

Periodontal Therapy Reduces the Rate of Preterm Low Birth Weight in Women With Pregnancy-Associated Gingivitis

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Background: One hypothesis to explain the association between periodontal disease (PD) preterm/low birth weight (PT/LBW) is that PT/LBW may be indirectly mediated through translocation of bacteria or bacterial products in the systemic circulation. Transient bacteremias occur in subjects with marginal periodontitis or with gingivitis, and it is possible that bacteria and their products may reach the placental membranes hematogenously and provide the inflammatory effect to induce preterm labor. The effect of gingivitis as a potential risk factor for PT/LBW has still not been studied. A randomized controlled trial was undertaken to determine the effect of routine plaque control and scaling on the pregnancy outcomes in women with gingivitis.

Methods: Eight hundred seventy (870) pregnant women with gingivitis, aged 18 to 42, were enrolled while receiving prenatal care in Santiago, Chile. Women were randomly assigned in a two-to-one fashion to either a treatment group (N = 580), receiving periodontal treatment before 28 weeks of gestation or to a control group (N = 290), receiving periodontal treatment after delivery. Periodontal therapy consisted of plaque control, scaling, and daily rinsing with 0.12% chlorhexidine. Maintenance therapy was provided every 2 to 3 weeks until delivery, and consisted of oral hygiene instruction and supragingival plaque removal by instrumentation, as needed. The primary outcomes assessed were delivery at less than 37 weeks of gestation or an infant weighing less than 2,500 g.

Results: Of the 870 women enrolled, 36 women (27 in the treatment group and nine in the control group) were excluded from the analyses for different reasons. The incidence of PT/LBW in the treatment group was 2.14% (12/560) and in the control group, 6.71% (19/283) (odds ratio [OR] 3.26; 95% confidence interval [CI] 1.56 to 6.83; $P = 0.0009$). Multivariate logistic regression analysis showed that, after adjusting for several known risk factors for PT/LBW, women with gingivitis were at a higher risk of PT/LBW than women who received periodontal treatment (OR 2.76; 95%CI 1.29 to 5.88; $P = 0.008$).

Conclusions: Periodontal treatment significantly reduced the PT/LBW rate in this population of women with pregnancy-associated gingivitis. Within the limitations of this study, we conclude that gingivitis appears to be an independent risk factor for PT/LBW for this population. *J Periodontol 2005;76:2144-2153.*

KEY WORDS

Clinical trials, controlled; clinical trials, randomized; gingivitis; infant, low birth weight; infant, premature; risk factors.

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One of the main causes of perinatal morbidity and mortality throughout the world is preterm delivery, and in about 50% of all preterm deliveries, the etiology is unknown.¹ Increasing evidence supports a relationship between symptomatic nongenital maternal infections and preterm labor, premature rupture of the membranes, and preterm delivery. Results from epidemiologic, molecular, microbiologic, obstetric, and animal model studies, as well as from interventional studies, show that infection and inflammation in the mother play primary roles in about 50% of episodes of preterm rupture of membranes and preterm birth (PT).^{2,3}

Results of two case-control studies^{4,5} have suggested that periodontal infections may be among the maternal infections associated with adverse pregnancy outcomes. If periodontal infections are a cause of preterm birth, it might be expected that eradication of such infections would reduce the risk of preterm birth. Randomized controlled trials testing interventions are considered to be the strongest evidence that the factor identified is in the causal chain. Results from some intervention studies⁶⁻⁹ have demonstrated a significant reduction of preterm births (PT) and of low birth weight (LBW) infants in women with chronic periodontitis who received periodontal therapy prepartum, compared to women who did not receive periodontal intervention. These preliminary intervention studies provide initial evidence that periodontitis is a risk factor for PT/LBW and that periodontal therapy may reduce the risk of PT/LBW. One of the hypotheses to explain the relation between periodontal disease and preterm birth is that periodontal infection is a source of bacteria and bacterial products that may spread from the infected periodontium to the amniotic cavity, as when transient bacteremia occurs in patients with periodontitis.^{4,10} It has been demonstrated that transient bacteremia commonly occurs in subjects with periodontitis¹¹ as well as in those with gingival inflammation,¹² and bacteria or their products may conceivably reach the placental tissues providing the inflammatory effect for labor induction.¹³

