Oral Health Behaviors, Periodontal Disease, and Pathogens in Preeclampsia: A Case-Control Study in Korea

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Background: The aim of this study is to confirm the association among oral health behaviors, periodontitis, and preeclampsia in Korean women.

Methods: This study is designed as a case-control study. Sixteen women with preeclampsia and 48 without preeclampsia post-delivery were included in this study from November 2007 to January 2010. Information was collected on demographics, health behaviors, and obstetric and systemic diseases that may influence the periodontal condition and preeclampsia. Full-mouth periodontal probing was conducted by one trained examiner (KHB). Localized periodontitis was defined as periodontal clinical attachment loss (AL) ≥3.5 mm on two or three sites not on the same tooth. In addition, generalized periodontitis was defined as clinical AL ≥3.5 mm on ≥4 sites not on the same tooth. Gingival crevicular fluid was collected using a sterilized paper point for quantitative analysis of *Treponema denticola*, *Porphyromonas gingivalis*, *Prevotella intermedia* (*Pi*), and *Tannerella forsythia* (previously *T. forsythensis*).

Results: After adjusting for confounders, the adjusted odds ratio (OR) was 4.79 (95% confidence interval [CI]: 1.02 to 29.72) for localized periodontitis and 6.60 (95% CI: 1.25 to 41.61) for generalized periodontitis. In addition, the proportion of floss or interdental brush users in women with preeclampsia was lower than that in women without (adjusted OR: 0.21; 95% CI: 0.02 to 0.93). *Pi* was significantly more prevalent in women with preeclampsia ($P = 0.028$).

Conclusion: These results indicate that preeclampsia could be associated with the maternal periodontal condition and interdental cleaning. *J Periodontol 2011;82:1685-1692.*

KEY WORDS

Epidemiology; periodontal diseases; pre-eclampsia; pregnancy complications.

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Preeclampsia is a pregnancy-specific disease characterized by hypertension and proteinuria. This disease occurs in ≈3% of pregnant women in developing countries and remains one of the major causes of maternal and neonatal mortality and morbidity throughout the world.[1,2] Although the causes of preeclampsia are not fully understood, infection is considered a main risk factor.[3-6]

Periodontal disease may provide a chronic burden of endotoxin and inflammatory cytokines, and the disease is considered a risk factor of systemic illnesses including cardiovascular disease, atherosclerosis, and cerebrovascular ischemia.[7-12] Because of the similarity between placental vascular damage and atherosclerosis, the potential for chronic oral infection to affect preeclampsia was raised.[13] Thus, Boggess et al.[13] suggested that women with active periodontal disease during pregnancy may have the translocation of oral organisms to the uteroplacental unit, inciting placental inflammation or oxidative stress early in pregnancy, which ultimately produces placental damage and the clinical manifestation of preeclampsia.

Several recent epidemiologic studies[14-18] found that periodontal disease was associated with a higher risk of preeclampsia. One cohort study[13] showed

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that maternal active periodontal disease during pregnancy was associated with an increased risk for the development of preeclampsia. Several case-control studies[14-17] also revealed that there was a significant relationship between active periodontitis detected within 48 hours of delivery or 3 to 28 months postpartum and preeclampsia. In contrast, one case-control study[19] did not identify the association between periodontal disease and preeclampsia. In a meta-analysis, Conde-Agudelo et al.[20] reported that women with evidence of periodontal disease during pregnancy had a 76% increased risk of preeclampsia compared to women without periodontal disease. Although the type of periodontal pathogen, which was more prevalent in preeclampsia, was different among studies,[15,17,21] these same microbiologic studies[15,17,21] showed that the prevalence of specific periodontal pathogens was higher in women with preeclampsia than in women without.

Despite efforts to understand the risk factors for preeclampsia through epidemiologic and microbiologic research in the past decade, there was no consideration of oral health behaviors which might be associated with the periodontal condition in most studies.[13-21] There was one study[19] about the association between periodontal disease and preeclampsia in Asia, even though there can be a difference according to ethnic background.

