

Evaluation of the Association Between Maternal Periodontal Health and Preeclampsia

R. Shariatmadar Ahmadi ¹, A. Lor ², F. Sayar ³, M. Kashanian ⁴, S. Hajisadeghi ⁵✉.

¹ Assistant Professor, Department of Periodontology, Dental Branch, Islamic Azad University, Tehran, Iran

² Dentist, Private Office, Tehran, Iran

³ Associate Professor, Department of Periodontology, Dental Branch, Islamic Azad University, Tehran, Iran

⁴ Professor, Department of Obstetrics and Gynecology, Akbarabadi Teaching Hospital, Tehran University of Medical Sciences, Tehran, Iran

⁵ Assistant Professor, Dental and Oral Research Center, Department of Oral and Maxillofacial Medicine, School of Dentistry, Qom University of Medical Sciences, Qom, Iran

Abstract

Background and Aim: Preeclampsia is a considerable complication of pregnancy. Chronic inflammations such as periodontitis may lead to a transient low-grade bacteremia in the maternal-fetal circulation, inducing systemic immune responses, placental abnormalities, and other clinical manifestations of preeclampsia. There are inconsistent findings regarding the correlation between periodontitis and preeclampsia. The aim of this study was to compare periodontal parameters in preeclamptic and normotensive pregnant women.

Materials and Methods: This case-control study was conducted among pregnant women visiting Akbarabadi Teaching Hospital, Tehran, Iran, for specialized care during 2015-16. From among 260 pregnant women, 100 with gestational hypertension were selected as the case group, and 100 without gestational hypertension were recruited as the control group. The examined periodontal parameters included Probing Depth (PD), Clinical Attachment Loss (CAL), Bleeding on Probing (BOP), and Plaque Control Record (PCR). The participants' demographic data, prenatal history, and family history were collected through interviewing and assessing their medical records. Data were analyzed by Mann-Whitney U test.

Results: Although there were significant statistical differences between the groups with regards to the mean \pm standard deviation (SD) of PD ($P < 0.0001$), CAL ($P < 0.0001$), PCR ($P = 0.001$), and BOP ($P = 0.016$) indices, yet the differences were clinically smaller than 0.3 mm and could not be measured with a periodontal probe. Also, the percentage of periodontal diseases was 98% in preeclamptic women and 93% in normotensive women ($P = 0.17$).

Conclusion: The present study did not support the theory of the relationship between periodontal parameters and preeclampsia.

Key Words: Periodontal Diseases, Pre-Eclampsia, Pregnancy

✉ Corresponding author:
S. Hajisadeghi, Assistant
Professor, Dental and Oral
Research Center, Department of
Oral and Maxillofacial Medicine,
School of Dentistry, Qom
University of Medical Sciences,
Qom, Iran

hajisadeghi@dnt.mui.ac.ir

Received: 12 Oct 2017

Accepted: 12 March 2018

➤ **Cite this article as:** Shariatmadar Ahmadi R, Lor A, Sayar F, Kashanian M, Hajisadeghi S. Evaluation of the Association Between Maternal Periodontal Health and Preeclampsia. J Islam Dent Assoc Iran. 2018; 30(2):58-65. DOI: 10.30699/JIsdreir.30.2.58

Introduction

Periodontal diseases are one of the most common chronic infectious disorders in human beings. Their prevalence varies between 35% and 60% in

adults. Periodontitis affects about 20% to $\leq 50\%$ of pregnant women [1]. New evidence indicates an association between periodontal diseases and increased risk of systemic diseases such as

atherosclerosis, myocardial infarction, stroke, diabetes mellitus, and adverse pregnancy outcomes such as premature birth, low birth weight, miscarriage, and preeclampsia [2,3].

The American College of Obstetricians and Gynecologists (ACOG) has defined preeclampsia as blood pressure $>140/90$ mmHg and/or $\geq 1+$ proteinuria on a catheterized urine specimen [4]. Preeclampsia is a common pregnancy complication, affecting 7% to 10% of pregnant women, and it has remained one of the two leading causes of maternal mortality worldwide [5,6]. The exact etiologies and pathogeneses of these outcomes are still elusive, but a comprehensive systemic inflammatory response during pregnancy may play a role in the development of preeclampsia [7]. In previous studies, a relationship between preeclampsia and inflammation has been suggested [8,9]. Periodontal disease is one of the most common chronic infectious disorders [10]. Periodontitis, as a chronic inflammatory disease, is a risk factor for adverse pregnancy outcomes, and since it is preventable and curable, it is of great public health importance [11].

