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Periodontal disease and perinatal outcomes: a case-control study

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Abstract

Aim: Our aim was to measure the association of maternal periodontitis with low birth weight (LBW), pre-term LBW, and intra-uterine growth restriction.

Material and Methods: An inclusive case–control design including subjects examined for periodontitis through attachment loss, information on perinatal outcomes and general health. Data were analysed through conditional logistic regression.

Results: Cases ($n = 304$) and controls ($n = 611$) had similar prevalence and severity of periodontitis, defined as at least three sites, in different teeth, with loss of three or more millimetres of clinical attachment level. Several factors were associated with the outcome, but the crude odds ratio for periodontitis was not significant. Odds ratio were 0.93 [95% confidence interval (CI): 0.63–1.41] for LBW and 0.92 (95% CI:0.54–1.57) for pre-term LBW in the presence of periodontitis, after adjustment for maternal age, previous pregnancies, pre-natal care, smoking, previous low birth or premature birth and other medical conditions, on a hierarchical model.

Conclusions: Results do not support the hypothesis of association observed in previous studies after appropriate controlling for confounding variables. Negative perinatal outcomes are better explained by determinants other than periodontal health. This study adds to the growing body of literature on the relationship between periodontal diseases and systemic health.

Key words: epidemiology; low birth weight; periodontal disease; periodontitis; prematurity

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The association of low birth weight (LBW), pre-term LBW and intra-uterine growth restriction with high health care costs and high infant mortality has been well established (McCormick 1985, Zaw et al. 2003). The recently observed increase in LBW incidence around the world (Victora et al. 1994, Monteiro et al. 2000, Ohmi et al. 2001, Nolte et al. 2002) raises the urgency of this public health issue and calls for the identification of preventable risk factors.

One such preventable risk factor may be maternal periodontitis. The association between periodontitis and LBW has been studied since the mid-1990s (Offenbacher et al. 1996). However, the risk estimates derived from a number of these studies vary greatly (Offenbacher et al. 1996, Dasanayake, 1998, Dasanayake et al. 2001, Mitchell-Lewis et al. 2001, Davenport et al. 2002, Lopez et al. 2002a b, Jeffcoat et al. 2003). In attempting to account for this wide variance in risk estimates, one theory that arises is that the observed association is linked to the confounding effects of risk factors other than periodontal infection (Pitiphat & Merchant 2002). This theory is supported by the fact that similar studies have yielded conflicting results (Offenbacher et al. 1996, Davenport et al. 2002), which are still being reported in recent publications (Buduneli et al. 2005, Cruz et al. 2005, Lunardelli & Peres 2005, 2006, Moliterno et al. 2005, Moreu et al. 2005, Noack, et al. 2005, Costa Mda 2006, Vettore et al. 2006).

As maternal periodontitis is associated with other exposures that predict or cause LBW, the objective of the present study is to measure the effect of maternal exposure to periodontitis on the incidence of LBW, pre-term LBW and intra-uterine growth restriction, after adjusting for these exposures.

Methods

A case–control study, matched for birth sequence and hospital, was conducted to explore the relation between maternal periodontitis and LBW. An inclusive design was adopted (Rodrigues & Kirkwood 1990), where controls were selected from the individuals of the target population, regardless of whether or not the outcome was present. Sample size calculation was performed to obtain 80% power and detect an odds ratio of

at least 1.6. The sample size was further increased by 20% to accommodate multivariate modelling and another 20% for losses and refusals. The total estimated sample size was 306 cases and 612 controls.

Case definition

Mothers who gave birth at one of the three hospitals in Porto Alegre, Brazil were included in the study, following written informed consent, and reviewed and approved by the Pelotas Federal University's Review Board and the hospitals' Review Boards.

The hospitals' birth registers were reviewed daily by the study staff to identify incident cases: singleton newborns with <2500 g of birth weight, at >27 weeks of gestational age (Horta et al. 1997).

The hospitals' scales were crosschecked daily for accuracy. All newborn cases were re-weighed for accuracy assurance, as was a 10% random sample of the newborn controls. Exclusion criteria included multiple gestations, maternal diabetes, stillborn at <28 weeks or severe physical defects that could compromise the weight or the survival chances. Stillborns were included as cases in the study if they were at least 28 weeks of gestational age, or if the age was unknown but if the newborn weighed at least 1000 g. Gestational age was assessed through the method described by Capurro et al. (1978), where a series of items from a physical examination of the newborn are considered in a scoring system.

Controls

Two controls were selected for each case. The controls were the two newborns (mother/child) delivered immediately after the case in the same hospital. The two controls were selected regardless of their birth weight, following the same exclusion criteria as cases. LBW controls were analysed ''as is'' in an inclusive case–control analysis (Santos et al. 1998).

Data collection

All mothers were interviewed after delivery. Interviewers were trained to gather data from cases and controls similarly through a structured questionnaire (closed questions). Although blinding to case–control status was attempted, it was not fully achieved due to the hospital's rooming system (mothers lodged with newborns unless either needed intensive care). Interviewers were not advised of the study hypothesis in order to reduce interviewer bias. The following information was collected from the mother and crosschecked with the hospital charts using a standardized template: socioeconomic factors (income, home assets, number of people living in the house, education level); demographic factors (age, skin colour, marital status). Reproductive variables (gestational history, previous delivery of a low weight baby, abortions, parity, quality of prenatal care, co-morbidities). Only information that could be confirmed from the hospital charts, with appropriate clinical and laboratorial assurance, was included in the study. Through the structured questionnaire, the mother was inquired of behavioural components (alcohol intake, drug usage, smoking during or before pregnancy).