Therefore, the objectives of this study are: 1) evaluate the association among periodontal disease, oral health behavior, and preeclampsia; and 2) compare the distributions of periodontal pathogens between preeclampsia and control groups.

MATERIALS AND METHODS

Study Design and Patient Sampling

This study is designed as a hospital-based case-control study. An examiner (KHB) and interviewer (JEH) were masked to whether patients had preeclampsia or not for the validity of the examination. Two obstetricians (KJO and HJY), who were masked to the oral health information of the patients, were responsible for the selection and medical history of patients in the study. The study was conducted in compliance with the principles of the Helsinki Declaration. Ethical clearance for the study was approved by the institutional review board of Seoul National University Hospital, Seoul, Korea (IRB number H-0709-046-219).

The study sample included inpatients of the Department of Obstetrics and Gynecology, Seoul National University Hospital. The following are criteria for inclusion in the study: 1) women with ≥20 teeth, 2) aged between 20 to 40 years, and 3) gave birth between November 2007 and January 2010. Only mothers with a single birth and preeclampsia were included in the case group. Preeclampsia was defined as blood pressure >140/90 mm Hg on two separate occasions and ≥1+ proteinuria on a random sample of urine.[13] Control mothers without preeclampsia who gave birth to a full-term, normal weight child were sampled by matching the following conditions with preeclampsia cases: 1) age ± 3 years of the case age; and 2) the same delivery mode (such as vaginal delivery versus a caesarean section). All patients provided written informed consent before participation in the study.

The appropriate sample size for this study was calculated using the power and sample-size calculation program.[22] A dichotomous output of independent cases and controls with three controls per case was modeled to estimate the sample size and detect differences between case and control groups. A type I error probability (α) associated with this test of the null hypothesis was 0.05, and the power ($1-\beta$) associated with correctly rejecting the null hypothesis was 0.8. The probability of exposure in controls (p_0) was 0.3. The odds ratio (OR) for disease in the exposed patients relative to the unexposed patients (ψ) was 4.5.

We obtained a sample size of 19 cases and 57 controls to be able to reject the null hypothesis. Seventy-six mothers were enrolled. Among them, 12 patients (three cases and nine controls) were excluded for systemic conditions such as chronic hypertension, pregestational diabetes, active hepatic disease, and any infectious disease requiring antibiotic treatment. Therefore, the remaining 64 women (16 cases and 48 controls) were included in the study.

The sample size was not sufficiently large enough to reject the null hypothesis. Therefore, we calculated the post hoc power of the study with 16 cases and 48 controls. In general periodontitis, the probability of exposure among controls was 0.104. The true OR for disease in exposed patients relative to unexposed patients was 6.60. When the type I error probability was 0.05, the post hoc power of the study was 0.797. In localized periodontitis, the probability of exposure among controls was 0.167. The true OR for disease in exposed patients relative to unexposed patients was 4.79. When the type I error probability was 0.05, the post hoc power of the study was 0.719.

Demographic and Health Information

A trained interviewer (JEH) asked all patients about information on demographics; health behaviors such as smoking, drinking, and weekly exercise; oral health behaviors such as the experience of scaling and the regular use of floss or an interdental brush; medication; diet; and the experience of oral health treatment before and during pregnancy. Obstetric information such as the history of a preterm birth, abortion, number of pregnancies, the experience of

delivery, the gestational age at delivery, and medical history including preeclampsia were collected by two obstetricians (KJO and HJY) from hospital records.

Measurement of Clinical Periodontal Condition

A periodontal examination was performed by one trained dentist (KHB), who participated four times in the Korean national oral health survey,[23-25] using dental mirrors, periodontal probes,‖ and a headset-type flashlight while the patient rested on a hospital bed within 5 days after delivery. Measurements of periodontal conditions recorded on the full-mouth basis included bleeding on probing (BOP) and periodontal clinical attachment loss (AL) that were determined at six sites (mesio-buccal, mid-buccal, disto-buccal, disto-lingual, mid-lingual, and mesio-lingual surfaces) of all teeth except the third molars and distal sites of second molars. Localized periodontitis was defined as periodontal clinical AL ≥3.5 mm on two or three sites not on the same tooth. In addition, generalized periodontitis was defined as clinical AL ≥3.5 mm on ≥4 sites not on the same tooth. Gingivitis was defined as >25% of sites showing BOP.

