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ORIGINAL ARTICLE

Effect of nonsurgical periodontal therapy and strict plaque control on preterm/low birth weight: a randomized controlled clinical trial

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Abstract
Objective This randomized controlled clinical trial was carried out to assess the effect of comprehensive nonsurgical periodontal treatment and strict plaque control performed during pregnancy on the reduction of preterm and/or low birth weight rates (PTLBW).
Material and methods Three hundred and three women were randomly allocated to receive periodontal treatment either during pregnancy (n=147, test group) or after delivery (n=156, control group). During pregnancy, the control group received only one session of supragingival scaling and oral hygiene instruction. In contrast, the test group received comprehensive periodontal treatment including multiple sessions of scaling and root planing, oral hygiene instructions, and frequent maintenance visits.
Results At baseline, periodontal inflammation was observed in approximately 50% of sites and attachment loss affected <15% of sites. Compared to controls, women in the test group had significant reductions in the percentage of sites with plaque (48.5% vs. 10.3%, p<0.001), gingival bleeding (23.3% vs. 2.5%, p<0.001), calculus (21.3% vs. 4.1%, p<0.001), bleeding on probing (38.1% vs. 2.6%, p<0.001) and probing depth ≥3 mm (19.97% vs. −2.45%, p<0.001). No significant differences were observed between the groups in the occurrence of PT (11.7% vs. 9.1%, p=0.57), LBW (5.6 % vs. 4.1%, p=0.59), and PTLBW (4.15% vs. 2.60%, p=0.53).
Conclusions Comprehensive periodontal treatment and strict plaque control significantly improved periodontal health; however, no reduction of PTLBW rates was observed. Thus, remaining periodontal inflammation posttreatment cannot explain the lack of effect of periodontal treatment on PTLBW.
Clinical relevance This study demonstrated that periodontal diseases may be successfully treated during pregnancy. Our results do not support a potential beneficial effect of periodontal treatment on PTLBW.

Keywords Periodontal diseases · Periodontal treatment · Pregnancy complications · Risk factors

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Introduction

Preterm affects approximately 9.6% of live births globally [1]. In USA, it is estimated that 75% and 50% of perinatal

mortality and long-term morbidity might be attributable to preterm birth, respectively [2]. Low birth weight affects 15.6% of births worldwide and is strongly associated with prematurity [3]. Primary and secondary prevention, whereas effective in reducing overall mortality rates, have had limited impact on preterm and/or low birth weight (PTLBW) rates [4]. Moreover, medical care intended to improve diagnosis, delay delivery, and treat preterm newborns is expensive and labor intensive. Thus, alternative interventions that may help decrease PTLBW incidence or mitigate its consequences are necessary.

In this context, periodontal treatment has been suggested as a possible intervention aimed at preventing PTLBW [4]. This assumption was based on early observational and clinical studies that observed an association between periodontal disease and adverse obstetric outcomes [5, 6] and a decreased incidence of PTLBW after periodontal treatment [7, 8]. However, recent epidemiological and intervention studies, supporting [9–14] and refuting [15–19] these early findings, have been published. Contradictory results were also observed in recent meta-analyses. Polyzos et al. [20] suggested a beneficial effect of periodontal treatment on PTLBW rates, whereas Fogacci et al. [21] could not corroborate this finding. Conflicting results might be explained, at least in part, by differences in sample characteristics, inclusion criteria, data analysis, and bias [22, 23].

Irrespective of these controversies, most studies have achieved limited treatment results with large amounts of remaining clinical inflammation after nonsurgical periodontal therapy [24]. In this regard, a recent clinical study observed a strong association between periodontal outcomes and full-term birth supporting the notion that possible beneficial effects on adverse obstetric outcomes might be dependent on the success of periodontal treatment [25]. Our experimental hypothesis was that periodontal treatment based on a strict plaque control regimen that results in very low levels of periodontal inflammation would reduce the PTLBW rates if a protective effect exists. The aim of the present randomized controlled clinical trial was to assess the effect of comprehensive nonsurgical periodontal treatment and strict plaque control performed during pregnancy on the reduction of PTLBW rates.

