

Chronic periodontitis and pre-term labour in Brazilian pregnant women: an association to be analysed

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Abstract

Aim: To investigate the association between chronic periodontitis (CP) and pre-maturity in a group of Brazilian pregnant women from the State of São Paulo.

Materials and Methods: One hundred and twenty-four women were investigated consecutively in a cross-sectional study, between December 2003 and May 2005. Sixty-eight women had pre-term labour (PTL) and 56 had term labour. A periodontal examination was carried out to identify the presence of CP. Statistical analysis used the Fisher's exact test or χ^2 for the discrete variables and the Mann–Whitney test for the non-parametric variables. Odds ratio (OR) was calculated with a 95% confidence interval (CI), to evaluate the relation between CP and pre-maturity.

Results: Periodontal indicators, such as clinical attachment loss ($p < 0.0001$) and bleeding on probing ($p = 0.012$), were observed more in the PTL group. The presence of CP increased the risk for PTL (OR: 4.7, 95% CI: 1.9–11.9), pre-term birth (PTB; OR: 4.9, 95% CI: 1.9–12.8) and low birth weight (<2500 g; OR: 4.2, 95% CI: 1.3–13.3). The pregnant women with PTL presented low levels of schooling ($p = 0.029$) and the lowest number of pre-natal appointments ($p = 0.0001$) when compared with those with term labour.

Conclusion: CP is strongly associated with PTL, PTB and low birth weight in a group of Brazilian pregnant women. These data point to the necessity of regularly investigating CP during pregnancy.

Key words: chronic periodontitis; low birth weight; periodontal diseases; pre-maturity; pre-term birth; pre-term labour

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Pre-maturity is responsible for 70% of perinatal deaths (Goldenberg et al. 2000) and for approximately 50% of the neurological sequelae of the newborn (McCormick 1985).

Conflict of interest and source of funding statement

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Pre-term birth (PTB), defined as the birth that occurs before 37 weeks of gestation (WHO 1977), is the main cause of low birth weight (LBW; <2500 g) and occurs in approximately 10% of pregnancies (Goldenberg et al. 2000) and that varies depending on the characteristics of the studied population.

Pre-term labour (PTL) frequently causes PTB and LBW and has been one of the main problems associated with perinatal mortality and morbidity particularly in countries with less development (Lamont & Husslein 2003). In

industrialized countries, investments in social programmes and the advent of new technologies in neonatal care have contributed significantly to the lowering of perinatal mortality/morbidity rates in the newborn (Zachariassen & Dennison 1998, Lumley 2003).

The main risk factors for PTL are previous PTL, chronic intrauterine infection and non-white ethnicity (Goldenberg et al. 2000). Pregnant women with a history of previous PTL presented a 15–80% risk factor of having another PTL in future pregnancies (Dizon-Townson 2001).

In the last decades, the role of infections in the aetiology of pre-maturity has been widely discussed, providing data that infection is an important risk factor for PTL (Hillier et al. 1988, Gibbs et al. 1992, Hill 1998, Offenbacher 1998).

More attention has been given recently to periodontal infections, especially chronic periodontitis (CP; Dasanayake 1998, Hill 1998, Jeffcoat et al. 2001, Radnai et al. 2004, Marin et al. 2005).

CP is a periodontal infection with multi-factorial characteristics (Armitage 2002, Nunn 2003). It is mainly caused by Gram-negative microorganisms and can progressively lead to an inflammatory destruction of the periodontal attachment apparatus. This is also linked to factors that are common in pre-maturity such as age, unfavourable socio-economical and cultural conditions, smoking and diabetes (Ezzo & Cutler 2003, Dixon et al. 2004).

Studies in different populations sustain the association between the presence of CP and pre-maturity. Multivariate logistic regression models point towards a variable risk between 3.5 and 7.9 (Offenbacher et al. 1996, Dasanayake 1998, Jeffcoat et al. 2001, Lopez et al. 2002a, Radnai et al. 2004).

In a case-control study, Offenbacher et al. (1996) showed that pregnant women with periodontal infection had seven times more risk of having a newborn with LBW as a consequence of PTL or due to pre-mature rupture of the ovular membranes (PROM).