Sampling Subgingival Bacteria and Microbial Analyses

A microbacterial examination was performed on selected patients of the study. All 16 case patients were included and one of every three controls was randomly selected per case for sampling subgingival biofilm and gingival crevicular fluid (GCF). At the end of the clinical periodontal examination, the subgingival biofilm and GCF samples were collected together from the mesio-buccal or mesio-lingual gingival surface of two teeth with the deepest probing depths. After supragingival plaque removal and isolation of the sample sites using cotton gauze, four sterilized paper points (#20) were inserted in the gingival sulcus for 20 seconds. The samples were analyzed using a real-time polymerase chain reaction (PCR) kit¶ for the presence of the following periodontal pathogens: *Porphyromonas gingivalis* (*Pg*), *Prevotella intermedia* (*Pi*), *Treponema denticola* (*Td*), and *Tannerella forsythia* (*Tf*).

DNA (1 μL) was mixed with 10 μL reagent and 200 nM of each primer in a total reaction volume of 20 μL. The thermal program chosen was 40 cycles of 95°C for 15 seconds, 58°C for 15 seconds, and 72°C for 33 seconds, with an initial denaturation at 95°C for 1 minute. All data were analyzed using sequenced-detection system software.# Sequences of primers used for real-time PCR were as follows: 5′-TGG AGC ATG TGG TTT AAT TCG A-3′ and 5′-TRY GGS ACT TAA SCC RAC A-3′ for eubacteria, 5′-TGC AAC TTG CCT TAC AGA GGG-3′ and 5′-ACT CGT ATC GCC CGT TAT TC-3′ for *Pg*, 5′-AAT ACC CGA TGT TGT CCA CA-3′ and 5′-TTA GCC GGT CCT TAT TCG AA-3′ for *Pi*, 5′-ATT GAA ATG TAG ACG ACG GAG AGT-3′ and 5′-TTA CCT GTT AGC AAC TGA CAG TCA-3′ for *Tf*, and 5′-TAA TAC CGA ATG TGC TCA TTT ACA T-3′ and 5′-TCA AAG AAG CAT TCC CTC TTC TTC TTA-3′ for *Td*. PCR products were subjected to a melting curve analysis to verify a single amplification product. The copy number of bacterial DNA was calculated with plasmid DNA (pGEM-T) that contained 16S ribosomal DNA for each bacterium (provided by Dr. J.K. Kook, Chosun University, Kwangju, Korea). Plasmid DNA was 10-fold serially diluted from 10^0 to 10^8 copies and subjected to real-time PCR to create a standard curve by plotting threshold cycles against the copy number of the plasmid DNA as previously described.[26] Plasmid standards and subgingival samples were run twice in duplicates, and average values were used to calculate the bacterial load. The detection of DNA $<10^2$ cells was regarded as negative. For a specificity test of primers used, DNA of various oral bacteria was included for real-time PCR, and non-specific amplification was not detected.

Statistical Analyses

The outcome variable was dichotomized into preeclampsia (case group) and non-preeclampsia (control group). The explanatory variables consisted of age, obstetric information, health condition, and health behaviors before and during pregnancy. A comparison between case and control groups for explanatory variables was performed by using the χ^2 test for categorical variables, independent samples *t* test for normally distributed continuous variables, the Mann-Whitney *U* test for abnormally distributed variables, and multivariable logistic regression for the estimation of ORs and 95% confidence intervals (CIs).