Material and methods

Study design

The present study used a randomized controlled clinical trial design (Fig. 1). Women were randomly allocated to the experimental groups using a block-stratified strategy according to smoking extent (≤5 or >5 cigarettes/day). Women smoking more than five cigarettes per day when interviewed were classified as smokers. A randomization table was computer generated and allocation to treatment was concealed in an opaque, sealed, and serially numbered envelope opened by the examiner after the baseline examination. Participants of the test group received comprehensive periodontal treatment and strict plaque control, whereas the control group received only one session of supragingival calculus removal and oral hygiene instructions (see "Intervention" section for details). The study protocol was reviewed and approved by the Presidente Vargas Maternal Hospital Ethical Committee, Porto Alegre, Brazil and all participants signed an informed consent form.

Study sample

All pregnant women seeking prenatal care at the Presidente Vargas Maternal Hospital were considered eligible. Recruitment for the study was carried out from April 2007 to June 2009. To be included, women should be 18 to 35 years old and had a gestational age of 20 weeks or less. Women with multiple fetuses, receiving orthodontic treatment or in need of antibiotic prophylaxis for dental treatment were not included in the study. All consenting eligible women who fulfilled the inclusion criteria were included in the study irrespective of periodontal status.

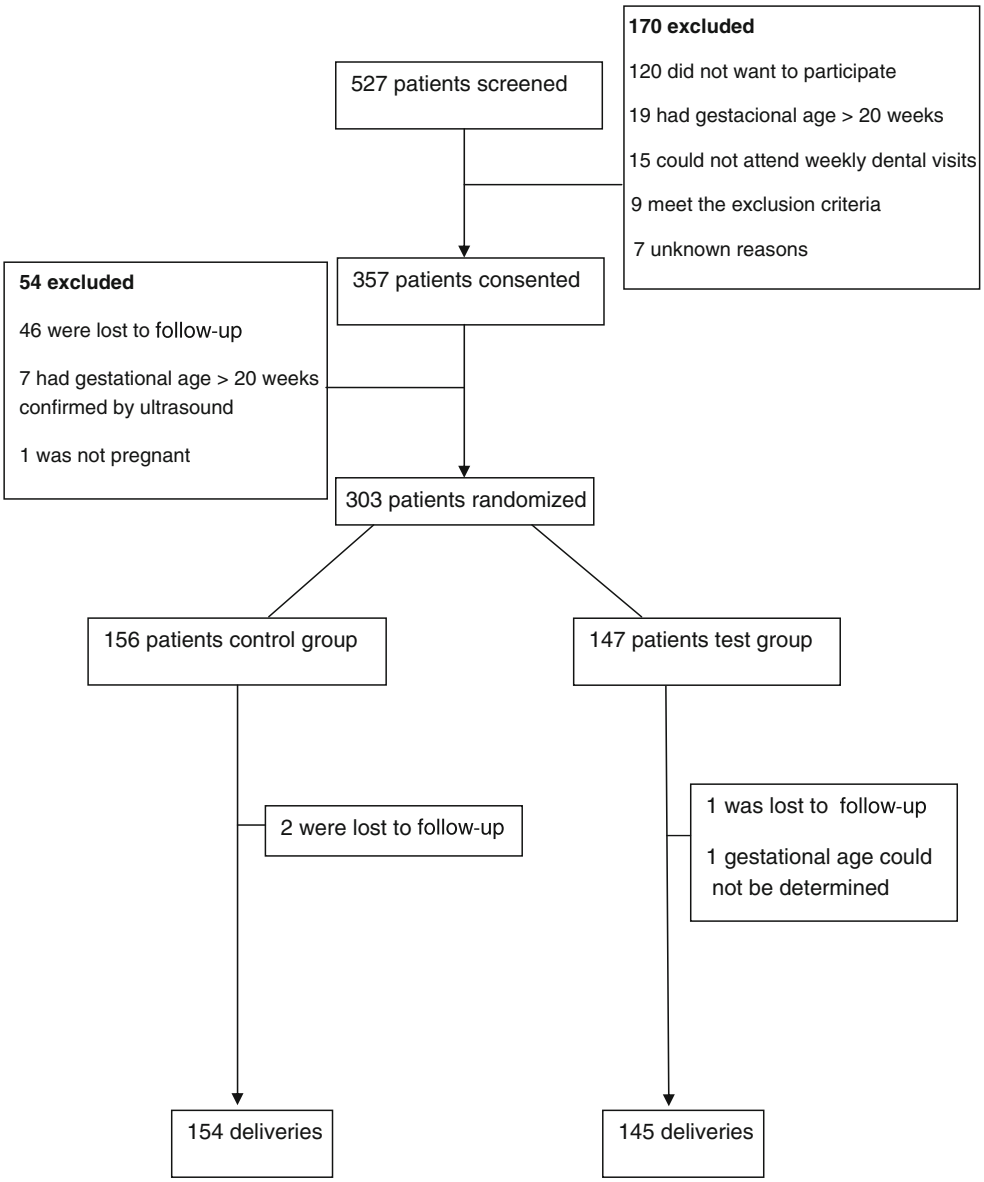
Maternal data

A structured questionnaire comprising demographics, socioeconomic status, medical and dental history was used to collect maternal data. In brief, anthropometric data, previous and current pregnancy conditions, hospitalization during pregnancy, use of medications, previous history of sexually transmitted diseases, personal and family medical history, smoking, alcohol consumption, and oral hygiene habits were recorded. During the study, the occurrence of gestational events such as vaginosis, urinary infections, preeclampsia, gestational diabetes, use of medications, and hospitalization were assessed using hospital records. The questionnaire used was previously tested and data were collected by trained interviewers. Reproducibility was evaluated by repeated assessment of key questions in 10% of the sample with a 1-week interval (kappa=0.79).

Periodontal clinical examination

Periodontal clinical examination was performed by three calibrated examiners (PW, CHCM, and MLM) and recorded in preset forms by trained assistants. Full-mouth, excluding third molars, six sites per tooth, periodontal examination was carried out using a manual periodontal probe (Neumar, North Caroline Probe 15, São Paulo, Brazil). Plaque index, gingival index, supragingival calculus, cavities, overhanging restorations, bleeding on probing (BOP), periodontal probing depth

