) and clinical attachment loss (CAL) was evaluated by using a Williams-type probe graduated in millimeters and carried out up to 3 days after delivery.

These examinations were carried out in six sites (distovestibular, mid-vestibular, mesiovestibular, distolingual, mid-lingual, mesiolingual) on every tooth in the mother's mouth excluding the third molars. A participant who presented at least four teeth with one or more sites with a PPD ≥4 mm and CAL ≥3 mm at the same site were considered to have periodontal disease.

Statistical analysis

Statistical analysis was performed using SPSS for Windows, version 15.0 (SPSS Inc, Chicago, IL). Mean ± standard deviation or median (minimum–maximum) values were given for continuous variables. Categorical variables were expressed as frequency and related percentage values and they were compared by the Chi-square test or Fisher's Exact test. Comparison of continuous variables was performed with parametric (Student's *t*-test) or non-parametric (Mann Whitney U-test) tests according to their distribution type. Multiple logistic regression analysis was carried out according to the forward selection method to determine the effects of demographic and clinical parameters on pre-term birth. The adjusted risk ratios were calculated with 95% confidence interval. A p-value < 0.05 was considered to be statistically significant.

Results

The mean age of the women enrolled in the case and control groups was 26 ± 5.23 years and 26.62 ± 5.28 years, respectively. Demographic and obstetric features, as well as daily habits of the study population, are presented in Table I. There was no difference between the groups in terms of type of delivery, total number of pregnancies, total number of births, educational level, occupation, family income, number of people living in the house, smoking, alcohol consumption and frequency of tooth brushing. The statistical difference between the groups was significant with regard to the number of previous spontaneous abortions, history of prior pre-term delivery, body mass index before pregnancy and average weight gain during pregnancy. Twenty-six per cent of the women in the case group had at least one previous spontaneous abortion, whereas this ratio remained at the level of 10% in the control group (p = 0.045). While none of the women in the control group had a history of prior pre-term delivery, 10% of the women in the case group had given birth to a premature infant in the past (p = 0.028). Women in the case group had lower body mass index and had gained significantly less weight than the controls (p = 0.039, p = 0.021). Most of the women in both groups had primary level of education. Although the difference did not reach the level of significance, the percentage of women with tertiary schooling level was higher in the control group than in the case group (p = 0.059). Most of the women in both groups were housewives and they belonged to the middle class with regard to their family income. The vast majority of the women in both groups were non-smokers. Alcohol consumption was eliminated from the analyses, since no woman declared drinking during pregnancy. The frequency of tooth brushing was higher in the control group. Although 70% of controls brushed their teeth at least once a day, this ratio was 56% for the cases. The difference was not significant (p = 0.214).

Periodontal clinical parameters of the study population are presented in Table II. Periodontal disease was diagnosed in 22% (n = 11/50) of the cases and 16% (n = 8/50) of the controls, but the difference was not statistically significant (p = 0.611). There was no difference between the cases and controls with regard to the median number of affected teeth, median number of sites with PPD ≥4 mm and CAL ≥3 mm and mean PPD and CAL measurements of patients with periodontitis.

The mean birth weight and GA of the case group were 1684.60 ± 549.16 g and 31.04 ± 2.79 weeks and of the control group were 3205.50 ± 523.05 g and 38.78 ± 1.14 weeks, respectively. In both groups, all cases were more likely to be AGA at birth (92% in the case group and 82% in the control group).

In the case group, 37 infants met the definition of very low birth weight (VLBW) pre-term infant (≤32 weeks and ≤1500 g), whereas the remaining 13 infants were relatively larger pre-terms. Mothers of seven neonates in the VLBW pre-term group and mothers of four neonates in the larger pre-term group were diagnosed to have periodontitis. However, no significant difference could be demonstrated (p = 0.386). When women in each study group were classified as periodontally healthy or not, no significant difference could be demonstrated between the sub-groups with regard to gestational age and birth weight (Table III).