Interactions between periodontitis and explanatory variables were assessed before constructing the multivariable logistic regression model. For the multivariable logistic analysis, we used conditional logistic regression while taking matching into consideration. To control for confounders, all variables with $P \leq 0.50$ were selected except matching variables such as age and delivery mode. The effects of selected confounders were investigated by a forward and backward procedure for the final model. All confounders included in the final model were determined to be independent assessing collinearity. Obstetric information (history of preterm birth and abortion), oral health conditions (number of missing teeth), and health behavior (smoking before pregnancy) were finally considered confounders in the conditional logistic regression model. Statistical significance was determined at *P*

‖ UNC PCP-15, Hu-Friedy, Chicago, IL.
¶ QIAamp DNA mini kit, QIAGEN, Venlo, The Netherlands.
# ABI PRISM 7300, Applied Biosystems, Foster City, CA.

Table 1.

Comparison Between Preeclampsia and Control Groups for Distributions of Age, Obstetric Information, and General and Oral Health Conditions (N = 64)

Variables	Preeclampsia (n = 16)	Control (n = 48)	P*
Age (years; mean ± SD [range])†	32.69 ± 5.30 (21 to 40)	32.69 ± 4.40 (21 to 40)	0.999
Obstetric information			
Age at first delivery (years; mean ± SD [range])†	31.27 ± 5.05 (21 to 39)	30.87 ± 4.44 (21 to 38)	0.773
Gestational age at delivery (weeks; mean ± SD [range])†	32.94 ± 3.19 (26 to 36)	38.60 ± 1.06 (37 to 41)	0.001
Number of pregnancies (mean ± SD [range])†	0.84 ± 1.35 (0 to 6)	1.19 ± 1.35 (0 to 5)	0.734
Delivery experience (n [%])			
Yes	7 (43.8)	25 (52.1)	0.774
No	9 (56.3)	23 (47.9)	
History of preterm-birth (n [%])			
Yes	7 (43.8)	3 (6.3)	0.001
No	9 (56.3)	45 (93.8)	
History of abortion (n [%])			
Yes	10 (62.5)	21 (43.8)	0.194
No	6 (37.5)	27 (56.3)	
General health conditions			
Anemia (n [%])‡			
Yes	2 (12.5)	5 (10.4)	0.817
No	14 (87.5)	43 (89.6)	
Oral health conditions			
Number of missing teeth (mean ± SD [range])†	0.81 ± 1.17 (0 to 3)	0.41 ± 0.79 (0 to 4)	0.221
Periodontal condition (n [%])			
Generalized periodontitis (clinical AL ≥3.5 mm on ≥4 teeth)	6 (37.5)	5 (10.4)	0.002
Localized periodontitis (clinical AL ≥3.5 mm on 2 or 3 teeth)	6 (37.5)	8 (16.7)	
Healthy periodontium	4 (25.0)	35 (72.9)	
BOP (n [%])			
≥25% of total sites (gingivitis)	5 (31.3)	14 (29.2)	0.874
<25% of total sites (healthy gingiva)	11 (68.8)	34 (70.8)	

* χ^2 test.
† *t* test.
‡ Hemoglobin concentration <11.0 g/dL.

<0.05. All analyses were performed using a statistical package.**

RESULTS

Table 1 compares demographic, obstetric, general, and oral health conditions between preeclampsia and control groups. The gestational age at delivery was significantly different between preeclampsia and control groups ($P = 0.001$). Preeclampsia cases had a significantly more frequent history of preterm birth ($P = 0.001$). Generalized and localized periodontitis were more prevalent in the preeclampsia group than in the control group ($P = 0.002$). Among health behaviors before pregnancy shown in Table 2, scaling in the last 12 months was higher in controls than in cases ($P = 0.034$). In the control group, 47.9% of patients used floss or an interdental brush regularly for their oral hygiene, whereas the proportion in the case group was only 12.5% ($P = 0.012$). The following adjusting variables were included in multiple logistic regression analysis: obstetric information (history of a preterm birth and abortion), oral health conditions (the number of missing teeth), and health behavior (smoking before pregnancy). In the final model after adjusting for these confounders, generalized periodontitis was significantly associated with preeclampsia, with an adjusted

** PASW, Version 18.0, IBM, Chicago, IL,

Table 2.

