

# Periodontitis during pregnancy as a risk factor for preterm birth and low birth weight

## *Periodontitis durante el embarazo como factor de riesgo de parto prematuro y bajo peso al nacer*

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### Abstract

**Introduction.** In recent years, periodontal diseases have been studied as a risk factor for the development of adverse pregnancy outcomes, mainly preterm birth (PB) and low birth weight (LBW). **Objective.** To determine if periodontitis correlates with the incidence of premature birth and low birth weight (PB/LBW). **Methodology.** The periodontal status of first-time pregnant women, between 18 and 35 years old, was evaluated in the second trimester of pregnancy, as a part of their prenatal care; the results were correlated with the presence of preterm birth and low birth weight. **Results.** No dependence was found between the presence or absence of periodontitis with the gestation weeks at the time of delivery ( $p$ -value= 0.055) and the weight of the product at birth ( $p$ -value = 0.566). On the other hand, no differences were observed regarding the analysis of clinical parameters that define the presence and severity of periodontitis, with birth conditions. **Conclusions.** In the present study, it does not seem to exist a dependency between the presence or absence of periodontitis with the development of PB and LBW; however, more research is needed to clarify this relationship.

**Key words:** periodontal diseases, periodontitis, risk factors, premature birth, low birth weight.

### Resumen

**Introducción.** En los últimos años, las enfermedades periodontales se han estudiado como factor de riesgo para el desarrollo de resultados adversos en el embarazo, principalmente el parto prematuro (PP) y el bajo peso al nacer (BPN). **Objetivo.** Determinar si la periodontitis se correlaciona con la incidencia de parto prematuro y bajo peso al nacer (PP/BPN). **Metodología.** Se evaluó el estado periodontal de las mujeres embarazadas primigestas, entre 18 y 35 años de edad, en el segundo trimestre del embarazo, como parte de su atención prenatal; los resultados se correlacionaron con la presencia de parto prematuro y bajo peso al nacer. **Resultados.** No se encontró dependencia entre la presencia o ausencia de periodontitis con las semanas de gestación al momento del parto ( $p = 0.055$ ) y el peso del producto al nacimiento ( $p = 0.566$ ). Por otro lado, no se observaron diferencias con respecto al análisis de los parámetros clínicos que definen la presencia y gravedad de la periodontitis con las condiciones de nacimiento. **Conclusiones.** En el presente estudio, no parece existir una dependencia entre la presencia o ausencia de periodontitis con el desarrollo de PB y BPN; sin embargo, se necesitan más estudios para aclarar esta relación.

**Palabras clave:** enfermedades periodontales, periodontitis, factor de riesgo, parto prematuro, bajo peso al nacer.

## INTRODUCTION

Pregnancy is the physiological state that brings temporary systemic changes to the pregnant woman, with the main objective to prepare the mother for the product development.<sup>1</sup> Some of these changes can lead the mother susceptibility to infections, within which are oral infections; an example of these are periodontal diseases.<sup>2</sup>

Periodontal disease is one of the most commonly chronic disorders of infectious origin known in humans, and can be present in two main types: gingivitis, the principal sign is an inflammation of the gums with no loss of periodontal attachment; and periodontitis.<sup>3,4</sup>

Periodontitis is one chronic multifactorial inflammatory disease associated with dysbiotic plaque biofilms and characterized by progressive destruction of the tooth-supporting apparatus.<sup>5</sup> Its prevalence is high, with rates of 20 to 50% in the world population,<sup>6</sup> 37 to 46% in women in reproductive age, and up to 30% in pregnant women (New York State Department of Health, 2006).<sup>7</sup>

In recent years, periodontal diseases have been studied as a risk factor for the development of adverse pregnancy outcomes, mainly premature birth (PB) and low birth weight (LBW).<sup>8,9</sup> These complications occur in the 10% of all obstetric cases and could be prevented;<sup>10,11</sup> otherwise, the newborn has a higher long-term risk of developing neurological, respiratory, cardiovascular, and metabolic problems, furthermore, a higher risk of perinatal mortality.<sup>12</sup>

Periodontal diseases could be a preventable risk factor for their evolution. For that reason, the American Academy of Periodontology (AAP), in 2004, published among its recommendations that every pregnant woman, or woman planning a pregnancy, should receive a complete periodontal assessment.<sup>13</sup>

In Mexico, there are only a few published studies concerning this association; therefore, the main objective of this study is to determine if periodontitis correlates with the development of PB and LBW.