In a prospective study with 1313 pregnant women, in Birmingham, Jeffcoat et al. (2001) reported that severe or generalized CP (90% or more sites with attachment loss of 3 mm or more) is associated with PTB [odds ratio (OR): 4.45, 95% confidence interval (CI): 2.16–9.18].

Others studies, however, have not presented such evidence (Davenport et al. 2002, Holbrook et al. 2004, Moore et al. 2004, 2005).

Davenport et al. (2002), in a case-control study with a multi-ethnic group of pregnant women from the East End of London, UK, predominantly the Bangladeshi community, showed no association between periodontal infection, PTB and LBW. The study was conducted in London, and the results did not support the fact that specific efforts to reduce periodontal disease could improve pregnancy outcomes.

Another prospective study with 3738 pregnant women, who were recruited

when they attended Guy's Hospital in London for a nuchal translucency scan at approximately 12 weeks gestational age (GA), investigated the relationship between periodontal infection and adverse pregnancy outcome. Regression analysis indicated that there was no significant relation between severity of periodontal disease and PTB or/and LBW (Moore et al. 2004).

Some interventional studies have suggested that non-surgical periodontal treatment during pregnancy reduces the incidence of pre-maturity (Lopez et al. 2002b, Jeffcoat et al. 2003).

In two Brazilian studies, a significant risk was observed between LBW and CP. In the first one, carried out at Carmela Dutra Maternity Hospital, Rio de Janeiro, which is part of the public health service network, cases of pregnant women with CP, who had at least four sites with probing pocket depth (PPD) ≥ 4 mm and clinical attachment loss (CAL) ≥ 3 mm, were associated with LBW (OR: 3.48, 95% CI: 1.17–10.36; Moliterno et al. 2005). In the second one, CP was associated with LBW, only in the Caucasian pregnant women from Joinville, Santa Catarina, who were over 25 years old. The mean weight of newborn was significantly lower in pregnant women with CP than without CP (Marin et al. 2005).

On the other hand, in a third study with pregnant women who gave birth in a public maternity hospital in Itajaí (the south of Brazil), no association between periodontal infection and PTB and/or LBW was observed (Lunardelli & Peres 2005).

Although most Brazilian studies have studied PTB and LBW, the authors did not mention the relation between PTL and CP.

Therefore, the main aim of this study was to investigate the association between CP and PTL. PTB with or without PROM and LBW in a group of Brazilian pregnant women were also evaluated. There are a limited number of studies in South American populations regarding CP and PTL.

Materials and Methods

Study population

One hundred and twenty-four pregnant women, 15–40 years of age, were enrolled consecutively to check the presence of CP in a cross-sectional study, between December 2003 and May 2005 at the hospital of the School of Medicine, Universidade Estadual de Campi-

nas, which is part of the public health service in the city of Campinas, São Paulo, Brazil. The hospital population came from an area of one million inhabitants and despite not being the only hospital in the area, this hospital is the most important one for high-risk pregnancy deliveries.

In this period, there were 5040 live births, a mean of 280 births per month.

Only pregnant women who needed to be admitted into the hospital for intravenous tocolysis with PTL (<37 weeks; PTL group) were enrolled in the study. For each patient admitted with PTL, the following pregnant woman in term labour (TL) was recruited to take part of the study in order to comprise the TL group.

A check list form was filled out by an obstetrician in order to identify the risk factors for PTL. Previous clinical and laboratory pre-natal patient records were used to avoid admitting patients with a history of hypertension, diabetes, miscarriages, genitourinary tract infections, sexually transmitted diseases, obstetric pathologies, smoking, alcoholism, use of chemotherapy and periodontal treatment during pregnancy. All the selected patients, after being informed the procedures, accepted to take part in the study, freely signing the informed terms of consent.

During the period of the study, 68 patients in PTL and 68 patients in TL were recruited. However, 12 cases belonging to the TL group were excluded due to the fact that the patients left the hospital before 36 h, making it impossible to perform the periodontal examination. This resulted in 68 patients in the PTL group and 56 patients in the TL group.

