

# Periodontal disease as a risk factor for adverse pregnancy outcomes: a prospective cohort study

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## Abstract

**Aim:** The aim of this study was to determine the association between periodontitis and the incidence of preterm birth (PB), low birth weight (LBW) and preterm low birth weight (PLBW)

**Material and Methods:** One thousand and ninety-six women were enrolled. Periodontal data, pregnancy outcome variables and information on other factors that may influence adverse pregnancy outcomes were collected. Data were analysed using a logistic regression model.

**Results:** The incidence of PB and LBW was 6.6% and 6.0%, respectively. The incidence of PLBW was 3.3%. PB was related to mother's age, systemic diseases, onset of prenatal care, previous PBs, complications of pregnancy, type of delivery, the presence of untreated caries and the presence of periodontitis (odds ratio 1.77, 95% confidence interval: 1.08–2.88). LBW was related to mother's smoking habits, ethnicity, systemic diseases, previous LBW babies, complications of pregnancy and type of delivery. PLBW was related to mother's age, onset of prenatal care, systemic diseases, previous LBW babies, complications of pregnancy and type of delivery.

**Conclusions:** The factors involved in many cases of adverse pregnancy outcomes have still not been identified, although systemic infections may play a role. This study found a modest association between periodontitis and PB. Further research is required to establish whether periodontitis is a risk factor for PB and/or LBW.

Key words: low birth weight; periodontitis; preterm birth; risk factors

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Preterm birth (PB) and low birth weight (LBW) are the leading perinatal problems world wide and have evident public health implications, because they are closely related to perinatal mortality and morbidity (Goldenberg & Rouse 1998). Multiple factors, some of

which are preventable, have been associated with PB and/or LBW, e.g., alcohol, smoking or drug use during pregnancy, high or low maternal age (>34 years old or <17 years old), African-American ancestry, low socioeconomic status, inadequate prenatal care, low maternal body mass index (BMI), hypertension, generalized infections, genitourinary tract infections, cervical incompetence, diabetes, nutritional status, stress and multiple pregnancies (Li et al. 2000, Mealey 2000, Mokeem et al. 2004). Increasing efforts have been made to diminish the effects of these

risk factors by preventive interventions during prenatal care. However, these have not reduced the frequency of PB and/or LBW infants partly because these risk factors are not present in approximately 50% of cases. Consequently, the search continues for other causes for PB and/or LBW (Mealey 2000, Mokeem et al. 2004, Moreu et al. 2005), including the presence of chronic infectious diseases. In recent years, periodontal infections have been associated with different systemic diseases, e.g., atherosclerosis, myocardial infarction, stroke and diabetes mellitus (Offenbacher et al. 1996,

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Champagne et al. 2000, García et al. 2001, Paquette 2002, Tonetti et al. 2007). In 1996, a case-control study by Offenbacher et al. reported that periodontal disease was a significant risk factor for preterm low birth weight (PLBW). Following this pioneering research, several investigations have been published on the possible association between periodontal disease, PB and/or LBW. Some of these investigations showed results similar to those of Offenbacher et al. (1996), whereas others found no association between periodontal disease and adverse pregnancy outcomes (Vettore et al. 2006, Xiong et al. 2006). These differences could be explained by a lack of power due to a small sample size, by inadequate adjustment for confounders or by distinct definitions of periodontitis, among other factors. Furthermore, other recent studies have considered whether or not periodontal treatment of pregnant women may reduce the prevalence of PB and LBW (Mitchell-Lewis et al. 2001, López et al. 2002a,b, Jeffcoat et al. 2003, Michalowicz et al. 2006, Offenbacher et al., 2006a,b). Again, conflicting results have been observed, which could be related, in part, to differences in study design. Nonetheless, according to Michalowicz & Durand (2007), "at present, however, there is no compelling evidence to indicate that treatment of periodontitis can improve birth outcomes".

Therefore, there is an urgent need to definitively establish the true role of periodontal disease in the etiology of PB and/or LBW because of their important medical and economical implications, with a current incidence of PB that can reach 12%, even in developed countries like the United States (Martin et al. 2006).

The objective of this prospective study was to determine the association between periodontal disease and the incidence of PB, LBW and PLBW deliveries in a cohort of pregnant women.