According to several studies, periodontal disease parameters such as Probing Depth (PD), Clinical Attachment Loss (CAL), and Bleeding on Probing (BOP) in women are highly linked with high blood pressure, and it is possible that maternal periodontal disease is associated with increased risk of preeclampsia [12-14]. However, some researchers have ruled out any correlation between periodontal disease parameters and blood pressure [15-17]. Because of this contradiction, the present study has been conducted to examine the association between periodontitis and preeclampsia in an Iranian population.

Materials and Methods

Study population:

This case-control study was conducted at Akbarabadi Teaching Hospital, Tehran, Iran and has been approved by the Ethics Committee of the Dental Branch of Islamic Azad University, Tehran, Iran (ethical code:24358/1394). The participants were informed about the aims of the study, and they signed a written informed consent form. The study's statistical population included

pregnant women who were admitted to the Obstetrics Department of Akbarabadi Teaching Hospital for their routine pregnancy visit between May 2015 and December 2016. Sample size estimation with PASS software (version 6.0; NCSS, LLC, Kaysville, Utah, USA) indicated that 95 patients were needed to attain 95% statistical power. Because of the risk of dropping subjects, 260 patients participated in the study. Women who had: 1) ≥ 18 years of age, 2) at least 15 teeth, and 3) gestational age between 25 and 28 weeks were eligible for enrollment. Women were excluded from the study if they: 1) were multiparous, 2) had infection during pregnancy, 3) had a history of any systemic disease such as diabetes, 4) had hypertension before pregnancy, 5) had consumed calcium channel blockers for more than three months, 6) were smokers, 7) had consumed antibiotics in the past three months, or 8) had received periodontal treatment in the past six months. According to the mentioned criteria, 60 women were excluded from the study.

According to the ACOG criteria, women were diagnosed with preeclampsia if they had blood pressure $\geq 140/90$ mmHg after 20 weeks of gestation with $+1$ proteinuria in the urine sample [4,13]. All of the women received information about the purpose of the study and provided an informed consent at the first interview.

Data collection:

Information about sociodemographic, pregnancy history and family history of systemic diseases were collected by a trained midwife. All the recruited women underwent a full periodontal examination by a trained dentistry student. Before the start of patient recruitment, a dental student was trained and calibrated by two periodontists (Roya Shariatmadar Ahmadi and Ferena Sayar) for measuring the clinical parameters of periodontal diseases. The dentistry student and the obstetricians were masked on the preeclamptic and periodontal status, respectively. The clinical parameters of periodontal conditions included BOP [18], Plaque Control Record (PCR) [19], PD [20] which is defined as the distance in millimeters (mm) from the gingival margin to the tip of the periodontal probe during probing, and CAL [21]. Measurements were taken at six sites per tooth using a periodontal probe (Hu-Friedy Mfg. Co.,

LLC, Chicago, IL, USA). CAL is the distance (mm) from the cement enamel junction (CEJ) to the tip of the periodontal probe during probing [21]. For measuring the CAL, we used disposable mirrors, #17-23 sterile explorers (Hu-Friedy Mfg. Co., LLC, Chicago, IL, USA), and the University of Michigan 'O' probe (Hu-Friedy Mfg. Co., LLC, Chicago, IL, USA) for each participant. Chronic periodontitis was classified according to the severity and the extent of the disease. If there was an involvement in less than 30% of the areas, local periodontitis would be reported. The severity of the disease according to the level of CAL was classified as follows: CAL equal to or less than 2mm and CAL equal to or greater than 3 mm were considered mild, and moderate to severe periodontitis, respectively.

Statistical analysis:

The data were analyzed by SPSS statistical software (version 22, SPSS Inc., Chicago, IL, USA) using Mann-Whitney U test.

Results

260 women participated in the present study. The subjects (100 women in each group) had no history of urinary tract infection, vaginal infection, systemic disease, smoking, or alcohol consumption. All the samples in the case and control groups were between 25 and 28 weeks' gestation. Table 1 revealed that the two groups were similar in terms of the age, occupation, education, income, and the number of children.

The distribution of the examined people based on their history of pregnancy shows that women in the case group had a higher blood pressure during pregnancy than the women in the control group, and the difference is statistically significant ($P=0.001$). Moreover, women in the case group had a significant difference with women in the control group in terms of the history of preeclampsia in a previous pregnancy ($P<0.0001$). The distribution of the examined people based on the family history of the disease shows that the case group had a significantly different family history of heart disease and hypertension in comparison with the control group ($P<0.0001$; Table 1).

