Acta Odontologica Scandinavica. 2016; 74: 73–80

informa
healthcare

ORIGINAL ARTICLE

Effect of maternal periodontitis and low birth weight—A case control study

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Abstract

Introduction. Since the 1990s, evidence has been raised that there is an association between maternal periodontal disease and undesirable gestational events, for example low birth weight; this issue is controversial. ***Objective.*** To evaluate whether there is an association between maternal periodontitis and low birth weight (LBW). ***Methods.*** A case-control study was carried out on 951 mothers that had been cared for by the Brazilian Unified Health System in Petrolina-PE and Juazeiro-BA, Brazil. The case group (n = 269) consisted of mothers of newborns with birth weight <2500 g and a control group (n = 682) of mothers of newborns with birth weight ≥2500 g. An interview was realized, using a questionnaire as well as a full mouth examination to diagnose the periodontal condition. Women who had at least four teeth with probing depth ≥4 mm and clinical attachment loss ≥3 mm, with bleeding on probing at the same site, were diagnosed with periodontitis. The birth weight was obtained through the hospital book record. The main association was evaluated using the multivariate regression model, considering confounders. ***Results.*** The frequency of periodontitis was 16.4% (case group) and 17.4% (control group). Periodontitis did not show an association with LBW (OR_{crude} = 0.92; 95% CI = 0.63–1.35), even after adjustment for the following confounders: maternal age, pre-gestational body mass index, number of pre-natal consultations, number of pregnancies, maternal schooling level, smoking habit during pregnancy and hypertension ($OR_{adjusted}$ = 1.00; 95% CI = 0.61–1.68). ***Conclusion.*** The findings of this study showed no association between maternal periodontal disease and low birth weight, even after appropriate adjustments for confounding factors.

Key Words: *Epidemiology, low birth weight, periodontitis*

Introduction

Periodontal disease is an oral inflammation, caused by an infection that exhibits high prevalence and affects mainly individuals in developing countries. This disease, in its various clinical entities, is the second biggest oral health problem worldwide. It is estimated that gingivitis affects ~ 40–85% of the adult population around the world and periodontitis ~ 11% [1–4].

This oral infection is defined as a multifactorial disease, caused by pathogenic bacteria from dental biofilm that stimulates an exacerbated inflammatory response in the gingival tissue, bone, cementum and periodontal ligament. When the inflammation results in the destruction of tooth supporting tissues, this disease is called periodontitis and the absence of treatment can result in tooth loss, pain and discomfort [5]. Other factors influence the development of periodontal disease such as smoking habit, increased age, genetics, stress, diabetes, unfavorable socioeconomic conditions, poor oral hygiene, among others [2,3,5–7].

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(Received 28 January 2015; accepted 4 May 2015)

ISSN 0001-6357 print/ISSN 1502-3850 online © 2015 Informa Healthcare
DOI: 10.3109/00016357.2015.1049374

Recently, some studies have shown that localized infection in periodontal tissues may interfere in the development of certain systemic diseases, demonstrating an association with the onset of kidney disease, ischemic disease, diabetes, respiratory conditions and prematurity and low birth weight [3,5–7].

The World Health Organization (WHO) defines low birth weight as any live birth under 2500 g and has been recognized as an important determinant of infant mortality, accounting for 60–80% of deaths in the neonatal period. This condition leads to an increased risk of infections, propensity to growth retardation and neuropsychological deficits that may impact on the living conditions of the adult [8,9].

Low birth weight is associated with unfavorable socioeconomic conditions, inadequate nutrition, twinning, primiparity, smoking habit and alcohol consumption during pregnancy, extremes of age, low body mass index (BMI) before pregnancy and complications during pregnancy, including other factors which contribute to the decrease in infant birth weight [8,9]. Despite numerous studies on low weight live births, its determinants are not completely clear. About 20% of the causes that lead to intrauterine growth retardation are unknown in developing countries [9].

Periodontitis is associated with the colonization of the surfaces of the teeth and the gingival sulcus by gram negative anaerobic bacteria, forming a reservoir of micro-organisms, endotoxin and mediators of inflammation that, upon entering the bloodstream, could lead to a systemic chronic inflammatory state able to affect both gestational period and the weight of the newborn [10,11].

Offenbacher et al. [12] were the first to test the above-mentioned hypothesis in the mid-1990s. They observed a strong association between maternal periodontal disease and low birth weight, even after adjustment for confounders such as smoking and drinking during pregnancy, pre-natal care, age and history of bacteremia. Since then, other researchers have conducted studies on the theme, using observational [13–16] and interventional [17–21] methodologies which corroborated the findings of Offenbacher et al. [12].