## Material and Methods

### Study sample

A prospective cohort study was designed to evaluate the association between periodontal disease and PB and/or LBW. A sample size of 1106 women was required, based on an estimated prevalence of periodontitis of 25% in pregnant women and a preva-

lence of PB of 7.1% and of LBW of 7.2%, for a relative risk of 2, an  $\alpha$  error of 5% and a  $\beta$  error of 10%. Because no data on the oral health of pregnant women in Spain were available, the prevalence of periodontal disease in Spanish adults (Llodra et al. 2002) was used as a reference. To allow for the possible loss of subjects to the study, the initial sample comprised 1404 pregnant women seeking prenatal care at the University Hospital of Lleida (Spain) between March 2003 and January 2005. All potential participants signed an informed consent form to participation in the study, which was approved by the Ethical Committee of the Hospital. Inclusion criteria were: age between 18 and 40 years, pregnancy duration of 20–24 weeks and the presence of  $\geq 18$  teeth. Exclusion criteria were: multiple gestation, a history of diabetes before pregnancy, alcoholism, drug abuse, HIV infection, antibiotic indication due to invasive procedures and the presence of  $< 18$  teeth. One thousand three hundred thirty-four women met the inclusion criteria.

Demographic data and medical history were assessed by interview during the 20th gestational week, when all pregnant women in prenatal care routinely undergo an ultrasound examination. The questionnaire included items on age, ethnicity (Caucasian, Black, Gypsy and other: Arab, Asian and Latin-American), socioeconomic level (five categories), educational level (primary or less, high school and university), area of residence (rural, semi-rural and urban, depending on the number of inhabitants), smoking habits (five categories), alcohol intake (0 or  $\geq 1$  drink/week), BMI ( $< 20$ , 20–25, 25.1–30, 30.1–35 and  $> 35$ ), systemic diseases (anaemia and/or hypertension during pregnancy), obstetric history (number of previous pregnancies, previous preterm delivery, previous LBW and previous spontaneous miscarriage and onset of prenatal care (up to the eighth week or later). The assessment of socioeconomic status was based on the employment of the woman and her partner (or the head of the family in the case of women without partner), and grouped into five categories, I being the highest and V the lowest. Smoking habit was divided into five categories: never smoked or former smoker before pregnancy, former smoker of  $< 15$  cigarettes/day just until pregnancy, smoker of  $\geq 15$  cigarettes just until pregnancy,

smoker of  $< 6$  cigarettes during pregnancy and smoker of  $\geq 6$  cigarettes during pregnancy. When necessary, further clinical data were obtained from the Obstetrics Department records. The following variables were recorded shortly after delivery: newborn weight and sex, duration of pregnancy, genitourinary tract infections and antibiotic intake during pregnancy, gestational diabetes, pregnancy complications (vaginal bleeding, placenta previa, emergency surgery) and type of delivery (vaginal or caesarean).

### Periodontal variables

Following the assessment of demographic data and medical and dental history, full-mouth data were recorded on pocket probing depths (PPD) and clinical attachment levels (CAL). Clinical parameters were assessed using a UNC-15 periodontal probe by a single calibrated examiner at six sites/tooth excluding third molars. The plaque index (O'Leary et al. 1972) was recorded by assigning a binary score to each surface (1 for plaque present, 0 for absent) and calculating the percentage of total tooth surfaces that revealed the presence of plaque detected by the use of a disclosing agent. Similarly, full-mouth bleeding on gentle probing (BOP) was calculated after assessing dichotomously the presence of bleeding from the bottom of the pocket with a manual probe. Full-mouth PPD and recession of the gingival margin (REC) were recorded at the same time, with measurements rounded to the nearest millimetre. Recession (REC) was recorded as a positive value if the free gingival margin occurred apical to the cemento-enamel junction (CEJ), whereas it was recorded as a negative value if it was coronal to the CEJ. In the latter case, the examiner reinserted the probe angled  $45^\circ$  into the site in order to detect the CEJ. Full-mouth CAL was calculated as PPD plus REC.

### Investigator calibration

A single examiner (A. A.) performed all the measurements: at the beginning of the study, the examiner was calibrated against an expert periodontist who represented the gold standard (J. J. E.). A total of eight non-study subjects with moderate to advanced periodontitis were recruited and used for the calibration exercise. The single designated examiner measured PPD and recession of the

gingival margin (REC) on Ramfjord teeth, at four sites per tooth. After 7 days, the examiner repeated the examination. Likewise, the expert periodontist performed an additional examination. Upon completion of all measurements, intra-examiner and inter-examiner reproducibilities for CAL measurement were assessed.