## MATERIAL AND METHODS

An observational cross-sectional study was conducted in a health clinic in Puebla State, Mexico. The study population consisted of first-time pregnant women, between 18 to 35 years old, in the second gestation trimester, referred to the stomatology department as part of their prenatal control, in the period from November 2018 to March 2019.

The study was approved by the Research Ethics Committee of the Universidad Popular Autónoma del Estado de Puebla (CONBIOETICA21CEI00620131021) and in accordance with the ethical principles of the World Medical Association Declaration of Helsinki (version 2008).

### Periodontal assessment

The project was thoroughly explained to the pregnant women, they were subsequently asked to read and sign a written informed consent if they agreed to participate. Each participant underwent an oral and periodontal evaluation, the variables

evaluated were plaque control, using a plaque disclosing tablet (expressed as percentages of pigmented sites); and probing depth (PD), measured with the aid of a periodontal probe calibrated in millimeters (probe of the University of North Carolina No. 15, Hu-Friedy, Chicago, IL, USA). In the same way, the presence of Bleeding on Probing (BOP), as well as measurements of the Clinical Attachment Level (CAL). PD and CAL were collected at six sites on each tooth.

Patient records were examined thoroughly, from which the relevant data were extracted and eligibility for the study was accurate.

The presence of two or more teeth with a CAL greater than or equal to 6 mm, like a site with a PD greater than or equal to 5 mm, were classified as patients with established periodontitis; those who did not meet this criterion, were classified as healthy patients.

### Diagnosis and treatment

The healthy patients were given hygiene techniques and, if is necessary, supragingival scaling was performed with a DTE-D1 (Guilin Woodpecker Medical Instrument Co., Ltd.) ultra sonic scaler that consists of a sonic device that emits waves accompanied by water irrigation, allowing the removal of food debris, additionally dental calculus.

The patients who presented established periodontitis were explained hygiene techniques and were monitored month by month to prevent the progression or deterioration of the disease and the need for emergency intervention. In these types of patients, the treatment which is usually more invasive, was suggested as an option at the end of pregnancy.

### Recording additional data

Possible known obstetric risk factors, the follow-up pregnancy, and the presence of adverse pregnancy outcomes, were obtained from the patient's medical records and an applied questionnaire at the same time as the periodontal assessment.

### Statistic analysis

The descriptive analysis of the data obtained was carried out using counts and percentages for the categorical variables, and measures of central tendency and dispersion for numerical variables.

The means of the numerical variables of interest were compared through the student's t-test and ANOVA. The  $\chi^2$  test of independence was applied to determine the association between categorical variables. Also, the Pearson Correlation Coefficient test was applied, and scatter plots were used to correlate the numerical variables.

Statistical analysis was performed in the SPSS® program (V 25.0). Statistical significance was defined as  $p$ -value < 0.05.

## RESULTS

A total of 54 pregnant women were attended for evaluation in the stomatology service; after the application of the established criteria, 24 patients did not meet the inclusion criteria (systemic commitment, multiparity, presence of infection and active antibiotic therapy) thus the final sample size was set in 30 participants.

Of the study group, 13% of the participants were diagnosed with established periodontitis, according to the Machtei *et al.*<sup>14</sup> criteria in 1992. These criteria are mainly based on two measures: CAL and PD ( $\geq 2$  teeth with a CAL  $\geq 6$  mm +  $\geq 1$  site with PD  $\geq 5$  mm), both considered as primary tools to measure periodontal status; besides, these criteria are widely used in cases definition for epidemiological studies, mainly in young populations.<sup>15-17</sup> According to these same criteria, the remaining 87% were classified as healthy patients. Thus, the participants were divided into two groups: the established periodontitis group and the healthy group.