Plaque-induced gingivitis is an inflammation of the gingiva resulting from bacterial infection, and this disease is the most common periodontal disease in pregnant women.^{14,15} During pregnancy, the prevalence and severity of gingivitis have been reported to be elevated yet unrelated to the amount of plaque present.^{16,17} However, the severity of gingivitis is correlated with sex steroid hormone levels during pregnancy.¹⁶ The characteristics of pregnancy-associated gingivitis are similar to plaque-induced gingivitis, but there is a tendency to a more severe gingival inflammation.^{14,15} There is evidence that some periodontal pathogens can cross the pla-

cental barrier and produce infection in the fetal membranes. *Prevotella intermedia* can be found at high concentrations in pregnancy-associated gingivitis,¹⁸ and the prevalence of positive fetal anti-IgM specific for *P. intermedia* was found to be significantly higher in preterm than in full-term neonates. The fetal antibody seropositivity for *P. intermedia*, as indexed by cord blood IgM, suggests in utero exposure to the fetus to this bacterium or its products.¹⁰

Fusobacterium nucleatum is one of the most commonly recovered organisms from sites with gingivitis,¹⁹ and is the most frequently isolated species from amniotic fluid cultures obtained from pregnant women with premature labor and intact placental membranes.²⁰ Recently, a study of pregnant mice showed that *F. nucleatum* can cross the placenta and spread to the amniotic fluid producing premature delivery and stillbirths.²¹ Thus, there is some basis to support the hypothesis that gingivitis may be a potential risk factor for PT/LBW, but the association between pregnancy-associated gingivitis with preterm birth has not been explored. A randomized controlled trial in pregnant women with gingivitis was undertaken to address the following questions: 1) Is pregnancy-associated gingivitis related to PT/LBW? and 2) Does periodontal therapy reduce the PT/LBW rate in pregnant women with gingivitis? The multivariate logistic analyses used in the current study determined the effect of each intervention or risk factor on the outcome.

MATERIALS AND METHODS

Patient Population

The study population consisted of pregnant women who received uniform prenatal care in a public health clinic in Santiago, Chile. Routine prenatal care included periodic examinations, screening for pregnancy complications, nutritional advice, stress reduction, education about symptoms of preterm labor, correction of identified risk factors, and referral to the high-risk obstetric clinic when appropriate.

Selection of Subjects

Criteria for inclusion were otherwise healthy pregnant women over age 18, with a single gestation, 22 weeks or less of gestation, gingival inflammation with $\geq 25\%$ of sites with bleeding on probing, and no sites with clinical attachment loss > 2 mm.

Exclusion criteria included fewer than 18 natural teeth, indication of prophylactic antibiotics for invasive procedures, diabetes previous to pregnancy, and the intention to deliver at a hospital other than that of the study.

Potential participants were identified by the midwives who attended the prenatal care clinics. A total of 1,296 women were screened, and 870 women with

gingivitis were selected. The study protocol was approved by the institutional ethics committee, and all women who participated did so voluntarily and gave their informed consent.

Sample Size

Assuming a probability of PT/LBW of 20% in the control group and of 10% in the treatment group, a sample of 290 women in each group might detect a significant difference of PT/LBW between groups ($P < 0.05$; two-sided) with a power of 80%. In order to increase the statistical power, it was decided to allocate unequal numbers of participants to each group. Thus, for each woman allocated to the control group, two women were placed in the treatment group.

Determining Periodontal Status

Upon entering the study, all women received a full-mouth periodontal examination and the following variables were measured: oral hygiene status, gingival inflammation, probing depth (PD), and clinical attachment level (CAL). Oral hygiene status was assessed as the percentage of surfaces demonstrating plaque. Dichotomous measures of supragingival plaque accumulation were made by running a periodontal probe at the cervical surface of each tooth. The presence of plaque was positive when a continuous band of plaque was found in contact with the gingival tissue on the cervical portion of mesial, buccal, distal, and lingual tooth surfaces. Plaque scores were calculated as the percentage of surfaces examined demonstrating plaque.

Probing depth and attachment level measurements were made at the mesio-buccal, buccal, disto-buccal, disto-lingual, lingual, and mesio-lingual positions of every tooth except third molars. CAL was measured using the cemento-enamel junction as a reference point. Bleeding on probing (BOP) was assessed on the six sites at which probing depth measurements were taken and deemed positive if bleeding occurred within 15 seconds after probing. BOP was expressed as the percentage of sites showing bleeding. Clinical measurements were recorded to the nearest millimeter using a calibrated periodontal probe by a single calibrated examiner.