Comparison Between Preeclampsia and Control Groups (n [%]) for Distributions of General and Oral Health Behaviors (N = 64)

Variables	Preeclampsia (n = 16)	Control (n = 48)	*P**
Smoking before pregnancy			
Yes	5 (31.3)	7 (14.6)	0.102
No	11 (68.8)	41 (85.4)	
Drinking before pregnancy			
No	9 (56.3)	30 (62.5)	0.685
1 to 2 times/month	6 (37.5)	17 (35.4)	
≥1 to 2 times/week	1 (6.3)	1 (2.1)	
Weekly exercise before pregnancy			
No	8 (50.0)	29 (60.4)	0.455
1 to 2 times	3 (18.8)	11 (22.9)	
≥3 times	5 (31.3)	8 (16.7)	
Scaling within 12 months before pregnancy			
Yes	2 (12.5)	19 (39.6)	0.034
No	14 (87.5)	29 (60.4)	
Scaling during pregnancy			
Yes	2 (12.5)	9 (18.8)	0.442
No	14 (87.5)	39 (81.3)	
Floss or interdental brush			
Regular use (2 or 3 times/week)	2 (12.5)	23 (47.9)	0.012
No	14 (87.5)	25 (52.1)	

* χ^2 test.

Table 3.

Crude and Adjusted ORs and 95% CIs of Preeclampsia With Periodontal Condition and Oral Health Behaviors

Variable	Crude OR (95% CI)	Adjusted OR (95% CI)
Periodontal condition		
Generalized periodontitis (clinical AL ≥3.5 mm on ≥4 teeth)	7.47 (1.33 to 41.94)	6.60 (1.25 to 41.61)
Localized periodontitis (clinical AL ≥3.5 mm on 2 or 3 teeth)	5.45 (1.06 to 28.56)	4.79 (1.02 to 29.72)
Scaling within 12 months before pregnancy (no = 0; yes = 1)	0.21 (0.04 to 0.98)	0.31 (0.03 to 1.31)
Floss or interdental brush (no = 0; regular use = 1)	0.15 (0.03 to 0.85)	0.21 (0.02 to 0.93)

Model was adjusted for the history of preterm birth, history of abortion, number of missing teeth, and smoking before pregnancy.

OR of 6.60 and 95% CI of 1.25 to 41.61 (Table 3). Localized periodontitis was also significantly associated with preeclampsia with an adjusted OR of 4.79 and 95% CI of 1.02 to 29.72. The regular use of floss or an interdental brush (adjusted OR: 0.21; 95% CI: 0.02 to 0.93) was significantly associated with preeclampsia.

Differences in the microbacterial distribution between preeclampsia and control groups are presented in Table 4. Only *Pi* showed a significant difference between case and control groups ($P = 0.028$). In addition, *Pg* was more prevalent in the preeclampsia group than in the control group, but the difference was not significant ($P = 0.056$). The other microbial pathogens *Td* and *Tf* were not significantly different in the comparison.

DISCUSSION

This case-control study was conducted to evaluate the association between periodontal disease and preeclampsia considering the oral health behaviors of patients. Our results show that periodontal disease measured by the presence of periodontal clinical AL ≥3.5 mm on two or three teeth (as localized periodontitis) or ≥4 teeth (as generalized periodontitis) was associated with an increased risk of preeclampsia. Patients who had generalized periodontitis were nearly six times more likely to have preeclampsia, and patients who had localized periodontitis were nearly five times more likely to have preeclampsia (Table 3). These results are consistent with previous findings. Canakci et al.[14] carried out a matched case-control study in 41 women with preeclampsia and 41 control women who were matched with each other for age, parity, and smoking. The results of that study[14] showed that periodontal disease during pregnancy was associated with preeclampsia (adjusted OR: 3.47; 95% CI: 1.07 to 11.95) after adjustment for maternal body weight, serum triglyceride level, and serum cholesterol level in the analysis. In addition, Kunnen et al.[17] confirmed that women with early onset preeclampsia had a more severe periodontal condition than did control women, taking into consideration the effects of age, smoking, educational level, and body mass index (adjusted OR: 7.9). However,

Table 4.

