J Clin Periodontol 2005; 32: 886–890 doi: 10.1111/j.1600-051X.2005.00781.x

Journal of Clinical Periodontology

Association between periodontitis and low birth weight: a case–control study

Luiz Flávio Martins Moliterno[1], Bruno Monteiro[1], Carlos Marcelo da Silva Figueredo[2] and Ricardo Guimarães Fischer[2]

Departments of [1]Pedodontics and [2]Periodontology, Rio de Janeiro State University, Rio de Janeiro, Brazil

Moliterno LFM, Monteiro B, da Silva Figueredo CM, Fischer RG. Association between periodontitis and low birth weight: a case–control study. J Clin Peridontol 2005; 32: 886–890. doi: 10.1111/j.1600–051X.2005.00781.x. © Blackwell Munksgaard, 2005.

Abstract

Objective: To verify a possible association between periodontitis and low-birth-weight babies.

Material and Methods: One hundred and fifty-one mothers were examined. The case group included 76 mothers (mean age 25.6 years), whose babies at birth weighed <2500 g and had a gestational age (GA) <37 weeks, while 75 mothers (mean age 24.4 years), whose babies were born with a weight of >2500 g and with a GA >37 weeks, were the control group. Data from the mothers and the babies were collected from the Hospital registration records and during an interview with the mother. The periodontal examination included measurements of probing pocket depth (PPD) and clinical attachment loss (CAL) in six sites from all existing teeth, except for third molars. Mothers with periodontitis had at least four sites with PPD $\geqslant 4$ and CAL $\geqslant 3$ mm, while healthy mothers had PPD $\leqslant 3$ mm and CAL $\leqslant 1$ mm.

Results: The median number of sites with PPD $\geqslant 4$ and CAL $\geqslant 3$ mm was eight in the case group, and four in the control group. The significant associations with low birth weight (LBW) babies were periodontitis (odds ratio (OR) = 3.48, 95% confidence interval (CI): 1.17; 10.36), arterial hypertension (OR = 9.65, 95% CI: 2.22; 41.91), haemorrhage during pregnancy (OR = 10.88, 95% CI: 1.95; 60.53), number of prenatal examinations (OR = 0.10, 95% CI: 0.02; 0.43) and genitourinary infection (OR = 3.21, 95% CI: 1.25; 8.20).

Conclusion: Periodontitis was considered a risk indicator for LBW in this sample, similar to other risk factors already recognized by obstetricians.

Key words: low birth weight; periodontal medicine; periodontitis; risk indicator

Accepted for publication 19 March 2005

The weight of the fetus at birth is the most important variable as far as the survival, growth and healthy development of a child is concerned. According to the World Health Organization, LBW is defined as being less than 2500 g and is considered to be a public health problem because of the consequent higher infancy sickness and neonatal mortality rates. A birth is considered premature if the fetus is born after a gestation period of under 37 weeks. In cases of premature birth, the baby's vital organs are immature and incapable of readily adapting to the start of life outside the uterus. As far as LBW, premature babies are concerned, risk factors which are known to medicine include tobacco consumption (Peacock et al. 1995, Jarvis et al. 2000), alcoholism (Peacock et al. 1995), use of illegal drugs (Rotta & Cunha 2000), genitourinary infections (Heyborne et al. 1992), arterial hypertension (Crombleholme 2000), haemorrhage during pregnancy, gestational diabetes and the lack of prenatal care among others (Rezende & Montenegro 1999). Nowadays, the number of days spent in hospital and the costs of intensive neonatal therapy units are high. This cost to society goes beyond the financial cost because it permeates the psycho-emotional situation of the families involved. There is also the possibility of future abnormalities during infancy. In developed countries, there has been a drop in the mortality rate resulting from LBW premature births. However, the number of premature births has not fallen (Challis 2001). It is estimated that 50% of LBW premature births are idiopathic (Haram et al. 2003). This fact in itself justifies the need for further studies to identify the causes and risk factors that lead to this type of obstetric complication.

