DOI: 10.21276/sajb.2016.4.9.1

Scholars Academic Journal of Biosciences (SAJB)
Sch. Acad. J. Biosci., 2016; 4(9):700-706
ISSN 2321-6883 (Online)
ISSN 2347-9515 (Print)

(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com

Original Research Article

Periodontal Disease as a Possible Risk Factor for Low birth Weight Infants –A Case Control Study

Dr. Peddengatagari Suresh[1], Dr. Sirigala Lavanya[2]

[1]Associate Professor, Department Of Periodontics, Government Dental College, RIMS, Kadapa, Andhra Pradesh, India
[2]Incharge Professor, Department Of Oral Pathology, Government Dental College, RIMS Kadapa, Andhra Pradesh, India

***Corresponding author**
Dr. Peddengatagari Suresh
Email: slavanyamds@yahoo.co.in

Abstract: The objective of this case-control study was to determine the influence of periodontal disease in pregnant women a possible risk factor for low birth weight infants. 200 postpartum women were included in this study population was grouped into: controls (TNBW, n=100) and cases (TLBW, n = 100). Periodontal disease presence and severity were clinically determined using Russell's periodontal index. The nutritional evaluation of the newborns was determined by Ballard's modified gestational age assessment chart. Results in this study concluded that the periodontal health appeared to be worsened as the mother's age increased. There was a decrease in the gestational age and birth weight of the infants as the mother's periodontal disease severity increased, although the values were not significant. An increase in the periodontal index score with increased periodontal disease severity was observed in cases as compared to controls. There was an association between periodontal disease and low birth weight, although this association has not reached statistical significance.
Keywords: Gestational age; Birth weight; Infant; Periodontal disease; Risk factor; TNBW; TLBW; PLBW.

INTRODUCTION

Periodontitis refers to the inflammatory loss of the attachment apparatus that includes the cementum, the periodontal ligament, and the bone supporting the tooth. As this supporting connective tissue around the tooth is lost, the epithelial attachment migrates towards the root apex, creating a periodontal pocket formation and eventually tooth exfoliation [1]. Periodontitis is a multifactorial disease, meaning that many risk factors may help create an altered or hyper-inflammatory trait that places the subject at risk for severe periodontal tissue breakdown when given a microbial challenge. This concept has gained tremendous experimental and population based evidence. Although we don't currently completely understand all of the components of the host response that seem to confer susceptibility, several biochemical markers seem critical in regulating connective tissue destruction and clinical disease [1].

The Gram-negative bacteria associated with progressive disease are capable of producing a variety of bioactive molecules that can directly affect the host. One of these microbial components, lipopolysaccharides (LPS, endotoxin), is shed in vesicles by Gram-negative oral microbes and has been demonstrated to penetrate into gingival tissues. LPS can activate macrophages and other cells to synthesize and secrete a wide array of molecules including the cytokines, interleukin-1beta (IL-1β), TNFα, IL-6 and prostaglandin E_2 (PGE_2), and matrix metalloproteinases [1].

Low birth weight (LBW) continues to be a significant cause of infant morbidity and mortality. LBW is associated with risk for mortality in the first year of life, with developmental problems in childhood, and with risk of several diseases in adulthood [2]. More than 60% of the mortality that occurs among infants without anatomic or chromosomal congenital defects is attributable to low birth weight (LBW) [3]. The prevalence of preterm birth varies from 6% to 15% of all deliveries, depending on the population and the prevalence has risen in recent years [4]. The factors that are generally thought to be related to increased likelihood low-birth weight infants are: genetic risk, demographic and psychosocial risk, nutritional risk, infection, toxic exposure, and antenatal care [5]. Periodontal infection, which is a reservoir for Gram-negative anaerobic microorganisms, lipopoly-saccharides, and inflammatory mediators, including prostaglandin E_2 and tumor necrosis factor-alpha, can represent a risk for adverse pregnancy results [6, 7]. Consequently, it is not surprising to find that increasing periodontal disease severity in the mother may result in a decreasing birth weight and gestational age [8].

Hence, on the basis of above evidence, the present study was undertaken to determine the influence of periodontal disease in pregnant women on their newborns. This study was based on the hypothesis that periodontal disease, an infectious process itself, may be related to gestational age and their birth weight.