The following sociodemographic and pregnancy variables were collected by a trained nurse, using a questionnaire on: age, ethnicity (white and non-white), marital status (married, single or divorced), level of schooling (elementary school, secondary school, graduate, no schooling), GA in weeks, number of pre-natal appointments and number of gestations and parity.

The study was approved by the Medical Ethics Committee of the Universidade Estadual de Campinas (Unicamp), São Paulo, Brazil.

Periodontal examination

All the periodontal examinations to identify the presence of CP were carried

out in the maternity ward with the patient lying flat on her bed, head placed at the end of the bed to facilitate a standard examination as reported by Davenport et al. 2002, with the use of an external light source.

The periodontal examination was carried out 36–48 h after delivery to avoid disturbing the patients. The periodontist did not know the clinical and obstetric status of the patients at the time of examination.

All the teeth were evaluated, except for the third molars. Measurement by PPD, the distance in millimetres between the gingival margin and the base of the periodontal pocket, CAL, the distance in millimetres between the cemento-enamel junction and the base of the pocket, bleeding on probing (BOP) and presence of dental plaque (DP) were evaluated with a Goldman-Fox-Williams periodontal probe (TMHu-Friedy, Chicago, IL, USA).

PPD and CAL were performed at six sites per tooth (midbuccal, mesiobuccal, distobuccal, midlingual, mesiolingual and distolingual). BOP was performed on the same six sites.

DP was evaluated at the cervical surface of each tooth. A periodontal probe was placed along the dental cervical on the buccal and lingual surface. A piece of dental floss was introduced into the inter-dental surfaces to check the presence of DP. The evaluation of gingival colour (GC) was performed on the same four dental surfaces.

All the data were recorded orally on a tape recorder and posteriorly transcribed to a periodontal examination sheet.

The presence of CP was established if there was at least one of six sites with CAL \geq 1 mm and gingival bleeding present in the same site of CAL.

Patients who did not reach this criterion were regarded as subjects without CP.

The severity of CP was classified as early (CAL < 3 mm), moderate (CAL \geq 3 mm and < 5 mm), severe (CAL \geq 5 mm) and extension in localized (CAL \leq 30% examined sites) and generalized (CAL > 30% examined sites; Armitage 1999).

All the patients received a toothbrush and dental floss kit and were sent for periodontal treatment if necessary.

Assessment of pregnancy outcomes

The PTL (< 37 weeks) and TL (\geq 37 weeks) were confirmed by the physician

based on GA, presence of uterine contractions with frequency \geq 2/10 min., cervical dilatation > 2 cm and 80% cervical shortening (Herron et al. 1982).

The GA was obtained based on the date of last menstrual occurrence and by the Capurro Method (Capurro et al. 1978), after delivery. In the case of discrepancies among the evaluations, the Capurro Method prevailed.

PTB was defined as the birth that occurs before 37 weeks of gestation (WHO 1977) and term birth (TB) as the birth that occurs after 37 weeks of gestation.

Forty-eight out of 68 patients with PTL ended the gestation in PTB and the remaining (20 cases) had a successful tocolysis reaching TB. Therefore, 56 plus those 20 cases resulted in a total of 76 patients who had term delivery.

The diagnostic of the integrity or PROM was carried out by the physician during labour.

Newborns with birth weight < 2500 g were considered LBW and those with

birth weight \geq 2500 g were considered as having adequate weight.

Statistical analysis

Statistical analysis used the Fisher's exact test and χ^2 for the discrete variables and the Mann-Whitney test for the analysis of the non-parametric variables. OR was calculated with a CI of 95%, so as to evaluate the relation between CP, PTL, PROM, PTB and LBW. The level of significance was 5%. The data were analysed using the SAS 8.2 statistical program (TMSAS Institute, Cary, NC, USA).

Results

The final analysis comprised 124 pregnant women: 68 patients had PTL and another 56 had TL.