It was demonstrated that the probability of women with periodontal disease to give a pre-term birth was 1.48-times higher than those who were periodontally healthy. However, the statistical difference was not significant (OR = 1.48; 95% CI = 0.54–4.06).

Discussion

In recent years, it is becoming increasingly clear that the factors that lead to pre-term labor are multiple and are part of a pathologic process leading to the onset of premature rupture of membranes. Recently it has been suggested that maternal periodontitis influences birth outcome since periodontal infections have the same pathophysiological mechanism with genitourinary infections which are accepted as the major risk factor for prematurity [7,12–14]. In this respect, we

Table I. Demographic features, obstetric history and daily habits of the study population.

	Case group (n = 50)		Control group (n = 50)		
	n	%	n	%	p
Age (years)	26 ± 5.23*		26.62 ± 5.28*		0.556
Educational level					
None	1	2	2	4	0.059
Primary	23	46	20	40	
Secondary	11	22	6	12	
Tertiary	15	30	22	44	
Occupation					
Remunerated	12	24	12	24	1.000
Housewife/unemployed	38	76	38	76	
Family income					
Low	21	42	14	28	0.357
Medium	23	46	28	56	
High	6	12	8	16	
Number of people living in the same house					
≤4	42	84	38	76	0.454
>4	8	16	12	24	
Smoking					
Yes	6	12	6	12	1.000
No	44	88	44	88	
Frequency of tooth brushing					
At least once a day	28	56	35	70	0.214
Nil	22	44	15	30	
Type of delivery					
Normal vaginal	25	50	31	62	0.314
Caesarean section	25	50	19	38	
Total number of pregnancies					
1	23	46	26	52	0.924
≥2	27	54	24	48	
Total number of births					
Primiparous	32	64	33	66	0.815
≥2	18	36	17	34	
Number of previous spontaneous abortions					
Nil	37	74	45	90	0.045†
At least 1	13	26	5	10	
History of prior pre-term delivery					
Yes	5	10	0	0	0.028†
No	45	90	50	100	
Body mass index before pregnancy					
Underweight	18	36	7	14	0.039†
Normal weight	27	54	38	76	
Overweight		10	5	10	
Weight gain during pregnancy (kg)	9.52 ± 3.4*		13.57 ± 5.2*		0.021

*Mean ± standard deviation; †$p < 0.05$.

Table II. Periodontal clinical parameters of the study population.

	Case group (n = 50)	Control group (n = 50)	p
Presence of periodontal disease (n/%)	11/22	8/16	0.611
Number of effected teeth in patients with periodontitis	5 (4–23)*	5.5 (4–5.5)*	0.492
Number of sites with PPD ≥4 mm and CAL ≥3 mm	9 (4–39)*	8.5 (5–38)*	0.545
PPD measurement of patients with periodontitis (mm)	4.17 ± 0.30†	4.11 ± 0.94†	0.545
CAL measurement of patients with periodontitis (mm)	3.69 ± 0.36†	3.48 ± 0.86†	0.442

*median (min–max); †Mean ± standard deviation.
PPD, Probing pocket depth; CAL, Clinical attachment loss.

Table III. Comparison of periodontally healthy women and women with periodontitis within the study groups with respect to the gestational age and birth weight of their infants.

	Case group (n = 50)			Control group (n = 50)		
	With periodontal disease (n = 11)	Periodontally healthy (n = 39)	p	With periodontal disease (n = 8)	Periodontally healthy (n = 42)	p
Birth weight (g)	1770 ± 540	1660 ± 556	0.661	3221 ± 368	3202 ± 551	0.717
Gestational age (weeks)	31.4 ± 3.1	30.9 ± 2.7	0.752	39.4 ± 1.18	38.7 ± 1.11	0.365

Data presented as mean ± standard deviation.

planned this study to determine if maternal periodontitis was associated with pre-term delivery in a sample of the Turkish population and the findings showed that the adjusted odds ratio (OR) for this association was 1.48, which was not meaningful for raising a risk indicator for pre-term birth. This result points in the same direction as the data published by Holbrook et al. [25], Mitchell-Lewis et al. [26], Moore et al. [23] and Buduneli et al. [21], whose studies were carried out in Iceland, the US, England and Turkey, respectively. Similar to this aspect, several other studies could not demonstrate an evidence of association between these two health problems either [20,27,28].