Obstetricians recognize that intrauterine infections act as a risk factor for prematurity and LBW. In this case, bacterial lipopolysaccharides (LPS) and inflammatory chemical intermediates

(PGE2, TNF-α and IL-1β) can speed up the physiological process of normal birth. Periodontal infections have much in common with genitourinary infections. In both these situations, the infection may be caused by Gram-negative micro-organisms which release LPS. The patient's defense system reacts to these antigens in a way that the blood levels of inflammatory cytokines such as PGE2, IL-1 β and TNF-α increase significantly (Ebersole & Cappelli 2000). High concentrations of these cytokines, in pregnant women, are responsible for the rupture of the uterine membranes causing premature birth and growth retardation (Romero et al. 1998).

Studies carried out with hamsters (Collins et al. 1994a, b) and with humans (Offenbacher et al. 1986, 1996, 1998a, b, Damaré et al. 1997, Dasanayake 1998, Mitchell-Lewis et al. 2001, Lopez et al. 2002, Radnai et al. 2004) showed evidence of an association between periodontitis and LBW, premature births in countries such as Chile and United States. However, studies carried out in England (Davenport et al. 2002, Moore et al. 2004) and Iceland (Holbrook et al. 2004) did not show such an association. Thus, the aim of this study was to verify if periodontitis was associated with LBW births, in a sample of the Brazilian population.

Materials and Methods

Patients

This case–control study involved 151 mothers consecutively examined who gave birth to naturally delivered babies. The case group consisted of 76 mothers (mean age = 25.6 years; SD = 7.3 years) who had given birth to babies of gestational age (GA) <37 weeks and weight <2500 g. The control group included 75 mothers (mean age = 24.4 years; SD = 5.8 years) who had given birth to babies of GA >37 weeks and weight >2500 g. Mothers of twins, those who were under 15 years old and HIV seropositive, were excluded from the sample. The mothers did not receive any systemic antibiotics during pregnancy. Some characteristics of the mothers such as race, educational level, occupation and marital status were registered. For the babies, data concerning the date of birth, type of birth, sex, weight at birth, GA and size classification (small for GA (SGA), adequate for (AGA) and large for GA (LGA)) were registered. This study was approved by the research ethics committees of the Rio de Janeiro State University and the Carmela Dutra Maternity Hospital. The participants signed a highly explicative authorization document of their own free will. The study was carried out over a period of 14 months at the Carmela Dutra Maternity Hospital, which is part of the public health service network in the city of Rio de Janeiro, Brazil. In this period, there were 6788 live births – an average of 484 births/month or 16 births/day. Of this total, 541 babies (7.97%) were LBW and premature.

Examiner

The same examiner collected the data of all the mothers and babies, using a structured interview and medical registers. Data concerning the periodontal status of the mothers, such as the probing pocket depth (PPD) and clinical attachment loss (CAL), were measured using a PCP 11.5B periodontal probe (Hu-Friedy, Chicago, IL, USA) and were carried out up to 3 days after giving birth. These examinations were carried out in six sites on every tooth in the mother's mouth excluding the third molars. A patient was considered to have periodontitis if there were at least four sites with PPD $\geqslant 4$ mm and CAL $\geqslant 3$ mm. Healthy mothers should have PPD $\leqslant 3$ mm and CAL $\leqslant 1$ mm.

Statistical analysis

SPSS 11.0 software was used to apply χ^2, Fisher, Mann–Whitney and multiple logistic regression tests to the data. The risk factors included into the analyses were smoking (yes or no), alcohol drinking problems (yes or no), educational level, diabetes mellitus (yes or no), genitourinary infection during pregnancy, including bacterial vaginosis (yes or no), haemorrhage during pregnancy (yes or no), arterial hypertension (yes or no), race (white and non-white), marital status (married and not married). In the first statistical analysis, a 2×2 table was set up for each independent variable in order to find out if there was any statistical association between periodontitis and LBW births. A p-value of 0.05 was decided on. In the second analysis, multiple logistic regression analysis was used to measure the effect of periodontitis on LBW, controlling the effects of the above-mentioned risk factors.

