

Maternal Periodontitis as a Potential Risk Variable for Preeclampsia: A Case-Control Study

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Background: Association studies between maternal periodontitis and an elevated risk for preeclampsia have shown conflicting results. The aims of the present case-control study were: 1) to evaluate the association between maternal periodontitis and preeclampsia before and after matching, assessing confounding and interaction; and 2) to evaluate the influence of the extent and severity of periodontal parameters, bleeding on probing (BOP), probing depth (PD), and clinical attachment loss (CAL), in association with preeclampsia.

Methods: Initially, 1,206 Brazilian women were included and divided into a control group (1,042 non-preeclamptic women who gave birth to infants with adequate gestational age and birth weight) and a case group (164 preeclamptic women). Further, 125 preeclamptic women were matched according to age, chronic hypertension, and primiparity to 375 non-preeclamptic women randomly selected from the control group. Maternal periodontitis was defined as PD \geq 4 mm and CAL \geq 3 mm at the same site in at least four teeth. The effect of variables of interest and confounding were assessed by univariate and multivariate analysis.

Results: After controlling for confounders, maternal periodontitis was included in the multivariate final model (odds ratio [OR] = 1.94; 95% confidence interval [CI]: 1.37 to 2.77; $P < 0.001$) and remained associated with preeclampsia after matching (OR = 1.52; 95% CI: 1.01 to 2.29; $P = 0.045$). The odds of preeclampsia were associated with an increase in the number of sites with BOP and PD and CAL \geq 4 mm.

Conclusion: Maternal periodontitis is a risk factor associated with preeclampsia, emphasizing the importance of periodontal care in prenatal programs. *J Periodontol* 2008;79:207-215.

KEY WORDS

Infection; inflammation; periodontal disease/adverse effects; preeclampsia; pregnancy; risk factors.

Periodontitis has a chronic infectious nature and leads to an inflammation and progressive destruction of supportive tissues of the teeth. An elevated level of cytokines and inflammatory mediators can be observed locally and systemically.¹ Periodontitis has been implicated as a systemic exposure and is considered a potential risk factor for some systemic illnesses, including cardiovascular diseases, diabetes mellitus, and adverse pregnancy outcomes, such as preeclampsia.¹⁻³

Preeclampsia is a pregnancy-specific syndrome usually occurring after 20 weeks of gestation and especially in first pregnancies. This disease is characterized by perturbations in volume and blood pressure control, gradual maternal blood pressure elevation, proteinuria, and generalized edema. In severe cases, alterations of the coagulation system and liver function may occur.⁴ Although preeclampsia is clinically complex and can be severe, it is reversible through the interruption of the pregnancy. However, this multifactorial disorder is one of the major causes of maternal and fetal morbidity and mortality.⁴⁻⁷

Studies⁸⁻¹³ have identified risk factors for preeclampsia, including nulliparity and primiparity, family history of preeclampsia, uterine abnormalities, obesity, chronic hypertension, renal diseases, diabetes mellitus, multiple gestation, and maternal age.

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The maternal hypertensive disorder, the proteinuria, and the edema are part of a severe systemic inflammation response that includes leukocyte and endothelial cell activation. Although the etiology of preeclampsia is not clear, reduced placental blood supply may be the key cause, leading to an oxidative and inflammatory endothelial dysfunction.^{6,7,14}

The characteristic lesion of preeclampsia, which is designated as acute atherosclerosis, is similar to the clinical and pathological alterations of atherosclerotic vascular changes.^{10,11,15} Atherosclerosis is characterized by local endothelial rupture, perivascular space invasion by mononuclear cells, and the formation of lipoprotein deposits.¹⁶

Atherogenic and thromboembolic events have been associated with infections of unknown origins. A study¹⁷ demonstrated that Gram-negative bacteria and bacterial endotoxins, when presented as a systemic stressor in animal models, can induce inflammatory cell infiltration in the main blood vessels, vascular muscular cell proliferation on the vascular wall, grease degeneration, and intravascular coagulation.