It is important to note that periodontal status and low birth weight have common risk factors in their causal chain, which may act as confounders or effect modifiers of the association referred to above [22]. More robust studies on this issue, with strict control for confounding, showed several results. Some studies have shown that periodontitis may affect the weight of newborns [17–21], while others found no association [23–33].

Given the importance of low birth weight in the public health context, the high prevalence of periodontal disease and, given that it is still a controversial issue, the aim of this study was to evaluate whether there is an association between maternal periodontitis and low birth weight.

Materials and methods

Study design and population

This is a case-control study with the participation of 951 mothers who sought care from June 2009 to December 2011, at the Hospital Dom Malan Petrolina, PE, Brazil, as well as at the Juazeiro Municipal Maternity and at Pró-Matre Hospital in Juazeiro, BA, Brazil. The study population was composed of women that had been cared for by the Brazilian Unified Health System. The **case group** consisted of 269 mothers of children with birth weight <2500 g and the **control group** of 682 mothers of newborns with birth weight ≥2500 g.

This study was approved by the Ethics and Research Committee of Feira de Santana State University, number 152/2008 (CAAE 0151.0.059.000-08).

Sample size

The minimum sample size was estimated at 103 cases and 206 controls, with the use of Epi Info software, assuming a confidence level of 95%, a study power of 80% and a ratio of 1:2 between case and controls. Moreover, the frequency of periodontitis was considered as 18% and 4.7%, respectively, for the case and control groups, based on records from a previous study [13].

Selection of the sample

Initially, this study conducted a preliminary selection of the participants of case and control groups from a survey carried out every day, about the information on newborns' weight in the book of records of birth from Don Malan, Juazeiro Maternity and Pro-Matre Hospitals. The records were updated daily.

At the time of selection, all mothers of newborns with birth weight <2500 g and who were still in the institution after delivery, were invited to join the case group. The control group, consisting of a random sample of mothers of newborns with birth weight ≥2500 g, was also selected employing the same source used for the case group. Participants received the necessary information about the survey and, subsequently, they signed the consent form.

The medical history of the patients was revised and those who had at least one of the following characteristics: (1) systemic change that required antibiotic prophylaxis for dental procedures, (2) periodontal treatment during pregnancy, (3) number of teeth less than four or (4) post-partum hospital stay longer than 7 days, were not included in the study.

Procedures for data collection

The data pertaining to the weight of newborns were collected from the birth registry of the participating hospitals. The volunteers were asked to reply to trained interviewers using a structured questionnaire. After the interview, one dentist, who was unaware of the group in which the woman had been allocated, performed a periodontal clinical examination to obtain the oral clinical parameters.

Registration of maternal characteristics

The identification of data related to the mothers was conducted based on data collected from the mother's gestational accompaniment card, hospital records and through interviews, with the application of a structured questionnaire developed specifically for this research.

Periodontal status assessment

After the questionnaire, the women were examined by one dentist, who was unaware of the outcome and who had received previous training from a specialist in periodontics. For intra-examiner agreement, the Kappa index (±1 mm) was 0.80 for probing depth and 0.88 for recession/hyperplasia.

The periodontal status of women in the survey was evaluated using the following clinical parameters: probing depth, bleeding on probing and clinical attachment loss. All teeth were examined in the oral cavity, with the exception of the third molars in six different sites: mesiobuccal, mediobuccal, distobuccal, mesiolingual, mediolingual and distolingual. The probing depth, the distance from the gingival margin to the most apical extent of probe penetration, was performed with a William probe (Hu-Friedy, Chicago, IL, USA). If the gingival margin was located between two probe marks, the entire value of the closest mark was used and, when the gingival margin was in a position equidistant from two marks, the greater was considered [34].

In addition, the presence of bleeding was evaluated at the moment of the probing depth measurement, observing after 20 s if there was some type of bleeding at the site after the removal of the periodontal probe from the sulcus/pocket.

Women who had at least four teeth with probing depth greater than or equal to 4 mm and clinical attachment loss of 3 mm or more, with bleeding on probing at the same site, were diagnosed with periodontitis. Mothers who did not fit this criterion were not considered to have the periodontal infection.

Outcome evaluation

After delivery, the recorded birth weight was collected from the hospital records of mothers who were admitted to the hospitals considered in the study. Babies weighing <2500 g were considered low weight cases. It is worth noting that, in accordance with the Health Care Neonatal Manual protocol of the Health Ministry, in use in the hospitals in which this study took place, the weighing of newborns was performed by a nursing assistant within an hour after childbirth, using a digital scale, before weight loss after delivery occurred.

