



Is Periodontal Disease a Risk Factor for Premature Birth and Low Birth Weight?

Periodontal Hastalıklar Erken Doğum ve Düşük Doğum Ağırlığı İçin Bir Risk Faktörü müdür?

Kübra CERAN DEVECİ*¹ 
k_crn@hotmail.com

Metin ÇALIŞIR² 
calisir_metin@hotmail.com

Mehmet Fatih DEVECİ³ 
dr-mfd@hotmail.com

Talip KARAÇOR⁴ 
talipkaracor@gmail.com

ABSTRACT

Aim: Preterm birth or low birth weight play an important role in neonatal mortality and morbidity. Even today, there are cases whose etiology is not fully understood. The aim of this study was to assess the impact of periodontal disease on adverse pregnancy outcomes using the current classification system accepted at the 2017 World Workshop.

Material and Methods: This study was conducted on 172 women. Demographic characteristics of all individuals were recorded and laboratory values were examined. While those with a gestational age <37 weeks and/or baby birth weight < 2500 g were constituted to the case group (n=85), those with a gestational age ≥ 37 weeks and/or baby birth weight ≥ 2500 g constituted the control group (n=87). Clinical periodontal and radiographic evaluations including plaque index (PI), gingival index (GI), bleeding on probing (BOP %), probing pocket depth (PPD) and clinical attachment level (CAL) values were performed for all individuals, and the diagnoses were made by the applied classification system. Analyses were performed between her two groups.

Results: PI, GI, BOP %, and PPD values in the case group were significantly higher compared to the control group (p<0.001). Although the CAL value was higher in the case group, the difference was not significant (p=0.058). WBC (p=0.020) and PLT (p<0.001) values were significantly higher in the case group.

Conclusion: According to the results of this study, periodontal diseases are associated with adverse pregnancy outcomes independent of other risk factors.

Keywords: Low birth weight, Preterm birth, Periodontal diseases, Plaque index, Gingival index

Received: 09.04.2023

Accepted: 02.09.2023

Published: 27.12.2023

ÖZ

Amaç: Erken doğum ya da düşük doğum ağırlığı, yenidoğan mortalite ve morbiditesinde önemli bir yer tutmaktadır. Günümüzde hala etyolojisi tam aydınlatılmayan vakalar mevcuttur. Bu çalışmanın amacı, 2017 Dünya Çalıştayı'nda kabul edilen güncel sınıflama sistemini kullanarak, periodontal hastalıkların olumsuz gebelik sonuçları üzerine etkisini değerlendirmektir.

Gereç ve Yöntemler: Bu çalışma, 172 kadın üzerinde gerçekleştirildi. Tüm bireylerin demografik özellikleri kaydedildi ve laboratuvar değerleri incelendi. Gebelik haftası < 37 hafta olan ve/veya bebek doğum ağırlığı < 2500 gr. olanlar vaka grubu (n=85) oluşturdu, gebelik haftası ≥ 37 hafta olan ve bebek doğum ağırlığı ≥ 2500 gr. olanlar ise kontrol grubunu (n=87) oluşturdu. Periodontal ve radyografik muayeneleri yapılan tüm bireylerin plak indeksi (PI), gingival indeksi (GI), sondlamada kanama yüzdesi (SK%), sondlama cep derinliği (SCD) ve klinik ataşman seviyesi (KAS) değerleri ölçüldü ve güncel sınıflama sistemine göre tanı konuldu. İki grup arasında analizler yapıldı.

Bulgular: Vaka grubunda; PI, GI, SK%, ve SCD değerleri kontrol grubuna kıyasla anlamlı olarak yüksek bulundu (p<0.001). Vaka grubunda KAS değeri daha yüksek olmasına rağmen fark anlamlı değildi (p=0.058). Vaka grubunda WBC (p=0.020) ve PLT (p<0.001) değerleri kontrol grubuna kıyasla anlamlı olarak yüksekti.