Because atherosclerosis has been associated strongly with chronic infections, some studies^{10,11,15} suggested that the presence of infections may be a potential risk factor in the pathogenesis of preeclampsia. Infection may be important to initiate the disorder by increasing the risk for the formation of atherosclerosis or boosting the process through the amplification of maternal inflammatory response.^{10,11,15}

Because the pathogenesis of atherosclerosis and preeclampsia are similar, periodontitis may represent a risk factor for this adverse pregnancy outcome. Studies^{9-11,15,16,18-20} have presented different odds ratios (ORs) for the association between periodontitis and preeclampsia. However, some studies¹³⁻²¹ failed to demonstrate such an association.

These conflicting findings may reflect methodological diversities among the studies. Moreover, this could be related to biases introduced by sample size, heterogeneity of the criteria to define periodontitis, and inadequate assessment of confounding and interaction.^{22,23}

In a previous study¹⁹ that included 588 Brazilian women, a risk association between maternal periodontitis and preeclampsia (OR = 1.88) was demonstrated. In addition, this study showed that chronic hypertension, maternal age, and primiparity were variables strongly related to preeclampsia.

For the present study, the number of women was increased to create an adequate matching process for the previously determined risk factors for preeclampsia. The rationale for this strategy was formulated based on the absence of matched case-control studies geared toward the investigation of the association between periodontitis and preeclampsia as well

as toward the review of the conflicting results from different studies^{9-16,18-21} assessing this association.

Thus, this case-control study was conducted to: 1) assess the risk association between maternal periodontitis and preeclampsia before and after matching for known risk factors of preeclampsia (maternal age, chronic hypertension, and primiparity); 2) assess the interaction between maternal periodontitis and prenatal visits and previous preterm birth on the risk for preeclampsia; and 3) assess the extent and severity of periodontal parameters, bleeding on probing (BOP), probing depth (PD), and clinical attachment loss (CAL), on the risk for an association with preeclampsia.

MATERIALS AND METHODS

The present study was conducted at a public hospital in Belo Horizonte and was approved by the Federal University of Minas Gerais Research Ethics Committee. Participants were informed of the aims of the study and provided written informed consent.

An eligible sample was selected based on the accessibility and availability of women in the postpartum period within 48 hours of delivery. Data were collected through subject questionnaires, periodontal examination, and medical records. The following variables were recorded: maternal age, educational level, marital status, chronic hypertension, diabetes mellitus, parity, alcohol and drug consumption during pregnancy, smoking during pregnancy, previous abortion, previous preterm birth, number of prenatal visits, genitourinary infection, birth weight and gestational age of the infant, occurrence of intrauterine growth restriction, and preeclampsia.

From February 2004 to June 2005, women 18 to 35 years of age who gave birth to live infants in the hospital unit were invited to participate in the study. Women were excluded from the study if they were <18 years of age and did not have a legal guardian; had had a multiple gestation; had suffered a spontaneous abortion; had undergone in vitro fertilization; or if they were diagnosed with pregestational diabetes, heart and renal diseases, placental, cervical, and/or uterine abnormalities, human immunodeficiency virus infection, or any medical condition requiring antibiotic prophylaxis for dental treatment. Some of these exclusion criteria were adopted because they were determined to be confounders and risk factors for preeclampsia.^{8-11,13}

During the 16-month period of data collection, 1,746 women were eligible and selected for a case-control study on adverse pregnancy outcomes and maternal periodontitis. From this total, 60 (3.43%) refused to participate, and 480 (27.5%) were excluded from the analysis because they did not meet the inclusion criteria. The final sample was composed

of 1,206 women from a multiethnic group with low socioeconomic status. Case and controls assignments were a post hoc definition. Women were divided as follows: a control group consisting of 1,042 non-preeclamptic women who gave birth to live term infants weighing $\geq 2,500$ g and a case group consisting of 164 preeclamptic women. Furthermore, 125 preeclamptic women were matched for age, chronic hypertension, and primiparity with 375 non-preeclamptic women selected randomly from the control group in a proportion of 1:3 (case/controls). The matching strategy was based on individual matching. Control selection from the sample during the matching process was performed through a random computer function. Thirty-nine women from the case group who presented no matching controls for the selected variables were excluded (Fig. 1). No significant differences were observed between the excluded and selected women in the case group.