Recording Maternal Characteristics

Demographic factors such as age, marital status, and educational level and detailed data about previous and current pregnancies were obtained from medical records and interviews during prenatal visits. A medical, obstetric, and social history was taken according to the protocol of the prenatal care program for each patient. Information on known risk factors and obstetric factors were collected and included the following: in relation to pregnancy history, the number carried to full term, previous preterm deliveries, low weight

births, previous pregnancies aborted, and live births were recorded. In relation to the current pregnancy, maternal age at time of study entry, onset of prenatal care, nutritional status, tobacco use, alcohol consumption, use of illicit drugs, sexually transmitted diseases, asymptomatic bacteriuria, urinary infections, vaginosis or any other maternal infectious disease, number of prenatal visits, intrauterine growth restriction, fetal death (the current pregnancy may end due to fetal death), gestational age, and birth weight were recorded.

Prenatal care included the following: blood pressure measurements, urine tests, blood tests, recording of maternal weight and height, and physical and pelvic examinations. At each prenatal visit, an evaluation of nutritional status was done to determine if weight gain was adequate. A normal standard of the weight-to-height proportion established for Chilean women was used for the evaluation of nutritional status. At every week of gestation, pregnant women should gain weight within the recommended range for her weight-to-height proportion. A nomogram for Chilean women²² was used to assess whether weight gain was adequate. Underweight women received supplementary nutrition. Women with symptomatic or asymptomatic bacteriuria (urine culture with $>100,000$ CFU) were treated with nitrofurantoin for 10 days.

All women with vaginosis were treated with locally applied antibiotics, either metronidazole, clotrimazole, or nistatine, according to the results of microbiological examinations of vaginal swabs.

Randomization

Randomization was done equalizing gingivitis as the relevant variable, and the percentage of BOP sites was selected as the variable describing gingivitis. Patients were assigned to one of two categories: those with $<50\%$ BOP sites and those with $\geq 50\%$ BOP sites. Three women with $<50\%$ BOP sites were grouped, and another three women with $\geq 50\%$ BOP sites were assigned to another group. Each one of the three women in both groups was given two numbers, simply because a die has six numbers. The numbers given were 1-2, 3-4, and 5-6, and were given in the same order in which the women were allocated to the group. One woman of each group of three was selected by rolling a die. The selected woman of each group was assigned to the control group, and the other two to the treatment group.

Periodontal Intervention and Timing

For women in the treatment group, periodontal therapy consisted of plaque control instructions, supra- and subgingival scaling, and crown polishing. At the beginning of treatment, each woman was provided with toothbrushes and chlorhexidine and instructed

to rinse once a day with 0.12% chlorhexidine until delivery. Periodontal therapy was completed before 28 weeks of gestation, and maintenance therapy was provided every 2 to 3 weeks until delivery. Maintenance therapy was provided every 2 to 3 weeks until delivery, and consisted of oral hygiene instruction and supragingival plaque removal by instrumentation, as needed. Carious lesions were treated, and all teeth indicated for extraction were extracted from both groups.

Women in the control group were monitored two to three times during pregnancy, and repeated periodontal examinations were performed after 30 weeks of gestation to assess changes in periodontal status.

Pregnancy Outcome Measures

Primary outcomes measured were preterm birth and low birth weight. Preterm birth was defined as a delivery before 37 complete weeks of gestation of an infant with a birth weight below 2,500 g which followed spontaneous labor and/or spontaneous rupture of the membranes, regardless of route of delivery. Preterm deliveries required for medical indications in which there was no spontaneous labor or no rupture of membranes were not included in preterm birth definition.

An infant born at term (≥ 37 weeks of gestation) with a birth weight less than 2,500 g was diagnosed as having intrauterine growth restriction if the birth weight was in the 10th percentile for gestational age as determined by the nomogram for Chilean newborn infants.²³ A birth outcome which occurred after 37 weeks of gestation or the birth of an infant with a weight $\geq 2,500$ g was defined as normal.

The delivery date was calculated from the last menstrual period and from ultrasound examination. Dates obtained from ultrasound examination were used in cases with unknown menstrual dates.

Labor and delivery management decisions were made by the resident staff and attending physicians at the hospital. They had no knowledge that the patients were participating in a research study. Information concerning the pregnancy outcomes was obtained from the hospital records by the obstetrician researcher (JG) who did not work at the study hospital. He was masked to the periodontal characteristics of the patient and to the group to which the patient belonged.