Sonuç: Bu çalışmanın sonuçlarına göre, periodontal hastalıklar olumsuz gebelik sonuçları ile ilişkilidir.

Anahtar Kelimeler: Düşük doğum ağırlığı, Erken doğum, Periodontal hastalıklar, Plak indeksi, Gingival indeks

Geliş: 09.04.2023

Kabul: 02.09.2023

Yayın: 27.12.2023

Atıf / Citation: Ceran Deveci K., Çalışır M., Deveci M. F., Karaçor T., Is periodontal disease a risk factor for premature birth and low birth weight? NEU Dent J. 2023;5:173-8.

* Sorumlu Yazar/Corresponding Author

1. DDS, Research Assistant, Adıyaman University, Faculty of Dentistry, Department of Periodontology, Adıyaman, Türkiye.
2. PhD, Assistant Professor, Adıyaman University, Faculty of Dentistry, Department of Periodontology, Adıyaman, Türkiye.
3. MD, Specialist, Adıyaman University, Faculty of Medicine, Department of Pediatrics, Adıyaman, Türkiye.
4. MD, Assistant Professor, Adıyaman University, Faculty of Medicine, Department of Obstetrics and Gynecology, Adıyaman, Türkiye.



"This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License. (CC BY-NC 4.0)"

INTRODUCTION

Periodontal diseases are chronic inflammatory diseases defined by the destruction of periodontal tissues as a result of dental plaque build-ups along the tooth's edge and gingiva.¹ The severity of the disease is affected by the host's response, genetics, personal factors, age, race, hormonal changes, and several other systemic conditions.² Periodontal diseases have been defined using various classification systems to date. Periodontal health and disease types were updated in detail in the most recent 2017 World Workshop. Periodontal conditions: according to the current classification made in 2017; are divided into periodontal and gingival health, biofilm-induced gingivitis, non-biofilm-induced gingivitis, and periodontitis. Periodontitis was specified in 4 stages (as stages I, II, III, IV) also into 3 grades (grades A, B, C).³

According to the World Health Organization, births that occur between 20 and 37 weeks of gestation are considered preterm births (PB).⁴ Births that are less than 2500 grams in weight are also considered low birth weight (LBW).⁵ Preterm birth and low birth weight are considered social problems because they are associated with high rates of neonatal morbidity and mortality.^{4,5} Among the risk factors associated with PB and/or LBW include maternal age below 17 years or over 34 years of age, race, low socioeconomic status, multiple pregnancies (e.g., twins, triplets), previous preterm birth history, stress or depression, smoking, alcohol use, high blood pressure, diabetes mellitus, and genitourinary system infections. Preterm and low birth weight newborns can occur in the absence of these risk factors. Non-genital infections including periodontal disease in the mother can be the reason of preterm birth and low birth weight. Although there is considerable evidence in the literature that periodontal diseases have a deleterious effect on pregnancy outcomes, the information is not completely clear.^{6,7} Although much epidemiological research supports the subject, there is also evidence to the contrary. Differences in the definition of periodontal disease are believed to be one of the reasons for these inconsistent results. Our aim was to reassess the impact of periodontal disease on adverse pregnancy outcomes in this study using the updated classification system adopted at the 2017 World Workshop.