Exposure assessment

The presence of periodontal disease in the mother was assessed through a full-mouth periodontal examination after delivery. One trained periodontist carried out the exam. Ten percent of the exams were repeated to ensure that the quality of the data was maintained throughout the study. Data from the training period and quality-control examinations were analysed according to the differences by mean plot (Bland & Altman 1986, 1995a, b) for reproducibility assessment, and it was found that 92% of the measures fell within the 95% confidence interval (CI) of the observed variance. Six sites per tooth were examined for probing depth and attachment level. Periodontitis was determined to be present when at least three sites, in different teeth, with loss of three or more millimetres of clinical attachment level were available. Presence of gingival recession was registered but excluded for diagnostic purposes when present in buccal or lingual surfaces.

For analytical purposes, periodontitis severity was coded as follows:

Mild: presenting at least three sites, in different teeth, with three or more millimetres of attachment loss, but not three or more sites with five or more millimetres of attachment loss.

Moderate: presenting at least three sites, in different teeth, with five or more millimetres of attachment loss, but not three sites with seven or more millimetres of attachment loss.

Severe: presenting at least three sites, in different teeth, with seven or more millimetres of attachment loss.

Statistical analysis

Data were entered through a relational database (Microsoft Access™) and analysed by means of Stata 7.0 (Stata Corporation, TX, USA). Univariate analysis was performed for data description. Odds ratios and 95% CIs were estimated through conditional logistic regression. Statistical significance was assessed through the likelihood ratio test. A conceptual framework was constructed to guide the conditional logistic regression procedures through different levels or domains (Victora et al. 1997). The model considered ethnicity, socioeconomic class and education in level 1. Level 2 included age, parity, pre-natal care and pre-natal care adequacy, cigarette smoking and alcohol use during pregnancy. The third level focused on previous delivery of an underweight or premature baby and co-morbidities (hypertension, pre-eclampsia, weight change during gestation and infections). Level 4 included urinary infection, vaginosis, HIV and syphilis. Different case categorization, focusing on pre-term LBW (<37 weeks of gestation and <2500 g of birth weight) and intra-uterine growth restriction [below the 10th percentile of ponderal index (PI = birthweight $\times$ 100/crown-heel length)] were each analysed separately in a secondary set of analysis based on the above-described conceptual model. All models were adjusted for the sex of the newborn.

Variables from the first level were entered in the conditional logistic model and those with $p \leqslant 0.25$ were kept in the final model as potential confounders when the appropriate criteria were met (Greenland & Morgenstern 2001). The same step was repeated for the subsequent levels, keeping the variables from a previous level in the model after the original level was adjusted, even if they lost significance. Analyses were performed for all cases, and separately for pre-term and growth-retarded cases and their respective controls.

Results

A total of 308 cases and 616 controls were recruited. Two cases and one control were lost due to early discharge; two cases were not examined for periodontitis and therefore were not included in the analysis. Fifty-two cases were also entered as controls. From these, five entered the study three times (once as case and twice as control). Four individuals were entered twice as controls. A total of 251 subjects entered the study as cases only (308 cases minus five cases that entered as controls twice and 52 cases that entered as controls once) and 550 as controls only (616 inclusive controls minus four controls that entered the study twice, five cases that were controls twice as well as cases, and 52 controls that were also cases). There were no refusals. Among cases, 106 were full-term births (34.6%), 197 were pre-term (64.4%), and three (1.0%) could not have gestational age assessed. The distribution of the exposure among cases and controls is presented in Table 1.

Table 1. Exposure distribution among cases and controls, Porto Alegre, Brazil

Exposure	Cases (no. = 304)		Controls (no. = 611)		χ^2
	n	%	*n*	%	*p*
Periodontal disease presence*					
Yes	178	58.5	333	54.5	0.3
No	126	41.5	278	45.5	
Periodontal disease severity†					
Mild	85	28.0	182	29.9	0.2
Moderate	70	23.0	122	19.8	
Severe	23	7.4	29	4.8	
Bleeding gingival sites					
50% or less	150	49.3	311	50.9	0.6
More than 50%	154	50.7	300	49.1	
Visible plaque sites					
50% or less	168	55.3	347	56.8	0.6
More than 50%	138	44.7	264	43.2	

*At least three sites, from different teeth, presenting at least 3 mm of periodontal attachment loss having the cement–enamel junction as reference.

†*Mild*: presenting at least three sites with 3 mm of attachment, but not three or more sites with more than 4 mm of attachment loss. *Moderate*: presenting at least three sites presenting at least 5 mm of attachment loss, but not three sites with more than 6 mm of attachment loss. *Severe*: at least three sites presenting more than 6 mm of attachment loss. Gingival recession was not considered when in buccal or lingual/palatal surface with probing depth of less than 2 mm.

Attachment level, the distance between the cement-enamel junction and the bottom of the probable pocket to the nearest whole millimetre.

Almost 59% of the cases and 55% of the controls had been born to mothers who showed some degree of periodontitis. The distributions of the severity grades of periodontitis were similar in cases and controls (χ^2; $p = 0.2$). The proportions of bleeding sites and of sites with visible plaque were also similar for cases and controls ($p = 0.6$).

Mothers with moderate or severe disease were more likely to be less educated, to be from a lower social class, to be older, to have been smokers before pregnancy, to have smoked during pregnancy, to be hypertensive and to have had fewer pre-natal appointments (χ^2; $p < 0.05$ – data not shown).

Table 2 shows the crude odds ratio and 95% CIs according to the conceptual framework. The association of the presence of periodontal destruction (measured through attachment loss) and LBW was not statistically significant. The crude analysis for pre-term LBW led to similar conclusions. Although the results show an increased risk of pre-term LBW associated with increased severity of periodontitis, they were not statistically significant (test for trend). The crude odds ratio for intra-uterine growth restriction in women exposed to periodontitis was not significant. However, the analysis with respect to categorized severity produces an odds ratio of 2.33 (1.01; 5.37) for moderate periodontitis, suggesting that there might be some risk associated with this condition. But power for statistical inference is low due to small counts.