The average PD was 1.99 mm in the case group and 1.73 mm in the control group, showing a

statistically significant difference ($P<0.0001$). The average CAL was 1.96 mm and 1.74 mm in the case and control groups, respectively, indicating that CAL was significantly higher in the case group ($P<0.0001$). The PCR was about 83.77% in the case group and 76.1% in the control group, indicating a statistically significant difference ($P=0.001$). The average BOP was about 48.6% in the case group and 38.2% in control group, showing a statistically significant difference ($P=0.016$; Table 2). Although there were statistically significant differences between the groups with regard to the mean \pm standard deviation (SD) of PD ($P<0.0001$), CAL ($P<0.0001$), PCR ($P=0.001$), and BOP ($P=0.016$) indices, yet the differences were clinically smaller than 0.3 mm and could not be measured with a periodontal probe.

Table 3 shows the distribution of the two groups according to the presence or absence of periodontal diseases and categorized by the pregnancy-induced hypertension status. This table shows that the prevalence of periodontal diseases in the case and control groups lacked a statistically significant difference ($P=0.17$).

Discussion

The purpose of this study was to assess the relationship between periodontal diseases and preeclampsia. Preeclampsia is the leading cause of many injuries and even mortality of mothers and babies around the world, affecting about 5% to 10% of pregnancies [22]. The treatment of preeclampsia is termination of pregnancy because of the probability of prenatal and maternal morbidity [17].

Some studies have suggested a correlation between periodontal disease and the development of certain adverse pregnancy outcomes such as low birth weight, preterm birth, and preeclampsia [3,23]. Periodontal infections lead to a transient low-grade bacteremia in the maternal-fetal circulation, which may cause systemic immune responses, placental abnormalities, and other clinical manifestations of preeclampsia [24,25]. From another point of view, the circulating C-reactive protein (CRP) level is elevated in both periodontal disease and adverse pregnancy outcomes [26]. Furthermore, some studies have shown that periodontal disease may

Table 1. Demographic and pregnancy-related characteristics of the studied groups

Variables		Preeclamptic	Control	P-value
Age		29.28 ± 6.02	28.91 ± 4.7	0.63
Housekeeper Occupation Employed		98	100	0.49
		2	0	
Below diploma Education Diploma Over diploma		58	61	0.43
		35	36	
		7	3	
Family income <300\$ 300\$-600\$		80	85	0.35
		20	15	
Number of children		0.66 ± 0.84	0.64 ± 0.84	0.86
Blood pressure during pregnancy		12.29 ± 0.27	10.61 ± 0.21	0.00
Number of previous pregnancies		1.03 ± 1.24	0.99 ± 1.07	0.81
Number of previous deliveries		0.63 ± 0.84	0.65 ± 0.84	0.86
Number of abortions		0.39 ± 0.77	0.43 ± 1.07	0.76
Interpregnancy intervals		2.21 ± 3.27	2.86 ± 3.54	0.18
History of low birth weight	Yes	0	1	1
	No	100	99	
History of premature infants	Yes	2	0	0.49
	No	98	100	
History of cesarean delivery	Yes	17	19	0.71
	No	83	81	
History of preeclampsia	Yes	16	0	0.00
	No	84	100	
Family history of heart disease	Yes	42	3	0.00
	No	58	97	
Family history of hypertension	Yes	56	10	0.00
	No	44	90	
Family history of premature infants	Yes	2	0	0.49
	No	98	100	
Family history of low birth weight	Yes	0	0	1
	No	100	100	
Family history of preeclampsia	Yes	2	0	0.49
	No	98	100	

Table 2. Distribution of pregnant women in case and control groups according to the preeclampsia status in terms of periodontal indices

Periodontal indices	Preeclamptic Mean±SD	Control Mean±SD	P-value
PD	1.99 ± 0.50	1.73 ± 0.34	<0.0001
CAL	1.96 ± 0.48	1.74 ± 0.34	<0.0001
PCR	83.77 ± 17.37	76.10 ± 22.22	0.001
BOP	48.60 ± 33.39	38.20 ± 27.01	0.016

PD=Probing Depth, CAL=Clinical Attachment Loss, PCR= Plaque Control Record, BOP=Bleeding on Probing, SD=Standard deviation