Data analysis procedures

Initially, an analysis of the distribution of main exposure (periodontitis) and all co-variables under consideration in this study for both the case and control groups was conducted. In the tabular analysis, the candidates for interaction and confounding for the modeling were selected and, using stratified analysis, the existence of potential effect modification and confounding was investigated for the following co-variables: age, sex, race, marital status, maternal schooling level, family income, current occupation, existing diseases, number of hospitalizations during pregnancy, history of low birth weight and intrauterine death, complications in previous childbirth and puerperal disorders, type and number of births, number of pregnancies, use of medication, pregestational body mass index (BMI), variables related to pre-natal care, examinations realized during pregnancy, immunization schedule, quality of pre-natal care, consumption and frequency of smoking, alcohol and drugs, dental care, type and frequency of cleaning.

The analysis of the study was based on a comparison of the frequency of periodontal disease between the two groups. This comparison was made by estimating the risk ratio, obtained by crude and adjusted *odds ratios*.

A logistic regression model was used to estimate the effect of the main association, simultaneously adjusting for the co-variables of interest using the backward procedure. The software R, version 12.0, was used for processing and analysis of the data.

Results

The sample of this study consisted of 951 mothers, 269 women in the case group, comprised of mothers of infants with birth weight <2500 g, and 682 women in the control group, composed of mothers of infants with birth weight equal to or greater than 2500 g. From the total of women invited to compose the sample, ~ 3% refused to participate in the study.

The comparison of the general characteristics of the case and control groups indicates that there is homogeneity between them, except for the following covariables (Table I): primiparity ($p < 0.001$), cesarean delivery ($p = 0.006$), history of LBW ($p = 0.004$),

Table I. Socio-demographics, obstetric and lifestyle characteristics of the case (mothers of newborns with birth weight <2500 g) and control (mothers of newborns with birth weight ≥2500 g) groups. Petrolina-PE/Juazeiro-BA, Brazil (n = 951).

Characteristics	Cases (n = 269)		Controls (n = 682)		p
	n	%	n	%	
Maternal schooling level*					
>4 years	232	86.9	585	86.2	0.77
0–4 years	35	13.1	94	13.8	
Family income (in minimum salary)*					
>1	75	29.2	200	29.9	0.84
0–1	182	70.8	470	70.1	
Maternal occupation during pregnancy*					
Paid	75	29.9	255	40.5	0.003
Housewife/student/unemployed	176	70.1	375	59.5	
Internation during pregnancy*					
No	218	81.0	605	89.1	< 0.001
Yes	51	19.0	74	10.9	
Type of delivery*					
Vaginal	176	65.7	508	74.4	0.01
Cesarean	92	34.3	174	25.5	
Primiparity*					
Yes	132	49.4	254	37.5	< 0.001
No	135	50.6	423	62.5	
History of low birth weight*					
Yes	34	13.4	48	7.3	0.004
No	220	86.6	608	92.7	
Marital status					
Married/stable union	214	79.9	557	81.8	0.49
Single/widow/divorced	54	20.1	124	18.8	
Age (years)*					
13–18	76	28.4	120	17.8	< 0.001
20–35	176	65.7	522	77.2	
>35	16	6.0	34	5.0	
Smoking habit during pregnancy*					
Yes	21	8.0	36	5.4	0.14
No	241	92.0	629	94.6	
Race/maternal color*					
White/yellow	46	17.3	92	13.9	0.18
Black	220	82.7	572	86.1	

* Some observations were lost due to lack of information about the variable.

hospitalizations during pregnancy ($p < 0.001$), maternal occupation ($p = 0.003$) and age ($p < 0.001$).

In accordance with Table II, it can be observed that the women in the case group, compared to the control group, had a higher frequency of pre-natal consultation <6 (60.1% vs 33.8%), pre-gestational body mass index ≤18.5 (8.9% vs 2.5%) and hypertension (26% vs 10.5%). Such differences showed high statistical significance ($p < 0.001$).

By observing co-variables related to oral health behavior (Table III), it was found that the study groups were similar for all aspects investigated, with the exception of visit to the dentist during pregnancy, in which mothers in the case group had lower frequency compared to the control group ($p = 0.038$). That is, visiting the dentist during pregnancy was found to be a protective factor against low birth weight.

Table II. Characteristics related to pre-natal care of the case (mothers of newborns with birth weight <2500 g) and control (mothers of newborns with birth weight ≥2500 g) groups. Petrolina-PE/Juazeiro-BA, Brazil (n = 951).