Table 3 shows the adjusted effect of periodontitis in the cases presenting LBW and premature birth. The model includes adjustment for maternal age, previous pregnancies, adequacy of pre-natal care, smoking during pregnancy, previous LBW child, previous premature birth, gestational hypertension, pre-eclampsia and weight change during pregnancy. Intra-uterine growth restriction cases were kept out of the adjusted analysis due to the low power of the sample for proper confounding adjustments and inferences. The inclusion of potential confounders in the analysis resulted in lowered odds ratios for the dichotomized effect of periodontitis on LBW and pre-term LBW. For the categorized exposure, adjusted odds ratios for LBW were lower than the crude ones (except for the severe disease, which varied from 1.78 to 1.9), but were not statistically significant.

When potential confounders were included, the odds ratios for premature birth for the categorized periodontitis were also reduced (Table 3). For the complete model see Table in Appendix.

Discussion

The results of the present study could not establish a statistically significant association between periodontitis and LBW. Except for the crude association between intra-uterine growth restriction and moderate (*versus* ''no'') periodontitis, there was no significant association between any of the three outcome measures and periodontitis. These results are supported by the preliminary findings of Mitchell-Lewis et al. (2001) and by the results from Davenport et al. (1998, 2002), Noack et al. (2005), Buduneli et al. (2005) and Lunardelli & Peres (2005). Except for the crude results showing an association between exposure to mild periodontitis and intra-uterine growth restriction, and between severe disease and LBW, no other value had significant effects. Controlling for factors related to exposure and outcome that met the confounding criteria (Greenland & Morgenstern 2001; i.e., maternal age, previous pregnancies, pre-natal care, adequate pre-natal care, smoking during pregnancy, previous low-weight birth, previous premature birth, gestational hypertension, pre-eclampsia and weight change during pregnancy) annulled the crude effects observed initially. In contrast to previous studies (Dasanayake 1998,

Table 2. Inclusive case–control analysis, distribution of the crude odds ratios (conditional logistic regression) for the effects of the covariates and main exposures on weight for low birth weight (LBW), intra-uterine growth restriction and pre-term LBW, Porto Alegre, Brazil

Level	Variable	Low birth weight			Intra-uterine growth restriction			Pre-term low birth weight		
		count (ca/co)	crude odds ratio	*p*-value†	count (ca/co)	crude odds ratio	*p*-value†	count (ca/co)	crude odds ratio	*p*-value†
Level 1	Skin color									
	White	232/461	1.00	0.82	56/379	1.00	0.86	157/531	1.00	0.29
	Not-white	72/150	0.95 (0.68, 1.33)		18/123	1.09 (0.53, 2.25)		39/181	0.78 (0.5, 1.21)	
	Social class									
	A and B	25/50	1.00	0.34	5/41	1.00	0.68	20/55	1.00	0.80
	C	99/239	0.87 (0.46, 1.62)		32/203	2.56 (0.74, 8.79)		69/267	0.9 (0.43, 1.87)	
	D	109/212	1.06 (0.56, 2.02)		21/171	2.37 (0.64, 8.8)		65/252	0.95 (0.43, 2.07)	
	Education									
	None	3/4	1.00	0.73	1/4	1.00	0.61	1/6	1.00	0.47
	Primary	188/390	0.65 (0.14, 2.91)		46/317	0.56 (0.03, 9.24)		122/454	0.96 (0.09, 10.71)	
	Secondary	102/191	0.71 (0.16, 3.23)		25/158	0.44 (0.03, 7.24)		64/225	1.04 (0.09, 11.52)	
	Tertiary	11/26	0.65 (0.12, 3.34)		2/23	0.87 (0.03, 26.41)		9/27	1.23 (0.1, 15.64)	
Level 2	Age group (years)									
	<15	12/25	1.00	0.78	1/19	1.00	0.87	6/31	1 .00	0.86
	16–19	67/109	1.25 (0.59, 2.66)		19/85	4.82 (0.45, 51.22)		50/125	1.83 (0.69, 4.90)	
	20–24	88/160	1.05 (0.5, 2.2)		19/137	2.95 (0.28, 30.7)		53/194	1.43 (0.53, 3.82)	
	25–29	49/144	0.67 (0.31, 1.47)		12/119	2.6 (0.24, 28.01)		32/159	1.07 (0.38, 2.97)	
	30–34	28/98	0.53 (0.23, 1.22)		8/79	3.94 (0.35, 44.33)		18/108	0.79 (0.27, 2.31)	
	>35	56/72	1.6 (0.73, 3.52)		12/63	4.26 (0.36, 50.29)		35/91	2.5 (0.88, 7.08)	
	Previous pregnancies									
	None	143/240	1.00	0.0031	39/195	1.00	0.07	92/290	1.00	0.09
	One	79/158	0.81 (0.58, 1.14)		22/130	0.87 (0.43, 1.73)		52/183	0.85 (0.55, 1.29)	
	Two	42/92	0.72 (0.47, 1.11)		4/71	0.30 (0.08, 1.09)		25/108	0.67 (0.38, 1.16)	
	Three or more	40/121	0.54 (0.35, 0.82)		9/106	0.56 (0.24, 1.28)		27/131	0.67 (0.4, 1.13)	
	Pre-natal care									
	Yes	282/583	1.00	0.19	65/478	1.00	0.5	177/682	1.00	0.03
	No	20/28	1.52 (0.81, 2.84)		8/24	1.47(0.48, 4.50)		18/30	2.28 (1.09, 4.75)	
	Adequate pre-natal care*									
	Yes	70/83	0.48 (0.33, 0.7)		47/409	0.15 (0.03, 0.66)	0.02	129/572	0.34 (0.20, 0.58)	
	No	210/494	1.00	0.0001	18/63	1.00		48/102	1.00	<0.001
	Smoking									
	Non-smoker	181/373	1.00	0.002	44/304	1.00	0.1	126/422	1.00	0.93
	Former smoker	43/126	0.69 (0.46, 1.03)		10/105	0.74 (0.28, 1.95)		28/140	0.63 (0.38, 1.04)	
	Smoker	80/112	1.56 (1.11, 2.19)		20/93	2.28 (1.02, 5.1)		42/150	1.13 (0.72, 1.76)	
	Alcohol consumption during pregnancy									
	Yes	20/44	0.91 (0.51, 1.61)	0.73	2/36	0.31(0.07, 1.47)	0.14	11/53	0.67 (0.30, 1.47)	0.32
	No	284/597	1.00		72/446	1.00		85/659	1.00	
Level 3	Previous LBW									
	Yes	59/66	1.97 (1.35, 2.87)		18/52	2.20 (1.01, 4.77)	0.03	40/85	2.30 (1.43, 3.71)	
	No	243/543	1.00	0.0004	55/448	1.00		155/625	1.00	<0.001
	Previous premature birth									
	Yes	52/54	2.17 (1.43, 3.28)		16/45	2.13 (0.97, 4.66)		42/64	3.93 (2.3, 6.72)	
	No	250/556	1.00	<0.001	57/456	1.00	0.04	153/647	1.00	<0.001