Because PD and CAL scores can be considered to be ordinal categorical variables, as they are measured in whole millimetres, weighted  $\kappa$  values were used. The weighted  $\kappa$  values for inter-examiner calibration were 0.79 [confidence interval (CI) 95% 0.71–0.88] for PPD and 0.69 (CI 95%, 0.55–0.85) for CAL, whereas intra-examiner calibration showed weighted  $\kappa$  values of 0.83 (0.69–0.97) for PPD and 0.88 (0.72–1.04) for CAL.

The oral examination also included the number of missing teeth, the presence of calculus and the number of untreated dental caries.

### Definitions

Periodontal disease was defined as the presence of  $\geq 4$  teeth with  $\geq 1$  site with PPD  $\geq 4$  mm and CAL  $\geq 3$  mm at the same site (López et al. 2002a, b). LBW was defined as newborn weight of  $< 2500$  g at  $\leq 1$  h after delivery. PB was defined as a delivery at  $< 37$  weeks of gestation (gestational age determined by last menstrual period and ultrasound foetal measurement). A PLBW infant was premature ( $< 37$  weeks) with a LBW ( $< 2500$  g).

### Statistical analysis

Data were entered into an Excel (Microsoft office 2003) database and were proofed for entry errors. The database was subsequently locked, imported into SPSS for Windows (SPSS Inc. version 12.0) formatted and analysed. The relationship between each variable and PB, LBW and PLBW were analysed. All variables were also compared between women with and without periodontitis. Independent samples *t*-test was performed for continuous variables (i.e., full-mouth mean PPD) whilst the chi-square test ( $\chi^2$ ) was used to analyse categorical variables (i.e. ethnicity). Statistical significance was set at  $p < 0.05$ . All variables showing an association with a  $p \leq 0.20$  in the bivariate analysis were included in a logistic regression model. Dependent variables were PB,

LBW and PLBW. Non-adjusted odds ratio (ORs) (95% CI) were obtained for all variables associated ( $p < 0.20$ ) with PB, LBW and PLBW. Adjusted ORs (95% CI) were obtained for all variables associated with PB, LBW and PLBW.

### Results

Out of the 1404 initially examined women, 1334 met the inclusion criteria. Thirty-four (2.6%) of these were excluded because the delivery took place at another hospital, whereas another four women were lost to the study because of miscarriage, resulting in a final sample of 1296 women. At delivery, 85 newborns (6.6%) were PB, 78 (6.0%) LBW and 43 (3.3%) PLBW. Periodontal disease was present in 338 (26.1%) women and absent in the remaining 958.

Table 1 lists the demographic and obstetric data for all subjects grouped by pregnancy outcome. Table 2 shows periodontal data for the women according to pregnancy outcome. A significant association was found between PB and mother's age, ethnicity, place of residence, number of untreated caries, plaque index, presence of systemic disease, previous PB, previous LBW, receipt of prenatal care, pregnancy complications, type of delivery and periodontal disease. A significant association was found between LBW and mother's age, ethnicity, smoking habit, number of untreated caries, presence of periodontitis, presence of systemic disease, previous PB, previous LBW, previous spontaneous abortions, pregnancy complications and type of delivery. Finally, a significant association was found between PLBW and mother's age, ethnicity, presence of systemic disease, previous PB, previous LBW, receipt of prenatal care, pregnancy complications and type of delivery. No statistically significant association was observed between periodontal disease and PLBW.

Tables 3–5 show the results of logistic regression analyses for variables influencing adverse pregnancy outcomes. After adjusting for confounding variables, a significant association was found between PB and mother's age, place of residence, plaque index, systemic disease, previous PB, receipt of prenatal care, presence of untreated caries, presence of periodontal disease and type of delivery. A significant association was also found between LBW and

mother's ethnicity, tobacco use, presence of systemic disease, pregnancy complications, previous LBW and type of delivery. No relationship was found between LBW and periodontal disease. PLBW was significantly associated with mother's age, presence of systemic disease, pregnancy complications, previous LBW, receipt of prenatal care and type of delivery. No relationship was found between PLBW and periodontal disease.