MATERIAL AND METHODS

Patients Incorporated in the Study

This study was conducted on 172 individuals between the ages of 18 and 35. Her follow-up care and delivery took place in the obstetrics and gynecology department of our university's training hospital. Approval has been received from Non-Invasive Clinical Research Ethics Committee on 20/03/2019 with the number 2019/2-16. The participants were informed about the purpose and content of the study. The study was started after written consent was obtained from the participants. Mothers were divided into two groups according to gestational age and baby birth weight. Gestational week <37 weeks and/or baby birth weight <2500 g was defined as the case group (n=85). Gestational age ≥37 weeks and birth weight of the baby ≥2500 g formed the control group (n=87). Mothers with systemic, genetic or metabolic diseases that may affect pregnancy outcomes and mothers who use substances such as cigarettes and alcohol were not included in the study. Mothers who received any hormone treatment or periodontal treatment in the last six months and who used anti-inflammatory and antibiotics drugs in the last three months were also excluded from the study. Mothers with conditions that may adversely affect pregnancy such as preeclampsia/eclampsia, placenta previa, ablatio placenta poly/oligohydramnios, uterus or cervical malformations, gestational diabetes, and multiple pregnancies were also excluded from the study. Weight, height, age, mode of delivery, and the previous number of pregnancies of all mothers included in the study were recorded mode of delivery, and the previous number of pregnancies of all mothers included in the study were recorded. The educational status and income level of the mother were recorded. To determine the oral hygiene habits of the mothers, the frequency of tooth brushing and whether they used dental floss were recorded. Laboratory values of mothers were scanned through the system. From the laboratory data obtained closest to the birth in the last month of pregnancy, hemoglobin (HGB), hematocrit (HCT), white blood cells (WBC), platelet (PLT), mean platelet volume (MPV) and calcium (Ca) values were recorded.

Periodontal Examination

Periodontal examinations of mothers were performed within 1 month after their birth in our University Faculty of Dentistry, Department of Periodontology. Evaluations were performed by a single self-calibrated clinician. Whole mouth clinical attachment level (CAL) and probing pocket depth (PPD) measurements were made and bleeding on probing (BOP), plaque index (PI), and gingival index (GI) found determined in individuals. Average values were received right after the indicators were received. Following the clinical and radiographic examinations of individuals, the new periodontal disease classification and criteria made by AAP and EFP in 2017 were used in the evaluation and clinical periodontal diagnosis of periodontal status.

Statistical Analysis

SPSS package for Windows version 24.0 was used for statistical analysis. The Shapiro-Wilk test was used to test the normality of data distribution. Student's t-test was used to compare normally distributed variables between two independent groups. Associations between categorical variables were examined using Fisher's exact and chi-square tests. Results are presented as \pm SD and n (%). A result of <0.05 was considered statistically significant.

RESULTS

A total of 172 patients were evaluated; the mean age of the case group (n=85) was 29.8 ± 5.8 , and the mean age of the control group (n=87) was 31 ± 5.32 . The two groups were statistically similar in terms of body mass index, age values, occupation, education level and income level ($p>0.05$). While 52.9% of the mothers in the case group gave birth to a boy, in the control group that rate was 41.4%. This difference was not statistically significant ($p>0.05$). It was determined that 70.6% of the mothers in the case group had cesarean section and 29.4% had vaginal delivery. The high rate of cesarean section was found to be statistically significant ($p<0.05$). Number of pregnancies were similar between the groups ($p>0.05$). (Table 1)

Table 1. Demographic characteristics and obstetric history of individuals.

	Case group (n=85)	Control group (n=87)	P values
Age (years) (mean \pm SD)	29.8 \pm 5.8	31 \pm 5,32	p=0.123 (a)
Body mass index (kg/m ²)(mean \pm SD)	26.73 \pm 3.9	28.35 \pm 5.19	p=0.055 (a)
Occupation n (%)			
Housewife/unemployed	78 (91.8)	82 (94.3)	p=0.564 (b)
Remunerated	7 (8.2)	5 (5.7)	
Socio-economicstatus n (%)			
Low	28 (32.9)	28(32.2)	
Middle	36 (42.4)	35(40.2)	p=0.909(b)
High	21 (24.7)	24(27.6)	
Educational level n (%)			
Primary	56 (65.9)	49 (56.3)	
Secondary	19 (22.4)	28 (32.2)	p=0,338(b)
Tertiary	10 (11.8)	10 (11.5)	
Gender of the baby n (%)			
Male	45 (52.9)	36 (41.4)	p=0.129(c)
Female	40 (47.1)	51 (58.6)	
Type of delivery n (%)			
Caesareansection	60 (70.6)	35 (40.2)	p<0.001*(c)
Vaginal	25 (29.4)	52 (59.8)	
Total number of pregnancies n (%)			
1	25 (29.4)	23 (26.4)	p=0.664(c)
≥ 2	60 (70.6)	64 (73.6)	