AIM OF THE STUDY

To determine maternal periodontal disease could be a possible risk factor for low birth weight infants.

MATERIALS

William's graduated periodontal probe, Straight probe, UNC – 15 probe, Explorer, Tweezer, Kidney tray, Mouth mask, surgical gloves, Cotton

METHOD

- Screening and sample selection
- Measurement of Periodontal status
- Evaluation of infant's nutritional state
- Statistical analysis

Screening and sample selection

A case control study design was chosen including 200 postpartum women between the ages of 18 to 35 years. (100 cases and 100 controls).

Study population was selected from the Department of Gynaecology and Obstetrics and Department of Paediatrics, Chigateri General Hospital, Bapuji Child Health Institute, Women and Children Hospital, Davangere. The study population was grouped as follows

I. Controls (n = 100) Term normal birth weight (TNBW) - the mothers who delivered infants after 37 weeks of gestation and infants weighing more than or equal to 2500 g at birth.

II. Cases (n = 100) Term low birth weight (TLBW)- the mothers who delivered infants after 37 weeks of gestation and infants weighing less than 2500 g at birth.

Inclusion criteria

- Pregnant women between the ages of 18 to 35 years were selected.
- Study participants having a Body Mass Index (BMI) ranging between 19 kg / m^2 and 25kg / m^2 were selected.

Exclusion criteria

- Systemic conditions: Severe anemia Diabetes, Cardiovascular disorders, Hepatic deficiency, High blood pressure, Venereal diseases ,Urinary infections, Bacterial vaginitis ,Viral infections .
- Environmental factors: Tobacco, alcohol, narcotic drug use, X-ray during the first trimester Anticonvulsive drugs.
- Obstetric history which included multiple pregnancies, more than 3 births, severe polyhydramnios Severe oligohydramnios, Umbilical cord coilings.

Data collection: All the data were collected within 48 hours after delivery. Clinical histories taken by the attending obstetrician were reviewed to ensure that none of the exclusion criteria mentioned above was present.

Measurement of periodontal status

Russell's periodontal index (PI) was used to define periodontal condition of the mother. Full mouth scores were obtained by totaling all the scores and dividing it by the number of teeth examined [9]. The periodontal index was intended to estimate the extent of deeper periodontal disease by measuring the presence or absence of gingival inflammation and its severity, pocket formation, and masticatory function. The PI is a composite index because it records both the reversible changes due to gingivitis and the more destructive and presumably irreversible changes brought by deeper periodontal disease.

All the teeth were examined. All of the gingival tissue circumscribing each tooth (i.e., all of the tissue circumscribing a tooth is considered a scoring or gingival unit) is assessed for gingival inflammation and periodontal involvement. A full mouth periodontal examination was performed and corroborated by one examiner on all the patients selected. The oral examination was carried out with the help of artificial light source, mouth mirror and William's graduated periodontal probe.

Criteria and scoring for field studies:

0 – Negative: There is neither overt inflammation in the investing tissues nor loss of function due to destruction of supporting tissues.
1 – Mild gingivitis: There is an overt area of inflammation in the free gingiva, but this area does not circumscribe the tooth.
2 – Gingivitis: Inflammation completely circumscribes the tooth, but there is no apparent break in the epithelial attachment.
6 – Gingivitis with pocket formation: The epithelial attachment has been broken, and there is a pocket (not merely a deepened gingival crevice due to swelling in the free gingiva). There is no interference with normal masticatory function, the tooth is firm in its socket, and it has not drifted.
8 – Advanced destruction with loss of masticatory function: The tooth may be loose, may have drifted, may sound dull on percussion with a metallic instrument, or may be depressible in its socket.