Statistical Methods

Women who had a preterm delivery or had a low birth weight infant (LBW) were grouped in the preterm/low birth weight group (PLBW) for the analyses of data to identify the risk factors. The analyses included descriptive statistics and both univariate and multivariate logistic regression analyses. Comparisons of proportions were performed using the chi square test

or Fisher's exact test and differences between continuous variables by the unpaired *t* test. Data to calculate the incidence and the odds ratios for PT, LBW, and PT/LBW were analyzed on an intention-to-treat basis, regardless of compliance with the protocol, and all women initially enrolled in the study were included except three in the treatment group and two in the control group who quit coming to the clinic. Unadjusted and adjusted odds ratios (OR) were calculated with 95% confidence interval (CI). Statistical significance was defined as $P < 0.05$. Statistical analysis was performed using a software program.[§]

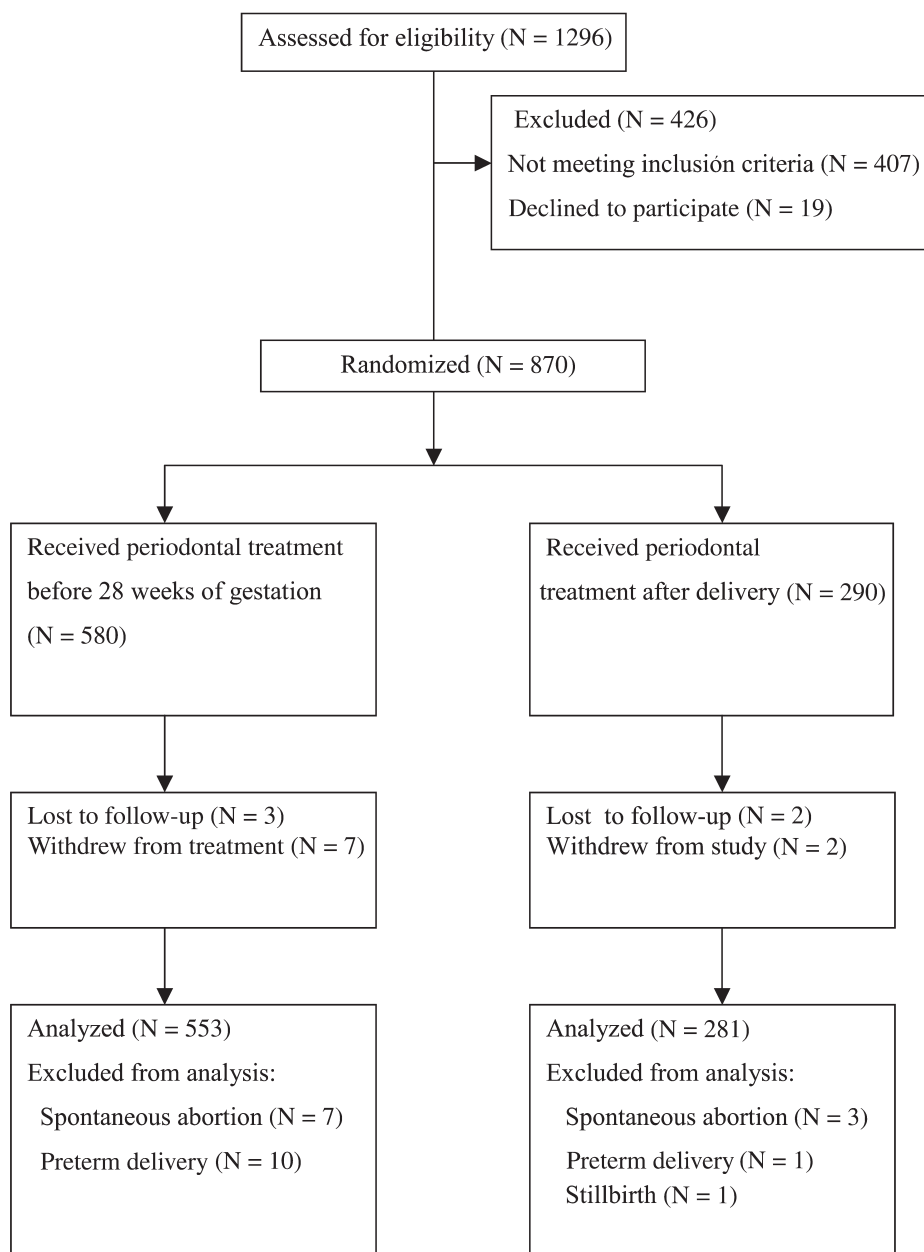
RESULTS

Figure 1 presents a flow diagram of participation and follow-up. Of the 870 women enrolled, 36 women (27 in the treatment group and nine in the control group) were excluded from the analyses. In the treatment group, seven had spontaneous abortion; 10 had preterm delivery due to placenta previa or abruption ($N = 4$), polyhydramnios ($N = 3$), preeclampsia ($N = 2$), or gestational diabetes ($N = 1$); seven women withdrew from the study because they moved from the residential area, and three were lost to follow-up. In the control group, three had spontaneous abortion, one had preterm delivery due to preeclampsia, and one had a stillbirth due to severe malformations; two withdrew from the study because they moved from the residential area, and two were lost to follow-up. The nine women who withdrew from the study had a normal parturition according to self-reported data, but their periodontal status before delivery could not be assessed. Thus, data of those women were not included in the logistic regression analyses.

Eight hundred thirty-four women with live births finished the study: 553 in the treatment group and 281 in the control group. The mean age of women was 25.35 (SD ± 5.1) years, 21.47% were unmarried, 78.77% had less than 12 years of education, 15.46% smoked, 34.98% were primiparous, and 4.79% had a history of previous PT/LBW. Table 1 shows the distribution of maternal characteristics in both groups at baseline. The control group had a significantly higher percentage of women with a history of a previous PT/LBW (7.47% versus 3.44%, $P = 0.009$). There were no other significant differences between the groups. Periodontal characteristics are shown in Table 2. Women in both groups had poor oral hygiene status and extensive gingival inflammation, with a mean percentage of BOP sites higher than 50%. There were no significant differences in the periodontal characteristics at baseline.