BMI: Body mass index, a:Student t test b: Chi-square test, c: Fisher's exact test, *: $p<0,05$,

Oral hygiene habits of participants were analyzed. The frequency of tooth brushing was grouped as those who brush regularly, those who brush irregularly, and those who do not brush at all. It was determined that 71.8% of the case group brushed regularly, 27.1% brushed irregularly and 1.2% did not brush at all. The use of dental floss was determined to be 5.9% in the case group and 3.4% in the control group. There were no statistical differences between the two groups in terms of individual oral health habits ($p>0.05$). (Table 2)

	Case group (n=85, %100)	Control group (n=87, %100)	P value
Frequency of toothbrushing n (%)			
Regular	61 (71.8)	55 (63.2)	p=0.267(b)
Irregular	23 (27.1)	28 (32.2)	
Nil	1 (1.2)	4 (4.6)	
Use of dentalfloss n (%)			
Yes	5 (5.9)	3 (3.4)	p=0.494(b)
No	80 (94.1)	84 (96.6)	

b: Chi-square test

Periodontal examination findings of the patients were analyzed between the two groups. PI was 1.29 ± 0.37 in the case group and 1.01 ± 0.46 ($p < 0.01$) within the control group; GI was 0.96 ± 0.36 in the case group and 0.66 ± 0.46 ($p < 0.01$) in the control group; BOP% was 70.26 ± 20.81 in the case group and $46.77 \pm 29.14\%$ ($p < 0.01$) in the control group; PPD was calculated as 2.42 ± 0.45 in the case group and 2.07 ± 0.47 ($p < 0.01$) in the control group. The clinical attachment level was statistically similar between the two groups. In conclusion, the periodontal status of the individuals was defined. 5 (5.9%) people in the case group and 24 (27.6%) people in the control group were found to be periodontally healthy. In the case group, 58 people were diagnosed with gingivitis, 21 people with periodontitis stage I, and 1 person with periodontitis stage II. In the control group, 50 people were diagnosed with gingivitis, 12 people with periodontitis stage I, and 1 person with periodontitis stage II. When compared in terms of periodontal status, the high rate of periodontal disease in the case group was found to be statistically significant ($p < 0.01$). (Table 3)

Table 3. Periodontal clinical parameters and periodontal diseases distribution of the study population.

	Case group (n=85, %100)	Control group (n=87, %100)	P value
PI (mean \pm SD)	1.29 \pm 0.37	1.01 \pm 0.46	p<0.001 *(a)
GI (mean \pm SD)	0.96 \pm 0.36	0.66 \pm 0.46	p<0.001 *(a)
BOP% (mean \pm SD)	70.26 \pm 20.81	46.77 \pm 29.14	p<0.001 *(a)
PPD (mm) (mean \pm SD)	2.42 \pm 0.45	2.07 \pm 0.47	p<0.001 *(a)
CAL(mm) (mean \pm SD)	0.72 \pm 1.25	0.39 \pm 0.95	p=0.058(a)
Periodontaldisease n (%)	80 (94.1)	63 (72.4)	p<0.001 *(b)
	Periodontal diseases distribution in the Case group (n=80, %100)	Periodontal diseases distribution in the control group (n=63, %100)	
Gingivitis n (%)	58 (72.5)	50 (79.37)	p=0.343(b)
Periodontitistage I n (%)	21 (26.25)	12 (19.04)	p=0.310(b)
Periodontitistage II n (%)	1 (1.25)	1 (1.59)	p=1.000*(b)

