

## Periodontal Disease as a Risk Factor for Preeclampsia

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**Background:** Preeclampsia is a unique idiopathic syndrome in human pregnancy that can involve almost all organ systems.

**Objectives:** The aim of the present study was to compare the periodontal diseases between the preeclamptic and normal pregnant women in order to find a possible risk factor relationship.

**Materials and Methods:** This case-control study was performed on 200 pregnant women, with maternal age  $\leq 35$  years and gestational age  $> 20$  weeks with singleton pregnancies. Of these, 100 women were preeclamptic with proteinuria and blood pressure  $\geq 140/90$  and 100 women with normal blood pressure in the control group. Oral examination was performed on all women by a dentist for detection of periodontal diseases. Gingivitis and periodontitis were diagnosed based on the American Academy of Periodontology (AAP)/American Dental Association (ADA) classification, using the measurement method of Ramfjord. The preeclamptic women were then sub-classified into mild and moderate and comparisons were made between all groups.

**Results:** The mean maternal age, BMI, neonatal birth weights and gestational age at delivery were not significantly different between the preeclamptic and normal groups. There was a significant association between preeclampsia and periodontal diseases ( $P < 0.01$ ). The mean number of involved teeth ( $P < 0.001$ ) and the mean pocket depth ( $P = 0.04$ ) were higher among the preeclamptic group. Gingivitis was more frequent among the cases with mild (56.8%) compared to (31.6%) in the severe preeclamptic group ( $P = 0.04$ ). Periodontitis was more prevalent among the cases with severe preeclampsia which was not statistically significant. The mean neonatal birth weight was significantly lower in the group with severe preeclampsia ( $P < 0.01$ ).

**Conclusions:** There was a significant association between preeclampsia and periodontal diseases. The number of involved teeth and pocket depth were higher among the preeclamptic mothers compared to normal pregnant women.

**Keywords:** Preeclampsia; Periodontal diseases; Gingivitis; Periodontitis; Low birth weight

### 1. Background

Preeclampsia is a unique idiopathic syndrome in human pregnancy that can involve almost all organ systems. Hypertensive disorders affect 5-10% of all pregnancies. However, preeclampsia syndrome is diagnosed in 3.9% of these women (1, 2). Hypertension during pregnancy is defined when blood pressure is  $\geq 140/90$  and preeclampsia syndrome is diagnosed when proteinuria as a specific sign of endothelial leakage is also added to the high blood pressure.

In the developed countries 16% of maternal deaths follow hypertensive disorders of pregnancy which is one of the deadly triad in obstetrics along with hemorrhage and infection (3). The rate is higher in the developing countries. In the analysis of maternal deaths published by World Health Organization (WHO) in 2006 hemorrhage was reported to be the leading cause of death in Africa and Asia but hypertensive disorders were the most common cause of death in Latin America and Caribbean that

accounted for 25.7% of the maternal deaths (4).

Although the etiology of preeclampsia is not well known, the syndrome is considered as a two-stage disease. The early stage is characterized by poor placental invasion and inappropriate development of placenta and the late stage is due to placental oxidative stress. Abnormal trophoblastic invasion, abnormal immunological tolerance between mother and the fetus, maternal maladaptation to the needed physiologic cardiovascular and inflammatory changes of pregnancy and genetic factors are considered as important pathophysiological factors for preeclampsia syndrome (1).

On the other hand periodontal diseases are the disorders that affect the surrounding and supporting tissues of the teeth. The American Dental Association (ADA) and American Academy of Periodontology (AAP) clinically classified the periodontal diseases. In this context, type I periodontal diseases are categorized as gingivitis and

#### Implication for health policy/practice/research/medical education:

Implications for general health policy, possibility for prevention of preeclampsia by good oral health, practice and management of pregnant women and also for medical education

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type II, III and IV are classified as early, moderate and advanced periodontitis respectively (5).

Gingivitis is caused by bacterial plaque and induces redness, swelling and bleeding of gingiva. If the inflammation extends deeper periodontitis develops. Periodontitis with destruction of the supporting tissues of the teeth and formation of soft tissue pockets and extension to the alveolar bone leads to tooth mobility and loss in the late stages of the disease (6).

The clinical finding that differentiates gingivitis from periodontitis is the presence of attachment loss that is often associated with pocket formation and subjacent alveolar bone changes. Periodontitis is usually evaluated in clinical studies by measurement of the mean probing dept, attachment loss and recession level. The grading of the severity is based on the degree of attachment loss (5).