Table 3. Distribution of case and control groups according to the presence or absence of periodontal disease, categorized by the pregnancy-induced hypertension status

		Preeclampsia		P-value
		Control	Case	
Periodontal disease	Negative	7	2	0.17
	Positive	93	98	
	Total	100	100	

be a potential risk factor for the initiation and development of preeclampsia because of the reduced antioxidant capacity and increased oxidative stress or free radicals [27,28]; therefore, we hypothesized that periodontitis during pregnancy was associated with preeclampsia. Several studies have reported the relationship between periodontitis and preeclampsia [29-31]. Ha et al [32] confirmed this correlation even in nonsmoker women. Also, Pattanashetti et al [33] showed that the degree of periodontal diseases is effective in pregnancy outcome. Furthermore, Sayar et al [14] demonstrated that preeclamptic women had greater attachment loss and gingival recession than normotensive women. The results of a study by Barak et al [34] showed that bacterial counts were significantly higher in preeclamptic women with regard to all periopathogenic bacteria. Varshney and Gautam [35] postulated that women with maternal periodontitis may have a transient translocation of oral microorganisms to the uteroplacental unit, inducing placental inflammation or oxidative stress early in pregnancy, which will eventually lead to placental

damage and the clinical manifestations of preeclampsia.

Numerous studies have found no association between these two disorders [2,17,36,37]. On the other hand, the effectiveness of periodontal treatment in preventing gestational complications has still not been established as it may be biased by several factors including the severity of the disease, the microbial community, the treatment protocol, and the duration of treatment during pregnancy; of course, treatment of periodontitis in pregnant women should be consistently considered [38]. A review of the literature showed that it is still not clear whether periodontal diseases have a causal role in adverse pregnancy outcomes such as preeclampsia [39]. Moreover, the validity of inflammatory markers, including CRP, as the indicators of potential preeclampsia associated with periodontal diseases, shows insufficiencies as these markers may be indicative of numerous systemic inflammatory conditions [40]. Also, inconsistent results, such as a higher prevalence of *Campylobacter rectus* in the control group, show that periopathogenic bacteria may not be a suitable

pointer of periodontitis in pregnant women [41]. Because of the conflicting results in this regard, the present case-control study was conducted on 100 pregnant women with pregnancy-induced hypertension and 100 pregnant women with normal blood pressure; we compared different periodontal disease measurements between preeclamptic women and normotensive controls and found that periodontal disease is not associated with preeclampsia.

Numerous factors may lead to conflicting results among different studies; for example, the differences in the studied populations (such as racial differences), various study designs, using different criteria for defining periodontal diseases, failing to provide a clear definition of preeclamptic patients, failing to determine the severity of the disease, major differences in the inclusion and exclusion criteria, and the number of the participants [42]. In the study by Cota et al [43], which its results are inconsistent with that of the present study, the studied groups were not matched in terms of the confounding variables related to the incidence of preeclampsia, such as smoking and alcohol consumption, the number of children, the number of abortions, and interpregnancy intervals. The unique feature of the present study, which distinguishes it from other studies (both aligned and non-aligned), is that it assessed the pregnant woman's blood pressure status after the 25th week of pregnancy; this means that firstly, the severity of the disease was almost the same among this group of pregnant women, and secondly, the periodontal status was under examination from the beginning of pregnancy-induced hypertension in order to prevent and treat undesirable pregnancy outcomes whenever a link between these two is proved, whereas, in previous studies, the women were evaluated near the end of pregnancy or after delivery, and therefore, they were heterogeneous in terms of the severity of preeclampsia.

Conclusion

Based on this study, there is no significant association between periodontal disease and preeclampsia in pregnant women. We did not find any difference in the prevalence of periodontal disease in preeclamptic pregnant women and normotensive pregnant women. However,

additional studies on a larger sample size are required to determine the role of periodontitis as a risk factor for preterm birth in preeclamptic pregnant women.

Acknowledgments

We would like to thank the Clinical Research Development Center of Akbarabadi Teaching Hospital, Dental Branch, Islamic Azad University, Tehran, Iran. Also, our appreciation is extended to all the participants for their kind cooperation.