Periodontal Index per person

$$= \frac{\text{Sum of individual scores}}{\text{Number of teeth present}}$$

Once the periodontal index scores were obtained, the women were divided into groups as follows:
Group I: Normal (PI = 0 to 0.2)
Group II: Simple gingivitis (PI = 0.3 to 0.9)
Group III: Initial periodontitis (PI = 0.7 to 1.9)
Group IV: Established periodontitis (PI = 1.6 to 5.0)

Evaluation of infant's nutritional state

Birth weight was attained within 1 hour of birth by placing the naked infant on a precise scale calibrated in grams. Infants were then placed into the following categories by birth weight-
Low birth weight < 2500 g
Normal birth weight – 2500 to 3900 g
High weight > 3900g

Gestational age of the infant was determined using Ballard's (Modified) gestational age assessment chart [10], which is based on physical and neurological examination to determine maturity. Analysis of examination values provided gestational age of the infant in weeks Term – 37 to 42 weeks.

The data obtained was tabulated and then subjected to statistical analysis.

Statistical analysis

Descriptive data that included mean and standard deviations were determined for each of the variables in each group. Categorical data was analyzed by Chi-square test. Multiple groups were compared by one-way ANOVA and group wise by Student's t-test. Relationship between Periodontal Index and other variables was assessed by Pearson's correlation coefficient. Significance for all the tests was predetermined at a probability value of 0.05 or less.

RESULTS

Study results were presented for each of the variables- maternal height, education level, socioeconomic status, periodontal condition of the mother, infant birth weight, gestational age, age of the mother and body mass index of the mother.

Table- 1.Comparison of Height, Education level, Socioeconomic status in Controls & Cases

S.No	Parameters		Controls (TNBW)	Cases (TLBW)	Statistical analysis
1	Height		156.0±3.9	155.6±2.8	F-0.35;P-0.70-NS (one way ANOVA)
2	Education Level	No Education	19	35	χ^2 - 28.8: P< 0.001 -HS Chi-square test
		Primary Level	63	58	
		Secondary Level	18	7	
3	socioeconomic status	Low	82	93	χ^2 - 21.8: P< 0.001 - HS Chi-square test
		Middle	18	7	

Table 1 shows comparison of, height, education levels, socioeconomic status between controls and cases.

- The mean height of the mothers in the Control group (TNBW) was 156.0 ± 3.9 cm, in the cases (TLBW) it was 155.6 ± 2.8 cm . Statistically, there was no significant difference between the controls and cases when height was compared (F = 0.35; P = 0.70).
- There was a highly significant difference between controls and cases when education level was compared (χ^2= 28.8; P < 0.001).
- There was a highly significant difference when socioeconomic status was compared between controls and cases (χ^2 = 21.8; P < 0.001).

Table- 2: Comparision of Russel's periodontal Index in controls and Cases

Groups	**No. of cases**	**Russell's index**			
		Range	**Mean**	**SD**	**CV (%)**
Controls (TNBW)	100	0.38 – 1.50	0.81	0.14	17.3 %
Cases (TLBW)	100	0.46 – 2.38	0.88	0.32	36.4 %

ANOVA	**F = 53.8**	**P<0.01**	**Sig.**
Controls	Cases (TLBW)	NS	

Table 2-Compares the Russell's periodontal index within and between controls and cases.

- In the control group the Russell's periodontal index was ranging from 0.38 to 1.50 with a mean of 0.81 and standard deviation of 0.14.

- In the cases (TLBW) the Russell's periodontal index was ranging from 0.46 to 2.38 with a mean of 0.88 and standard deviation of 0.32.When Russell's periodontal index was compared between control group and cases, there was an increase in the periodontal index scores in cases, but statistically not significant.

Table-3: Relationship of Infant birth weight to Periodontal condition

Periodontal condition	Controls (TNBW)		Cases (TLBW)	
	n	x ± SD	n	x ± SD
Simple Gingivitis	90	2950 ± 377	76	2205 ± 251
Initial periodontitis	10	2811 ± 252	22	2237 ± 173
Established periodontitis	-	-	2	2125 ± 125
Total	100	2936 ± 369	100	2211 ± 199
Statistical analysis	P=0.26(NS)		P=0.67(NS)	

Table 3, shows the relationship of infant's birth weight to periodontal condition of the mothers.