The mean age of the patients with PTL and TL was 24.65 \pm 5.73 and 22.63 \pm 5.28 years, respectively

Table 1. Sociodemographic characteristics of the pregnant women with pre-term labour and term labour ($n = 124$)

	PTL (68)		TL (56)		<i>p</i> value
Age (mean \pm SD)	24.65 \pm 5.73		22.63 \pm 5.28		0.035*
Ethnicity, <i>n</i> (%)					
White	44	64.70	30	53.60	0.208 [†]
Non-white	24	35.30	26	46.40	
Marital status, <i>n</i> (%)					
Married	59	86.80	42	75.00	0.093 [†]
Single/divorced	9	13.20	14	25.00	
Schooling, <i>n</i> (%)					
Elementary school	40	58.80	22	39.30	0.029 [‡]
Secondary school/superior	27	39.70	34	60.70	
No schooling	1	1.50	0	0	

*Mann-Whitney test.

[†] χ^2 test.

[‡]Fisher's exact test.

Mean \pm SD, Mean values (standard deviation); PTL, pre-term labour; TL, term labour.

Table 2. Clinical and obstetric characteristics related to pregnant women with pre-term and term labour ($n = 124$)

	Mean \pm SD		<i>p</i> value
	PTL (68)	TL (56)	
Gestational age (weeks)	32.99 \pm 3.16	38.98 \pm 1.93	< 0.0001*
Number of pre-natal appointments (<i>n</i>)	6.40 \pm 3.53 [‡]	8.13 \pm 2.70	0.0001*
CAPURRO (weeks)	35.29 \pm 2.46	39.30 \pm 1.22	< 0.0001*
Weight of newborn (g)	2379.53 \pm 566.83	3203.21 \pm 418.96	< 0.0001 [†]
Number of gestations (<i>n</i>)	2.07 \pm 1.42	1.82 \pm 1.16	0.412*
Parity (<i>n</i>)	1.82 \pm 1.29	1.54 \pm 1.09	0.278*

*Mann-Whitney test.

[†]Student's *T*-test.

[‡]Five cases ignored.

Mean \pm SD, Mean values (standard deviation); PTL, pre-term labour; TL, term labour.

Table 3. Periodontal indicators related to pregnant women with pre-term and term labour ($n = 124$)

	Mean \pm SD		<i>p</i> value*
	PTL (68)	TL (56)	
Clinical attachment level (mm)	1.00 \pm 0.94	0.42 \pm 0.73	<0.0001
Probing pocket depth (mm)	1.33 \pm 0.29	1.27 \pm 0.27	0.090
Dental plaque (%)	77.84 \pm 25.88	70.58 \pm 30.12	0.199
Altered gingival colour (%)	53.14 \pm 32.24	44.03 \pm 34.52	0.097
Bleeding on probing (%)	54.61 \pm 30.76	41.48 \pm 31.81	0.012

*Mann-Whitney test.

Mean \pm SD, Mean values (standard deviation); PTL, pre-term labour; TL, term labour.Table 4. Distribution of pregnant women with pre-term labour, pre-mature rupture of the ovular membranes, pre-term birth and low birth weight, based on the presence or not of chronic periodontitis and odds ratio (OR) with a 95% confidence interval (95% CI; $n = 124$).

	<i>n</i> = 124	Chronic periodontitis, <i>n</i> (%)		OR (95% CI) Adjusted*
		yes	no	
Pre-term labour				
Yes	68	42 (61.80)	26 (38.20)	4.7 (1.9–11.9)
No	56	15 (26.80)	41 (73.20)	
Pre-mature rupture of the ovular membranes				
Yes	62	29 (46.80)	33 (53.20)	1.0 (0.4–2.3)
No	62	28 (45.20)	34 (54.80)	
Birth				
Pre-term	48	31 (64.60)	17 (35.40)	4.9 (1.9–12.8)
Term	76	26 (34.20)	50 (65.80)	
Newborn (g)				
<2500	40	23 (57.50)	17 (42.50)	4.2 (1.3–13.3)
\geq 2500	84	34 (40.50)	50 (59.50)	

*Adjusted for age (< 18 and > 34 years), number of gestations (nulliparous), schooling (elementary), ethnicity (non-white), marital status (single) and number of pre-natal appointments.

PTL, pre-term labour; TL, term labour.