References

1. Pihlstrom BL, Michalowicz BS, Johnson NW. Periodontal diseases. *Lancet*. 2005 Nov 19; 366 (9499):1809-20.
2. Winning L, Linden GJ. Periodontitis and Systemic Disease: Association or Causality? *Curr Oral Health Rep*. 2017;4(1):1-7.
3. Xiong X, Buekens P, Vastardis S, Yu SM. Periodontal disease and pregnancy outcomes: state-of-the-science. *Obstet Gynecol Surv*. 2007 Sep;62(9):605-15.
4. Chen BA, Parviainen K, Jeyabalan A. Correlation of catheterized and clean catch urine protein/creatinine ratios in preeclampsia evaluation. *Obstet Gynecol*. 2008 Sep;112(3):606-10.
5. Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. *Lancet*. 2005 Feb 26-Mar 4;365 (9461):785-99.
6. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. *Am J Obstet Gynecol*. 2000 Jul;183(1):S1-S22.
7. Harmon AC, Cornelius DC, Amaral LM, Faulkner JL, Cunningham MW Jr, Wallace K, et al. The role of inflammation in the pathology of preeclampsia. *Clin Sci (Lond)*. 2016 Mar; 130(6): 409-19.
8. Gibbs RS, Romero R, Hillier SL, Eschenbach DA, Sweet RL. A review of premature birth and subclinical infection. *Am J Obstet Gynecol*. 1992 May;166(5):1515-28.
9. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008 Jan 5;371(9606):75-84.
10. Loesche WJ, Grossman NS. Periodontal disease as a specific, albeit chronic, infection:

- diagnosis and treatment. Clin Microbiol Rev. 2001 Oct; 14(4):727-52.
11. Yaghini J, Mostajeran F, Afshari E, Naghsh N. Is periodontal disease related to preeclampsia? Dent Res J (Isfahan). 2012 Nov;9(6):770-3.
 12. Moura da Silva G, Coutinho SB, Piscoya MD, Ximenes RA, Jamelli SR. Periodontitis as a risk factor for preeclampsia. J Periodontol. 2012 Nov; 83(11):1388-96.
 13. Nabet C, Lelong N, Colombier ML, Sixou M, Musset AM, Goffinet F, et al. Maternal periodontitis and the causes of preterm birth: the case-control Epipap study. J Clin Periodontol. 2010 Jan; 37(1):37-45.
 14. Sayar F, Hoseini MS, Abbaspour S. Effect of Periodontal Disease on Preeclampsia. Iran J Public Health. 2011;40(3):122-7.
 15. Khader YS, Jibreal M, Al-Omiri M, Amarin Z. Lack of association between periodontal parameters and preeclampsia. J Periodontol. 2006 Oct; 77(10):1681-7.
 16. Srinivas SK, Sammel MD, Stamillo DM, Clothier B, Jeffcoat MK, Parry S, et al. Periodontal disease and adverse pregnancy outcomes: is there an association? Am J Obstet Gynecol. 2009 May; 200(5):497.e1-8.
 17. Lohsoonthorn V, Kungsadalpipob K, Chanchareonsook P, Limpongsanurak S, Vanichjakvong O, Sutdhibhisal S, et al. Maternal periodontal disease and risk of preeclampsia: a case-control study. Am J Hypertens. 2009 Apr; 22(4):457-63.
 18. Lenox JA, Kopczyk RA. A clinical system for scoring a patient's oral hygiene performance. J Am Dent Assoc. 1973 Apr;86(4):849-52.
 19. O'Leary TJ, Drake RB, Naylor JE. The plaque control record. J Periodontol. 1972 Jan;43(1):38.
 20. Ainamo J, Bay I. Problems and proposals for recording gingivitis and plaque. Int Dent J. 1975 Dec;25(4):229-35.
 21. Silness J, Loe H. Periodontal disease in pregnancy. II. Correlation between oral hygiene and periodontal condition. Acta Odontol Scand. 1964 Feb;22:121-35.
 22. Tooher J, Thornton C, Makris A, Ogle R, Korda A, Hennessy A. All Hypertensive Disorders of Pregnancy Increase the Risk of Future Cardiovascular Disease. Hypertension. 2017 Oct; 70(4):798-803.
 23. Bobetsis YA, Barros SP, Offenbacher S. Exploring the relationship between periodontal disease and pregnancy complications. J Am Dent Assoc. 2006 Oct;137 Suppl:7S-13S.
 24. Xiong X, Buekens P, Fraser WD, Beck J, Offenbacher S. Periodontal disease and adverse pregnancy outcomes: a systematic review. BJOG. 2006 Feb;113(2):135-43.
 25. Nagpal R, Yamashiro Y, Izumi Y. The Two-Way Association of Periodontal Infection with Systemic Disorders: An Overview. Mediators Inflamm. 2015;2015:793898.
 26. Sharma A, Ramesh A, Thomas B. Evaluation of plasma C-reactive protein levels in pregnant women with and without periodontal disease: A comparative study. J Indian Soc Periodontol. 2009 Sep;13(3):145-9.
 27. Shetty MS, Ramesh A, Shetty PK, Agumbe P. Salivary and Serum Antioxidants in Women with Preeclampsia with or Without Periodontal Disease. J Obstet Gynaecol India. 2018 Feb;68(1):33-38.
 28. Dahiya P, Kamal R, Gupta R, Saini H. Evaluation of the serum antioxidant status in patients with chronic periodontitis. Indian J Multidiscip Dent. 2016 Aug;6(1):3-6.
 29. Durand R, Gunselman EL, Hodges JS, Diangelis AJ, Michalowicz BS. A pilot study of the association between cariogenic oral bacteria and preterm birth. Oral Dis. 2009 Sep;15(6):400-6.
 30. Shetty M, Shetty PK, Ramesh A, Thomas B, Prabhu S, Rao A. Periodontal disease in pregnancy is a risk factor for preeclampsia. Acta Obstet Gynecol Scand. 2010 May;89(5):718-21.
 31. Desai K, Desai P, Duseja S, Kumar S, Mahendra J, Duseja S. Significance of maternal periodontal health in preeclampsia. J Int Soc Prev Community Dent. 2015 Mar-Apr;5(2):103-7.
 32. Ha JE, Jun JK, Ko HJ, Paik DI, Bae KH. Association between periodontitis and preeclampsia in never-smokers: a prospective study. J Clin Periodontol. 2014 Sep;41(9):869-74.
 33. Pattanashetti JI, Nagathan VM, Rao SM. Evaluation of Periodontitis as a Risk for Preterm Birth among Preeclamptic and Non-Preeclamptic Pregnant Women - A Case Control Study. J Clin and Diagn Res. 2013 Aug;7(8):1776-8.
 34. Barak S, Oettinger-Barak O, Machtei EE, Sprecher H, Ohel G. Evidence of periopathogenic microorganisms in placentas of women with