- In the control group, the mean infant's birth weight was 2936 ± 369g. The mean birth weight of the infants delivered by mothers with simple gingivitis was 2950 ± 377 g and that of mothers with initial periodontitis was 2811 ± 252g. As the severity of periodontal disease increased there was a reduction in the infant's birth weight. However, there was no statistically significant association between these two variables (P = 0.26).
- In the cases (TLBW), the mean infant's birth weight was 2211 ± 199 g. The mean birth weight of the infants delivered by mothers with simple gingivitis was 2205 ± 251 g, that of mothers with initial periodontitis was 2237 ± 173 g and the mean birth weight of infants delivered by mothers with established periodontitis was 2125 ± 125g. As the periodontal disease increased in its severity from initial periodontitis to established periodontitis, there was a decrease in the infant's birth weight i.e. from 2237 ± 173 g to 2125 ± 125 g. The statistical analysis revealed no significance between the examined variables (P = 0.67).

Table-4: Relationship of PI WITH BW, GA, MATERNAL AGE and BMI

Correlation between	Controls (TNBW)		Cases (TLBW)		Total	
	r	P	r	P	r	P
PI and BW	-0.02	0.81 NS	-0.04	0.67 NS	-0.40	<0.001 HS
PI and GA	-0.16	0.12 NS	-	-	-0.50	<0.001 HS
PI and Maternal Age	0.02	0.87 NS	+0.50	<0.001 HS	+0.23	<0.001 HS
PI and BMI	0.15	0.12 NS	-0.01	0.96 NS	-0.09	0.11 NS

Table 4 shows comparison of infant's birth weight and gestational age, maternal age and BMI according to the mother's periodontal condition using Pearson's correlation coefficient.

- In the control group; the correlation between periodontal index and infant's birth weight showed a negative relation (r = - 0.02), stating that as the periodontal health worsened; there was a decrease in the infant's birth weight. The P value, P = 0.81 confirmed that this relation was not statistically significant. The correlation between periodontal index and infant's gestational age showed a negative relation (r = - 0.16), stating that there was a decrease in the gestational age as the mother's periodontal disease increased in severity. However, P value, P = 0.12 revealed that the relation was not statistically significant.

The correlation between periodontal index and maternal age was not statistically significant with corresponding values (r = 0.02, P = 0.87).

- In the cases (TLBW); the correlation between periodontal index and the infant's birth weight showed a negative relation (r = - 0.04) stating that an increase in the periodontal disease severity resulted in a decrease in the infant's birth weight. But the P value, P = 0.67 proved that this relation was not statistically significant.

The correlation between periodontal index and the maternal age showed a positive relation (r = + 0.50) stating that there was an increase in the periodontal disease severity as the maternal age increased. The P value, P < 0.001 revealed that this relation was statistically highly significant.

- When all the study population (n = 200) were compared, the correlation between periodontal index and infant's birth weight showed a negative relation (r = - 0.40) stating that as the periodontal disease increased in severity, there was a decrease in the infant's birth weight. This relation was proved to be statistically highly significant with corresponding P value, $P < 0.001$.

The correlation between periodontal index and maternal age showed a positive relation ($r = + 0.23$) inferring that periodontal health worsened as the maternal age increased. This relation was proved to be statistically highly significant ($P < 0.001$).

- The correlation between periodontal index and body mass index of the mother was not statistically significant with corresponding values ($r = - 0.09$, $P = 0.11$). Periodontal disease severity was not significantly related to mother's body mass index as the study participants with body mass index in the range of 19 kg/m^2 to 25 kg/m^2 were selected as per the inclusion criteria mentioned in the methodology.

Table-5: Relationship of BMI to Periodontal condition

Periodontal condition	Control (TNBW)		Cases (TLBW)	
	n	$\bar{x} \pm$ SD	n	$\bar{x} \pm$ SD
Simple Gingivitis	90	20.7 ± 1.3	76	19.8 ± 0.7
Initial periodontitis	10	21.5 ± 1.6	22	20.2 ± 1.2
Established periodontitis	-	-	2	19.3 ± 0.1
Total	100	20.8 ± 1.4	100	19.9 ± 1.0

Table 5 shows the relationship of mother's BMI to periodontal condition.

- In the Controls (TNBW), the mean BMI of the mothers was 20.8 ± 1.4 kg/m^2. BMI of the mothers with simple gingivitis was 20.7 ± 1.3 kg/m^2 and BMI of the mothers with initial periodontitis was 21.5 ± 1.6 kg/m^2. When the mother's BMI was compared to periodontal condition there was no statistical significance ($P = 0.12$).