Differences (colony forming units) in Microbacterial Distribution Between Preeclampsia and Control Groups (n = 32)

	Preeclampsia (n = 16)			Control (n = 16)			
Microbacterial Factors	25%	50%	75%	25%	50%	75%	*P**
Td	0	15,128.0	95,375.1	0	2,591.9	85,998.1	0.985
Pg	0	69,190.6	357,325.9	0	0	545.7	0.056
Pi	0	3,576.9	29,519.4	0	0	2,123.1	0.028
Tf	0	0	158,481.1	0	0	226.7	0.251

* Mann-Whitney *U* test for non-parametric distribution (25%, 50%, and 75%).

a study by Khader et al.[19] in Jordan showed that there was no significant association between preeclampsia and periodontal disease after adjustment for potential confounders such as age at delivery, prepregnancy body mass index, history of preeclampsia, family history of cardiovascular disease, and family history of preeclampsia. Differences among previous studies[14,17,19] could have been caused by study designs, sample sizes, control-matching variables, and, especially, the definition of periodontal disease.

Nevertheless, Siqueira et al.[18] revealed that the extent and severity of periodontal parameters were strongly related to the occurrence of preeclampsia. Contreras et al.[15] also found that mothers with preeclampsia had a higher risk of periodontal destruction. In our study, the extent of periodontitis (clinical AL ≥3.5 mm on two, three, or ≥4 teeth), was associated with an increased risk of preeclampsia. The adjusted OR of generalized periodontitis was higher than that of localized periodontitis. Thus, the extent and severity of periodontal disease may significantly affect the chronic burden of endotoxin and inflammatory cytokines, which serve to initiate and exacerbate preeclampsia.

Boggess et al.[13] suggested that women with active periodontal disease during pregnancy may have the translocation of periopathogenic bacteria to the uteroplacental unit, which ultimately produces placental damage and preeclampsia. One epidemiologic study[15] revealed that periodontal pathogens such as *Pg* and *Tf* were significantly more prevalent in the subgingival plaque of a preeclampsia group than in the control group. Kunnen et al.[17] also reported that *Parvimonas micra*, which is known as a bacterial marker of destructive periodontitis, was more prevalent in GCF of preeclamptic women. Barak et al.[21] revealed that the bacterial counts of *Aggregatibacter actinomycetemcomitans*, *Fusobacterium nucleatum*, *Pg*, *Pi*, *Tf*, and *Td*, which are considered major periodontal pathogens, were statistically significantly higher in placentas of women with preeclampsia than in the control group. However, among periodontal pathogens in our study, only *Pi* showed a significant difference between case and control groups, and the prevalence of *Pg* was higher in the preeclampsia group than in the control group, but the difference was not significant (Table 4). Our results are consistent with the study of Raber-Durlacher et al.,[27] which showed that the mean proportion of *Pi* in the subgingival biofilm increased in experimental gingivitis during pregnancy. According to our results as well as previous results,[15,17,21,27] periodontal pathogens such as *Pi* were detected in periodontal and placental tissues, and there was a potential for the translocation of periopathogenic bacteria to the uteroplacental unit.

With regard to the association between periodontal disease/pathogen and preeclampsia, some studies[13,17] suggested that the treatment of periodontal disease during pregnancy may represent a novel approach to the prevention of preeclampsia. However, a randomized controlled trial in Western Australia revealed that there was no difference between the control and treatment of periodontitis groups in preeclampsia (OR: 0.82; 95% CI: 0.44 to 1.56).[28] In the multivariable logistic regression analysis in our study, the regular use of floss or an interdental brush showed a significant correlation with a decreased risk of preeclampsia. Therefore, according to our results, oral health behaviors before pregnancy such as interdental plaque control, which can decrease the level of a periodontal pathogen,[29] may be more important as a new approach to prevent preeclampsia than the treatment of periodontal disease during pregnancy.