Fig. 1 Study flow chart



(PPD), and clinical attachment level (CAL) were recorded. Reproducibility during the study was assessed in 10% of the participants with at least 1-h intervals between clinical examinations. One experienced periodontist (PW) served as the reference examiner. The intraclass correlation coefficient ranged between 0.95 and 0.96 for PPD and between 0.84 and 0.93 for CAL. Weighted kappa (±1 mm) ranged between 0.89 and 0.90 for PPD and between 0.84 and 0.88 for CAL. The participants were examined at baseline and at 26–28 gestational weeks. All participants were examined at baseline and 261 (138 in the control group and 123 in the test group) were available for examination at 26–28 gestational weeks.

Intervention

Periodontal treatment was performed by two periodontists (TF and JMR) at the hospital dental unit. The test group received comprehensive nonsurgical periodontal therapy before the 24th gestational week. Treatment included excavation and sealing of cavities, removal of overhanging restorations, extraction of hopeless teeth, supragingival calculus removal, and subgingival scaling and root planing under local anesthesia. Oral hygiene instructions were given at each appointment. No limits were imposed to the number of dental visits needed to accomplish periodontal therapy. After active treatment, patients were seen at least once a month according to individual needs in order to maintain optimal plaque control. The control group received the standard dental treatment provided to all patients at the hospital, comprising one session of supragingival calculus removal and oral hygiene instruction. The same comprehensive periodontal therapy provided to the test group was offered to the control group after delivery. Patients in both experimental groups received pain relief treatment whenever

necessary. Teeth diagnosed with pulpitis or obvious endodontic involvement were referred for endodontic treatment.

Outcomes

Preterm birth and low birth weight were the primary outcomes of the present study. Births before the 37 gestational week were considered preterm and newborns under 2,500 g were considered low birth weight, irrespectively of gestational age, according to the World Health Organization [3]. Gestational age was determined by a gynecologist using information of sequential physical exams, data from menstrual cycles, and ultrasounds. Birth was assisted by attending physicians and examination of newborn infants was performed by neonatologists using standardized hospital procedures.