The average age of the population with periodontitis was  $25.5 \pm 4.7$  and  $28.0 \pm 4.1$  years old for the healthy group, also, the average gestational age at the time of the review for each group was  $18.8 \pm 7.0$  and  $16.0 \pm 7.0$  gestation weeks, respectively. In the periodontitis group, the average birth weight of the product was 3 070 grams and mean gestational age at the time of delivery of 37.8 weeks; the healthy group reported an average of 3 027 grams of birth weight and 38.5 gestation

weeks. Variables such as weight, height, BMI, and the total number of prenatal visits, were too analyzed in both groups; however, no significant differences were obtained regarding these (*table 1*).

Clinical parameters such as BOP, CAL, PD, and Presence of Biofilm (BIOFILM %) were analyzed. The group with established periodontitis showed an average PD of 2.51 mm and an average CAL of 2.45 mm, unlike the healthy group, which showed an average PD of 2.36 mm and an average CAL of 2.32 mm. An analysis of the student t-test was carried out to obtain the difference of means between both groups, obtaining a *p*-value of 0.010\* concerning PD and of 0.001\* for CAL, both being significant; although, regarding BIOFILM % and BOP parameters, no significant differences were observed (*table 2*).

According to the follow-up that was given to each patient during the gestational period, none of the participants with periodontitis showed an advance in the severity and progression of the presented disease, i.e., there was no increase in the CAL and PD compared to the initial survey.

**Table 1.** Study group characteristics.

	Machtei criteria				<i>p</i> -value <sup>a</sup>
	Healthy group		Periodontitis group		
	Mean	SD	Mean	SD	
Age (years)	28.0	4.1	25.5	4.7	0.326
Gestational age (weeks)	18.8	7.0	16.0	7.0	0.460
Height (m)	1.55	0.07	1.54	0.04	0.782
Weight (kg)	66.37	19.66	60.63	9.53	0.575
BMI (kg/m <sup>2</sup> )	27.32	6.18	25.75	5.23	0.634
Prenatal care (appointments)	7.5	2.6	6.5	1.3	0.451
Infant mean weight (g)	3027.1	404.6	3070.0	455.6	0.847
Gestational weeks period	38.5	1.4	37.8	2.1	0.393

SD: standard deviation.

<sup>a</sup> T-Student test.

**Table 2.** Study group clinical parameters.

	Healthy group		Periodontitis group		<i>p</i> -value <sup>a</sup>
	Mean	SD	Mean	SD	
Bleeding on probing (BOP)	53.8%	17.8%	71.3%	15.6%	0.075
Biofilm %	69.0	11.2	70.8	11.8	0.770
Probing depth (PD)	2.36	0.10	2.51	0.09	0.010*
Clinical attachment level (CAL)	2.32	0.06	2.45	0.09	0.001*

SD: standard deviation.

<sup>a</sup> T-Student test. \* Statistically significant.

The results of the total study population, healthy group, and group with established periodontitis, showed that 80% of the births went without obstetric complications; 14% presented PB, 3% LBW, and 3% PLBW (**table 3**).

Reviewing the direct comparisons between PB, LBW, and PLBW with periodontitis, it can be observed that, of the healthy group, 7.7% had products with LBW; 11.5% presented PB; and only 3% presented PLBW; on the other hand, in the periodontitis group, none of the cases presented LBW; nevertheless, 50% were premature. A  $\chi^2$  independence test was performed to determine the dependence between the variables, regardless, no

dependence was found between the presence or absence of periodontitis, with the gestation weeks at the time of delivery ( $p$ -value = 0.055) and the weight of the product at birth ( $p$ -value = 0.566) (**table 4**).