- preeclampsia. *J Periodontol.* 2007 Apr;78(4):670-6.
35. Varshney S, Gautam A. Poor periodontal health as a risk factor for development of pre-eclampsia in pregnant women. *J Indian Soc Periodontol.* 2014 May;18(3):321-5.
36. Kunnen A, van Doormaal JJ, Abbas F, Aarnoudse JG, van Pampus MG, Faas MM. Periodontal disease and pre-eclampsia: a systematic review. *J Clin Periodontol.* 2010 Dec; 37(12):1075-87.
37. Taghzouti N, Xiong X, Gornitsky M, Chandad F, Voyer R, Gagnon G, et al. Periodontal disease is not associated with preeclampsia in Canadian pregnant women. *J Periodontol.* 2012 Jul; 83(7): 871-7.
38. Zi MY, Longo PL, Bueno-Silva B, Mayer MP. Mechanisms involved in the association between periodontitis and complications in pregnancy. *Front Public Health.* 2015 Jan 29;2:290.
39. Scannapieco FA, Bush RB, Paju S. Periodontal disease as a risk factor for adverse pregnancy outcomes. A systematic review. *Ann Periodontol.* 2003 Dec;8(1):70-8.
40. Herrera JA, Parra B, Herrera E, Botero JE, Arce RM, Contreras A, et al. Periodontal disease severity is related to high levels of C-reactive protein in pre-eclampsia. *J Hypertens.* 2007 Jul; 25 (7):1459-64.
41. Kunnen A, Blaauw J, van Doormaal JJ, van Pampus MG, van der Schans CP, Aarnoudse JG, et al. Women with a recent history of early-onset pre-eclampsia have a worse periodontal condition. *J Clin Periodontol.* 2007 Mar;34(3):202-7.
42. Vivares-Builes AM, Rangel-Rincón LJ, Botero JE, Agudelo-Suárez AA. Gaps in knowledge about the association between maternal periodontitis and adverse obstetric outcomes: an umbrella review. *J Evid Based Dent Pract.* 2018 Mar;18(1):1-27.
43. Cota LO, Guimarães AN, Costa JE, Lorentz TC, Costa FO. Association between maternal periodontitis and an increased risk of preeclampsia. *J Periodontol.* 2006 Dec;77(12):2063-9.