Sample size estimate

The sample size calculation was based on results obtained in a similar South American sample [7]. A sample size of 290 women was calculated based on a reduction in this population prematurity from 10.7% [26] to 2% taking into consideration an alpha of 5% and power of 80%. Based on previous clinical studies performed by our research group, a dropout rate of approximately 5% was added to the sample size totaling 304 participants.

Data analysis

The data bank was carefully examined to assure quality control. Categorical data were summarized by absolute and relative frequencies, and comparisons between groups were performed using Chi-square and Fisher's exact test. Continuous data were summarized by means, standard deviations, and confidence intervals, and groups were compared by independent sample *t* tests. The distribution of continuous data was evaluated by dispersion graphics and no major departure from the normal distribution was observed. Plaque and gingival indexes were dichotomized and presented as percentage of sites with visible plaque and gingival bleeding. Self-reported skin color was collected using criteria proposed by the Brazilian Institute of Geography and Statistics, and data were categorized into white, black, and other. Socioeconomic status was assessed using the Brazilian Criteria for Economic Classification [27] and participants were categorized into low, medium low, medium high, and high. Preterm birth and low birth weight rates were computed as a fraction of the total number of participants randomized for each experimental group. The individual was the unit of analysis and data collected at teeth/sites were aggregated at the individual level. Statistical significance was set at 5%.

Results

From the 527 women evaluated to participate in the study, 303 were randomized to the experimental groups (Fig. 1). No statistically significant differences were observed between groups with regards to demographic, socioeconomic, behavioral, and medical data at baseline for the participants that completed the study protocol (Table 1). The mean gestational age at baseline was 12.4±4.24 weeks for the control group and 12.3±4.56 weeks for the test group (p=0.92). Two participants in each group were lost to follow-up yielding an overall dropout rate of 1.3% (Fig. 1).

No significant differences between experimental groups were observed in the percentage of women who were primiparous and had previous history of preterm birth or abortions

Table 1 Demographic, socioeconomic, behavioral, and medical data at baseline

	Control (n=154)		Test (n=145)		
	n	%	*n*	%	*p* value
Age (years)					
<20	13	8.45	13	8.96	
≥20 and <25	51	33.11	46	31.73	
≥25 and <30	48	31.17	51	35.17	
≥30	42	27.27	35	24.14	0.90
Skin color					
White	106	68.83	98	67.59	
Black	22	14.30	25	17.24	
Other	26	16.87	22	15.17	0.75
Education					
Elementary	72	46.75	75	51.73	
High school	74	48.05	60	41.38	
College/university	8	5.20	10	6.89	0.48
Socioeconomic status					
Low	35	22.73	32	22.07	
Medium low	78	50.65	74	51.04	
Medium high	35	22.73	29	20.00	
High	6	3.89	10	6.89	0.67
Smoking					
Never	80	51.95	74	51.04	
Former	48	31.17	44	30.34	
Current	26	16.88	27	18.62	0.92
BMI[a]					
Underweight	5	3.55	10	7.81	
Normal	89	63.12	67	52.34	
Overweight	28	19.86	30	23.44	
Obese	19	13.47	21	16.41	0.23
Total	154	100	145	100	

[a] Data available for 141 women in test group and 128 women in control group

(Table 2). During the study pregnancy, no significant differences were observed in the occurrence of genitourinary infection, gestational diabetes, and preeclampsia for the control and test groups. Both groups had access to prenatal care and no differences were observed in the number of appointments (control, 9.12±3.15 vs. test, 9.00±2.79, $p=0.74$).