Table 2. (Contd.)

Level	Variable	Low birth weight			Intra-uterine growth restriction			Pre-term low birth weight		
		count (ca/co)	crude odds ratio	*p*-value†	count (ca/co)	crude odds ratio	*p*-value†	count (ca/co)	crude odds ratio	*p*-value†
	Gestational Hypertension									
	Yes	92/111	2.00 (1.44, 2.77)		27/84	3.3 (1.56, 6.98)		57/142	2.08 (1.37, 3.15)	
	No	202/491	1.00	0.0001	45/411	1.00	0.003	131/560	1.00	0.001
	Pre-eclampsia									
	Yes	63/48	3.07 (2.03, 4.65)		25/33	8.72 (2.98, 25.53)		48/63	3.79 (2.27, 6.32)	
	No	241/563	1.00	<0.001	49/469	1.00	<0.001	148/649	1.00	<0.001
	Weight change during pregnancy									
	Loss or <5 Kg gain	27/37	1.4 (0.8, 2.44)	0.0009	5/31	0.39 (0.09, 1.7)	0.02	22/40	1.53 (0.79, 2.96)	0.001
	5–15 Kg gain	188/327	1.00		48/268	1.00		125/387	1.00	
	>16 Kg gain	47/176	0.51 (0.35, 0.75)		8/144	0.26 (0.09, 0.74)		25/197	0.38 (0.23, 0.63)	
	Infections during pregnancy‡									
	None	164/352	1.00	0.99	39/285	1.00	0.39	108/403	1.00	0.13
	One	87/173	1.01 (0.72, 1.42)		19/150	0.73 (0.35, 1.54)		45/215	0.82 (0.53, 1.28)	
	Two or more	29/61	0.99 (0.61, 1.63)		12/48	2.85 (0.84, 9.63)		24/65	1.69 (0.91, 3.15)	
Level 4	Urinary infection									
	Yes	78/165	0.89 (0.65, 1.23)		22/136	1.26 (0.77, 2.07)		50/192	0.97 (0.64, 1.46)	
	No	216/438	1.00	0.55	51/359	1.00	0.6	139/510	1.00	0.95
	Vaginosis (tricomonas)									
	Yes	69/124	1.20 (0.85, 1.69)		21/101	1.7 (0.72, 3.97)		46/146	1.5 (0.96, 2.36)	
	No	224/475	1.00	0.38	51/391	1.00	0.16	142/552	1.00	0.09
	HIV infection									
	Yes	4/10	0.89 (0.27, 2.89)		1/9	2.00 (0.13, 31.98)		2/12	0.67 (0.13, 3.3)	
	No	283/592	1.00	0.85	71/487	1.00	1.00	180/689	1.00	0.62
	Positive VDRL									
	Yes	3/7	1.00 (0.25, 4.0)		0/7	-		3/7	1.1 (0.26, 4.63)	
	No	283/587	1.00	1.00	71/483	1.00	-	179/685	1.00	0.9
	Periodontitis									
	Yes	178/333	1.18 (0.89, 1.56)		46/279	1.24 (0.67, 2.31)		118/388	1.25 (0.86, 1.81)	
	No	126/278	1.00	0.21	28/223	1.00	0.68	78/324	1.00	0.24
	Periodontitis									
	Absent	126/278	1.00	0.17	28/224	1.00	0.06	78/325	1.00	0.33
	Mild	85/182	1.04 (0.74, 1.46)		19/156	0.67 (0.3, 1.46)		58/205	1.08 (0.71, 1.67)	
	Moderate	70/121	1.32 (0.91, 1.93)		21/98	2.67 (1.13, 6.32)		45/145	1.40 (0.86, 2.26)	
	Severe	23/29	1.79 (0.98, 3.25)		6/24	2.04 (0.57, 7.29)		15/37	1.71 (0.83, 3.54)	
	Sex of the newborn									
	Male	138/328	1.00	0.010	39/269	1.00	0.56	99/362	1.00	0.12
	Female	166/283	1.44 (1.09, 1.92)		35/233	1.28 (0.67, 2.42)		97/350	1.32 (0.93, 1.88)	

Owing to missing data, the sums may not reach the sample size.

*Adequate pre-natal care: more than three visits starting before the fifth month.

†*p*-value according to the χ^2 test for heterogeneity between models.

‡Excluding genital-urinary infections, included in level 4.