Medical Data and Case Definition

Demographic data, medical history, and detailed information on events during pregnancy and delivery were obtained from medical records (Latin American Center for Perinatology form). The subjects' medical records were examined thoroughly, and data were confirmed through subject questionnaires upon oral examination. All medical data were reviewed by an obstetrician to confirm criteria for inclusion and exclusion.

Preeclampsia was defined as blood pressure $>140/90$ mm Hg on two separate occasions after week 20 of

gestation and $\geq 1+$ proteinuria.¹⁰ Blood pressure was assessed by a trained medical group from the hospital unit under strict conditions to avoid observer and instrumental errors. The assessments focused on the protocols of the Obstetric High Risk Unit from the hospital, which were based on previous reports.^{10,16,17} All subjects included in this study were tested for proteinuria, which was defined as a protein concentration ≥ 0.30 g/dl, equivalent to a $\geq 1+$ urine dipstick value, on two separate urine samples taken 6 hours apart. Upon a positive result, 24-hour urine specimens were collected for analysis of quantitative protein excretion during the monitoring period in cases of conservative routine procedures.¹⁹

Chronic hypertension was defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg confirmed by multiple measurements and detected before conception or before gestation week 20.²⁴

Smoking during pregnancy and alcohol use were defined as self-reported consumption during any trimester of pregnancy. This study did not attempt to clarify the exposure or patterns of consumption because there was substantial within-person fluctuation during pregnancy.¹⁹

Women with conjugal stability were considered those who reported official marriage or stable unions with their partners.

Periodontal Assessment

A full-mouth periodontal examination was performed with a University of North Carolina-15 periodontal probe at six sites per tooth. Two periodontists, trained and masked to each subject's identity and medical history, were calibrated at the start of the study and 3 months later using PD and CAL. Intra- and interexaminer reliability scores were tested, and unweighted *k* scores up to 0.81 were attained.

Periodontal examination was performed in the hospital bed under proper light and infection control conditions. When necessary, teeth were cleaned with sterile gauze for adequate assessment of periodontal parameters. Clinical signs of inflammation and periodontal tissue destruction were assessed using BOP, PD, and CAL.

BOP was defined as the presence of bleeding from the gingival crevice after periodontal probing. PD was measured as the distance from the gingival margin to the bottom of the clinical sulcus or to the base of the probable gingival crevice. CAL was determined by measuring the distance from the cemento-enamel junction to the bottom of the clinical sulcus or to the base of the probable gingival crevice.

For the purpose of this analysis, maternal periodontitis was defined as PD ≥ 4 mm and CAL ≥ 3 mm at the same site in at least four teeth.²⁵

Teeth were excluded from the examination if the cemento-enamel junction could not be determined

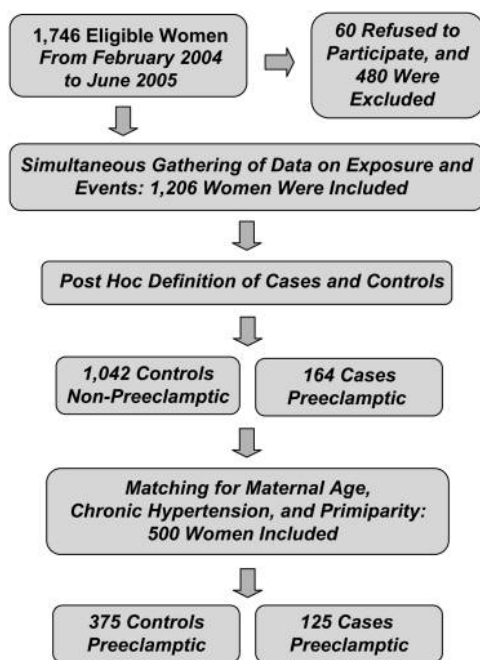


Figure 1.

Sampling strategy and study sample.

properly, if they were in the eruption process, if they had unsatisfactory restorations, extent caries lesions, or fracture, or if they were third molars.

Statistical Analysis

Descriptive, univariate, and logistic regression analyses were performed. The periodontal status of the sample was described, and the groups were compared using the two-sample *t* test. Groups also were compared in relation to variables of interest (age, educational level, marital status, chronic hypertension, diabetes mellitus, parity, alcohol use and drug consumption during pregnancy, smoking during pregnancy, previous abortion, previous preterm birth, number of prenatal visits, and maternal periodontitis) using the χ^2 and Fisher exact tests when appropriate.