On the contrary, a positive relationship between maternal periodontitis and PLBW was originally suggested by Offenbacher et al. [14] and confirmed by many other studies from different countries worldwide [9,15–19,29–31]. While some of these studies reported a strong association, some could only present limited evidence [32,33]. In their review, Clothier et al. [34] discussed that a positive association between periodontal disease and pre-term labor existed in 22 of 31 studies, most of which were performed in North America and a few in Europe. Criticizing for the homogeneity of the population, association between poor periodontal health and pre-term birth has been predominantly described in African-American and Hispanic-Caucasian women [35]. Conversely to this report, Mitchell-Lewis et al. [26] could not find such a relationship in African-American and Hispanic women of low socio-economic status, but focused on the finding that PLBW mothers appeared to harbor substantially higher load of periodontal pathogens than women with a normal birth outcome. Holbrook et al. [25], in a detailed clinical study performed on women of high socio-economic status in Iceland in 2004, found no association between periodontal disease and pre-term birth and related this result with socio-economic status. They stated that, since the Icelandic population has access to subsidized dental care until the age of 17 years, it is possible that this may have had some beneficial effect in reducing periodontal disease and, thus, the risk of pre-term birth. In this respect one of the factors that may have affected our results is that, although dental care is mostly provided by the government hospitals and it is free of charge in Turkey, only a small percentage of the population has the habit of routine dentist visits. As viewed from past studies, Holbrook et al. [25] also commented that the reason for the higher rates among African-American women could be racially or life-style linked. However, up to date there has been insufficient data regarding ethnical groups.

Conflicting results from various studies in the current literature can be enlightened by different definitions of periodontitis. In our opinion, heterogeneity in diagnostic criteria for periodontal disease on the studies leads to spurious conclusions. For example, Offenbacher et al. [9,14] defined periodontitis as PPD of >4 mm or average CAL of >3 mm. On the other hand, Lopez et al. [29] and Cruz et al. [19], who were methodologically parallel to our study, examined six sites in all the teeth that were present

in the dental arch and considered those mothers who had at least four teeth with one or more sites with PPD ≥4 mm and CAL ≥3 mm at the same site to be suffering from periodontitis. Moliterno et al. [18] also defined periodontitis as PPD ≥4 mm and CAL ≥3 mm in their study and found a positive relationship similar to the above-mentioned authors. Dasanayake [30] and Davenport et al. [20], analyzing a large sample, used the Community Periodontal Index of Treatment Needs (CPITN) to diagnose periodontitis. Gomes-Filho et al. [36] conducted a study comparing the use of different definitions for measuring exposures in order to evaluate whether there was any distortion from the use of these measurements. The authors concluded that the magnitude of correlation between PLBW and maternal periodontitis varied according to the definition established. In another study performed by Vettore et al. [37], 13 methods of defining the extent of periodontal disease was used to avoid objections about measuring periodontal disease. They did not find any relationship between PLBW and periodontal disease with the measurement of PPD ≥4 mm and CAL ≥3 mm. In the present study, we used the definition of PPD ≥4 mm and CAL ≥3 mm that indicated no significant difference between the case and control groups.