### Discussion

Preterm delivery and LBW are the leading causes of neonatal morbidity and mortality, and contribute to nearly half of all severe long term, birth related, neurological morbidities, including cerebral palsy (McCormick 1985). Despite efforts made, there has been no reduction in their incidence. In fact, the percentage of premature babies in the United States has increased nearly 30% since 1983, and represents  $> 12.5\%$  (17.9 % for non-hispanic black women) of all deliveries (Martin et al. 2006). Although many risk factors associated with PB and/or LBW have been identified, including genitourinary tract infections, about 50% of all cases of PB are of unknown aetiology. Over the last two decades, several investigations have shown an association between periodontitis and PB and/or LBW. Periodontitis is an infection that affects tooth-supporting tissues. The rationale for considering it capable of influencing pregnancy outcome is that it is a Gram-negative anaerobic infection that may trigger earlier production of cytokines and prostaglandins (as in the case of genitourinary tract infections) thereby promoting premature onset of labor contractions and PB and LBW deliveries (Offenbacher et al. 1996). However, a causal relationship between periodontitis and PB or LBW has yet to be demonstrated.

Most of the variables found to be associated with PB, LWB and PLBW in the present cohort study of 1296 pregnant women are well known risk factors explaining PB and/or LBW (e.g. presence of systemic diseases, pregnancy complications, onset of prenatal care, type of delivery, and a history of deliveries of these types, among other factors). A modestly significant relationship was observed between periodontitis and PB (adjusted OR of 1.77), whereas

Table 1. Frequency of study subjects by pregnancy outcome and explanatory variables

	All subjects, <i>n</i> = 1296	PB, <i>n</i> = 85; 6.6% <i>n</i> (%)	<i>p</i> value	LBW, <i>n</i> = 78; 6.0% <i>n</i> (%)	<i>p</i> value	PLBW, <i>n</i> = 43; 3.3% <i>n</i> (%)	<i>p</i> value
Age (years)	29.6	28.0 (5.2)*	0.003	29.6 (5.1)*	0.250	28.2 (5.1)*	0.065
Ethnicity			0.012		0.018		0.045
Caucasian	1019 (78.6)	65 (6.4)		60 (5.9)		32 (3.1)	
Black	58 (4.5)	8 (13.8)		8 (13.8)		5 (8.6)	
Gipsy	24 (1.9)	4 (16.7)		3 (12.5)		2 (8.3)	
Others	195 (15)	8 (4.1)		7 (3.6)		4 (2.1)	
Socioeconomic level			0.907		0.921		0.993
I	89 (6.9)	6 (6.7)		6 (6.7)		3 (3.4)	
II	138 (10.6)	9 (6.5)		8 (5.8)		4 (2.9)	
III	281 (21.7)	15 (5.3)		15 (5.3)		9 (3.2)	
IV	229 (17.7)	17 (7.4)		12 (5.2)		7 (3.1)	
V	559 (43.1)	38 (6.8)		37 (6.6)		20 (3.6)	
Education level			0.914		0.583		0.532
Primary or less	537 (41.1)	36 (6.7)		36 (6.7)		20 (3.7)	
High school	492 (38.0)	33 (6.7)		29 (5.9)		17 (3.5)	
University	267 (20.6)	16 (6.0)		13 (4.9)		6 (2.2)	
Single	163 (12.6)	11 (6.7)	0.919	9 (5.5)	0.773	4 (2.5)	0.509
Residence			0.004		0.279		0.478
Rural	142 (11.0)	6 (4.2)		5 (3.5)		5 (3.5)	
Semi-rural	657 (50.7)	32 (4.9)		38 (5.8)		18 (2.7)	
Urban	497 (38.5)	47 (9.5)		35 (7.0)		20 (4.0)	
Body mass index			0.129		0.102		0.339
< 20	212 (16.4)	21 (9.9)		21 (9.9)		11 (5.2)	
20–25	753 (58.1)	42 (5.6)		37 (4.9)		21 (2.8)	
25.01–30	252 (19.4)	14 (5.6)		14 (5.6)		7 (2.8)	
30.01–35	51 (3.9)	5 (9.8)		4 (7.8)		2 (3.9)	
> 35	28 (2.2)	3 (10.7)		2 (6.0)		2 (7.1)	
Smoking			0.060		0.000		0.102
Never or ex-smoker	820 (63.3)	48 (5.9)		35 (4.3)		21 (2.6)	
Ex-smoker pregnancy < 15 cigarette	160 (12.4)	7 (4.4)		11 (6.9)		5 (3.1)	
Ex-smoker pregnancy ≥ 15 cigarettes	43 (3.3)	5 (11.6)		3 (6.7)		3 (4.7)	
Smoker < 6 cigarettes	109 (8.4)	7 (6.4)		6 (5.5)		4 (3.7)	
Smoker ≥ 6 cigarettes	163 (12.6)	18 (11.0)		23 (14.0)		11 (6.7)	
≥ 1 alcohol unit per week <i>n</i> (%)	73 (5.6)	3 (4.1)	0.383	4 (5.4)	0.841	3 (4.1)	0.698
Systemic diseases	60 (4.6)	12 (20.0)	0.000	9 (15.0)	0.003	8 (13.3)	0.000
> 1 previous pregnancy	269 (20.8)	24 (8.9)	0.079	21 (7.8)	0.167	13 (4.8)	0.120
Previous preterm delivery	75 (5.8)	12 (16.0)	0.001	11 (14.7)	0.001	6 (8.0)	0.020
Previous low birth weight	66 (5.1)	14 (21.2)	0.000	12 (18.2)	0.000	8 (12.0)	0.000
Previous miscarriage	303 (23.4)	22 (9.4)	0.052	21 (9.0)	0.036	12 (5.1)	0.088
Onset prenatal care > 8th week	646 (49.9)	58 (9.2)	0.000	42 (6.5)	0.466	30 (4.6)	0.008
Pregnancy complications	53 (3.4)	9 (18.0)	0.001	8 (16.0)	0.002	6 (12.0)	0.000
Genitourinary infections	271 (20.9)	16 (5.9)	0.622	20 (7.4)	0.291	11 (4.0)	0.445
Antibiotic intake	338 (26.1)	26 (7.7)	0.330	24 (7.1)	0.333	14 (4.1)	0.327
Gestational diabetes	98 (7.6)	5 (5.1)	0.543	6 (6.1)	0.966	0 (0.0)	0.056
Caesarean delivery	276 (21.3)	34 (12.3)	0.000	36 (13.0)	0.000	23 (8.3)	0.000