Characteristics	Cases (n = 269)		Controls (n = 682)		p
	n	%	n	%	
Realization of pre-natal care*					
Yes	261	97.8	671	98.5	0.40
No	6	2.2	10	1.5	
Number of pre-natal consultations*					
≥6	91	39.9	407	66.2	< 0.001
<6	137	60.1	208	33.8	
Urinary infection*					
Yes	109	42.6	282	42.2	0.82
No	147	57.4	388	57.8	
Hypertension*					
Yes	67	26.0	71	10.5	< 0.001
No	191	74.0	602	89.5	
Diabetes*					
Yes	9	3.5	12	1.8	0.25
No	251	96.5	659	98.1	
Other diseases*					
Yes	19	8.1	48	7.7	0.87
No	217	91.9	574	92.3	
Pre-gestational BMI*					
>18.5 kg/m^2	173	91.1	511	97.5	< 0.001
≤18.5 kg/m^2	17	8.9	13	2.5	
Educational activity during pre-natal care*					
Yes	50	20.6	159	25.5	0.13
No	193	79.4	465	74.5	

* Some observations were lost due to lack of information about the variable.

Table III. Characteristics related to maternal oral hygiene during the pregnancy of the case (mothers of newborns with birth weight <2500 g) and control (mothers of newborns with birth weight ≥2500 g) groups. Petrolina-PE/Juazeiro-BA, Brazil (n = 951).

Characteristics	Cases (n = 269)		Controls (n = 682)		p
	n	%	n	%	
Tooth brushing after the meal*					
Yes	263	97.8	662	97.2	0.63
No	6	2.2	19	2.8	
Frequency of brushing*					
≥3	97	36.1	435	64.0	0.99
<3	172	63.9	245	36.0	
Use of dental floss*					
Yes	89	33.2	245	36.2	0.38
No	179	66.8	431	63.8	
Visit to the dentist*					
Yes	58	22.1	191	28.7	0.04
No	205	77.9	474	71.3	

* Some observations were lost due to lack of information about the variable.

Table IV. Periodontal clinical parameters of the case (mothers of newborns with birth weight <2500 g) and control (mothers of newborns with birth weight ≥2500 g) groups. Petrolina-PE/ Juazeiro-BA, Brazil (n = 951).

Periodontal clinical parameters	Cases (n = 269)	Controls (n = 682)
Bleeding on probing index (%)		
Mean	10.8	8.6
Median	6.0	5.0
Range	0–92.0	0–68.0
Probing depth (mm)		
Mean	1.60	1.60
Median	1.52	1.55
Range	0.34–3.04	0.06–5.5
Clinical attachment loss (mm)		
Mean	1.59	1.60
Median	1.47	1.55
Range	0.69–4.3	0.06–5.5

Table IV shows the following periodontal clinical parameters among cases and controls: bleeding on probing index, probing depth and clinical attachment loss. They were almost similar between the groups.

The proportion of periodontal disease in the case group was approximately the same as found in the control group and the differences were irrelevant, statistically (16.4% vs 17.4%, p = 0.68). The crude association analysis (Table V) showed that, among women with periodontal infection, the chance of having children with low birth weight was 8% lower than that observed among mothers without such disease (ORcrude = 0.92, 95% CI = 0.63–1.35). This finding was not statistically significant.

In the stratified analysis using Mantel-Henzel method, assuming a relative difference of at most 10% between crude and adjusted ORs, the following co-variables presented as potential confounders of the association under study: pre-gestational body mass index, number of pre-natal consultations and hypertension. However, even at this stage of the analysis, potential modifier effects were not identified.

After multivariate non-conditional logistic regression analysis, there was no confirmation of confounding. However, the following co-variables were included in the final mathematical model, because they are recognized as classical confounders of the studied association: maternal age, smoking during pregnancy, pre-gestational body mass index, number of pregnancies, hypertension, number of pre-natal consultations and maternal schooling level. The adjusted model also showed no association between maternal periodontal disease and low birth weight (ORadjusted = 1.00, 95% CI = 0.57–1.69).

Discussion

The findings of this study showed no association between maternal periodontal disease and low birth weight, even after appropriate adjustments for confounding factors such as *maternal age*, *smoking during pregnancy*, *pre-gestational body mass index*, *number of pregnancies*, *hypertension*, *number of pre-natal consultations* and *maternal schooling level* (ORcrude = 0.92, 95% CI = 0.63–1.35; ORadjusted = 1.00, 95% CI = 0.61–1.68).