- In the Cases (TLBW), the mean BMI of the mothers was 19.9 ± 1.0 kg/ m^2. BMI of the mothers with simple gingivitis was 19.8 ± 0.7 kg/ m^2, BMI of the mothers with initial periodontitis was 20.2 ± 1.2 kg/m^2 and that of mothers with established periodontitis was 19.3 ± 0.1 kg/m^2. Statistically no significance was found between these two variables ($P = 0.20$).

DISCUSSION

Birth weight is considered to be an important determinant of the chances of an infant to survive, growth and mature [11]. Low birth weight babies are about 20 times, and very low birth weight babies (< 1500 g) are about 80 times more likely to die before their first birthday [12]. Various factors have been associated with the delivery of low-birth weight infants [11].

Periodontal diseases are a group of infectious diseases resulting in inflammation of gingival and periodontal tissues and progressive loss of alveolar bone. The periodontal infection is initiated and sustained by several bacteria, predominantly Gram-negative, anaerobic and microaerophilic bacteria that colonize the subgingival area. Host defense mechanisms play integral role in the pathogenesis of periodontal disease. It has been postulated that the association between periodontal disease and low birth weight (LBW) may have similar pathogenic mechanisms as other maternal infections. Inflamed periodontal tissues produce significant amounts of proinflammatory cytokines, mainly interleukin 1 beta (IL-1β), IL-6, prostaglandin E_2, and tumor necrosis factor alpha (TNF-α), which may have systemic effects on the host [13].

There is an evidence of association between periodontal disease, especially severe periodontitis, and a variety of systemic conditions. Among these are cardiovascular disease, including endocarditis and coronary heart disease, insulin-dependent diabetes mellitus, and respiratory disease Collins and co-workers reported that there was a 25% reduction in birth weight in pregnant hamsters challenged subcutaneously in the dorsal region with the periodontal pathogen Porphyromonas gingivalis, compared with normal healthy pregnant hamsters [11].

Based on the evidence from the above review of information, this study was intended to determine whether maternal periodontal disease could be associated to low birth weight infants.

The selected study population was in the age range of 18-35 years. Selection was carried out as per the inclusion and exclusion criteria mentioned in the methodology. A proforma was used to record all the details and clinical observations of the study population.

In this case-control study, selection bias was avoided by excluding all the traditional risk factors and confounding variables were controlled in a well defined population (mothers giving birth at particular hospitals) and almost all mothers agreed to participate in the study. Where feasible, details ascertained in the questionnaire were evaluated from the maternity notes. We can therefore be confident that selection bias has not influenced our results. Variables like low socioeconomic status (labourers/farmers), education level (no/primary level) were found to be associated with the increased risk of having a LBW infant and were statistically highly significant ($P< 0.001$), which was in correlation with Dasanayake AP (1998) [14] which lends further credibility to the validity of this study. However, the maternal height compared between the groups was not found to be significant ($P= 0.70$).

In studies of clinical periodontal disease, a great many potential measures of disease severity are available. Our choice of periodontal indices was essentially determined by the need to carry out the clinical examination in the ward. Russell's periodontal index is an epidemiologic index with true biologic gradient and was seen to provide the most appropriate screening system for the chosen setting. It is unlikely that different choices of outcome would have produced different results.

Various factors have been associated with the delivery of low birth weight infants. However, the significant proportion of low birth weight is of unknown etiology. LBW is not the single pathologic entity. Studies on etiological factors for LBW should make the conceptual distinction between intrauterine growth and gestational age duration. Thus, our findings can be safely regarded as possible etiological factors for low birth weight independent of gestational duration. In this study, in the A Cases (TLBW), wherein gestational duration being normal with low birth weight has shown decrease in infant birth weight with increase in periodontal disease severity from initial periodontitis to established periodontitis which was found to be nonsignificant. Collins JG *et al.*, [15] suggested that infection with Gram-negative periodontal pathogens may induce adverse effects on the fetus, depending on the degree of infection. The authors reported that the lipopolysaccharide from oral bacteria can cause adverse pregnancy outcomes and have shown that increasing doses of lipopolysaccharide from both Escherichia coli and Porphyromonas gingivalis produced biphasic effects on fetal weight with significant decreases in fetal weight at higher doses. Dasanayake AP [14] suggested that periodontal disease, which is a Gram-negative anaerobic infection, can affect pregnancy outcome either by the direct or indirect effect of periodontal pathogens on the developing fetus.