Table 3. Distribution of the adjusted odds ratios (conditional logistic regression) for the effects of the main exposure on low birth weight (LBW) and pre-term LBW, Porto Alegre, Brazil

LBW	Cases		Controls		Conditional logistic regression	
	n	%	nI/nT†	%I/%T	adjusted odds ratio (95% confidence interval)	*p*-value*
Periodontitis						
Yes	178	58.5	333/288	54.5/53.9	0.93 (0.63, 1.41)	
No	126	41.5	278/246	45.5/46.1	1.00	0.97
Periodontitis						
Absent	126	41.5	278/246	45.5/46.1	1.00	0.76
Mild	85	28	182/159	29.9/29.8	0.98 (0.60, 1.56)	
Moderate	70	23	122/105	19.8/19.7	0.77 (0.46, 1.32)	
Severe	23	7.4	29/23	4.8/4.3	1.94 (0.80, 4.71)	
PTLBW						
Periodontitis						
Yes	118	60.2	330/297	54.4/55.5	0.92 (0.54, 1.57)	
No	78	39.8	277/238	45.6/44.5	1.00	0.77
Periodontitis						
Absent	78	39.8	278/239	45.8/44.6	1.00	0.49
Mild	58	29.6	180/160	29.7/29.9	0.89 (0.48, 1.64)	
Moderate	45	23	120/110	19.8/20.6	0.87 (0.41, 1.57)	
Severe	15	7.7	29/26	4.8/4.9	1.87 (0.64, 5.45)	

Adjusted for maternal age, previous pregnancies, adequate pre-natal care, smoking during pregnancy, previous low weight birth, previous premature birth, gestational hypertension, pre-eclampsia and weight change during pregnancy.

*Likelihood-ratio test for heterogeneity between the models.

†I, Inclusive design; T, Traditional design (LBW controls excluded)

Offenbacher et al. 1996, Lopez et al. 2002a b), the present model adjusted the exposure effect for adverse events that can take place during pregnancy, as well as for socioeconomic variables (hospital matching). In addition to the matching, socioeconomic variables were tested for their association with the outcomes and exposures to prevent residual confounding.

Results from previous studies are not consistent, and, as mentioned above, another case–control study also failed to detect an association between periodontitis and LBW after the proper adjustment for confounders (Davenport et al. 1998, 2002), as well as other study designs (Buduneli et al. 2005, Lunardelli & Peres 2005, Noack et al. 2005). Inconsistent controlling for confounding should be added to the reasons for differences among the published results. The present study was conducted according to sound case–control principles. Selection bias was minimized by selecting controls and cases from the same study population. Data were collected in a similar fashion from cases and controls, and although the clinical examiner could not be blinded for case/control status, the objectivity of the exams and the training meant that the exposure measures were unaffected. Furthermore, data were cross checked through the hospital charts,and it is not likely that any influence from the outcome was exerted on the interviewers.

The decision to rely on clinical attachment level for diagnosis was based on the fact that this parameter is not seriously affected by the pregnancy, and the diagnosis based on attachment loss has higher sensitivity and specificity than the one relying on probing depth (Bassani et al. 2006). Although to some extent past history of periodontitis may be included when applying these criteria, the sample population was mainly untreated, and the prevalence of other clinical signs of periodontal disease did not differ among cases and controls (Table 1). Adjustment for previous periodontal treatment did not alter the results (data not shown).

As the inclusive case–control design (Rodrigues & Kirkwood 1990) includes controls chosen from the source population regardless of their birth weight status, these controls can be used to estimate the frequency of exposure among the population. As mentioned by (Santos et al. 1998), if the exposure under investigation is associated positively with the outcome, excluding cases from the control group would result in an odds ratio that overestimates the relative risks.

The sample size calculations were performed to obtain 80% power and detect an odds ratio of at least 1.6. The sample size was increased by 20% to accommodate multivariate modelling and another 20% for losses and refusals. As there were only 13 exclusions (1.4%) (two cases, four respective controls, and one control, plus no information on the periodontal status for two cases, hence excluding the four respective controls), the sample accounts for greater than the planned 80% power. Thus, the lack of power cannot be implicated as the source of non-significant associations between periodontal status and full or pre-term LBW. However, low prevalence of severe periodontitis may well have led to a power issue, in particular if only a severe periodontal condition affects pregnancy. Overall, power is slightly lower for the other two outcomes of interest, namely, intra-uterine growth restriction and pre-term LBW, with smaller sample sizes. Therefore, results for intra-uterine growth restriction were not significant and are not presented.

The disparity of the results observed in the literature, towards different magnitudes of risk, may also be a result of publication bias, as negative-result studies may not be favoured for publication. Further, as suggested by Davenport et al. (2002), ethnicity of the population and cultural factors may account for some of the observed differences between studies.

Data from the present study were not supportive of the hypothesis of association between periodontitis and LBW, pre-term LBW and intra-uterine growth restriction. Results presented for the pre-term LBW and intra-uterine growth restriction may be interpreted in light of reduced sample size. Although the sample presents a high prevalence of periodontitis, probably reflecting low SES status (Khan & Jamal 2003), other characteristics of this population also known to be concomitants of periodontitis, such as cultural aspects, health care behaviour/access to health care (Mohsin et al. 2003), nutritional factors, and habits such as smoking and alcohol consumption (Jaffee & Perloff 2003), may account for the prevalence of LBW to a greater extent than periodontitis, but the possibility of type-II error and the borderline *p*-values observed for Table 2 (moderate and severe periodontitis) and Table 3 (severe periodontitis) should be accounted for. Further studies on the

effects of periodontitis on intra-uterine growth restriction might be necessary to clarify the issue.

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References

Bassani, D., Silva, C. & Oppermann, R. (2006) Validity of the community Periodontal Index of Treatment Needs (CPITN) for population periodontitis screening. *Cadernos de Saude Publica* **22**, 109–118.

Bland, J. M. & Altman, D. G. (1986) Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* **1**, 307–310.

Bland, J. M. & Altman, D. G. (1995a) Calculating correlation coefficients with repeated observations: part 1 – correlation within subjects. *BMJ* **310**, 446.