Table 3 shows the periodontal characteristics in the treatment group after receiving periodontal

§ Version 6.12, SAS, Cary, NC.



in the treatment group had a higher mean gestational age and a higher mean birth weight than women in the control group.

There were 31 PT/LBW infants (3.67%) in the 843 live births: 24 were due to preterm birth (2.84%) and seven were low birth weight infants (0.83%) (Table 5). Women in the control group had a significantly higher incidence of PT (5.65%) compared to women in the treatment group (1.42%, $P = 0.001$). The rate of LBW was also higher in the control group (1.15%) than in the treatment group (0.71%), but the difference was not statistically significant. The incidence of PT/LBW was more than three times higher in control group (6.71%) than in the treatment group (2.14%, $P = 0.002$). Preterm prelabor rupture of the membranes was found in three of the eight women with PT in the treatment group compared to 8 of the 16 women in the control group (non-significant). Two of the 16 preterm births in the control group and three of the eight preterm births in the treatment group occurred in women with a previous PT/LBW. Four of the 16 preterm deliveries in the control group (1.41%) and four of the eight preterm deliveries in the treatment group (0.71%) occurred at less than 34 weeks of gestation, but the difference was not significant.

Figure 1.
Study flow diagram.

therapy, and those in the control group after 30 weeks of gestation. The characteristics of the treatment group were compatible with periodontal health, and all parameters were significantly higher in the control group. The periodontal characteristics of the control group did not change significantly throughout pregnancy, except for mean probing depth which increased from 2.22 ± 0.46 mm at baseline to 2.33 ± 0.57 mm ($P = 0.012$) after 30 weeks of gestation. Maternal characteristics of women in both groups after delivery are shown in Table 4. There were no significant differences between the groups, although women

Table 6 shows the OR for PT, LBW, and PT/LBW in women in both groups. The OR for PT for women in the control group was 4.11 (95% CI: 1.73 to 9.73), and for PT/LBW 3.26 (95% CI: 1.56 to 6.83). However, the relationship between gingivitis and LBW was not statistically significant (OR 1.47, 95% CI: 0.32 to 6.54). The reduction in the incidence of PT/LBW in the treatment group was 67.89%.