The world-wide prevalence of moderate to severe periodontitis in most populations is reported to be about 15-20% (7). Periodontal disease as a chronic Gram-negative anaerobic inflammation has been recently considered to trigger unwanted effects during pregnancy. Periodontal disease may induce both local and systemic inflammation. It can promote local tissue damage produced by the bacterial plaque infection and also indirectly by activation of the host immune system (8).

It is hypothesized that the immunologic reaction that is induced following the inflammation caused by periodontal disease may contribute to the development of preeclampsia syndrome. There are few published studies on this topic. However, some of them suggested an increased risk of preeclampsia in the women with periodontal disease but there are also reports against the idea (9-11).

## 2. Objectives

The present study was carried out to compare the incidence of periodontal diseases in the preeclamptic and normal pregnant women. It also sub-classified the patients with preeclampsia into mild and severe forms and compared them for periodontal diseases, their gestational age at the time of delivery and the neonatal birth weight.

## 3. Material and Methods

This case-control study was performed on mothers aged less than 35 years, with gestational ages of more than 20 weeks, singleton pregnancies and a fetus without congenital anomaly. They had no history of previous hypertension or other clinical diseases. The mothers were observed during their pregnancy for presence of preeclampsia symptoms and maximum blood pressure (BP). The case group included 100 women with blood pressure  $\geq 140/90$  and 24-hour urine protein excretion  $> 300$  mg or persistent dipstick urine protein  $\geq 1+$  in random samples. The control group comprised 100 women without

high blood pressure or proteinuria. All subjects signed an informed consent form and were examined by a dentist for detection of periodontal diseases upon entering the study. Gingivitis and periodontitis were diagnosed based on the AAP/ADA classification, using the measurement method of Ramfjord by a calibrated periodontal probe (5). Gingivitis was indicated by redness, swelling and probably bleeding of the gingiva. Gingival recession was measured from the cement-enamel junction to the gingival margin. Probing dept was measured from the gingival margin to the base of the periodontal pocket. Clinical attachment loss was calculated by the addition of gingival recession and periodontal pocket (7).

The fetal weight and gestational age at delivery were also evaluated. The association of gingivitis, periodontitis and periodontal disease were compared and analyzed among the groups.

The women in the preeclamptic group were then sub-classified into mild and severe forms of preeclampsia according to the published criteria (12). There were 19 women with the signs and symptoms of severe preeclampsia and 81 women in the mild group. The variables were also compared between these two groups.

This project was approved by the Institutional Review Board and the Ethics Committee of Shiraz University of Medical Sciences. Statistical analyses were performed by SPSS software (Version 15, Chicago, IL, USA). Chi-Square test was used for comparison of proportions that were presented as number (%) and independent sample t test was used for comparison of means. Statistical significance was considered as  $P < 0.05$ .

## 4. Results

Twohundred pregnant women entered the study, of which 100 had preeclampsia and 100 women had normal pregnancies. The mean maternal age was  $26.72 \pm 4.6$  in the preeclamptic and  $26.24 \pm 4.1$  in the normal group. The mean BMI and mean gravid number were not significantly different between two groups. Periodontal disease was more frequently seen in the preeclamptic group ( $P < 0.01$ ). The number of involved teeth was significantly higher among the preeclamptic group ( $P < 0.001$ ). Periodontal pocket dept was significantly more in the preeclamptic group  $4.35 \pm 1.1$  vs  $4.01 \pm 1.23$  mm ( $P = 0.04$ ). Although the rates of gingivitis and periodontitis, measured separately, were higher in the preeclamptic group, they did not reach a statistically significant value. As shown in Table 1, neonatal birth weight and gestational age at delivery were not significantly different between the two groups.

The preeclamptic women were sub-classified into the mild and severe forms and the corresponding variables were also compared between them. There were 19 and 81 women with severe and mild signs and symptoms of preeclampsia respectively (Table 2).

Gingivitis was more frequently seen among the cases

with mild preeclampsia 46 (56.8%) compared to 6 (31.6%) in the severe group ( $P = 0.04$ ). Periodontitis was more prevalent among the cases with severe preeclampsia, but it did not reach the statistically significant level. Periodontal diseases as the summation of gingivitis and periodontitis were more frequent in the mild group without any statistically significant difference found between them. The mean neonatal birth weight was significantly lower in the severe group of preeclampsia ( $P < 0.01$ ). No other significant difference was found between the groups with mild and severe preeclampsia.