The results of periodontal therapy are presented in Table 3. After periodontal therapy, the test group showed a significant higher reduction than the control group in the percentage of sites with visible plaque (48.50% vs. 10.32%, $p<0.001$), gingival bleeding (23.31% vs. 2.50%, $p<0.001$), supragingival calculus (21.33% vs. 4.13%, $p<0.001$), BOP (38.05% vs. 2.56%, $p<0.001$), and PPD ≥3 mm (19.97% vs. −2.45%, $p<0.001$). No significant differences were observed in CAL between groups. Periodontal therapy was completed in 123 out of 145 women (84.83%) in the test group. Out of 22 patients that did not complete periodontal treatment, 13 discontinued treatment for unknown reasons, 4 were recommended to stay in bed, 4 had spontaneous abortion, and 1 moved to another city. One session of supragingival calculus removal and oral hygiene instruction was completed for 138 out of 154 women in the control group as indicated by the study protocol. The test group had, in average, 4.2 (±2.48) appointments for periodontal treatment and 1.8 (±0.78) appointments for periodontal maintenance.

The mean gestational duration was 269.75 (±32.70) days for the control group and 270.41 (±28.95) days for the test group. Mean weight and height at birth were 3,264.10 (±519.82) g and 48.51 (±2.82) cm for the control group and 3,302.08 (±524.83) g and 48.72 (±2.41) cm for the test group. No statistically significant differences were observed between groups for these variables.

Table 2 Obstetric data regarding previous and current pregnancies

	Control ($n=154$)		Test ($n=145$)		
	n	%	*n*	%	*p* value
Previous pregnancies					
Any previous pregnancy	93	60.38	92	63.44	0.59
Any preterm birth	19	12.33	21	14.48	0.89
Any miscarriage	30	19.48	29	20.00	0.85
Current pregnancy					
Genitorurinary infection	17	11.04	21	14.48	0.30
Diabetes	4	2.60	7	4.83	0.37
Preeclampsia	3	1.95	2	1.38	0.99
Other disease and conditions[a]	10	6.49	5	3.45	0.30
Antibiotics	30	19.48	36	24.83	0.33
Alcohol consumption	4	2.59	4	2.75	0.93

[a] Depression, polyhydramnios, pericoronaritis, periapical abscess

Table 4 shows neonatal and obstetric outcomes. No significant differences in preterm birth (<37 weeks) rates were observed between experimental groups (control, 9.09% vs. test, 11.72%, $p=0.57$). Similarly, very preterm birth (<32 and <35 weeks) rates did not differ between control and test groups ($p>0.05$). Occurrence of newborns with LBW was not significantly different between groups irrespective of weight thresholds ($p>0.05$). PTLBW rates were not significantly different between groups (control, 2.6% vs. test, 4.1%, $p=0.53$).

No significant differences were observed between groups in the incidence of serious adverse events such as stillbirth (test, 4.5% vs. control, 3.5%, $p=0.77$) and hospitalization (test, 6.15% vs. control, 8.98%, $p=0.59$). Dental adverse events including dental hypersensitivity, gingival abrasion, toothbrush sensitivity, and traumatic brushing were more frequent in the test group (test, 8.8% vs. control, 3.8%, $p=0.07$). No significant differences were observed in the occurrence of acute dental infections between groups (test, 6.2% vs. control, 7.8%, $p=0.24$).

Discussion

The present randomized controlled clinical trial was carried out to assess the effect of nonsurgical periodontal treatment and strict plaque control during pregnancy on the reduction of PTLBW rates. Contrary to previous studies, our results demonstrated that successful periodontal treatment performed up to the second trimester of gestation may significantly improve periodontal inflammation. Nevertheless, this reduction in periodontal inflammation did not affect the occurrence of adverse obstetric outcomes in this population. PTB rates for the experimental groups (control, 9.1% and test, 11.7%) were somewhat comparable to those observed in North America (10.6%), Latin America (8.1%), and Asia (9.1%) but higher than the incidence in Europe (6.2%) and Oceania (6.4%) [1]. Similar to our findings, the overall PTB incidence observed in Porto Alegre was 10.7% [26].