Table 7 shows the results of the univariate analysis for risk factors for PT/LBW. PT/LBW was significantly associated with gingivitis (OR 3.26, 95% CI: 1.56 to 6.83), and to a previous PT/LBW (OR 4.22, 95% CI:

Table 1.
Maternal Characteristics of Patients at Baseline

Characteristic	Treatment N = 580	Control N = 290	P Value
Age, years (mean ± SD)	25.54 ± 5.41	24.98 ± 4.55	0.31
Unmarried (%)	21.16	22.06	0.76
<12 years education (%)	77.76	80.78	0.31
Primiparous (%)	35.80	33.45	0.50
Previous PLBW (%)	3.44	7.47	0.009
Previous abortion (%)	11.21	13.17	0.40
Smoked (%)	14.47	17.44	0.26

Table 2.
Periodontal Characteristics of Patients at Baseline (mean ± SD)

Characteristic	Treatment N = 580	Control N = 290	P Value
N teeth	25 ± 2.9	24.8 ± 2.7	NS
% sites with:			
Plaque	88.34 ± 9.0	86.70 ± 11.3	NS
BOP	55.09 ± 8.2	51.42 ± 9.4	NS
PD ≥4 mm	9.24 ± 3.9	12.23 ± 4.8	NS
PD (mm)	2.26 ± 0.34	2.22 ± 0.46	NS
CAL (mm)	1.12 ± 0.45	1.17 ± 0.49	NS

1.53 to 11.6). The other variables studied did not influence the incidence of PT/LBW.

After multivariate adjustment, the only factor significantly associated with PT/LBW was gingivitis (OR 2.76, 95% CI: 1.29 to 5.88) (Table 8), and a previous PT/LBW was no longer associated with PT/LBW.

DISCUSSION

The present randomized controlled trial was carried out in an ethnically and demographically homogeneous population at low risk for PT/LBW (the total incidence of PT/LBW was 3.17%, which is 40% lower than in the total population of pregnant women in Chile [6%] and 63% lower than in the U.S. [10%]), with a historically low PT/LBW rate. In the present study, women who received periodontal treatment had sig-

Table 3.
Periodontal Characteristics of Patients After 30 Weeks of Gestation (mean ± SD)

Characteristic	Treatment N = 573	Control N = 287	P Value
N teeth	24.82 ± 2.8	24.5 ± 2.6	NS
% sites with:			
Plaque	38.64 ± 13.0	88.70 ± 9.3	0.0001
BOP	15.09 ± 7.9	56.52 ± 13.9	0.0001
PD ≥4 mm	1.8 ± 2.9	14.5 ± 2.8	0.0001
PD (mm)	1.93 ± 0.33	2.33 ± 0.57	0.0001
CAL (mm)	0.93 ± 0.54	1.18 ± 0.43	0.0001

Table 4.
Maternal Characteristics of Patients After Delivery

Characteristic	Treatment N = 560	Control N = 283	P Value
Gestational age (mean ± SD)	39.26 ± 1.50	38.9 ± 1.70	NS
Infant mean weight (g) (mean ± SD)	3,426 ± 477	3,325 ± 535	NS
N prenatal visits (mean ± SD)	8.78 ± 1.81	8.21 ± 2.26	NS
Percentage:			
With urinary infection	11.21	11.39	0.93
With vaginosis	17.18	18.15	0.72
Underweight	12.12	12.46	0.88
Onset prenatal care after 20 weeks of gestation	18.99	22.06	0.29

nificantly fewer PT/LBW than women with untreated gingivitis.

One of the essential characteristics of randomized controlled trials is that the study groups must be similar at the start of the trial.²⁴ Women of the present study were randomly allocated to each group equalizing gingivitis as the relevant variable. Since the study sample was obtained from a homogenous population in relation to demographic characteristics and known risk factors for PT/LBW, and all women were receiving uniform prenatal care, it was assumed that the distribution of the other relevant variables would be similar in both groups of women. Although proper

Table 5.
Incidence of Preterm Births (PT), Low Birth Weight (LBW), and Preterm/Low Birth Weight (PT/LBW) in Intention-to-Treat Analysis

	Treatment Group N = 560		Control Group N = 283		P Value
	N	%	N	%	
PT	8	1.42	16	5.65	0.001
LBW	4	0.71	3	1.15	0.79
PT/LBW	12	2.14	19	6.71	0.002

Table 6.
Odds Ratios for Preterm Births (PT), Low Birth Weight (LBW), and Preterm/Low Birth Weight (PT/LBW) in Women With Gingivitis