Interactions between maternal periodontitis and independent variables of interest (previous preterm birth and prenatal visits) were assessed before constructing the multivariate logistic models.

To control for confounders, all variables with *P* value ≤ 0.20 were selected and entered in an unconditional multivariate logistic regression model. In the analysis of matched data, a conditional logistic regression analysis was performed. Variables selected for the conditional model also included the matching variables. The effects of variables of interest on the estimate for periodontitis were investigated by a forward and backward procedure for unconditional and conditional models. The elimination procedure was based on the changes in the estimate of periodontitis, and variables were removed manually from the models when no changes were observed. All variables included in the final model were determined to be independent assessing collinearity. Consequently, there is no degree of redundancy or overlap among these variables, and their coefficients are reliable estimates.

In addition, the influence of the extent and severity of periodontal parameters on the OR for preeclampsia was evaluated by means of a multivariate regression analysis. Clinical periodontal parameters, including the number of sites with BOP and the number of sites with PD and CAL ≥ 4 , ≥ 5 , and ≥ 7 mm were tested separately because of their multicollinearity. All analyses were performed using statistical software.†

RESULTS

Demographic, medical, and obstetric data for control and case groups before matching are detailed in Table 1. The mean age of the sample was 25.87 ± 5.97 years. The frequency of chronic hypertension, diabetes mellitus, smoking during pregnancy, and alcohol and drug consumption during pregnancy were low. Primiparity was noted in 36.2% of the women in the control group and 46.3% in the case group. A small number of women had previous preterm births (2.6%

in the control group and 5.5% in the case group), and a greater number had previous abortions (17.8% in the control group and 20.1% in the case group) (Table 1). The frequency of preeclampsia in the sample was 13.6%. The frequency of periodontitis was 41.4% in the total sample, 39.0% among non-preeclamptic women, and 56.7% among preeclamptic women.

The periodontal status of the sample is described in Table 2. The mean number of sites with BOP and PD and CAL ≥ 4 or ≥ 5 mm was significantly greater in the case group.

When the interaction between maternal periodontitis and prenatal visits was tested, an OR = 1.27 (95% confidence interval [CI]: 0.64 to 2.50; *P* < 0.483) for preeclampsia was observed. When the interaction between maternal periodontitis and previous preterm birth was tested, an OR = 1.64 (95% CI: 0.27 to 9.72; *P* < 0.582) for preeclampsia was observed. Although the point estimates of OR for both interactions terms were positive, the 95% CIs included the null. Therefore, these OR estimates were considered not significant, and they were not selected for the multivariate logistic models.

Findings from the unconditional multivariate logistic regression analysis are detailed in Table 3. After adjustments, maternal age ≥ 30 years (OR = 2.21; *P* < 0.001), chronic hypertension (OR = 5.19; *P* < 0.001), primiparity (OR = 2.37; *P* < 0.001), previous preterm birth (OR = 2.74; *P* = 0.021), at least six prenatal visits (OR = 0.65; *P* < 0.021), and maternal periodontitis (OR = 1.94; *P* < 0.001) were retained in the final model.

After matching for age, chronic hypertension, and primiparity, previous preterm birth (OR = 3.15; 95% CI: 1.04 to 9.52; *P* = 0.042) and maternal periodontitis (OR = 1.52; 95% CI: 1.01 to 2.29; *P* = 0.045) were determined to be independent variables significantly associated with preeclampsia in the final conditional logistic regression model (Table 4).

The influence of the extent and severity of periodontal parameters, BOP and PD and CAL ≥ 4 , ≥ 5 , or ≥ 7 mm, on the risk association for preeclampsia after the matching process are detailed in Figures 2 and 3. With an increase in the number of sites with BOP, the OR for preeclampsia also increased (Fig. 2). Results showed OR = 1.33 (95% CI: 1.08 to 1.65) and OR = 1.61 (95% CI: 1.44 to 2.29) for BOP in 30% and 50% of sites, respectively. The odds for the development of preeclampsia increased with an increase in the number of sites with PD and CAL ≥ 4 mm (Fig. 3). The results showed OR = 1.63 (95% CI: 1.04 to 2.57) and OR = 2.27 (95% CI: 1.07 to 4.92) for PD and CAL ≥ 4 mm in 30% and 50% of sites, respectively. When PD and CAL were tested with cut-off points of ≥ 5

† Statistical Package for the Social Sciences, version 9.0 for Windows, SPSS, Chicago, IL.