Bland, J. M. & Altman, D. G. (1995b) Comparing two methods of clinical measurement: a personal history. *International Journal of Epidemiology* **24** (Suppl. 1), S7–S14.

Buduneli, N., Baylas, H., Buduneli, E., Turkoglu, O., Kose, T. & Dahlen, G. (2005) Periodontal Infections and pre-term low birth weight: a case control study. *Journal of Clinical Periodontology* **32**, 174–181.

Capurro, H., Konichezky, S., Fonseca, D. & Caldeyro-Barcia, R. (1978) A simplified method for diagnosis of gestational age in the newborn infant. *Journal of Pediatrics* **93**, 120–122.

Costa Mda, C. (2006) Low birth weight and periodontal disease association. *Revista de Saude Publica* **40**, 353.

Cruz, S. S., Costa Mda, C., Gomes Filho, I. S., Vianna, M. I. & Santos, C. T. (2005) Maternal periodontal disease as a factor associated with low birth weight. *Revista de Saude Publica* **39**, 782–787.

Dasanayake, A. P. (1998) Poor periodontal health of the pregnant woman as a risk factor for low birth weight. *Annals of Periodontology* **3**, 206–212.

Dasanayake, A. P., Boyd, D., Madianos, P. N., Offenbacher, S. & Hills, E. (2001) The association between *Porphyromonas gingivalis*-specific maternal serum IgG and low birth weight. *Journal of Periodontology* **72**, 1491–1497.

Davenport, E. S., Williams, C. E., Sterne, J. A., Murad, S., Sivapathasundram, V. & Curtis, M. A. (2002) Maternal periodontal disease and preterm low birthweight: case–control study. *Journal of Dental Research* **81**, 313–318.

Davenport, E. S., Williams, C. E., Sterne, J. A., Sivapathasundram, V., Fearne, J. M. & Curtis, M. A. (1998) The East London Study of maternal chronic periodontal disease and preterm low birth weight infants: study design and prevalence data. *Annals of Periodontology* **3**, 213–221.

Greenland, S. & Morgenstern, H. (2001) Confounding in health research. *Annual Review of Public Health* **22**, 189–212.

Horta, B. L., Victora, C. G., Menezes, A. M., Halpern, R. & Barros, F. C. (1997) Low birthweight, preterm births and intrauterine growth retardation in relation to maternal smoking. *Paediatrics and Perinatal Epidemiology* **11**, 140–151.

Jaffee, K. D. & Perloff, J. D. (2003) An ecological analysis of racial differences in low birthweight: implications for maternal and child health social work. *Health & Social Work* **28**, 9–22.

Jeffcoat, M. K., Hauth, J. C., Geurs, N. C., Reddy, M. S., Cliver, S. P., Hodgkins, P. M. & Goldenberg, R. L. (2003) Periodontal disease and preterm birth: results of a pilot intervention study. *Journal of Periodontology* **74**, 1214–1218.

Khan, N. & Jamal, M. (2003) Maternal risk factors associated with low birth weight. *Journal of the College of Physicians and Surgeons of Pakistan* **13**, 25–28.

Lopez, N. J., Smith, P. C. & Gutierrez, J. (2002a) Higher risk of preterm birth and low birth weight in women with periodontal disease. *Journal of Dental Research* **81**, 58–63.

Lopez, N. J., Smith, P. C. & Gutierrez, J. (2002b) Periodontal therapy may reduce the risk of preterm low birth weight in women with periodontal disease: a randomized controlled trial. *Journal of Periodontology* **73**, 911–924.

Lunardelli, A. & Peres, M. (2005) Is there an association between periodontal disease, prematurity and low birth weight? A population-based study. *Journal of Clinical Periodontology* **32**, 938–946.

Lunardelli, A. N. & Peres, M. A. (2006) Is there an association between periodontal disease, prematurity and low birth weight? A population-based study. *British Dental Journal* **200**, 325.

McCormick, M. C. (1985) The contribution of low birth weight to infant mortality and childhood morbidity. *New England Journal of Medicine* **312**, 82–90.

Mitchell-Lewis, D., Engebretson, S. P., Chen, J., Lamster, I. B. & Papapanou, P. N. (2001) Periodontal infections and pre-term birth: early findings from a cohort of young minority women in New York. *European Journal of Oral Science* **109**, 34–39.

Mohsin, M., Wong, F., Bauman, A. & Bai, J. (2003) Maternal and neonatal factors influencing premature birth and low birth weight in Australia. *Journal of Biosocial Science* **35**, 161–174.

Moliterno, L. F., Monteiro, B., Figueredo, C. M. & Fischer, R. G. (2005) Association between periodontitis and low birth weight: a case–control study. *Journal of Clinical Periodontology* **32**, 886–890.

Monteiro, C. A., Benicio, M. H. & Ortiz, L. P. (2000) Secular trends in birth weight in the city of Sao Paulo, Brazil (1976–1998). *Revista de Saude Publica* **34**, 26–40.

Moreu, G., Tellez, L. & Gonzalez-Jaranay, M. (2005) Relationship between maternal periodontal disease and low-birth-weight pre-term infants. *Journal of Clinical Periodontology* **32**, 622–627.

Noack, B., Klingenberg, J., Weigelt, J. & Hoffmann, T. (2005) Periodontal status and preterm low birth weight: a case control study. *Journal of Periodontal Research* **40**, 339–345.

Nolte, E., Koupilova, I. & McKee, M. (2002) The increase in very-low-birthweight infants sin Germany: artefact or reality? *Paediatrics and Perinatal Epidemiology* **16**, 131–140.

Offenbacher, S., Katz, V., Fertik, G., Collins, J., Boyd, D., Maynor, G., McKaig, R. & Beck, J. (1996) Periodontal infection as a possible risk factor for preterm low birth weight. *Journal of Periodontology* **67**, 1103–1113.