The results of the present study are in contrast to early findings from two randomized clinical trials carried out in similar Latin American samples from Chile [7, 8]. In the first study, Lopez and coworkers showed that the treatment of periodontitis significantly reduced the occurrence of preterm birth from 6.8% to 1.1% [7]. Subsequently, the same research group showed similar results when pregnant women with pregnancy-associated gingivitis were treated. PTLBW rates were 2.1% for the test group and 6.7% for the control group [8]. A large pilot study also observed a borderline significant decrease in the occurrence of PTLBW after periodontal therapy from 4.9% to 0.8% in USA [28]. Somewhat beneficial results of periodontal treatment have

Table 3 Periodontal parameters at baseline and 26–28 weeks of gestation

	Control (n=154)		Test (n=145)		
	Mean	95%CI	Mean	95%CI	p value
Baseline					
Number of teeth	25.47	24.97–25.97	25.68	25.17–26.19	0.56
Visible plaque (% sites)	55.23	51.39–59.08	56.34	52.50–60.18	0.69
Gingival bleeding (% sites)	32.60	29.81–35.40	32.85	29.97–35.74	0.90
Supragingival calculus (% sites)	21.73	19.40–24.07	22	19.59–24.40	0.88
BOP (% sites)	49.40	46.28–52.53	49.56	46.03–53.09	0.95
PPD ≥3 mm (% sites)	48.88	46.55–51.22	48.78	46.39–5.18	0.95
PPD ≥4 mm (% sites)	11.27	9.49–13.06	10.28	8.77–11.78	0.41
CAL ≥1 mm (% sites)	13.98	10.81–17.15	11.04	8.41–13.68	0.16
CAL ≥2 mm (% sites)	7.89	5.29–10.49	5.07	3.30–6.85	0.08
	Control (n=138)		Test (n=123)		
26–28 weeks of gestation					
Number of teeth	25.41	24.87–25.94	25.55	25.00–26.09	0.72
Visible plaque (% sites)	44.91	40.39–49.43	7.84	6.02–9.67	<0.001
Gingival bleeding (% sites)	30.10	27.34–32.86	9.54	8.32–10.85	<0.001
Supragingival calculus (% sites)	17.61	15.23–19.98	0.67	0.23–1.10	<0.001
BOP (% sites)	46.84	43.18–50.50	11.51	10.05–12.97	<0.001
PPD ≥3 mm (% sites)	51.33	48.48–53.86	28.81	25.77–31.85	<0.001
PPD ≥4 mm (% sites)	13.01	11.09–14.94	2.86	2.10–3.62	<0.001
CAL ≥1 mm (% sites)	15.32	11.81–18.68	11.10	8.48–13.72	0.64
CAL ≥2 mm (% sites)	7.00	4.46–9.55	4.03	2.31–5.76	0.63

BOP bleeding on probing, *PPD* periodontal probing depth, *CAL* clinical attachment loss

also been observed in randomized [10, 12] and nonrandomized [29, 30] clinical studies published recently.

Table 4 Distribution of obstetric and birth outcomes

	Control (n=154)		Test (n=145)		
	n	%	n	%	p value
Preterm birth					
<32 weeks	7	4.55	5	3.45	0.77
<35 weeks	9	5.84	8	5.52	0.99
<37 weeks	14	9.09	17	11.72	0.57
Birth weight					
<1,500 g	1	0.68	0	0.00	0.99
<2,000 g	2	1.35	2	1.41	0.99
<2,500 g	6	4.05	8	5.63	0.59
Preterm and low birth weight	4	2.60	6	4.15	0.53
Live births	147	95.45	140	96.55	
Abortion	5	3.25	4	2.76	
Stillbirth	2	1.30	1	0.69	0.99

These positive results were not confirmed in subsequent clinical trials. In 2006, Michalowicz et al. [15] published a multicenter clinical trial performed in USA with 823 pregnant women. Their results demonstrated that periodontal therapy did not alter the occurrence of preterm birth or low birth weight. Recently, three large clinical trials conducted in USA [17, 19, 25] and Australia [16] have also failed to observe a positive effect of periodontal therapy on PTLBW. The largest clinical trial included 1,806 participants that received scaling and root planing either in the second trimester of gestation or after delivery. The test group had an incidence of preterm delivery of 13.1% whereas in the control group the incidence was 11.5% [17]. A smaller clinical study including a Brazilian sample did not find any differences in the occurrence of adverse obstetric outcomes [18].