\*Mean (standard deviation).

PLBW, preterm low birth weight; LBW, low birth weight; PB, preterm birth.

no significant association was found between periodontitis and LBW/PLBW. These results differ from the findings of some previously published cohort studies, case-control studies, and clinical trials (Xiong et al. 2006). Eleven cohort studies found such associations (Jeffcoat et al. 2001, Offenbacher et al. 2001, López et al. 2002a,b, Boggess et al. 2003, Hasegawa et al. 2003, Dortbudak et al. 2005, Marín et al. 2005, Moreu et al. 2005, Rajapakse et al. 2005, Boggess et al. 2006, Offenbacher et al. 2006a, b) and one reported that this

association may be present (Romero et al. 2002). However, four cohort studies found no association (Holbrook et al. 2004, Moore et al. 2004, Farrell et al. 2006, Meurman et al. 2006). These cohort studies varied in sample size, type of population, presence and management of aetiological or risk factors, and definition of periodontal disease. While the definitions of PB and LBW are well established, no consensus has yet been achieved on the definition of periodontitis in periodontal research, essential to optimize the interpretation,

comparison and validation of clinical data (Borrell & Papapanou 2005). It seems reasonable to assume that a difference in the definition of periodontitis could influence findings on its association with pregnancy outcomes, although it was recently reported that the use of varied definitions of periodontitis did not affect the association found with other systemic diseases, e.g., myocardial infection (Adriankaja et al. 2006). For the present study, the definition of periodontitis used by López et al. (2002a,b) was selected, which includes PPD, CAL

Table 2. Periodontal parameters mean SD for subjects that experienced PB, LBW and PLBW and those who did not