Table 1.**Demographic, Obstetric, and Medical Data for Preeclamptic and Non-Preeclamptic Women**

Variable	Groups				P	OR (95% CI)
	Controls (N = 1,042)		Cases (N = 164)			
	n	%	n	%		
Educational level						
None/primary school	552	53.0	78	47.5	NS	NS
Secondary school/higher	490	47.0	86	52.5		
Maternal age (years)						
<30	779	74.7	95	57.9	<0.001	2.15 (1.53 to 3.02)
≥30	263	25.3	69	42.1		
Prenatal visits (N)						
≤6	406	38.9	74	45.1	NS	NS
>6	636	61.1	90	54.9		
Chronic hypertension	33	3.2	27	16.5	<0.001	6.03 (3.52 to 10.33)
Poor conjugal stability	278	26.7	41	25.0	NS	NS
Diabetes mellitus	4	0.4	2	1.2	NA	NA
Primiparity	377	36.2	76	46.3	0.014	1.52 (1.09 to 2.12)
Smoking during pregnancy	94	9.0	8	4.9	NS	0.52 (0.25 to 1.08)
Alcohol use during pregnancy	110	10.5	12	7.3	NS	NS
Drug use during pregnancy	2	0.2	1	0.6	NA	NA
Previous abortion	186	17.8	33	20.1	NS	NS
Previous preterm birth	27	2.6	9	5.5	0.048	2.18 (1.01 to 4.73)
Maternal periodontitis	406	39.0	93	56.7	<0.001	2.04 (1.67 to 2.85)

NS = not significant; NA = not applicable.

Table 2.**Periodontal Status (mean [95% CI]) of the Sample**

Variable	Preeclamptic Women (n = 164)	Non-Preeclamptic Women (n = 1,042)	P Value
Sites with BOP	22.93 (19.51 to 26.36)	15.14 (13.86 to 16.41)	<0.001*
Sites with PD and CAL ≥4 mm [†]	11.49 (9.49 to 13.50)	7.46 (6.72 to 8.20)	<0.001*
Sites with PD and CAL ≥5 mm [†]	4.71 (3.54 to 5.87)	3.63 (3.15 to 4.11)	0.0104*
Sites with PD and CAL ≥7 mm [†]	0.73 (0.39 to 1.06)	0.48 (0.31 to 0.64)	0.190 [‡]

* The two-sample *t* test with equal variance was used.

† At the same site.

‡ The two-sample *t* test with unequal variance was used.

and ≥7 mm, the ORs for preeclampsia were not significant (data not shown). The upper and lower limits for the CIs in these associations presented great discrepancy and included 1.

DISCUSSION

In the present study, maternal periodontitis was associated with an elevated risk for preeclampsia. The biologic plausibility for such an association is supported

Table 3.
Logistic Regression Multivariate Analysis for Preeclampsia: Unconditional Final Model (cases: n = 164; controls: n = 1,042)

Variable	Coefficient	OR (95% CI)	P Value
Maternal age ≥30 years	0.79	2.21 (1.52 to 3.22)	<0.001
Chronic hypertension	1.65	5.19 (2.88 to 9.34)	<0.001
Primiparity	0.86	2.37 (1.63 to 3.45)	<0.001
Prenatal visits ≥6	-0.42	0.65 (0.46 to 0.94)	0.021
Previous preterm birth	1.01	2.74 (1.16 to 6.46)	0.021
Maternal periodontitis	0.66	1.94 (1.37 to 2.77)	<0.001

Table 4.
Logistic Regression Analysis for Preeclampsia After Matching for Age, Chronic Hypertension, and Primiparity: Conditional Final Model (cases: n = 125; controls: n = 375)