The mean neonatal birth weights were compared between the women with normal oral examination (40

women) and those who had periodontal disease (160 cases), without any statistically significant difference found between them ( $P = 0.546$ ).

### 5. Discussion

Preeclampsia as a member of the deadly triad with unknown etiology attracted great attention in experimental studies. However despite considerable efforts made to clarify the cause and effect, the exact responsible etiologic pathway has not yet been identified. It is a fact that after expulsion of placenta and termination of pregnancy the preeclampsia symptoms regress. So it is concluded

**Table 1.** Comparison of Demographic, Oral and Neonatal Findings in the Preeclamptic and Normal Pregnant Women

Variable *	Preeclamptic, N = 100	Normal, N = 100	P Value
Maternal age, year	26.72 ± 4.61	26.24 ± 4.13	0.439
BMI	24.03 ± 3.72	23.30 ± 3.50	0.155
Gravida, No.	1.96 ± 0.931	2.01 ± 0.882	0.697
Teeth involved, No.	3.64 ± 1.81	2.70 ± 2.05	0.001
Periodontal pocket dept, mm	4.34 ± 1.09	4.01 ± 1.23	0.044
Gingival Recession, mm	0.13 ± 0.47	0.11 ± 0.47	0.702
Clinical attachment loss, mm	1.89 ± 2.69	1.41 ± 2.55	0.196
Women with Normal oral exam	13 (13%)	27 (27%)	0.01
Women with Gingivitis	52 (52%)	48 (48%)	0.336
Women with Periodontitis	35 (35%)	25 (25%)	0.082
Women with Periodontal disease	87 (87%)	73 (73%)	0.01
Gestational age at delivery, weeks	37.50 ± 2.27	37.81 ± 2.68	0.379
Neonatal birth weight, gr	2884.50 ± 563.65	2960.40 ± 635.60	0.373

\* The values are presented as mean ± SD or No. (%)

**Table 2.** Comparison of the Parturients with Severe and Mild Preeclampsia for their Demographic, oral and Neonatal Findings

Variable *	Severe Preeclampsia, N = 19	Mild Preeclampsia, N = 81	P Value
Maternal age, year	27.47 ± 4.37	26.54 ± 4.67	0.431
BMI	24.89 ± 4.64	23.83 ± 3.48	0.356
Gravida, No.	1.95 ± 0.84	1.96 ± 0.95	0.948
Maximum systolic blood pressure, mmHg	164.47 ± 10.39	144.26 ± 5.19	0.000
Teeth involved, No.	3.32 ± 2.02	3.72 ± 1.76	0.389
Dept of periodontal pocket, mm	4.1937 ± 1.18	4.3842 ± 1.07	0.497
Gingival recession, mm	0.13 ± 0.59	0.12 ± 0.44	0.953
Clinical attachment loss, mm	2.52 ± 2.91	1.74 ± 2.63	0.262
Patients with normal oral exam	4 (21.1%)	9 (11.1%)	0.263
Patients with Gingivitis	6 (31.6%)	46 (56.8%)	0.048
Patients with Periodontitis	9 (47.4%)	26 (32.1%)	0.209
Patients with Periodontal disease	15 (78.9%)	72 (88.9%)	0.246
Gestational age at delivery, weeks	36.68 ± 3.87	37.69 ± 1.68	0.281
Neonatal birth weight, gr	2610.53 ± 864.35	2948.77 ± 450.62	0.018

\* The values are presented as Mean ± SD or No. (%)

that the abnormal placenta plays an important role in the pathogenesis. Among the pathogenetic theories the immunogenic and inflammatory hypothesis has gained more acceptability. In fact preeclampsia starts early during pregnancy and gradually worsens in its spectrum of severity with vascular spasm and generalized endothelial cell dysfunction. The hallmark of endothelial dysfunction is the leakage of protein from renal glomeruli and proteinuria.

The responsible factor or factors triggering the immunogenic cascade that leads to preeclampsia syndrome is not exactly known. Although, multiple genetic, nutritional, environmental and infectious entities may lead to the final common pathway. Even acute primary viral infections during pregnancy are suggested to play a role in the pathogenesis of preeclampsia among the seronegative women (13).