	Full term, <i>n</i> = 1211	PB, <i>n</i> = 85	<i>p</i> value	Normal weight, <i>n</i> = 1218	LBW, <i>n</i> = 78	<i>p</i> value	Non PLBW, <i>n</i> = 1253	PLBW, <i>n</i> = 43	<i>p</i> value
Periodontitis*	307 (25.4)*	31 (36.5)*	0.024	310 (25.5)*	28 (35.9)*	0.042	322 (25.7)*	16 (37.2)*	0.091
% Gingival bleeding	27.2 (29.5)	26.8 (26.0)	0.907	27.2 (9.4)	26.2 (26.8)	0.756	27.1 (29.3)	30.0 (28.9)	0.518
% Plaque (plaque index)	49.0 (24.4)	56.2 (28.2)	0.024	49.3 (24.4)	56.8 (29.2)	0.306	49.4 (24.5)	54.3 (30.4)	0.303
Probing pocket depth (PPD)	2.1 (0.9)	2.2 (1.1)	0.308	2.1 (0.9)	2.2 (1.1)	0.372	2.1 (0.9)	2.2 (1.1)	0.236
% teeth PPD 0–3 mm	81.9 (29.4)	75.6 (34.1)	0.061	81.8 (29.4)	76.4 (34.6)	0.124	81.7 (29.6)	73.9 (35.5)	0.092
% teeth PPD 4–5 mm	19.3 (23.0)	18.4 (25.0)	0.116	14.4 (23.1)	17.2 (24.7)	0.314	14.5 (23.1)	18.4 (24.8)	0.272
% teeth PPD ≥ 6 mm	3.8 (13.7)	6.0 (17.4)	0.164	3.8 (13.7)	6.4 (17.9)	0.106	3.8 (13.7)	7.7 (20.0)	0.076
Clinical attachment level (CAL)	1.9 (0.8)	2.1 (1.1)	0.194	1.9 (0.8)	2.0 (1.0)	0.210	1.9 (0.8)	2.1 (1.0)	0.125
% teeth CAL 0–3 mm	86.7 (24.5)	79.9 (31.2)	0.052	86.7 (24.5)	79.7 (32.1)	0.063	86.6 (24.7)	77.9 (32.5)	0.091
% teeth CAL 4–5 mm	10.9 (19.1)	14.9 (21.9)	0.103	10.9 (19.0)	15.6 (23.7)	0.089	11.0 (19.2)	16.1 (21.9)	0.087
% teeth CAL > 6 mm	2.4 (10.2)	5.2 (16.7)	0.132	2.5 (10.5)	4.7 (17.0)	0.165	2.5 (10.5)	6.0 (16.9)	0.183

\*Number (percentage).

LBW, low-birth weight; PB, preterm birth; PLBW, preterm low birth weight.

Table 3. Adjusted odds ratios (OR) for the variables influencing preterm birth

Variable	OR	95% CI
Age <sup>†</sup>	0.93*	0.89–0.98
Area of residence		
Urban	1	
Semi-rural	0.51	0.20–1.28
Rural	0.51*	0.31–0.83
Systemic diseases		
No	1	
Yes	3.65*	1.78–7.51
Pregnancy complications		
No	1	
Yes	2.81*	1.26–6.24
Previous pre-term birth		
No	1	
Yes	3.49*	1.70–7.15
Onset prenatal care		
≤ 8th week	1	
> 8th week	2.12*	1.30–3.48
Type of delivery		
Vaginal	1	
Caesarean	3.10*	1.90–5.05
Untreated caries		
No	1	
Yes	1.83*	1.04–3.21
Periodontal disease		
No	1	
Yes	1.77*	1.08–2.88

\*Adjusted OR statistically significant.

<sup>†</sup>Age in years is a quantitative variable; in this case the OR given is the odds ratio for each increasing unit (year) of age.

CI, confidence interval.

and threshold values associated with the assessment of the presence of periodontitis (Tonetti & Claffey 2005). López et al. (2002a, b) found that periodontal disease was an independent risk factor for PB with higher OR than ours (OR of 2.9 *versus* 1.7, respectively). A similar finding has been reported by other authors, in many cases with even

Table 4. Adjusted odds ratios (OR) for the variables influencing low birth weight

Variable	Odds ratio	95% CI
Ethnicity	1	
White	3.65*	1.53–8.74
Black	2.02	0.55–7.40
Gipsy	0.79	0.34–1.88
Others		
Smoking habit		
No smoker or ex-smoker	1	
Ex-smoker in pregnancy < 15 cigarettes	1.74	0.88–3.6
Ex-smoker in pregnancy ≥ 15 cigarettes	1.59	0.44–5.72
Smoker < 6 cigarettes	1.48	0.58–3.78
Smoker ≥ 6 cigarettes	4.17*	2.25–7.75
Systemic diseases		
No	1	
Yes	2.47*	1.12–5.48
Pregnancy complications		
No	1	
Yes	3.00*	1.28–7.04
Previous low birth weight		
No	1	
Yes	4.24*	2.07–8.67
Type of delivery		
Vaginal	1	
Caesarean	3.59*	2.19–5.90

\*Adjusted OR statistically significant.