Results

The median number and percentage of sites with PPD $\geqslant 4$ and CAL $\geqslant 3$ mm was 8% and 5.6%, respectively, in the case group. The corresponding numbers for the control group were 4% and 2.5%, respectively (Table 1). There was no statistically significant difference in the frequency of smokers and diabetics in the case and control groups; however, there was a significant higher number of mothers with alcohol drinking problems in the case group (Table 1). The mean number of teeth examined in the case and control groups was 25.2 ($\pm$ 3.9) and 25.4 ($\pm$ 3.9), respectively.

The mean weight at birth was 1924 ($\pm$ 417) g in the case group and 3253 ($\pm$ 412) g in the control group. In the sample studied, 16 babies weighed under 1500 g and one of these weighed only 980 g. The mean GA in the case group was 33.5 ($\pm$ 2.1) weeks and 39.1 ($\pm$ 1.3) weeks in the control group. In the case group, 76.3% of the babies were born with a GA of between 33 and 36 weeks, 17.1% with GA between 29 and 32 weeks and 6.6% with GA below 28 weeks. That is, the majority of the babies were born near to the minimum of 37 weeks. There was a significantly higher frequency of babies considered SGA in the case group. All the babies from the control group were an AGA at birth (Table 2).

The adjusted odds ratio (OR) for the presence of periodontitis was 3.48, similar to the adjusted OR for the presence of genitourinary infection (3.21). Other significant associations were arterial hypertension, haemorrhage during pregnancy and the number of pre-natal examinations. Race, smoking, alcohol drinking problems, diabetes and educational level were not significant risk indicators for this sample (Table 3).

Discussion

The results of the present study showed that the adjusted OR for the association between periodontitis and LBW was 3.48. This association was originally suggested by Offenbacher et al. (1996) and confirmed in further studies carried out in the United States (Offenbacher et al. 1998a, b), Chile (Lopez et al. 2002), Thailand (Dasanayake 1998) and Hungary (Radnai et al. 2004), with ORs varying between 3.5 and 7.9. On the other hand, Davenport et al. (2002) and Moore et al. (2004), in studies

Table 1. Frequency of smokers, diabetics and patients with alcohol drinking problems, and median (minimum and maximum) number and percentage of sites with probing pocket depth (PPD) $\geqslant$ 4mm and clinical attachment loss (CAL) $\geqslant$ 3 mm in the case and control groups

	Case group ($n = 76$)	Control group ($n = 75$)
Smokers	21%	19%
Diabetics	3.9%	1.3%
Alcohol	10.5%	1.3%
Number of sites with PPD $\geqslant$ 4mm and CAL $\geqslant$ 3mm	8 (0–98)	4 (0–113)
Percentage of sites with PPD $\geqslant$ 4mm and CAL $\geqslant$ 3mm	5.8 (0–60.5)	2.5 (0–67.2)

Table 2. Mean and standard deviation (SD) of birth weight (g) and number of gestational weeks, in the case and control groups

	Case group ($n = 76$)	Control group ($n = 75$)
Birth weight	1924 ($\pm$ 417)*	3253 ($\pm$ 412)
Gestational weeks	33.5 ($\pm$ 2.1)*	39.1 ($\pm$ 1.3)

*$p < 0.05$.

Table 3. Multiple logistic regression analysis of the factors associated with low birth weight

Associated factors	OR	95% CI	Adjusted OR	95% CI
Periodontitis	2.17	1.03; 4.53	3.48*	1.17; 10.36
Genitourinary infection	2.77	1.43; 5.36	3.21*	1.25; 8.20
Race	1.41	0.74; 2.68	1.42	0.57; 3.58
Pre-natal location	0.39	0.07; 2.07	4.41	0.22; 89.08
Arterial hypertension	4.37	1.53; 12.52	9.65*	2.22; 41.91
Hemorrhage during pregnancy	4.06	1.09; 15.20	10.88*	1.95; 60.53
Alcohol drinking problems	8.71	1.06; 71.43	116.33	0.000; 8.20
Number of pre-natal exams	0.15	0.05; 0.41	0.10*	0.02; 0.43
Diabetes	3.04	0.31; 29.92	1.34	0.07; 24.32
Education level	0.49	0.21; 1.13	1.85	0.72; 4.79
Smoking	1.16	0.52; 2.59	0.95	0.30; 3.03