There was a possible association between the periodontal condition of mothers and the nutritional condition of their newborns. The association was significant when Controls were compared with Cases ($\chi^2 = 7.68$; $P < 0.5$). The above results agree with those reported by Romero BC *et al*., [16] who stated that there was a clinical association between an increase in the severity of periodontal disease and nutritional condition of their newborns.

The relationship of maternal age with the periodontal condition was not significant in the Control group (mean= 22.5 ± 3.1 years; $P = 0.87$), highly significant in the Cases (mean = 22.6 ±3.1 years; $P < 0.001$). The above results agree with those reported by Dasanayake AP [14]. He reported in his study that mothers who delivered low birth weight infants appeared to be slightly older than the mothers who delivered term normal birth weight infants.

There was a slight decrease in the infant's birth weight and gestational age as the periodontal disease severity increased. The relationship between the infant's birth weight and periodontal condition was not significant in the Controls (mean= 2936 ± 369 g; $P = 0.26$), Cases (mean = 2211±199 g; $P = 0.67$). The association between the infant's gestational age and the periodontal condition was not significant in the Controls (mean = 38.2 ± 0.6 weeks; $P = 0.27$). The above results agree with those reported by Dempsey *et al*[17]. The authors stated that the high risk group was found to have significantly ($P< 0.01$) more plaque (mean plaque indexes 1.52 vs 0.79), more gingival inflammation (mean gingival indexes 1.56 vs 0.62), and more bleeding on examination (mean percentage of sites bleeding 30.7% vs 11.92%) than the low risk group.

When Russell's periodontal index was compared between Controls and Cases, there was no statistical significance. The above results agree with those reported by Romero BC *et al*.,[16] who stated that a decrease in the average newborn's weight and gestational age was observed as the mother's level of periodontal disease increased and suggested that periodontal disease in pregnant women would be a clinically significant risk factor for low birth weight.

The relationship between periodontal condition and BMI was not statistically significant in the Controls (mean= 20.8 ± 1.4 kg/m^2; $P = 0.12$), A Cases (mean = 19.9 ± 1.0 kg / m^2; $P = 0.20$), Above results agree with those reported by Romero BC et al., [11] who stated that in their study Corporal Mass Index, CMI (19.8 to 26.0 kg / m^2) covered a wide range and no significant difference was found when CMI was compared to periodontal condition ($P = 0.8839$).

Theoretically, compromised oral health of the mother can affect the fetus in many different ways. One possible mechanism would be through the decreased nutritional intake as a result of poor oral health. For this to be true, the nature of the oral illness should be severe enough to interfere with food intake and should last for a considerable time period [14].

On the other hand, periodontal disease, which is a Gram-negative anaerobic infection, can affect pregnancy outcome either by the direct or indirect effect of periodontal pathogens on the developing fetus. While there is no evidence to date as to whether specific periodontal pathogens are found in relation to the developing fetus or the feto-placental unit, there is ample evidence for the effect of other infectious agents found in the genitourinary tract on the pregnancy outcome. Bacterial vaginosis and a high prevalence of maternal lower genitourinary tract infections are associated with poor pregnancy outcomes. Colonization of the vagina and cervix with Gram-negative Bacteroides is also associated with poor pregnancy outcomes. The possibility that the inflammation of the placental membranes could occur even without signs of infection, and that such inflammation is associated with poor pregnancy outcomes, lends credibility to the idea of an indirect effect of periodontal pathogens on the developing fetus.

Dasanayake *et al*. hypothesized that Gram-negative anaerobic pathogens from the periodontium and associated endotoxins and maternal inflammatory mediators could have a possible adverse effect on the developing fetus. This view is further supported by the results obtained from animal models, where subcutaneous infection with a periodontal pathogen and experimental periodontal disease in pregnant hamsters resulted in decreased fetal growth as well as increased inflammatory mediator levels [14].