Despite not having verified an association between periodontal infection and low birth weight, *visit to the dentist during pregnancy* showed a protective effect for the referred outcome. This variable, most probably, functioned as a proxy factor for *access to the health service* and *health behavior* co-variables.

The frequency of periodontitis in the control group (17.4%) was slightly higher compared to the cases (16.4%). However, no significant differences were detected. Similar results were found in studies by Vettore et al. [26] and Buduneli et al. [32], in which the mothers of children with normal weight had a higher prevalence of periodontal disease, when compared to mothers of newborns with low birth weight. In contrast, Bassani et al. [24] detected higher frequency of periodontitis cases compared to the control group. However, these findings do not indicate the statistical significance of the association, consistent with other previous studies [25–32].

However, there are several case-control studies that defend the existence of the referred association

Table V. Odds ratio (OR) and confidence interval (CI) of the association between maternal periodontitis and low birth weight. Petrolina-PE/ Juazeiro-BA, Brazil (n = 951).

Maternal periodontitis	Cases (n = 269)		Controls (n = 682)		Crude analysis		Adjusted analysis[a]	
	n	%	n	%	OR	95% CI	OR	95% CI
Yes	44	16.4	119	17.4	0.92	0.63–1.35	1.00	0.61–1.68
No	225	83.6	563	82.6				

[a] Adjustment for: maternal age, smoking during pregnancy, pre-gestational body mass index, number of pregnancies, hypertension, number of pre-natal consultations and maternal schooling level.

contradicting the results obtained in the present study. Among these studies, there are those that dealt appropriately with confounders, such as Moliterno et al. [35] (OR = 3.48, 95% CI = 1.17–10.36), Cruz et al. [14] (OR = 2.30, 95% CI = 1.14–4.60), Siqueira et al. [17] (OR = 1.67, 95% CI = 1.11–2.56) and Khader et al. [16] ($p < 0.001$) that found a statistically significant association between periodontitis and low birth weight. Thus, this variability of findings reinforces a lack of consensus on the hypothesis.

Even among randomized and controlled intervention studies considered the gold standard in search of evidence for causation, there is disagreement about the existence of this association. On one hand, the results of Michalowicz et al. [27], Offenbacher et al. [29], Ebersole et al. [28], Marcones et al. [31] and Oliveira et al. [23] corroborate the findings of this research. On the other hand, the studies of Lopez et al. [21] and Taranum and Faizundin [18] found that periodontal infection is a risk factor for low birth weight.

A possible explanation for the disagreement concerning the studied association is related to different definitions for periodontitis, since, by adopting different criteria for the diagnosis of periodontal disease, the strength of association is changed, as well as its statistical significance [13,36]. In this study, a combination of three clinical parameters (pocket depth, attachment loss and bleeding on probing) was used to obtain a robust criteria for determining the existence of exposure, thereby avoiding the inclusion of false-positives.

Taking into consideration the above issues, the findings of this study should be evaluated with caution. First, it should be subject to the limitations of the chosen epidemiologic methodological design. It is known that case-control investigations are subject to selection bias in the control group, as well as recall bias because of its retrospective nature, compared to cohort and intervention studies.

However, since there is a small number of randomized clinical trials able to give a categorical answer on this theme, an increase in the number of observational studies is contributing to a better understanding of this subject. It is important to note that this study was planned according to the recommendations of STROBE [37], a guide for observational studies in the epidemiology area.

Furthermore, to ensure greater credibility, certain methodological safeguards have been adopted in this study, such as robust exposure and outcome measurements, standardization of the examiner and adjustment procedures in the phase of data analysis.

The criterion for low birth weight was the same as used by the World Health Organization [8], obtained through hospital records. Regarding the diagnosis of periodontal disease, we adopted a robust criterion, with good specificity [13]. From a methodological point of view, the sample size was much higher than the original estimated and the final model was adjusted for potential confounders of the association, thereby giving greater reliability to the results.

Despite the limitations of this investigation, and this is still a controversial topic in the literature, the results can contribute to the body of evidence in question. Although we have not found an association between maternal periodontal disease and low birth weight, we must stress also the need for large studies with methodological rigor, which take into account the inflammatory response of individuals to this oral infection, besides the need for a consensus around the clinical measure of exposure to obtain a better comparison between investigations, giving greater consistency to the theme.

Conclusion

The findings of the present study, in accordance with the employed method and the limitations, did not verify the association between maternal periodontitis and low birth weight.

***Declaration of interest*:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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