CI, confidence interval.

higher OR (Vergnes & Sixou 2007). Differences among studies may also derive from a failure to control for potentially confounding risk factors that may be responsible for the association between pregnancy outcomes and PB or LBW. For instance, numerous variables were controlled for in the present analysis, but not all of them were considered by some authors (Jeffcoat et al. 2001, Holbrook et al. 2004, Buduneli et al. 2005, Dörtbudak et al. 2005, Moore et al. 2005, Offenbacher et al. 2006a, b) such as socioeconomic status and smoking, ethnicity, history of

adverse pregnancy outcomes, infections (e.g. bacterial vaginosis and chorioamnionitis), antibiotic use during pregnancies, BMI, maternal disorders (hypertension, diabetes), and onset of prenatal care, many of which are considered crucial in explaining PB and/or LBW. In fact, despite efforts made in the present study, it is even possible that an unknown confounding effect might have influenced our results. A third factor which should be taken into account when considering the association between periodontitis and PB and/or LBW is whether the sample size is

Table 5. Adjusted odds ratios (OR) for the variables influencing preterm low birth weight

Variable	OR	95% CI
Age (continuous variable)	0.93*	0.87–0.99
Systemic diseases		
No	1	2.06–11.64
Yes	4.90*	
Pregnancy complications		
No	1	1.58–10.78
Yes	4.13*	
Previous low birth weight		
No	1	2.67–15.34
Yes	6.40*	
Onset prenatal care		
≤8th week	1	1.19–4.73
>8th week	2.38*	
Type of delivery		
Vaginal	1	2.52–9.22
Cesarean	4.82*	

\*Adjusted OR statistically significant.  
CI, confidence interval.

inadequate (Romero et al. 2002, Holbrook et al. 2004, Mokeem et al. 2004, Radnai et al. 2004, Dörtbudak et al. 2005) especially when a non-significant association is found (Holbrook et al. 2004). In the present study, the sample size was designed to obtain a power of 90% and an OR of 2, recruiting 20% more women than required for this purpose to compensate for any possible loss of subjects to the study.

Interestingly, a significant association between periodontal disease and adverse pregnancy outcomes has consistently been found in populations with a high incidence of preterm deliveries, including African-American women and those from economically disadvantaged families (Offenbacher et al. 1996, Dasanayake 1998, Jeffcoat et al. 2001, Louro et al. 2001, Offenbacher et al. 2001, López et al. 2002a,b, Romero et al. 2002, Boggess et al. 2003, Goepfert et al. 2004, Mokeem et al. 2004, Jarjoura et al. 2005). In contrast, most studies conducted in European countries or Canada, which offer universal health care, have shown significantly lower percentages of PB and/or LBW and no association between periodontal disease and adverse pregnancy outcomes (Davenport et al. 2002, Holbrook et al. 2004, Moore et al. 2004, 2005, Farrell et al. 2006, Meurman et al. 2006). Hence, it could be speculated that the effect of periodontal disease on pregnancy outcomes might differ according to the socioeconomic status and access to prenatal care of the

women. In the present study, no relationship was found between socioeconomic status and adverse pregnancy outcomes, and all participants had free access to medical and prenatal medical care, which might offer a better explanation of the low percentage of PB and/or LBW deliveries in this study.

In conclusion, the present study found a modest association between periodontitis and PB but not between periodontitis and LBW or PBLW.

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**Clinical Relevance**

*Scientific rationale for the study:* Contradictory reports on the association between periodontitis and adverse perinatal outcomes suggest the need for methodological improvements in this area of research.

*Principal findings:* A modest association was found between perio-

donitis and PB. Although a slightly lower weight was observed in newborns from mothers with periodontitis, no significant association was found between periodontitis and LBW or PBLW deliveries.

*Practical implications:* To date, the nature of the association between periodontitis and PB/LBW remains

unclear, and the interventional studies do not fully support the need to screen pregnant women for periodontitis to apply preventive therapy. Nevertheless, clinicians should be alert to the possibility that future well-conducted investigations may indicate the need for a change in this approach.

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