Variable	Coefficient	OR (95% CI)	P Value
Previous preterm birth	1.15	3.15 (1.04 to 9.52)	0.042
Maternal periodontitis	0.42	1.52 (1.01 to 2.29)	0.045

by the hypothesis that infection is a risk factor for preeclampsia. It has been speculated that preeclampsia may develop as the result of a maternal predisposition to endothelial dysfunction, leading to an insufficient placenta implantation. In addition, this endothelial dysfunction may involve cytokine production. In this manner, maternal infection should accelerate cytokine liberation, and periodontitis, as a maternal infection, may well contribute to this process.²⁶

Chronic periodontitis is caused by the host immune response to periodontal pathogens.²⁷ Many studies^{5,28-32} have postulated that the effect of periodontitis on the development of adverse pregnancy outcomes may stem from the hematogenous translocation of inflammatory mediators and bacterial products to the fetal-placenta unit. This process may interfere with fetal growth and uterine contractions.

The criteria proposed by Lopez et al.²⁵ to describe periodontitis were used in the present study because they contain the parameters PD and CAL in their definitions. We believe that these criteria could appropriately reflect the periodontal condition in terms of extent and severity. The frequency of periodontitis observed in the sample (41.4%) was similar to that reported in previous studies.^{10,11,18}

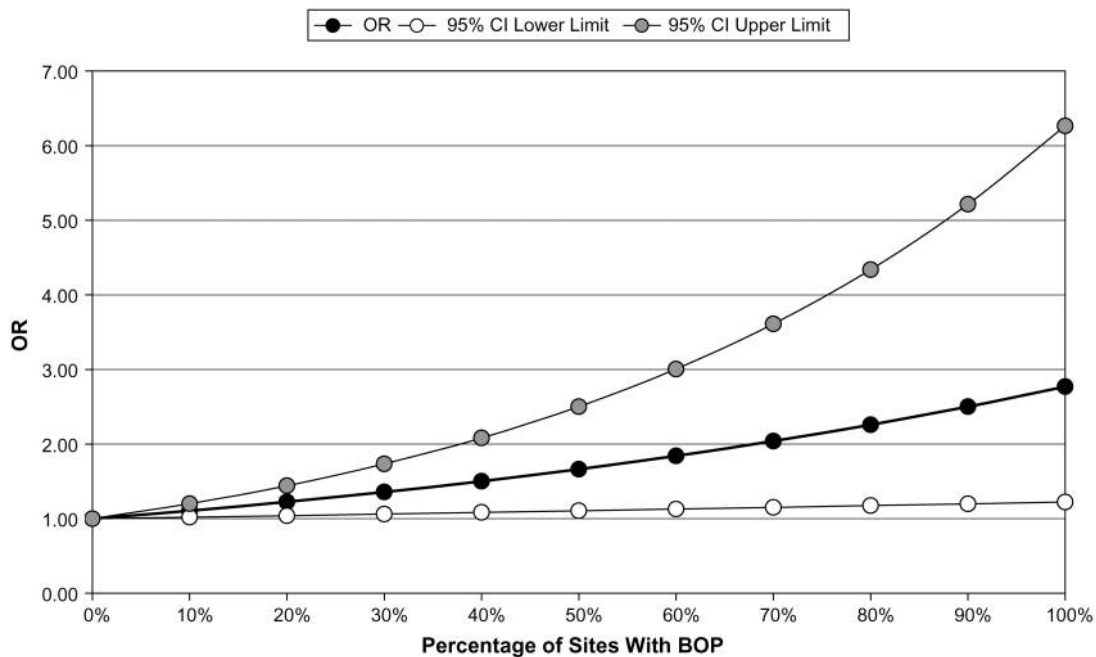


Figure 2.
 OR for preeclampsia and percentage of sites with BOP after matching for age, chronic hypertension, and primiparity (cases: n = 125; controls: n = 375).