This study may have some limitations. The plaque status, which can be more of an objective factor than the variable of interdental cleaning to estimate the level of plaque-induced periodontal infection, was not investigated. The socioeconomic status, which may be associated with the prevalence of periodontal disease and preeclampsia, was not also considered a confounder. Although our study presents the meaningful

results without these confounders, there was a marginal contribution to the understanding of association between periodontitis and preeclampsia. If unmeasured confounders were included in our final model, the marginal difference may have been changed to insignificant. There was also another shortcoming: a post hoc power (0.797 for generalized periodontitis and 0.719 for localized periodontitis) <0.8 because some patients were later excluded. Therefore, additional epidemiologic research with a large sample including possible confounders will be needed to confirm the clear association between the periodontal condition and onset of preeclampsia. Also, the present study may have some bias, such as a selection bias, in the control sampling and a recall bias in interviewing or questioning as in other case-control studies, even though it was strengthened by the one examiner–masked design. Because the selection bias in control sampling was minimized by matching controls to cases, the influence on results was not significant. A recall bias in the questionnaire about health behaviors before pregnancy may have occurred. However, the influence of the recall bias could be ignored because health behaviors before pregnancy except smoking were not inserted into the final model as confounders. Because the experience of smoking before pregnancy was investigated as a dichotomous output (yes or no), there was no recall bias of smoking.

This study was worthwhile because studies on the association between the periodontal condition and preeclampsia with matched cases and controls have been relatively rare in Asian countries. Because preeclampsia and periodontal disease may share common risk factors such as socioeconomic status, genetics, and health behaviors, more comprehensive cohort studies and randomized controlled clinical trials are needed to determine whether the relationship between periodontal disease and preeclampsia is causal or simply associative.

CONCLUSION

These results indicate that preeclampsia may be associated with the maternal periodontal condition and interdental cleaning.

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REFERENCES

1. Villar J, Say L, Shennan A, et al. Methodological and technical issues related to the diagnosis, screening, prevention, and treatment of pre-eclampsia and eclampsia. *Int J Gynaecol Obstet* 2004;85(Suppl. 1):S28-S41.
2. Dolea C, AbouZahr C. Global burden of hypertensive disorders of pregnancy in the year 2000. Global Burden of Disease Working Paper. 2003. Available at: http://www.who.int/healthinfo/statistics/bod_hypertensivedisordersofpregnancy.pdf. Accessed August 3, 2010.
3. von Dadelszen P, Magee LA. Could an infectious trigger explain the differential maternal response to the shared placental pathology of preeclampsia and normotensive intrauterine growth restriction? *Acta Obstet Gynecol Scand* 2002;81:642-648.
4. Trogstad LIS, Eskild A, Bruu AL, Jeansson S, Jenum PA. Is preeclampsia an infectious disease? *Acta Obstet Gynecol Scand* 2001;80:1036-1038.
5. Odegård RA, Vatten LJ, Nilsen ST, Salvesen KA, Austgulen R. Preeclampsia and fetal growth. *Obstet Gynecol* 2000;96:950-955.
6. Walker JJ. Pre-eclampsia. *Lancet* 2000;356:1260-1265.
7. Seymour GJ, Ford PJ, Cullinan MP, Leishman S, Yamazaki K. Relationship between periodontal infections and systemic disease. *Clin Microbiol Infect* 2007;13(Suppl. 4):3-10.
8. Beck JD, Garcia R, Heiss G, Vokonas PS, Offenbacher S. Periodontal disease and cardiovascular disease. *J Periodontol* 1996;67(Suppl. 10):1123-1137.
9. Hung HC, Willett W, Merchant A, Rosner BA, Ascherio A, Joshipura KJ. Oral health and peripheral arterial disease. *Circulation* 2003;107:1152-1157.
10. Janket SJ, Baird AE, Chuang SK, Jones JA. Meta-analysis of periodontal disease and risk of coronary heart disease and stroke. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003;95:559-569.
11. Mealey BL, Oates TW; American Academy of Periodontology. Diabetes mellitus and periodontal diseases. *J Periodontol* 2006;77:1289-1303.
12. Khader Y, Khassawneh B, Obeidat B, et al. Periodontal status of patients with metabolic syndrome compared to those without metabolic syndrome. *J Periodontol* 2008;79:2048-2053.
13. Boggess KA, Lieff S, Murtha AP, Moss K, Beck J, Offenbacher S. Maternal periodontal disease is associated with an increased risk for preeclampsia. *Obstet Gynecol* 2003;101:227-231.
14. Canakci V, Canakci CF, Canakci H, et al. Periodontal disease as a risk factor for pre-eclampsia: A case control study. *Aust N Z J Obstet Gynaecol* 2004;44:568-573.
15. Contreras A, Herrera JA, Soto JE, Arce RM, Jaramillo A, Botero JE. Periodontitis is associated with preeclampsia in pregnant women. *J Periodontol* 2006;77:182-188.
16. Cota LO, Guimarães AN, Costa JE, Lorentz TC, Costa FO. Association between maternal periodontitis and an increased risk of preeclampsia. *J Periodontol* 2006;77:2063-2069.
17. Kunnen A, Blaauw J, van Doormaal JJ, et al. Women with a recent history of early-onset pre-eclampsia have a worse periodontal condition. *J Clin Periodontol* 2007;34:202-207.
18. Siqueira FM, Cota LO, Costa JE, Haddad JP, Lana AM, Costa FO. Maternal periodontitis as a potential risk variable for preeclampsia: A case-control study. *J Periodontol* 2008;79:207-215.
19. Khader YS, Jibreal M, Al-Omiri M, Amarin Z. Lack of association between periodontal parameters and preeclampsia. *J Periodontol* 2006;77:1681-1687.