PI: Plaque index, GI:Gingival index, BOP% : Bleeding on probing, PPD: Probing pocketdepth, CAL:Clinical attachment level*: p<0,05, a:Student t test b: Chi-square and Fisher's exact test

When maternal laboratory values were compared; high PLT and WBC values in the case group were found to be statistically significant ($p < 0.01$). (Table 4)

Table 4. Hematological parameters of individuals

	Case group (n=85, %100)	Control group (n=87, %100)	P value
WBC ($\times 10^3/\text{mm}^3$) (mean \pm SD)	11.96 \pm 3.92	10.55 \pm 2.45	p=0.020 *(a)
HGB (g/dL) (mean \pm SD)	11.72 \pm 1.22	11.78 \pm 1.71	p=0.198(a)
HTC (%) (mean \pm SD)	35.89 \pm 3.19	36.39 \pm 3.57	p=0.344(a)
PLT ($\times 10^3/\text{mm}^3$) (mean \pm SD)	258.32 \pm 69.93	225.07 \pm 65.77	p<0.001 *(a)
MPV(fL) (mean \pm SD)	8.78 \pm 1.78	8.86 \pm 1.92	p=0.802(a)
Ca(mg/dL) (mean \pm SD)	8.70 \pm 0.41 (n=56)	8.83 \pm 0.51 (n=60)	p=0.055(a)

WBC: White blood cell, HGB: Hemoglobin, HTC: Hematocrit, PLT: Platelet volume, MPV: Mean platelet volume, Ca: Calcium. *p<0.05 a: Student t test

DISCUSSION

According to the consensus report published at the World Workshop by AAP and EFP in 2017, the adverse effects of periodontal diseases on pregnancy are still current.⁸ It is a researched fact that periodontal diseases that occur during pregnancy affect not only the expectant mother but also the baby. It has been shown in studies that periodontal disease has many side effects on pregnant women leading to PB, LBW, miscarriage and preeclampsia.^{9,10} However, there are some studies that have not found any association between periodontal disease and pregnant women.^{11,12} Offenbach et al.¹³ conducted the first clinical trial investigating the relationship between periodontal disease, LBW and PB in 1996 and right after, a very powerful connection between periodontal disease with PB and LBW has been outlined. A prospective cohort study by Ali and Abidin¹⁴ found that periodontitis was not associated with PB or LBW in pregnant women between 28 and 36 weeks of gestation. Although the definition of PM and LBW is very clear, different definitions of periodontitis have been used in periodontal research to date. The results of the studies in the literature are very heterogeneous due to the different criteria used in both the diagnosis and classification of periodontal diseases.¹⁵ Therefore, we aimed to re-evaluate the impact of periodontitis on adverse pregnancy outcomes using the current classification system adopted at the 2017 World Workshop, in this study.

Our study was conducted in two groups: as case (n=85) and control (n=87) group with similar demographic characteristics and oral hygiene habits. We found that the cesarean delivery rate was statistically higher in our case group. Lohana et al.¹⁶ explained that cesarean section is the most common method in the delivery of premature and LBW babies. Additionally, studies depicting there is no crucial connection between the way of delivery also PB and/or LBW still exists.¹⁷ We think that this high rate of cesarean section may be related to the negative outcome of pregnancies and the necessity of urgent delivery.

In our study which we investigated the negative pregnancy relationship with periodontal disease, the PI, GI, and BOP% values of the mothers in the case group were found to be statistically higher according to the mothers in the control group. Some studies have reported that the amount of plaque and inflammation in gingivitis is connected with PB and/or LBW.^{18,19} By using PPD and CAL together, the periodontal status of the individual from the past to the present is evaluated.²⁰ Lopez et al.²¹ found the PPD higher in individuals with preterm birth and low birth weight infants. Jarjoura et al.²² performed a study using 203 individuals, and the bond loss turned out to be higher in individuals delivering a premature baby as opposed to full-term deliveries. We found that the PPD values of the mothers in the case group were statistically higher according to the mothers in the control group. Although CAL was higher in the case group, the difference was not significant. In this study, the diagnosis and measurement criteria of periodontal disease were made according to the current classification system accepted in the 2017 World Workshop, the rate of periodontal disease was found to be higher in the case group.