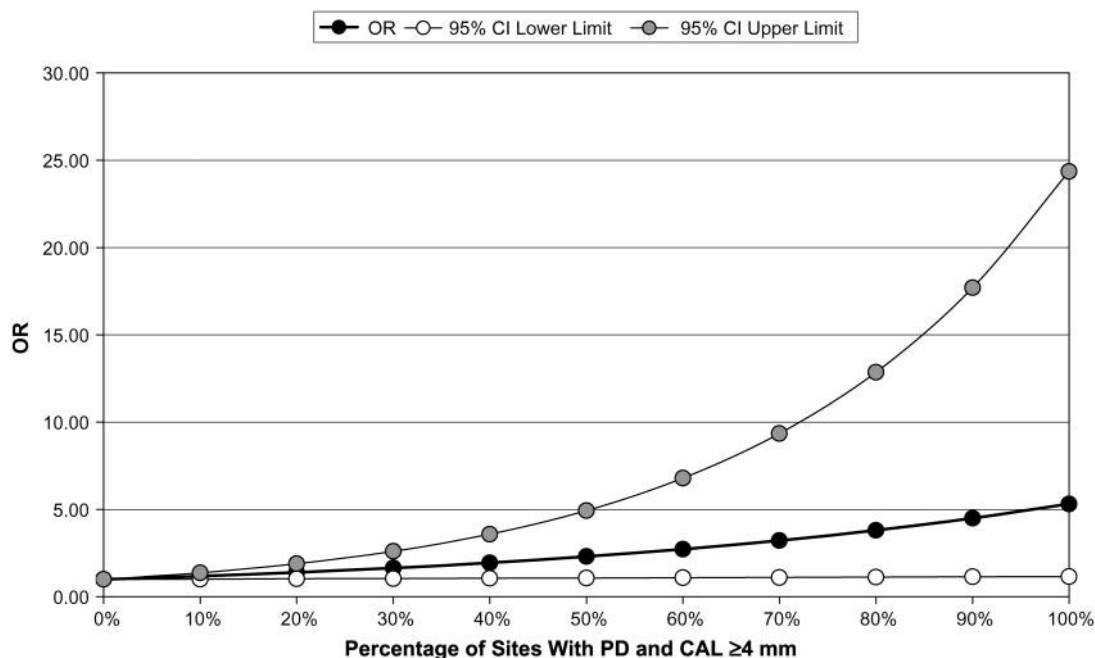


Figure 3.

OR for preeclampsia and percentage of sites with PD and CAL ≥ 4 mm after matching for age, chronic hypertension, and primiparity (cases: $n = 125$; controls: $n = 375$).

The frequency of preeclampsia in the present study (13.6%) was higher compared to the reports of Riché et al.⁹ (4.6%) and Boggess et al.¹⁰ (4.4%), but it was similar to the study of Castaldi et al.²¹ (10.0%). It has been suggested that the prevalence of preeclampsia could be influenced by geographic characteristics, socioeconomic status, ethnicity, as well as access to and availability of medical care.⁹ The hospital at which this study was carried out is a local obstetric referral center, which may have contributed to the prevalence observed.

Findings from the present study showed a significant risk association between maternal periodontitis and preeclampsia, considering other variables analyzed. The adjusted OR for preeclampsia was 1.94 (95% CI: 1.37 to 2.77; $P < 0.001$). This type of association was reported first by Boggess et al.¹⁰ who reported an OR = 2.4. Other studies also reported significant associations, such as those by Canakci et al.¹¹ (OR = 3.47), Contreras et al.¹⁸ (OR = 3.0), Cota et al.¹⁹ (OR = 1.88), and Kunnen et al.²⁰ (OR = 7.9). However, the studies of Khader et al.¹³ and Castaldi et al.²¹ failed to demonstrate such an association.

The OR reported by Kunnen et al.²⁰ is notably higher compared to other studies. This most likely can be explained by the smaller number of subjects in the study sample (17 cases and 35 controls).

After matching for age, chronic hypertension, and primiparity, maternal periodontitis remained as a sig-

nificant independent variable in the conditional logistic regression model (OR = 1.52; 95% CI: 1.01 to 2.29; $P = 0.045$). These variables were selected for the matching process because many studies^{4,9-11,15,19} demonstrated that they are associated strongly with preeclampsia.