Ohmi, H., Hirooka, K., Hata, A. & Mochizuki, Y. (2001) Recent trend of increase in proportion of low birthweight infants in Japan. *International Journal of Epidemiology* **30**, 1269–1271.

Pitiphat, W. & Merchant, A. (2002) The association between maternal periodontitis and adverse pregnancy outcomes among poor Chilean women. *Journal of Dental Research* **81**, 516–517; author reply 517.

Rodrigues, L. & Kirkwood, B. R. (1990) Case-control designs in the study of common diseases: updates on the demise of the rare disease assumption and the choice of sampling scheme for controls. *International Journal of Epidemiology* **19**, 205–213.

Santos, I. S., Victora, C. G., Huttly, S. & Carvalhal, J. B. (1998) Caffeine intake and low birth weight: a population-based case-control study. *American Journal of Epidemiology* **147**, 620–627.

Vettore, M. V., Sheiham, A. & Peres, M. A. (2006) Low birth weight and periodontal diseases association. *Revista de Saude Publica* **40**, 184–185, 181–182; author reply 185–186, 182–183.

Victora, C. G., Grassi, P. R. & Schmidt, A. M. (1994) Health status of children in an area of southern Brazil, 1980–1992: temporal trends and spatial distribution. *Revista de Saude Publica* **28**, 423–432.

Victora, C. G., Huttly, S. R., Fuchs, S. C. & Olinto, M. T. (1997) The role of conceptual frameworks in epidemiological analysis: a hierarchical approach. *International Journal of Epidemiology* **26**, 224–227.

Zaw, W., Gagnon, R. & da Silva, O. (2003) The risks of adverse neonatal outcome among preterm small for gestational age infants according to neonatal versus fetal growth standards. *Pediatrics* **111**, 1273–1277.

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Clinical Relevance

Scientific rationale for study: The role of periodontitis in the occurrence of LBW episodes and other negative perinatal outcomes has been broadly discussed since 1996 but methodologically sound observational studies had difficulty detecting the association of maternal periodontal disease and LBW.

Principal findings: Our findings support the hypothesis of a weak or non-existing association between these events, especially because after proper adjustment for important risk factors for LBW, no association of perinatal outcomes and periodontal disease could be detected in the present study.

Practical implications: Clinicians should be aware of several important health and behavioural characteristics of the patients that contribute significantly to LBW and that can be associated with periodontal disease. The association of this infection, especially severe stages, with perinatal outcomes should be further studied.

Appendix. Distribution of variables among cases and controls, adjusted odds ratios for the effects of periodontitis and severity of periodontitis during pregnancy on low birth weight and pre-term low birth weight, Porto Alegre, Brazil

Level	Variable	Cases ($n = 306$)		Controls ($n = 611$)		LBW		PTLBW	
		n	(%)	*n*	(%)	adjusted odds ratio	*p*-value*	adjusted odds ratio	*p*-value†
Level 1	Skin color								
	White	233	(76.1)	461	(75.4)	1.00	0.41[A]	1.00	0.48[A]
	Not-white	73	(23.9)	150	(24.6)	0.84 (0.56, 1.27)		0.83 (0.49, 1.40)	
	Social class								
	A and B	25	(10.7)	50	(10)	1.00	0.27[A]	1.00	0.64[A]
	C	99	(42.3)	239	(47.7)	0.94 (0.50, 1.79)		1.01 (0.48, 2.16)	
	D	110	(47.0)	212	(42.3)	1.19 (0.61, 2.34)		1.14 (0.50, 2.59)	
	Education								
	None	3	(1.0)	4	(0.6)	1.00	0.68[A]	1.00	0.57[A]
	Primary	189	(61.8)	390	(63.8)	0.34 (0.05, 2.09)		0.66 (0.03, 11.33)	
	Secondary	102	(33.3)	191	(31.3)	0.39 (0.06, 2.43)		0.71 (0.04, 12.23)	
	Tertiary	12	(3.9)	26	(4.3)	0.35 (0.05, 2.53)		0.89 (0.04, 17.88)	
Level 2	Age group (years)								
	<15	12	(4.0)	25	(4.1)	1.00	0.03[B3]	1.00	0.04[B4]
	16–19	67	(22.2)	109	(17.9)	1.28 (0.55, 2.98)		1.86 (0.57, 6.00)	
	20–24	88	(29.1)	160	(26.3)	1.27 (0.54, 2.96)		1.63 (0.49, 5.46)	
	25–29	50	(16.6)	144	(23.7)	0.96 (0.39, 2.37)		1.55 (0.44, 5.45)	
	30–34	29	(9.6)	98	(16.1)	1.01 (0.39, 2.68)		1.57 (0.41, 5.96)	
	>35	56	(18.5)	72	(11.8)	3.17 (1.24, 8.12)		4.49 (1.19, 16.90)	
	Previous pregnancies								
	None	143	(46.7)	240	(39.2)	1.00	<0.01[B3]	1.00	0.01[B4]
	One	81	(26.5)	158	(25.9)	0.68 (0.45, 1.03)		0.71 (0.41, 1.21)	
	Two	42	(13.7)	92	(15.1)	0.54 (0.32, 0.91)		0.49 (0.25, 0.97)	
	Three or more	40	(13.1)	121	(19.8)	0.33 (0.19, 0.59)		0.45 (0.22, 0.90)	
	Pre-natal care								
	Yes	284	(93.4)	583	(95.4)	1.00	0.72[B2]	1.00	0.64[B1]
	No	20	(6.6)	28	(4.6)	0.45 (0.07, 3.01)		0.40 (0.05, 2.98)	
	Adequate pre-natal care‡								
	Yes	211	(74.8)	494	(85.6)	0.43 (0.28, 0.66)		0.29 (0.17, 0.52)	
	No	71	(25.2)	83	(14.4)	1.00	<0.01[B3]	1.00	<0.01[B4]
	Smoking								
	Non smoker	182	(59.5)	373	(61.1)	1.00	0.11[B3]	1.00	0.58[B2]
	Former smoker	43	(14.1)	126	(20.6)	0.60 (0.38, 0.94)		0.54 (0.30, 0.96)	

Appendix. (Contd.)