*Statistically significant.
OR, odds ratio; CI, confidence interval.

carried out in England, and Holbrook et al. (2004), in Iceland, did not show that periodontitis was a risk factor for LBW, premature babies. The difference in these results may be explained by different definitions of periodontitis. Offenbacher et al. (1996, 1998a) stated that periodontitis corresponded to an average attachment loss of >3 or 4 mm. Lopez et al. (2002), similar to our study, examined six sites in all the teeth that were present in the dental arch and considered those mothers who had at least four sites with PPD $\geqslant$ 4 mm and PAL $\geqslant$ 3 mm to be suffering from periodontitis. Dasanayake et al. (1998) and Davenport et al. (2002) used the Community Periodontal Index of Treatment Needs (CPITN) to diagnose periodontitis. Although, according to Papapanou (1996), the CPITN is not a satisfactory method for evaluating the prevalence of periodontitis, since it can underestimate the true values, it must be remembered that Davenport et al. (2002) analysed a large sample. A prospective study with also a large sample, performed in London (Moore et al. 2004), examined two sites of all teeth present. The authors made correlations between pre-term birth and LBW with different combinations of probing depth and/or loss of attachment cut-off points, and did not find association between periodontal disease and pre-term birth and LBW. In the present study, six sites in all the teeth in the mouth were analysed, which enabled us to have a clearer idea of the prevalence of periodontitis in the sample. The population analysed was very homogeneous, their ages were similar, the women were from a low socio-economic background and were treated by a hospital that is part of the public health service of the city of Rio de Janeiro. Analysis of the periodontal disease in the mothers in the case group and the control group showed these patients had localized, chronic periodontitis. In spite of this similarity in the sample, there was a significantly greater number of mothers who had periodontitis in the case group. Another possible explanation why Davenport et al. (2002), Moore et al. (2004) and Holbrook et al. (2004) did not find periodontitis to be a risk factor for the birth of LBW, premature babies might be that different populations may be subject to different risk factors/indicators for the development of a specific pathology.

In our study, genitourinary infection was a risk indicator similar to that observed for periodontitis. Genitourinary infection is a widely accepted risk for prematurity and LBW (Gomez et al. 1997). In genital and/or urinary infections, LPS stimulate inflammation in women, where the levels of PGE2 and TNF-α increase at an inappropriate moment during pregnancy, causing uterine contractions and premature rupture of the membranes. The physiopathological mechanism by which periodontitis may increase the risk of prematurity and LBW could be similar. LPS from oral microorganisms have a retarding effect on fetal growth rate in hamsters, as a consequence of the increased levels of PGE2 and TNF-α (Collins et al. 1994b). In humans, Offenbach et al. (1996) observed that the progress of periodontal destruction was associated with an increase in the PGE2 levels in the gingival fluid. The levels of PGE2 in the gingival fluid was significantly associated with the levels of PGE2 in the amniotic fluid, which suggests that the PGE2 levels in the gingival fluid could give an indirect estimate of the levels of PGE2 in the amniotic fluid (Damaré et al. 1997).

There are various risk factors that are related to LBW, premature babies. These include: (1) fetal factors (multiple gestation, erythroblastosis, non-immune hydrops), (2) uterine factors (bicornuate uterus, premature dilation), (3) placental factors (low-lying placenta and premature detachment of the placenta) and (4) maternal factors (pre-eclampsia, heart disease, genitourinary infections, use of drugs) (Cunningham et al. 1997). In the population analysed, the greatest risk indicators were related to the maternal factors; these were the number of pre-natal examinations, haemorrhage during pregnancy and arterial hypertension. Smoking was not found to be associated with LBW babies in this population. Lopez et al. (2002) also did not show the habit of smoking tobacco to be a risk factor. On the other hand, Davenport et al. (2002) observed that the OR for smokers

was 2.15. These differences may indicate that different populations are subject to different risk factors/indicators associated with specific pathologies.