Controversial results in the current literature can be also related to the variation of patient selection and exclusion criteria among different studies. Periodontal diseases share many common risk factors with pre-term delivery and low birth weight such as age, systemic health status, smoking, poor hygiene habits and low socioeconomic level. Women with systemic medical conditions and obstetric disorders, as well as women who received systemic antibiotics during pregnancy and who had multiple gestation were excluded from our study, since major risk indicators for pre-term birth are related to maternal medical conditions and pregnancy complications. Opposite to our study, several authors included such women and observed a positive relationship between periodontitis and PLBW [9,18,29,31,32]. Nabet et al. [32] have stated that maternal periodontitis was associated specifically with an increased risk of pre-eclampsia induced pre-term birth and not associated with spontaneous pre-term birth. As mentioned before, genitourinary infections are accepted as the major risk factors for prematurity and low birth weight [38]. In our research, patients suffering from these infections were excluded in order not to interfere with the effects of periodontal disease, since both infections share a common pathophysiological pathway causing early rupture of membranes. However, most studies supporting a positive relationship between prematurity and periodontitis have not paid much attention to this issue [9,18,29–31]. Therefore, we think that in these study groups the effects of genitourinary infections interfered with the effects of periodontal inflammation leading to spurious conclusions. The population in our study was unselected regarding the demographic characteristics. We especially paid extreme attention to exclude women who received an inadequate number of pre-natal consultations.

Lifestyle characteristics and daily habits may be potentially confounding factors that may influence the association between periodontitis and pre-term labor. In the present study, we could not demonstrate a significant difference between the patient groups in terms of daily habits and lifestyle characteristics, except that poor nutrition and underweight was recorded to be higher in the case group. In terms of obstetric history, the women enrolled in each group showed an important difference. Thus, the ratio of previous spontaneous abortions and prior pre-term delivery was higher in cases. These results were compatible with the data reported by Buduneli et al. [21]. On the other hand, when we evaluated the study groups together we found that women having periodontal disease had worse smoking habits, lower educational level, higher ratio of pregnancy and labor, higher ratio of previous spontaneous abortion, lower ratio of tooth brushing and worse oral hygiene compared to periodontally healthy women. In other words, similar to previous studies in the literature, we demonstrated that the above-mentioned independent factors strongly contribute to pre-term delivery.

To date, only a few authors have investigated the association between periodontitis and very low birthweight pre-term delivery (≤32 weeks and ≤1500 g) [39,40]. Our results are consistent with previous studies that found no significant association between periodontitis and the risk for pre-term birth at <37 weeks [39,40]. We also found no evidence that periodontal disease increases very pre-term birth risk of women (≤32 weeks), as reported by Michalowicz et al. [40], whereas Offenbacher et al. [39] reported a positive relation between periodontitis and very pre-term birth (≤32 weeks).

As distinct from other studies in the current literature, we believe that the strength of our study arises from the fact of being a blind study, having been examined by one dentist only, having rigid criteria for patient selection and being one of the rare studies in the medical literature evaluating the association between periodontitis and very low birth-weight preterm delivery. With regard to the study design and the data presented, it can be concluded that there is no association between periodontal disease and pre-term birth. In addition, there isn't a noteworthy difference between the study groups in terms of other risk factors inducing pre-term labor.

Early identification of various epidemiologic, clinical and environmental risk factors that are related to pre-term labor may allow modification of the traditional approaches to pre-natal care and,

ultimately, may reduce the rate of pre-term deliveries. In this respect, despite conflicting data in the current literature, early identification of maternal periodontal diseases by obstetricians and dentists is crucial because, unlike other medical conditions causing pre-term birth, periodontitis is preventable and treatable. Therefore, by means of this study we recommend routine periodontal screening to become a part of antenatal care for all pregnant women.

Declaration of interest: The authors alone are responsible for the content and writing of the paper.

Ethics: This study was undertaken in compliance with the guidelines of the Declaration of Helsinki and it was approved by the local ethics committee of the Dr. Behcet Uz Children's Hospital (2010/03). The participants signed an explicative authorization document of their own free will before enrollment in the study.

The authors of this study declare that they have no conflicts of interest and any financial agreements with pharmaceutical or biomedical firms whose products are pertinent to the subject matter dealt within the manuscript.

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