Through an ANOVA test, the clinical parameters that define the presence and severity of periodontitis (BOP, BIOFILM %, PD, CAL), with birth conditions (normal, PB, LBW, and PLBW) were analyzed, no differences in the means were observed within each group, i.e., no significant differences were no in the clinical parameters between patients with normal birth, PB, LBW or PLBW (**table 5**). In contrast, a Pearson correlation was performed to determine significant relationships between the same clinical parameters with the final weight of the product and the gestation weeks at the time of delivery; even so, no correlation was found ( $r = 0.000$ ,  $p$ -value = 0.100) (**table 6**).

**Table 3.** Birth conditions.

	N	%
Normal	24	80.0
Premature birth	4	14
Low birth weight	1	3
PLBW	1	3
<b>Total</b>	<b>30</b>	<b>100.0</b>

## DISCUSSION

Research on the possible association between periodontitis and maternal and fetal health is a matter of great concern to the scientific community.<sup>18</sup> LBW, PB, and preeclampsia, have been associated with exposure to maternal periodontitis. Nonetheless, the strength of the observed associations based on clinical parameters is modest and seems to vary according to the population studied, the means of periodontal evaluation, and the periodontal disease classification used.<sup>19</sup>

**Table 4.** Groups by categories.

		Healthy group		Periodontitis group		$p$ -value <sup>b</sup>
		n	%	n	%	
Weight categories	LBW	2	7.7%	0	0.0%	0.566
	Normal	24	92.3%	4	100.0%	
Gestation weeks categories	Premature	3	11.5%	2	50.0%	0.055
	Term	23	88.5%	2	50.0%	

<sup>b</sup>  $\chi^2$  Test of independence.

**Table 5.** Birth conditions/clinical parameters.

	Normal		PB		LBW		PLBW		$p$ -value <sup>c</sup>
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Bleeding on probing (BOP)	58.3%	17.0%	51.8%	25.1%	26.0%	.	52.0%	.	0.354
Biofilm %	69.4%	10.5%	73.8%	12.9%	48.0%	.	68.0%	.	0.232
Probing depth (PD)	2.38	0.11	2.41	0.11	2.28	.	2.53	.	0.415
Clinical attachment level (CAL)	2.34	0.08	2.35	0.07	2.28	.	2.45	.	0.423

SD: Standard Deviation

<sup>c</sup> One way ANOVA

**Table 6.** Correlations between final weight and gestation weeks with clinical parameters.

Final weight (g)	BOP (%)	BIOFILM %	PD	CAL
correlation coefficient	-0.003	0.188	-0.017	0.060
<i>p</i> -value <sup>d</sup>	0.989	0.320	0.928	0.752
Gestation weeks	BOP (%)	BIOFILM %	PD	CAL
correlation coefficient	0.295	0.092	-0.023	0.079
<i>p</i> -value <sup>d</sup>	0.114	0.630	0.904	0.680

<sup>d</sup> Pearson correlation coefficient test.

In this work, it was possible to observe the presence of periodontitis in 13% of the study population, contrary to the reported in previous studies; one of them conducted in Brazil, found a high prevalence of periodontal disease during pregnancy (47%).<sup>20</sup> So, these prevalences seem to vary in different regions of the world, where the figures range between 10 and 74%.<sup>21</sup>

Bleeding, inflammation, and sensitive gums are common oral problems reported by pregnant women. These conditions generally reflect tissue responses to increased levels of progesterone and estrogen and can be prevented mainly if good oral hygiene is maintained during pregnancy.<sup>22</sup> In the present work, an average of 71.3% BOP and the presence of biofilm of 70.8% was observed in the periodontitis group, despite these numbers, no significant differences were found regarding these variables compared to the healthy group. Besides, PD and CAL were significant, since, in a patient with periodontitis, there is a loss of hard and soft tissue support around the teeth, for that reason, these levels tend to be increased.

There are data in the literature that shows an exacerbation of pre-existing periodontal status as pregnancy progresses.<sup>20</sup> Nevertheless, as previously mentioned, no participant in the group with periodontitis showed negative progress of their initial periodontal state, but the gestation weeks reported at the beginning of their follow-up (mean of 16 weeks) could have been a crucial factor to prevent a more considerable periodontal damage, by having been guided on the correct oral hygiene.