20. Conde-Agudelo A, Villar J, Lindheimer M. Maternal infection and risk of preeclampsia: Systematic review and metaanalysis. *Am J Obstet Gynecol* 2008;198:7-22.
21. Barak S, Oettinger-Barak O, Machtei EE, Sprecher H, Ohel G. Evidence of periopathogenic microorganisms in placentas of women with preeclampsia. *J Periodontol* 2007;78:670-676.
22. Dupont WD, Plummer WD Jr. Power and sample size calculations. A review and computer program. *Control Clin Trials* 1990;11:116-128.
23. Ministry of Health and Welfare Affairs. 2000 Korea National Oral Health Survey. In: *National Oral Health Survey*. Seoul: Ministry of Health Welfare and Family Affairs; 2001:40.
24. Ministry of Health and Welfare Affairs. 2006 Korea National Oral Health Survey. In: *National Oral Health Survey*. Seoul: Ministry of Health Welfare and Family Affairs; 2007:16.
25. Ministry of Health and Welfare Affairs. 2010 Korea National Oral Health Survey. In: *National Oral Health Survey*. Seoul: Ministry of Health Welfare and Family Affairs; 2011:19.
26. Nonnenmacher C, Dalpke A, Mutters R, Heeg K. Quantitative detection of periodontopathogens by real-time PCR. *J Microbiol Methods* 2004;59:117-125.
27. Raber-Durlacher JE, van Steenbergen TJ, Van der Velden U, de Graaff J, Abraham-Inpijn L. Experimental gingivitis during pregnancy and post-partum: Clinical, endocrinological, and microbiological aspects. *J Clin Periodontol* 1994;21:549-558.
28. Newnham JP, Newnham IA, Ball CM, et al. Treatment of periodontal disease during pregnancy: A randomized controlled trial. *Obstet Gynecol* 2009;114:1239-1248.
29. Corby PM, Biesbrock A, Bartizek R, et al. Treatment outcomes of dental flossing in twins: Molecular analysis of the interproximal microflora. *J Periodontol* 2008; 79:1426-1433.

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