CONCLUSION

It is not yet clear that periodontal disease plays a causal role in adverse pregnancy outcomes. Hence, according to this study periodontal disease in pregnant women could have influence on their newborn's nutritional condition. Preliminary evidence to date suggests that periodontal intervention may reduce adverse pregnancy outcomes. Additional large-scale longitudinal epidemiologic and interventional studies are necessary to validate this association and to determine if the association is causal. Further studies should include measurement of bacteriological profiles and molecular epidemiological and randomized clinical trials. Poor periodontal health of pregnant women as a potential independent risk factor for low birth weight needs to be studied further which includes large sample size and analysis of periodontal pathogens and cellular inflammatory mediators.

REFERENCES

1. Offenbacher S, Beck JD, Lieff S, Slade G; Role of periodontitis in systemic health: spontaneous preterm birth. Journal of dental education, 1998; 62(10): 852-858.
2. Scannapieco FA, Bush RB, Paju S; Periodontal disease as a risk factor for adverse pregnancy outcomes. A systematic review. Ann Periodontol, 2003; 8: 70-78
3. Gibbs RS, Romero R, Hillier SL, Eschenbach DA, and Sweet RL. A review of premature birth and subclinical infection. Am J Obstet Gynecol, 1992; 166: 1515-28
4. Madianos PN, Bobetsis GA, Kinane DF; Is periodontitis associated with an increased risk of coronary heart disease and preterm and / or low birth weights? J Clin Periodontol, 2002; 19 (Suppl.3): 22-36.
5. Williams CECS, Davenport ES, Sterne JAC, Sivapathasundram V, Fearne JM, Curtis MA; Mechanisms of risk in preterm low-birth weight infants. Periodontol, 2000; 23: 142-150.
6. Collins JG, Windley HW, Arnold RR, Offenbacher S; Effect of a Porphyromonas gingivalis infection on inflammatory mediator response and pregnancy outcome in the hamster. Infect Immun, 1994; 62: 4356-61.
7. Collins JG, Kirtland BC, Arnold RR, Offenbacher S. Experimental periodontitis retards hamster fetal growth. J Dent Res, 1995; 74 (Spl. Issue): 158 (Abstr. 1171).
8. Offenbacher S, Lin YY, Boyd DL, Arnold RR; Actinobacillus actinomycetemcomitans infection associated with low birth weight. J Dent Res, 1993; 72 (Spl. Issue): 373 (Abstr. 2157).
9. Newman MG, Carranza FA; Clinical Periodontology. 8th Edition. Saunders, 1996.
10. Cloherty JP, Eichenwald EC, Stark AR; Manual of neonatal care. 5th Edition. Lippincott Williams & Wilkins, 2008.
11. Davenport ES, Williams CECS, Sterne JAC, Murad S, Sivapathasundram V, and Curtis MA. Maternal periodontal disease and preterm low birth weight: Case-control study. J Dent Res, 2002; 81(5): 313-318.
12. Dasanayake AP, Russell S, Boyd D, Madianos PN, Forster T; Preterm low birth weight and periodontal disease among African Americans. Dent Clin N Am, 2003; 47: 115-125.
13. Lopez NJ, Smith PC, and Gutierrez J; Higher risk of preterm birth and low birth weight in women with periodontal disease. J Dent Res, 2002; 81(1): 58-63.
14. Dasanayake A. Poor periodontal health of the pregnant woman as a risk factor for low birth weight. Ann Periodontol, 1998; 3: 206-212.
15. Collins JG, Smith MA, Aronld RR, and Offenbacher S; Effects of Escherichia coli and Porphyromonas gingivalis lipopolysaccharide on pregnancy outcome in the golden hamster. Infect Immun, 1994; 62: 4652-4655.
16. Romero BC, Chiquito CS, Elejalde LE, Bernardoni CB; Relationship between periodontal disease in pregnant women and the nutritional conditions of their newborns. J Periodontol, 2002; 73: 1177-1183
17. Dempsey R, Ashmead G, Cissada N, Clapp J, Amini S; Periodontitis and preterm labor. Am J Obstet Gynecol, 2000; 182: 82.