Regarding the relationship between the presence or absence of periodontitis with the development of PB, LBW, and PLBW, previous literature from developed countries does not conclusively show a positive association between periodontitis and PB, in contrast to the reported evidence by developing countries, which show a more consistent connection.<sup>23</sup>

In this research, PLBW was observed in 3% of the total population studied; this figure is comparable with 3.17% obtained by López *et al.*<sup>24</sup> in Chile in 2005, which was lower than the reported in that country and worldwide (up to 10%). On the other hand, 50% of pregnant women with periodontitis had PB; even so, there was not a significant relationship between the presence or absence of periodontitis with birth weight or gestation weeks at birth; these results were similar to those reported by Zermeño *et al.*<sup>25</sup> in 2011, and Wang *et al.*<sup>26</sup> in 2013; which they could not demonstrate a significant

relationship between periodontal disease and PB; regardless, Wang's work describes that the association between periodontal disease and LBW was significant, which suggests that a possible association between the presence of periodontal disease and LBW could exist in the population of this study; however, it is necessary to increase the size of the sample to corroborate this information.

Martínez *et al.*<sup>27</sup> in 2016, concluded that infectious processes during pregnancy are confounding variables that, if controlled, show that periodontitis is not associated with premature birth; in addition, Fogacci *et al.*<sup>18</sup> argues that the systematic control of important risk factors would minimize the incidence of adverse pregnancy outcomes. In this study, pregnant women that presented a history of risk for the development of PB, LBW, or both were excluded; despite that, different variables can influence the final results of pregnancy.

Otherwise, some studies support and demonstrate a relationship between periodontitis and PLBW. In a systematic review conducted by Corbella<sup>28</sup> in 2016 of 17 053 participants from 22 studies, it was confirmed that periodontitis could be considered as a risk factor for PB, LBW, and PLBW. Despite that, the last correlation was supported by fewer participants compared to individual results (PB and LBW).

The most reliable evidence made in animals and humans supports the concept that periodontal infections provide a portal for the hematogenous spread of oral microorganisms and their products, which reach the fetal-placental unit. This direct route is associated with the inflammatory/immune response in the fetal-placental unit that induces a variety of adverse outcomes, which will depend on the timing and severity of exposure. It is mentioned that periodontal disease could influence the production of proinflammatory cytokines, which are considered physiological mediators during childbirth (indirect route). Lower exposures can induce hypercontractility of the uterus, cervical dilation, and loss of membrane integrity, which leads to premature birth.<sup>29-31</sup>

According to the clinical parameters that define the presence and severity of periodontitis (BOP, BIOFILM %, PD, CAL), with birth conditions, no significant differences there were. These results differ from those reported by Meqa *et al.*<sup>32</sup> in 2017, where they concluded that PD and CAL were significantly higher in patients with premature birth; similarly, higher BIOFILM % was observed, as well as higher PD and

CAL in patients who had products with LBW. In another study carried out in Brazil by Santos *et al.*<sup>33</sup> in 2007, a significant loss in CAL and greater BOP was reported significantly in patients who had PB; meanwhile, Manemm *et al.*<sup>34</sup> in India in 2011, observed an association between PD and PLBW.

### CONCLUSIONS

In the present study, it was not possible to demonstrate any relationship between the presence or absence of periodontitis with the development of adverse pregnancy outcomes, such as PB and LBW. Nevertheless, the results are controversial in the literature, since they suggest that certain conditions external to periodontal diseases, such as the socioeconomic status of the pregnant woman, the presence of infections, the consumption of some medications, among others, could influence the development of these complications.

Despite the similarity found with previous studies, some differences could be due to the number of participants in the study population and the different methods of defining periodontitis, so the results of the present study cannot be extrapolated to the general population.

More studies are still required to determine the importance of periodontal diseases during pregnancy, and take into account periodontal assessment in prenatal control.