The majority of babies in the case group (90%) and the control group (100%) had an AGA at birth. However, there were eight babies in the case group SGA. There are certain conditions that have a negative effect on the fetus, making it SGA, such as tobacco smoking, or LGA, such as diabetes mellitus (Ounsted et al. 1985). In our sample, smoking was not found to be a significant risk factor and only four mothers were diabetic, three in the case group and one in the control group. Seventy-four percent of the babies in the case group were born with a GA of between 33 and 36 weeks. In this case, in spite of the babies in the case group being born prematurely, the number of weeks that they were premature was small. The average weight of the babies in the case group was 1924 ($\pm$ 420) g, whereas the corresponding weight of the babies in the control group was 3261 ($\pm$ 410) g. According to Rezende & Montenegro (1999), children born atraumatically, with a weight of up to 1000 g, have a 90% survival rate. In the sample studied, 16 babies weighed under 1500 g and one of these weighed only 980 g. This study did not propose to study the survival of these low weight children over time. That would have been interesting, because the survival rate of these children could have been evaluated, as well as the corresponding financial costs, including the number of days for which they were interned in a neonatal unit, the medicine prescribed and the necessary medical steps taken for the complete recovery of these children.

In conclusion, there was an association between the existence of periodontitis and low-weight births along with other cofactors such as number of pre-natal examinations, maternal arterial hypertension, genitourinary infection and the presence of haemorrhage during pregnancy.

References

Challis, J. R. (2001) Understanding preterm birth. *Clinical Investigations in Medicine* **24**, 60–67.

Collins, J. G., Smith, M. A., Arnold, R. R. & Offenbacher, S. (1994a) Effects of *Escherichia coli* and *Porphyromonas gingivalis* lipopolysaccharide on pregnancy outcome in golden hamster. *Infection and Immunity* **62**, 4652–4655.

Collins, J. G., Windley, H. W., Arnold, R. R. & Offenbacher, S. (1994b) Effects of *Porphyromonas gingivalis* infection on inflammatory mediator response and pregnancy outcome in hamsters. *Infection and Immunity* **62**, 4356–4361.

Crombleholme, W. R. (2000) Obstetrics. In: Tierney Jr., LM Jr., Mc Phee, SJ & Papadakis, MA (eds). *Current Medical Diagnosis and Treatment*, 39th edition, pp. 758–782. New York: McGraw-Hill.

Cunningham, F. G., Mac Donald, P. C., Gant, N. F., Leveno, K. J., Gilstrap III, L. C. Hankins, G. D. V. & Clark, S. L. (1997) Pre term birth. In: Cunningham, F. G., Mac Donald, P. C., Gant, N. F., Leveno, K. J., Clark, S. L. & Hankins, G. D. V. (eds). *Williams Obstetrics*, 20th edition, pp. 797–826. Stanford: Appleton & Lange.

Damaré, S. M., Wells, S. & Offenbacher, S. (1997) Eicosanoids in periodontal diseases: potential for systemic involvement. In: Sinzinger, H., Vane, J. R., Samuelsson, B., Paoletti, R., Ramwell, P. W. & Wong, P. Y. -K. (eds) *Recent Advances in Prostaglandin, Thromboxane, and Leukotriene Research*, pp. 23–35. New York: Plenum Publishing Corp.

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.

Davenport, E. S., Williams, C. E. C. S, Sterne, J. A. C., 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.

Ebersole, J. L. & Cappelli, D. (2000) Acute-phase reactants in infections and inflammatory disease. *Periodontology 2000* **23**, 19–49.

Gomez, R., Romero, R., Edwin, S. S. & David, C. (1997) Pathogenesis of preterm labor and preterm premature rupture of membranes associated with intraamniotic infection. *Infection Disease Clinics of North America* **11**, 135–175.

Haram, K., Mortensen, J. H. S. & Wollen, A-L. (2003) Preterm delivery: an overview. *Acta Obstetricia et Gynecologica Scandinavia* **82**, 687–704.

Heyborne, K. D., Witkin, S. S. & McGregor, J. A. (1992) Tumor necrosis factor-α in midtrimester amniotic fluid is associated with impaired intrauterine fetal growth. *American Journal of Obstetrics and Gynecololy* **167**, 920–925.