	OR	95% CI	P Value
PT	4.11	1.73 - 9.73	0.0005
LBW	1.47	0.32 - 6.54	0.61
PT/LBW	3.26	1.56 - 6.83	0.0009

randomization is aimed to prevent selection bias, it does not always guarantee that the groups are totally equivalent at baseline, especially when a high number of risk factors may affect the outcome under study, as occurs with PT/LBW. In the present study, there was a significantly higher proportion of women with a previous PT/LBW in the control group (Table 1), and a history of PT/LBW is an important risk factor for subsequent pregnancies.²⁵⁻²⁸ In the present study, a previous PT/LBW showed to be a risk factor for PT/LBW in the univariate logistic regression analysis, with an unadjusted OR = 4.22. Thus, women in the control group appeared to be at higher risk of PT/LBW than women in the treatment group. However, the low rate of PT/LBW in women with a previous PT/LBW in both groups explains why, after multivariate adjustment, a previous PT/LBW was no longer associated with PT/LBW. The recurrence of PT/LBW may be associated with the presence of some conditions in the mother that make her more susceptible to the effects of infection and inflammation. The success of periodontal treatment in reducing the risk of preterm birth in women with a history of PT/LBW supports the hy-

pothesis that these women may have greater susceptibility to the effect of periodontal infection. There may be a variation between women in the activation threshold at which periodontal infections trigger the mechanisms of preterm labor. A genetic factor that determines a low threshold to the effect of infection or a hyper-inflammatory response could account for the repeated occurrence of spontaneous preterm birth in certain women. Results of some studies^{29,30} have suggested that polymorphisms in proinflammatory cytokine genes may be associated with spontaneous preterm labor in some populations.

Urinary infections and vaginosis are well known risk factors of PT/LBW. In the current study, there was a similar proportion of women with urinary infection or with vaginosis in the treatment and control groups (Table 4). All women with urinary infections were treated with nitrofurantoin, and women with vaginosis were treated with locally applied antibiotics. As women with vaginosis were treated with locally applied antibiotics, no effect of the antibiotics on the progression of gingivitis can be expected.

No association was found between genitourinary infections and PT/LBW, probably due to the fact that the treatment given to women in the present study was effective in controlling these infections. There were 64 women in the treatment group (11.21%) and 33 (11.39%) in the control group who were treated with systemic nitrofurantoin. There may be some concern about the effect of nitrofurantoin as a confounding variable in gingivitis. In a previous study in pregnant women,⁸ no differences were found in patients with untreated periodontitis who received nitrofurantoin when their baseline periodontal characteristics were compared with those after receiving the antibiotic and with patients who did not receive nitrofurantoin. Additionally, in the current study, the proportion of patients treated with nitrofurantoin was similar both in the treatment and control groups, and the logistic regression analyses found no relationship between nitrofurantoin therapy and PT/LBW.

A significant association between gingivitis and preterm birth was found after adjusting for the major risk factors for preterm delivery, suggesting that gingivitis is an independent risk factor for PT/LBW. The results of the present study showing that periodontal therapy reduced PT/LBW rate by 68% in women with pregnancy-associated gingivitis are in concordance with two intervention studies^{7,8} in which periodontal treatment reduced the incidence of PT/LBW between 71% and 84% in pregnant women with moderate to severe chronic periodontitis.

In the present study, a higher number of medically indicated preterm deliveries occurred in the treatment group than in the control group, although the

Table 7.
Unadjusted Odds Ratios for Preterm/Low Birth Weight Risk Factors

	Normal Birth (N = 803)		PT/LBW (N = 31)		OR	95% CI	P Value
	N	%	N	%			
Gingivitis							
Yes	262	93.23	19	6.76	3.26	0.0009	1.56 - 6.83
No	541	97.83	12	2.17			
Previous PT/LBW							
Yes	35	4.4	5	16.1	4.22	0.01	1.53 - 11.6
No	768	95.6	26	83.9			
<12 years education							
Yes	634	91.82	23	8.18	1.87	0.44	0.36 - 9.57
No	169	98.55	8	1.44			
Unmarried							
Yes	173	21.5	6	19.4	1.14	0.77	0.46 - 2.8
No	630	78.5	25	80.7			
Primiparous							
Yes	282	35.1	10	32.2	0.88	0.74	0.41 - 1.9
No	521	64.9	21	67.7			
Tobacco use							
Yes	125	15.6	4	12.9	0.80	0.69	0.28 - 2.3
No	678	84.4	27	87.1			
Low maternal weight gain							
Yes	95	11.8	7	22.6	2.17	0.09	0.91 - 5.2
No	708	88.2	24	77.4			
Onset of prenatal care after 20 weeks gestation							
Yes	157	19.6	10	32.3	1.96	0.08	0.90 - 4.2
No	646	80.5	21	67.7			
Previous abortion							
Yes	93	11.6	6	16.1	1.83	0.19	0.73 - 4.6
No	710	88.4	25	83.9			
Urinary infection							
Yes	89	11.1	5	16.1	0.38	1.54	0.58 - 4.1
No	714	88.9	26	83.9			
Vaginosis							
Yes	143	17.8	3	9.7	0.49	0.24	0.15 - 1.6
No	660	82.2	28	90.3			