Level	Variable	Cases ($n = 306$)		Controls ($n = 611$)		LBW		PTLBW	
		n	(%)	*n*	(%)	adjusted odds ratio	*p*-value*	adjusted odds ratio	*p*-value†
	Smoker	81	(26.4)	112	(18.3)	1.49 (1.01, 2.21)		0.95 (0.56, 1.61)	
	Alcohol consumption during pregnancy								
	Yes	20	(6.5)	44	(7.2)	0.83 (0.41, 1.70)		0.68 (0.25, 1.81)	
	No	286	(93.5)	567	(92.8)	1.00	0.87[B1]	1.00	0.46[B3]
Level 3	Previous LBW								
	Yes	60	(19.7)	66	(10.8)	2.81 (1.59, 4.96)		0.94 (0.34, 2.59)	
	No	244	(80.3)	543	(9.2)	1.00	<0.01[C3]	1.00	0.71[C1]
	Previous premature birth								
	Yes	53	(17.4)	54	(8.8)	1.70 (0.83, 3.48)		5.63 (2.42, 13.08)	
	No	251	(82.6)	556	(91.2)	1.00	0.14[C2]	1.00	<0.001[C3]
	Gestational hypertension								
	Yes	92	(31.1)	111	(18.4)	1.54 (0.89, 2.67)		1.61 (0.69, 3.79)	
	No	204	(68.9)	491	(81.6)	1.00	0.15[C3]	1.00	0.31[C2]
	Pre-eclampsia								
	Yes	63	(20.6)	48	(7.9)	2.86 (1.45, 5.61)		5.87 (2.76, 12.47)	
	No	243	(79.4)	563	(92.1)	1.00	<0.01[C3]	1.00	<0.01[C3]
	Weight change during pregnancy								
	Loss or < 5Kg gain	27	(10.2)	37	(6.8)	1.50 (0.75, 2.96)		1.89 (0.76, 4.74)	
	5–15 Kg gain	190	(72.0)	327	(60.6)	1.00	<0.01[C3]	1.00	<0.01[C3]
	> 16 Kg gain	47	(17.8)	176	(32.6)	0.49 (0.31, 0.77)		0.35 (0.18, 0.67)	
	Other infections during pregnancy								
	None	165	(58.5)	352	(60.1)	1.00	0.49[C1]	1.00	0.13[C3]
	One	88	(31.2)	173	(29.5)	1.19 (0.76, 1.85)		0.95 (0.53, 1.74)	
	Two or more	29	(10.3)	61	(10.4)	1.19 (0.66, 2.17)		2.19 (0.95, 5.05)	
Level 4	Urinary infection								
	Yes	79	(26.7)	165	(27.4)	0.96 (0.62, 1.46)		1.06 (0.57, 1.96)	
	No	217	(73.3)	438	(72.6)	1.00	0.66[D]	1.00	0.85[D1]
	Vaginosis (tricomonas)								
	Yes	69	(23.4)	124	(20.7)	1.12 (0.72, 1.75)		1.29 (0.69, 2.44)	
	No	226	(76.6)	475	(79.3)	1.00	0.54[D]	1.00	0.41[D2]
	HIV infection								
	Yes	4	(1.4)	10	(1.7)	0.90 (0.19, 4.18)		0.04 (0.00, 0.89)	
	No	285	(98.6)	592	(98.3)	1.00	0.80[D]	1.00	0.04[D3]
	Positive VDRL								
	Yes	3	(1.0)	7	(1.00)2	3.48 (0.63, 19.19)		11.49 (1.31, 100.84)	
	No	285	(99.0)	587	(98.8)	1.00	0.14[D]	1.00	0.02[D3]
	Periodontitis§								
	Yes	180	(58.8)	333	(54.5)	0.93 (0.63, 1.41)		0.92 (0.54, 1.57)	
	No	126	(41.2)	278	(45.5)	1.00	0.97[E]	1.00	0.77[E]
	Periodontitis§								
	Absent	126	(41.4)	278	(45.7)	1.00	0.76[E]	1.00	0.49[E]
	Mild	86	(28.0)	184	(29.8)	0.98 (0.60, 1.56)		0.89 (0.48, 1.64)	
	Moderate	70	(23.0)	122	(19.8)	0.77 (0.46, 1.32)		0.87 (0.41, 1.57)	
	Severe	23	(7.6)	30	(4.7)	1.94 (0.80, 4.71)		1.87 (0.64, 5.45)	
	Sex of the newborn								
	Male	138	(45.1)	328	(53.7)	1.00	0.13	1.00	0.09
	Female	168	(54.9)	283	(46.3)	1.40 (0.94, 2.07)		1.57 (0.93, 2.64)	

Owing to missing data, the sums may not reach the sample size.

*p-value according to the χ^2 test for heterogeneity between models.

†Adjusted p-value according to the likelihood ratios test for heterogeneity between models.

‡Adequate pre-natal care: more than three visits starting before the fifth month.

§Analysed separately in the model.

[A]Adjusted for variables in the same conceptual level. [B1]Adjusted for variables in the same conceptual level. [B2]Adjusted for variables in the same conceptual level except alcohol consumption during pregnancy. [B3]Adjusted for variables in the same conceptual level except alcohol consumption during pregnancy and pre-natal care (yes/no). [C1]Adjusted for the upper level [B3]variables and variables from the same level. [C2]Adjusted for the upper level [B3]variables and variables from the same level except other infections during pregnancy. [D]Adjusted for [B3]variables, [C3]variables and variables from the same conceptual level. [E]Adjusted for [B3]variables, [C3]variables and sex of the newborn.