Holbrook, W. P., Oskarsdottir, A., Fridjonsson, T., Einarsson, H., Hauksson, A. & Geirsson, R. T. (2004) No link between low-grade periodontal disease and preterm birth: a pilot study in a healthy Caucasian population. *Acta Odontologica Scandinavia* **62**, 177–179.

Jarvis, M. J., Goddard, E., Higgins, V., Feyerabend, C., Bryant, A. & Cook, D. G. (2000) Children's expose to passive smoking in England since the 1980s: cotinine evidence from population survey. *British Medical Journal* **321**, 343–345.

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

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

Moore, S., Ide, M., Coward, P. Y., Randhawa, M., Borkowska, E., Baylis, R. & Wilson, R. F. (2004) A prospective study to investigate the relationship between periodontal disease and adverse pregnancy outcome. *British Dental Journal* **197**, 251–258.

Offenbacher, S., Beck, J. D., Lieff, S. & Slade, G. (1998a) Role of periodontitis in systemic health: spontaneous preterm birth. *Journal of Dental Education* **62**, 852–858.

Offenbacher, S., Jared, H. L., O'Reilly, P. G., Wells, S. R., Salvi, G. E. Lawrence, H. P., Socransky, S. S. & Beck, J. (1998b) Potential pathogenic mechanisms of periodontitis associated pregnancy complications. *Annals of Periodontology* **3**, 233–250.

Offenbacher, S., Kats, 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** (Suppl.), 1103–1113.

Offenbacher, S., Odle, B. M. & Van Dyke, T. E. (1986) The use of crevicular fluid prostaglandin E2 levels as a predictor of periodontal attachment loss. *Journal of Periodontal Research* **21**, 101–112.

Ounsted, M., Moar, V. A. & Scott, A. (1985) Risk factors associated with small-for-dates and large-for-dates infants. *British Journal of Obstetric and Gynecology* **92**, 226–232.

Papapanou, P. N. (1996) Periodontal diseases: epidemiology. *Annals of Periodontology* **1**, 1–36.

Peacock, J. L., Bland, J. M. & Anderson, H. R. (1995) Preterm delivery: effects of socioeconomic factors, psychological stress, smoking, alcohol, and caffeine. *British Medical Journal* **311**, 531–535.

Radnai, M., Gorzó, I., Nagy, E., Urbán, E., Norak, T. & Pál, A. (2004) A possible association between preterm birth and early periodontitis. Pilot Study. *Journal of Clinical Periodontology* **31**, 736–741.

Rezende, J & Montenegro, CAB. 1999 Prematurity. In: Rezende, J. & Montenegro, C. A. B. (eds) *Fundamental Obstetrics*, pp. 384–391. Rio de Janeiro: Guanabara Koogan.

Romero, R., Mazor, M., Wu, Y. K., Sirtori, M., Oyarzum, E. Mitchell, M. D. & Hobbins, J. C. (1998) Infection in the pathogenesis of preterm birth. *Seminars in Perinatology* **12**, 262.

Rotta, N. T. & Cunha, G. B. (2000) Pre natal exposure to cocaine: review of the neurobehaviourist effects (in Portuguese). *Journal of Pediatrics* **76**, 179–184.

Address:
Ricardo G. Fischer
Faculdade de Odontologia
Rio de Janeiro State University
Boulevard 28 de Setembro 157, 2°. Andar
Vila Isabel, Rio de Janeiro, RJ
Cep 20551-030
Brazil
E-mail: ricfischer@globo.com

Clinical Relevance

Periodontitis has been associated with increased risk for the premature and low birth weight (LBW) babies in many countries, such as United States, Chile, Hungary and Thailand. In England and Iceland, this association was not confirmed. Different criteria to diagnose periodontitis may explain these results. Our results showed that periodontitis was a significant risk indicator to LBW babies, as well as other traditional risk factors, such as arterial hypertension, haemorrhage during pregnancy, number of prenatal examinations and genitourinary infection. Studies in populations with different geographical and ethnical characteristics may extend the validity of the association between periodontitis and LBW babies.