No matched case-control study for the association between periodontitis and preeclampsia was found in the dental or medical literature. Matching is an important strategy for minimizing the effects of confounding in epidemiologic studies. In addition, the matching process has the advantage of choosing controls that are comparable to the study group with respect to extraneous factors. It promotes a restriction of controls to reduce confounding.³³

It must be highlighted that the number of subjects in the present study seemed to be well founded for the association analysis before and after matching. In addition, subjects were matched for variables associated strongly with the development of preeclampsia. The proportion of case/controls (1:3) used in this study increased the consistency and validity of the results obtained.

In the present study, smoking during pregnancy was associated with a lower OR for the development of preeclampsia in the multivariate analysis. This finding is supported by other studies^{4,10,19,34,35} that demonstrated a protector effect of this variable. It is hypothesized that smoking can affect angiogenic

factors, the endothelial function, and the immune system. In addition, smoking can inhibit the production of interleukin-2 and tumor necrosis factor- α by mononuclear cells, which decreases the risk for preeclampsia.³⁶⁻³⁹

However, it was demonstrated that smoking during pregnancy is responsible for hazardous effects to the mother and the infant. Smoking can induce the development of abnormalities in the brain, leading to psychological, behavioral, and cognitive disorders.⁴⁰

The selection of variables for the analysis of interaction was based on the biologic plausibility of each interaction. The interaction between periodontitis and prenatal visits was tested based on one's own health and self-care. The interaction between periodontitis and previous preterm birth was tested based on the hypothesis that because periodontitis may serve as a risk factor for preterm birth, women with periodontitis and previous preterm birth may be at a higher risk for preeclampsia. However, there was no interaction between the independent variables tested because no combined effect was observed, and the 95% CI included the null.

It also has been suggested that the number of previous preterm births is associated with an elevated risk for adverse pregnancy outcomes.²⁸ Findings from the present study showed that the number of previous preterm births was associated with preeclampsia (OR = 3.15; 95% CI: 1.04 to 9.52; $P=0.042$) before and after matching.

Findings from Cota et al.¹⁹ involving 588 Brazilian women showed an OR = 1.88 between preeclampsia and maternal periodontitis. The present study greatly expanded the sample from our previous work¹⁹ (814 women were added) in an attempt to reach a simultaneous matching process for three important variables: chronic hypertension, primiparity, and maternal age. It also provided new strategies for the analysis of unmatched and matched data as well as new interaction terms. In this manner, the influence of the matching process and the severity and extent of periodontal parameters on OR estimates were tested as a new hypothesis. The results of the present study showed estimates for the association between preeclampsia and maternal periodontitis (unconditional analysis: OR = 1.94; conditional analysis: OR = 1.52) similar to that reported by Cota et al.¹⁹

Our results demonstrated that the higher the percentage of sites with BOP and PD and CAL ≥ 4 mm, the higher the OR for the development of preeclampsia. This finding suggests a dose-response effect for maternal periodontitis. The OR for PD and CAL ≥ 4 mm in $>50\%$ of sites (OR = 2.27), which denotes a generalized pattern of disease, is greater than the OR calculated after matching (OR = 1.52) based on the criteria used to define periodontitis.²⁵ However, when

the severity of periodontitis was analyzed with cut-off points of PD and CAL ≥ 5 or ≥ 7 mm, the OR was not significant. Very discrepant upper and lower limits for the CI were observed. This fact could be related to the small number of samples with these specific cut-off points for PD and CAL. There was a small number of women affected by severe periodontitis in the study sample. These findings were demonstrated after matching, which reinforces its consistency because known risk variables were controlled.

Beck and Offenbacher⁴¹ demonstrated that the extent and severity of periodontal parameters (BOP, PD, and CAL) could reflect different systemic exposures. Investigators stated that BOP and PD can be relevant clinical parameters to represent systemic inflammation exposure. In the present study, the extent of these periodontal parameters was related strongly to the occurrence of preeclampsia.

CONCLUSIONS

The present study showed a risk association between maternal periodontitis and preeclampsia (OR = 1.94). This association remained significant after matching for age, chronic hypertension, and primiparity (OR = 1.52). Consequently, these findings emphasize the importance of periodontal care in prenatal and pregnancy health care programs. However, because both events are influenced by multiple factors, association studies must be analyzed with care. Longitudinal and intervention studies are necessary to better address the association between periodontitis and preeclampsia as well as the benefits of periodontal treatment on the prevention of adverse pregnancy outcomes.

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