Recently, posttreatment outcomes have received greater attention due to contradictory results regarding the systemic impact of periodontal therapy [24, 31, 32]. In this context, it has been proposed that the lack of periodontal therapy effect on decreasing PTLBW rates observed in some studies could be explained, at least in part, by remaining high levels of periodontal inflammation after therapy [24]. This hypothesis was based on the fact that previous studies did not achieve substantial reduction on periodontal inflammation, questioning the efficacy of the treatment provided. BOP affecting between 29% and 47% of the sites were observed in large

clinical studies with negative results [15–17]. Unfortunately, other large studies did not report periodontal outcomes hindering the assessment of periodontal therapy and consequently its relationship with obstetric outcomes [19, 28]. Supporting this argument, Jeffcoat et al. [25] observed a strong positive correlation between periodontal therapy outcomes and full-term birth in a high-risk population. The present study does not support the contention that "unsuccessful" periodontal therapy could explain the lack of protective effect observed in some clinical studies with remaining high levels of periodontal inflammation. No effect on PTLBW was observed in the present study irrespective of very low levels of plaque (7.8% of sites) and periodontal inflammation (9.5% of sites with gingival bleeding and 11.5% of sites with BOP).

Interestingly, large epidemiological studies have consistently observed a significant association between periodontitis and PTLBW [9, 11, 14, 33]. Conflicting results between clinical and epidemiological studies are not unique to studies concerning periodontal diseases and risk for preterm birth. Genitourinary infections are well-known risk factors for preterm birth [34]. Although several studies have demonstrated that antimicrobial therapy during pregnancy or in the preconception period is efficacious in treating vaginal infections, they have failed to demonstrate a reduction in the occurrence of preterm birth [35–37]. Nevertheless, possible explanations for this lack of consistency between different lines of evidence should be further investigated.

The major strengths of the present investigation reside on the study design employed and very low attrition rate achieved. Experimental groups were well balanced for possible confounders by design and randomization. Moreover, meticulous periodontal treatment and strict plaque control were implemented and maintained throughout the study. The present sample size could be seen as a weakness since it is smaller than other recent studies [15–17, 19]. Whereas our study had enough power (0.80) to show that a decrease in the incidence of preterm birth to less than 3% is unlikely in this and similar populations of young pregnant women; it is conceivable that studies with larger sample sizes could show smaller but significant reductions in the incidence of adverse pregnancy outcomes in other patient populations. Endodontic treatment was provided whenever necessary during this study; nevertheless, it is important to acknowledge that periapical lesions may have not been diagnosed if teeth were asymptomatic or did not have obvious endodontic involvement. Dental radiographies were taken according to the ALARA principle to allow proper diagnosis and treatment of these conditions; however, full-mouth radiographic examination was not performed due to safety concerns. Another possible limitation of this study could be the sample periodontal disease pattern. Contrary to other studies, a high-risk sampling strategy designed to select women with high levels of periodontal destruction was not used. Caution should be taken when extrapolating these findings to subjects with greater disease severity. Nevertheless, our strategy of including all eligible women irrespective of periodontal status yielded a sample of women with localized periodontal destruction and widespread periodontal inflammation. This is likely to increase the external validity of the findings to this and similar populations since only a small proportion of women in childbearing age would have severe periodontitis [38–40]. Intervention studies [41–43] have shown an immediate increase in serum inflammatory mediators after intense periodontal therapy (full-mouth scaling and root planing) which resolves shortly after the intervention. The systemic effect of this transient release of inflammatory markers is yet to be determined. In the present study, periodontal treatment was provided on a weekly basis (mean ± SD, 4.2±2.5 appointments per patient) possibly minimizing undesirable systemic effects associated with this intervention [43].

In conclusion, comprehensive periodontal treatment and strict plaque control performed up to the second trimester of gestation may significantly improve periodontal health; however, this reduction in periodontal inflammation did not affect PTLBW rates. Furthermore, the present findings do not support the contention that remaining periodontal inflammation after periodontal treatment could explain the lack of effect on PTLBW rates observed in previous clinical studies.

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Conflicts of interest The authors declare no conflicts of interest.

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