In the present study we found a significant association between preeclampsia and periodontal diseases. The number of involved teeth and pocket depth were significantly higher among the preeclamptic mothers compared to normal pregnant women. Therefore, this suggests a possible relationship of risk factor to disease development. Regarding the fact that pathogenesis of preeclampsia and periodontal diseases are both complex and multifactorial, we believe that periodontal disease may help the development of the preeclamptic syndrome.

The possible relationship between periodontal infection and preterm birth was first reported in 1996 (14). Since then, the idea that periodontal disease may have adverse effects on pregnancy induced several researchers to investigate the association between periodontal diseases and preterm birth, low birth weight, and preeclampsia (15, 16).

It is hypothesized that periodontal disease triggers serial pathologic and immunologic reactions that may help preeclampsia syndrome to develop. Several mechanisms have been suggested to explain the possible relationship between preeclampsia and periodontal diseases. These include movement of the periodontal microorganisms to the placenta, effect of the endotoxins produced in the periodontal pockets on the placenta or action of the other inflammatory mediators such as interleukins (ILs), tumor necrotizing factor (TNF), prostaglandins (PGs) or increasing cytokines on the fetoplacental unit (17).

In this study we examined the women's dental status by an experienced dentist for detection of periodontal diseases, and found that periodontal diseases were more frequent among the preeclamptic group compared to the normal pregnant women. There are several studies that reported similar result (9, 18, 19). These studies support the inflammatory model of preeclampsia with an indirect infectious trigger leading to acute atherosclerosis in preeclampsia and subsequent chronic atherosclerosis and development of cardiovascular disease (20).

Also, the association between periodontal disease and several disorders including cardiovascular disease, osteoporosis, diabetes and respiratory infections has been investigated (6). Periodontal disease is reported to be associated with atherosclerotic thromboemboly and hypercholesterolemia. It is suggested that the production of chronic endotoxins and cytokines may induce atherogenesis and thrombogenesis in the placenta which leads to fetal growth restriction in a preeclamptic mother (21).

In our research the cases with mild and severe preeclampsia were compared in relation to periodontal diseases. The results showed that periodontitis was more frequently seen among the cases with severe than in the women with mild preeclampsia, but the difference was not statistically significant. In contrast, gingivitis was more frequent in women having mild than in the cases with severe preeclampsia, and the difference was statistically significant ( $P = 0.04$ ). In this study periodontal disease as a combination of gingivitis and periodontitis was more frequently observed among the cases with mild preeclampsia compared to the severe form. However, a positive association was found between severity of preeclampsia and the intensity of periodontal disease in a recent study (18). Ruma et al. reported that the risk of preeclampsia was increased with the severity of periodontal disease and C-reactive protein  $\geq 75^{\text{th}}$  percentile being an indicator of maternal systemic inflammation (22). Accepting a causal relationship, logically the more severe the periodontal disease the more profound the immunogenic reactions which lead to a more severe form of preeclampsia. However, our results were not consistent with this assumption, and the reason may be due to our small sample size in the severe group (19 cases) or it may be related to the activation and remission-phases of periodontal diseases. A recent meta-analysis performed to evaluate the relationship between periodontal disease and preterm birth pointed to a likely association which needs to be confirmed by further studies (16). Our study did not show a significant difference in gestational age at delivery or neonatal birth weight between the normal and preeclamptic groups. However, we think that our small sample size of 200 with only 19 cases in the severe preeclamptic group may not be enough to arrive at a definite conclusion.

There are several reports concluding that periodontal disease may be associated with increased risk of adverse pregnancy outcomes or other systemic diseases but there are inconsistencies regarding the results of these studies. It seems that large, randomized controlled clinical trials are needed to confirm such relationships (23, 24). Recently a meta-analysis also concluded that there is a significant correlation between preeclampsia and periodontal diseases (odds ratio = 2.79 and 95% CI: 2.01-3.01) but the idea still warrants further studies to evaluate the biologic causal mechanisms (25).

Despite lack of convincing evidence to confirm the caus-

al relationship between periodontal disease and adverse pregnancy outcomes, the prevention and management of periodontal diseases should be among the priorities in public health planning and programs. We believe that for the general population and the pregnant women in particular, educational and screening programs should be implemented by health care providers to achieve a good public oral health.

There is a significant association between preeclampsia and periodontal diseases. The number of involved teeth and pocket depth were significantly higher among the preeclamptic mothers compared to normal pregnant women, indicating a possible risk factor relationship.

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### Authors' Contribution

All of the authors contributed in the study design, performing the study, data analysis and writing the manuscript.

### Financial Disclosure

There is no conflict of interest.

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