difference was not statistically significant. None of the preterm deliveries in the present study were preceded by spontaneous labor or premature rupture of membranes, and were associated with conditions not related to maternal or fetal infections, such as polyhydramnios, placenta previa or abruption, gestational diabetes, and preeclampsia.

Significantly high health care costs are generated by preterm birth, and any strategy that reduces the preterm birth rate is likely to produce both health and economic benefits for mothers and infants. The present study and other published controlled trials^{7,8} demonstrate that significant reduction of preterm births can be obtained in women considered to be at

Table 8.**Multivariate Logistic Regression Model for Preterm/Low Birth Weight**

Risk Factor	Parameter Estimate	Standard Error	Adjusted OR	95% CI	P Value
Gingivitis	1.01	0.3858	2.76	1.29 - 5.88	0.0085

normal or low risk for preterm birth by treating periodontal infections. In the present study, as well as in the two previous intervention studies,^{7,8} periodontal therapy was finished before 28 weeks of gestation in order to eliminate periodontal infection at a similar early stage of the pregnancy in all women in the treatment group. Because infection is more likely to cause very early preterm birth, trials focusing on women at later gestational ages may not show an effect.³¹

Ideally, women should begin their pregnancy without periodontal infections, and they should be educated and motivated to maintain a high level of oral hygiene prior to and throughout pregnancy. However, if a periodontal infection is diagnosed at any time during pregnancy, the treatment should be administered as soon as possible in order to reduce the risk of PT/LBW. Pregnancy-associated gingivitis is a preventable and easy to treat disease, and any cost-benefit analysis of the administration of periodontal therapy to pregnant women in order to reduce preterm birth rates would show a high direct cost-benefit saving. However, the real cost saving of reduction in the rate of preterm birth ascribable to periodontal treatment is best represented by the lives of children saved from premature death and biological, social, and economic impairment.

The current knowledge of the pathologic mechanism involved in the association between periodontal diseases and PT/LBW supports this relationship, but more investigations are still needed to determine if periodontal infections have a causal role in adverse pregnancy outcomes in other populations. Most cases of preterm labor and preterm birth are multifaceted, multiple-step, and interactive fetal and maternal processes.³ It has been shown that some maternal factors, such as short cervix, are more likely to be associated with preterm birth when the mother also has a bacterial vaginosis.³³ Thus, it is probable that maternal periodontal infection may interact synergistically with other maternal factors to trigger preterm birth.

It is still not known what are the precise mechanisms involved in the association between periodontal infections and preterm birth. In the history of medicine there are several examples of effective control or dis-

ease prevention before the precise mechanisms that caused the disease had been established. The puerperal fever was controlled many years before bacteria were discovered through the careful hand washing of the midwives and obstetricians before assisting women at delivery. The consumption of citric fruit was used to prevent and to treat scurvy more than 200 years before vitamin C was discovered. In the same way, malaria was controlled by draining marshes before knowing that mosquitoes transmitted the disease.³³ Results of intervention studies in pregnant women with periodontitis⁷⁻⁹ and the results of the present study in women with gingivitis show that eradication of periodontal infection significantly reduces the risk of PT/LBW, and no harmful damaging effect caused by periodontal intervention in pregnant women has been reported.

CONCLUSIONS

In this study, women with gingivitis who received periodontal therapy before 28 weeks of gestation had a significantly lower incidence of PT/LBW than women who did not receive periodontal therapy. Pregnancy-associated gingivitis appeared to be an independent risk factor for PT/LBW and affords more than a two-fold increase in the risk for PT/LBW.

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