### CONFLICT OF INTERESTS

None.

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### REFERENCES

- Duarte-Tencio A. El embarazo y la práctica odontológica: Generalidades. *Rev. Cient. Odontol.* 2011;7(2): 70-4.
- Russell SL, Mayberry LJ. Pregnancy and oral health: a review and recommendations to reduce gaps in practice and research. *MCN Am J Matern Nurs.* 2008; 33(1): 32-7.
- Xiong X, Buekens P, Fraser WD, Beck J, Offenbacher S. Periodontal disease and adverse pregnancy outcomes: A systematic review. *BJOG.* 2006; 113(2): 135-43.
- Iheozor-Ejiofor Z, Middleton P, Esposito M, Glennly AM. Treating periodontal disease for preventing adverse birth outcomes in pregnant women. *Cochrane Database Syst Rev.* 2017 Jun 12; 6(6): CD005297.
- Papapanou PN, Sanz M, Buduneli N, Dietrich T, Feres M, Fine DH, *et al.* Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Periodontol.* 2018; 89(Suppl 1): S173-82.
- Nazir MA. Prevalence of periodontal disease, its association with systemic diseases and prevention. *Int J Health Sci (Qassim).* 2017; 11(2): 72-80.
- Dasanayake AP, Gennaro S, Hendricks-Muñoz KD, Chhun N. Maternal periodontal disease, pregnancy, and neonatal outcomes. *MCN Am J Matern Nurs.* 2008; 33(1): 45-9.
- Parihar AS, Katoch V, Rajguru SA, Rajpoot N, Singh P, Wakhle S. Periodontal Disease: A Possible Risk-Factor for Adverse Pregnancy Outcome. *J Int Oral Heal.* 2015; 7(7): 137-42.
- Boutigny H, de Moegen ML, Egea L, Badran Z, Boschin F, Delcourt-Debruyne E, *et al.* Oral infections and pregnancy: knowledge of gynecologists/obstetricians, midwives and dentists. *Oral Health Prev Dent.* 2016; 14(1): 41-7.
- Murray-Davis B, McDonald H, Cross-Sudworth F, Ahmed R, Simioni J, Dore S, *et al.* Learning from Adverse Events in Obstetrics: Is a Standardized Computer Tool an Effective Strategy for Root Cause Analysis? *J Obstet Gynaecol Canada.* 2015; 37(8): 728-35.
- Class QA, Lichtenstein P, Långström N, D'Onofrio BM. Timing of prenatal maternal exposure to severe life events and adverse pregnancy outcomes: A population study of 2.6 million pregnancies. *Psychosom Med.* 2011; 73(3): 234-41.
- Bobetsis YA, Barros SP, Offenbacher S. Exploring the relationship between periodontal disease and pregnancy complications. *J Am Dent Assoc.* 2006; 137(Suppl): 7S-13S.
- Bogges KA; Society for Maternal-Fetal Medicine Publications Committee. Maternal oral health in pregnancy. *Obstet Gynecol.* 2008; 111(4): 976-86.
- Machtei EE, Christersson LA, Grossi SG, Dunford R, Zambon JJ, Genco RJ. Clinical criteria for the definition of "established periodontitis". *J Periodontol.* 1992; 63(3): 206-14.
- Savage A, Eaton KA, Moles DR, Needleman I. A systematic review of definitions of periodontitis and methods that have been used to identify this disease. *J Clin Periodontol.* 2009; 36(6): 458-67.
- Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. *J Periodontol.* 2007; 78(7 Suppl): 1387-99.
- Shaju-Jacob P. Measuring periodontitis in population studies: a literature review. *Rev Odonto Cienc.* 2011; 26(4): 346-54.
- Fogacci MF, Cardoso EOC, Barbirato DDS, de Carvalho DP, Sansone C. No association between periodontitis and preterm low birth weight: a case-control study. *Arch Gynecol Obstet.* 2018; 297(1): 71-6.
- Sanz M, Kornman K; working group 3 of the joint EFP/AAP workshop. Periodontitis and adverse pregnancy outcomes: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *J Periodontol.* 2013 Apr 1; 84(4 Suppl): S164-9.
- Vogt M, Sallum AW, Cecatti JG, Morais SS. Factors associated with the prevalence of periodontal disease in low-risk pregnant women. *Reprod Health.* 2012; 9(1): 3.
- Jiang H, Su Y, Xiong X, Harville E, Wu H, Jiang Z, *et al.* Prevalence and risk factors of periodontal disease among pre-conception Chinese women. *Reprod Health.* 2016; 13(1): 141.
- Kloetzel MK, Huebner CE, Milgrom P. Referrals for dental care during pregnancy. *J Midwifery Womens Health.* 2011; 56(2): 110-7.
- Manrique-Corredor EJ, Orozco-Beltran D, Lopez-Pineda A, Quesada JA, Gil-Guillen VF, Carratala-Munuera C. Maternal periodontitis and preterm birth: Systematic review and meta-analysis. *Community Dent Oral Epidemiol.* 2019; 47(3): 243-51.