Hematological parameters are frequently used in the diagnosis and prognosis of various diseases, including periodontal diseases. WBC level counts as a marker of the existence of the systemic contamination or aggravation within the person. Local inflammatory responses are maintained by the PLT under mediator conditions.²³ Studies have shown that as the severity and prevalence of periodontal disease increases, WBC increases.²⁴ Reason of increment in PLT levels and activation, was indicated as dental plaque bacteria and for the most part P.gingivalis. Leukocytes and PLT rise in response to periodontal pathogens and decrease after periodontal treatment.^{25,26} In our

study; WBC and PLT values were statistically higher in the case group with worse periodontal status. This result is compatible with the literature.²⁷

The limitations of our study are the lack of use of grading, which has a significant place in the new classification, it is single-centered, and the prenatal periodontal status of the mothers is not known. Our study found that mothers who gave birth to preterm or low birth weight babies had worse periodontal conditions than mothers who gave birth to healthy babies.

CONCLUSION

The results show that periodontal disease might be an important risk factor for PB and LBW. Women should take care of their oral hygiene and dental check-ups before and during pregnancy. However, there is a need for more detailed, highly standardized studies using consensus criteria in defining periodontal conditions to be able to talk about a full cause and effect relationship.

ETİK KURUL ONAYI

Bu çalışma için gerekli etik onay Adıyaman Üniversitesi İlaç ve Tıbbi Cihaz dışı etik kurul tarafından alınmıştır. (2019/2-16)

FİNANSAL DESTEK

Bu çalışma 'Adıyaman Üniversitesi Bilimsel Araştırma Proje Koordinatörlüğü' tarafından maddi olarak desteklenmiştir. (proje no. DHFDUP/2019-0001).

ÇIKAR ÇATIŞMASI

Yazarlar arasında herhangi bir çıkar çatışması yoktur.

YAZAR KATKILARI

Tasarım: KCD, MÇ, TK. Veri toplama veya veri girişi yapma: KCD, MFD. Analiz ve yorum: KCD, MFD. Literatür tarama: KCD. Yazma: KCD.

REFERENCES

1. Tonetti MS, Van Dyke TE, working group 1 of the joint EFP/AAPworkshop. Periodontitis and atherosclerotic cardiovascular disease: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. J Periodontol. 2013;84:24-9.
2. Carrillo-de-Albornoz A, Figuero E, Herrera D, Bascones-Martínez A. Gingival changes during pregnancy: II. Influence of hormonal variations on the subgingival biofilm. J Clin Periodontol. 2010;37:230-40.

3. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *J Periodontol.* 2018;89:159-72.
4. World Health Organization. The incidence of low birth weight: an update. *Weekly Epidemiol Rec* 1984;59:205-11.
5. World Health Organization. International Classification of Diseases. 1975 revision. Volume 1. Geneva: WHO, 1977
6. Bey A, Gupta ND, Khan S, Ashfaq N, Hadi SA. Periodontitis: a significant risk factor for preterm low birth weight (PTLBW) babies. *Biol Med.* 2011;3:158-63.
7. Dasanayake AP, Boyd D, Madianos PN, Offenbacher S, Hills E. The association between Porphyromonas gingivalis-specific maternal serum IgG and low birth weight. *J Periodontol.* 2001;72:1491-7.
8. Chapple ILC, Mealey BL, Van Dyke TE, Bartold PM, Dommisch H, Eickholz P, et al. Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Periodontol.* 2018;89:S74-S84.
9. Vergnes JN, Sixou M. Preterm low birth weight and maternal periodontal status: a meta-analysis. *Am J Obstet Gynecol.* 2007;196:135-e1.
10. Daalderop LA, Wieland BV, Tomsin K, Reyes L, Kramer BW, Vanterpool SF, et al. Periodontal disease and pregnancy outcomes: overview of systematic reviews. *JDR Clin Trans Res.* 2018;3:10-27.
11. Armitage GC. Bi-directional relationship between pregnancy and periodontal disease. *Periodontol* 2000. 2013;61:160-7.
12. Ide M, Papapanou PN. Epidemiology of association between maternal periodontal disease and adverse pregnancy outcomes--systematic review. *J Periodontol* 2013;84:181-94.
13. Offenbacher S, Katz V, Fertik G, Collins J, Boyd D, Maynor G, et al. Periodontal infection as a possible risk factor for preterm low birth weight. *J Periodontol.* 1996;67:1103-13.
14. Ali T, Abidin K. Relationship of periodontal disease to preterm low birth weight infants in a selected population- a prospective study. *Community Dent Health.* 2012;29:100-5.
15. Borrell L, Papapanou PN. Analytical epidemiology of periodontitis. *J Clin Periodontol.* 2005;32:132-58.
16. Lohana MH, Suragimath G, Patange RP, Varma S, Zope SA. Prospective cohort study to assess and correlate the maternal periodontal status with their pregnancy outcome. *J Obstet Gynaecol India.* 2017;67:27-32.
17. Vettore MV, Leao AT, Leal Mdo C, Feres M, Sheiham A. The relationship between periodontal disease and preterm low birthweight: clinical and microbiological results. *J Periodontol Res.* 2008;43:615-26.
18. Santos-Pereira SA, Giraldo PC, Saba-Chujfi E, Amaral RL, Morais SS, Fachini AM, et al. Chronic periodontitis and pre-term labour in Brazilian pregnant women: an association to be analysed. *J Clin Periodontol.* 2007;34:208-13.
19. Moss KL, Beck JD, Offenbacher S. Clinical risk factors associated with incidence and progression of periodontal conditions in pregnant women. *J Clin Periodontol.* 2005;32:492-8.
20. Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. *J periodontol.* 2007;78:1387-99.
21. Lopez NJ, Smith PC, Gutierrez J. Periodontal therapy may reduce the risk of preterm low birth weight in women with periodontal disease: a randomized controlled trial. *J Periodontol.* 2002;73:911-24.
22. Jarjoura K, Devine PC, Perez-Delboy A, Herrera-Abreu M, D'Alton M, Papapanou PN. Markers of periodontal infection and preterm birth. *American J Obstet Gynecol.* 2005;192:513-19.
23. Croce K, Libby P. Intertwining of thrombosis and inflammation in atherosclerosis. *Curr Opin Hematol.* 2007;14:55-61.
24. Loos BG, Craandijk J, Hoek FJ, Wertheim-van Dillen PM, Velden UVD. Elevation of systemic markers related to cardiovascular diseases in the peripheral blood of periodontitis patients. *J Periodontol.* 2000;71:1528-34.
25. Loubakos A, Yuan YP, Jenkins AL, Travis J, Andrade-Gordon P, Santulli R, et al. Activation of protease-activated receptors by gingipains from Porphyromonas gingivalis leads to platelet aggregation: a new trait in microbial pathogenicity. *Blood.* 2001;97:3790-7.
26. Acharya AB, Shetty IP, Jain S, Padakannaya I, Acharya S, Shettar L. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in chronic periodontitis before and after nonsurgical therapy. *J Indian Soc Periodontol.* 2019;23:419-23.
27. Papapanagiotou D, Nicu E, Bizzarro S, Gerdes V, Meijers J, Nieuwland R. Periodontitis is associated with platelet activation. *Atherosclerosis.* 2009;202:605-11.