($p = 0.035$). The level of schooling was also different between the two patient groups ($p = 0.029$). There was no significant difference between the two groups of women related to ethnicity, marital status (Table 1), parity and number of gestation (Table 2).

Patients who presented PTL had significantly less pre-natal appointments than patients with TL (6.40 ± 3.53 versus 8.13 ± 2.70 , $p = 0.0001$). The mean newborn weight (g) in the patients who presented PTL was $2.379.53 \pm 566.83$ and there was a significant difference when compared with the newborns of patients who presented TL that was 3203.21 ± 418.26 ($p < 0.0001$; Table 2).

The ratios of PPD, CAL, DP, BOP and GC were greater in the PTL group. Statistically significant differences were observed only in relation to CAL (1.00 ± 0.94 versus 0.42 ± 0.73 , $p < 0.0001$) and BOP (54.61 ± 30.76 versus 41.48 ± 31.81 , $p = 0.012$; Table 3).

The periodontal examination showed that the frequency of CP was signifi-

cantly higher in the PTL group (61.80%) than the TL group (26.80%, $p < 0.0001$; Table 4).

In terms of the severity and extension of CP, 32 of the 42 patients with PTL presented early CP (76.20%), 13 of whom presented the localized form and 19 the generalized form. In eight pregnant women, CP was moderate (19.00%), in seven it was localized and in one generalized and in two pregnant women with severe CP (4.80%), it was only found in the generalized form.

Thirteen out of the 15 pregnant women with TL presented early CP (86.67%), it was localized in seven cases, generalized in six cases and moderate plus generalized in two cases (13.33%).

The severity of CP did not show any differences between the PTL and TL groups ($p = 0.843$).

The multivariate regression analysis adjusted by age, number of gestations, level of schooling, ethnicity, marital status and number of pre-natal appoint-

ments showed that women with CP had 4.7 times more chance of PTL. A strong association was also observed between CP, PTB and LBW. Adjusted multivariate regression analysis also increased the chances of PTB and LBW by 4.9 times and 4.2 times, respectively (Table 4).

Discussion

This study demonstrated that the presence of CP was associated with a significant risk for PTL (OR: 4.7, 95% CI: 1.9–11.9), PTB (OR: 4.9, 95% CI: 1.9–12.8) and LBW (OR: 4.2, 95% CI: 1.3–13.3) in a group of Brazilian pregnant women.

Several studies carried out on different populations and different study designs showed associations between moderate and severe CP, PTB and LBW (Offenbacher et al. 1996, Dasanayake 1998, Jeffcoat et al. 2001, Lopez et al. 2002a, b).

In our cross-sectional study, the frequency of moderate, severe and mainly early CP in a generalized form was more related in the PTL group than in the TL group.

In a case-control study with 85 pregnant women, Radnai et al. (2004) also showed that early CP (bleeding $\geq 50\%$ and at least in one site ≥ 4 mm PPD, $p = 0.001$) is a significant risk factor for PTB (OR: 5.46, 95% CI: 1.72–17.32).

Contrary to Radnai's criteria and other studies (Holbrook et al. 2004, Lunardelli & Peres 2005) that used PPD as a marker of periodontal disease, the authors considered subjects with CP based in sites with CAL ≥ 1 mm and gingival bleeding as a clinical sign of gingival inflammation.

CAL (active and inactive sites) sometimes can under- or overestimate the presence, severity and extension of CP. Despite this, the authors believed that CAL constitutes a useful parameter to estimate CP status when associated to gingival inflammation (bleeding).

In this study, the PPD in the PTL group had a greater mean (1.33) than in the TL group (1.27), but lower when compared with other studies with different designs (Offenbacher et al. 1996, Davenport et al. 2002, Moore et al. 2005).

The presence of periodontal pockets, CAL and gingival bleeding are shown to be important factors associated to adverse pregnancy outcome. Perio-

dontal pockets, as a consequence of loss of attachment, are potential reservoirs for microorganisms. In exposed areas without gingival epithelium, gingival bleeding facilitates the entrance of microorganisms, especially the LPS-rich ones (Offenbacher et al. 1996, Offenbacher 1998, Radnai et al. 2004).