24. López NJ, Da Silva I, Ipinza J, Gutiérrez J. Periodontal therapy reduces the rate of preterm low birth weight in women with pregnancy-associated gingivitis. *J Periodontol.* 2005; 76(11): 2144-53.
25. Zermeño NJJ, Flores ACC, Saldívar RD, Soria LJA, Garza RM, Iglesias BJJ. Enfermedad periodontal como factor de riesgo para presentar resultados perinatales adversos. *Rev Chil Obstet Ginecol.* 2011; 76(5): 338-43.
26. Wang YL, Liou JD, Pan WL. Association between maternal periodontal disease and preterm delivery and low birth weight. *Taiwan J Obstet Gynecol.* 2013 Mar; 52(1): 71-6.
27. Martínez-Martínez RE, Moreno-Castillo DF, Loyola-Rodríguez JP, Sánchez-Medrano AG, Miguel-Hernández JHS, Olvera-Delgado JH, *et al.* Association between periodontitis, periodontopathogens and preterm birth: is it real? *Arch Gynecol Obstet.* 2016 Jul 1; 294(1): 47-54.
28. Corbella S, Taschieri S, Del Fabbro M, Francetti L, Weinstein R, Ferrazzi E. Adverse pregnancy outcomes and periodontitis: A systematic review and meta-analysis exploring potential association. *Quintessence Int.* 2016; 47(3): 193-204.
29. Pitiphat W, Joshipura KJ, Gillman MW, Williams PL, Douglass CW, Rich-Edwards JW. Maternal periodontitis and adverse pregnancy outcomes. *Community Dent Oral Epidemiol.* 2008; 36(1): 3-11.
30. Afshari P, Sheinizadeh S, Ranjbari A, Khalilinejad F. Maternal Periodontitis, Preeclampsia and Adverse Pregnancy Outcomes. *J Midwifery Reprod Heal.* 2013; 1(1): 19-25.
31. Madianos PN, Bobetsis YA, Offenbacher S. Adverse pregnancy outcomes (APOs) and periodontal disease: pathogenic mechanisms. *J Periodontol.* 2013; 84(4 Suppl): S170-80.
32. Meqa K, Dragidella F, Disha M, Sllamniku-Dalipi Z. The Association between Periodontal Disease and Preterm Low Birthweight in Kosovo. *Acta Stomatol Croat.* 2017; 51(1): 33-40.
33. Santos-Pereira SA, Giraldo PC, Saba-Chujfi E, Amaral RLG, Morais SS, Fachini AM, *et al.* Chronic periodontitis and preterm labour in Brazilian pregnant women: an association to be analysed. *J Clin Periodontol.* 2007; 34(3): 208-13.
34. Mannem S, Chava VK. The relationship between maternal periodontitis and preterm low birth weight: A case-control study. *Contemp Clin Dent.* 2011; 2(2): 88-93.