It is still not clear how the microorganisms that are rich in LPS can cause sufficient immunoinflammatory response that can compromise pregnancy.

It is possible that some of the bacterial species present in the periodontal infection can colonize the placental tissues by means of the blood stream (Hill 1998, Bearfield et al. 2002) or even that the production of pro-inflammatory cytokines and PGE₂ can reach elevated levels in the maternal serum and stimulate pre-mature uterine contractions (Offenbacher et al. 1996, Offenbacher 1998, Dörtbudak et al. 2005).

In an animal model, periodontal infections due to *Porphyromonas gingivalis* increased the levels of PGE₂ in the amniotic fluid and interfered with the development of the foetus (Collins et al. 1994a, b).

Despite differences between PTL and TL groups ($p < 0.0001$), this study also revealed that most pregnant women needed periodontal treatment. Ferris (1993) reported that during gestation, physiologic changes (oestrogen and progesterone levels) and behaviour associated with poor oral hygiene have been observed.

An inadequate DP control was observed in the Brazilian pregnant sample in both groups (Table 3) probably because most of the patients had a low level of schooling, low socioeconomic status, anxiety and/or worries about the pregnancy more than with themselves.

The sociodemographic data showed that white and non-white ethnicity was very homogeneous ($p = 0.208$) and did not relate to pre-maturity in this study, but other studies had a greater proportion of African Americans (Offenbacher et al. 1996, Jeffcoat et al. 2001).

No association was observed in relation to PROM. One possible explanation for this finding is the very rigid exclusion criteria, where pregnant women with a diagnosis of infection, especially in the genitourinary tract, did not participate in this study, although the aetiology of PROM is multi-factorial and appears as a result of the altered collagen structure, diminished synthesis, acceleration of the degrading mechanism

apart from the presence of infection and immunoinflammatory response (Aagaard-Tillery et al. 2005).

Owing to fact that the bivariate statistical analysis showed that schooling and the number of pre-natal appointments were related to PTL, the multivariate regression analysis was adjusted to eliminate its influence and to check the real influence of CP on the PTL, PROM, PTB and LBW.

An important study limitation to be pointed out is the small number of patients. However, to minimize this problem, for each patient in PTL admitted into the study, the following patient to be admitted in TL was used as the control. Also, very rigid criteria were applied when selecting the subjects, in order to eliminate all the other confounding factors, even though the CP OR pointed to a 4.7 risk for PTL with a reasonable range of CI.

As is well known, there are many risk factors for PTL. Smoking and alcohol abuse, diabetes mellitus, hypertension, genitourinary tract infection and multiple pregnancies are frequently cited by the authors (Hillier et al. 1988, Gibbs et al. 1992, Hill 1998, Offenbacher 1998, Goldenberg et al. 2000, Dizon-Townson 2001, McGaw 2002). If we had included patients with any other risk factor, it could interfere with the final results in order to evaluate the influence of CP leading to PTL. It is very clear that, for example, multiple pregnancies can induce PTL. Other studies have used similar selection criteria as were used here (Radnai et al. 2004, Marin et al. 2005, Noack et al. 2005).

CP was strongly associated with PTL, PTB and LBW in a group of Brazilian pregnant women. The authors did not have the intention of generalizing the results for the entire Brazilian population, but to emphasize the importance of the role of CP in pre-maturity as it is very important in Brazil.

More prospective and interventional studies on Brazilian pregnant women should be carried out in order to help understand the PTL physiopathogenesis and its association with CP.

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Clinical Relevance

Scientific rationale for the study: Several studies have tried to relate chronic periodontitis (CP), and prematurity or low birth weight. However, none have shown the cause-effect relation. This association has been only sporadically studied in

Brazil, being in need of more data that can help to elucidate it.

Principal findings: This study pointed to a strong association between CP and prematurity in Brazilian pregnancies, supporting international scientific data. PC was also strongly associated to low birth

weight and low level of schooling. *Practical implications:* We have shown high rates of CP in pregnant women with low educational levels, suggesting the necessity of pre-natal dental care.