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The Prevalence and Relationship between Periodontal Disease and Pre-term Low Birth Weight Infants at King Khalid University Hospital in Riyadh, Saudi Arabia

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Abstract

The aim of this study was to examine the prevalence and relationship between periodontal disease and pre-term low birth weight (PLBW) among Saudi mothers at King Khalid University Hospital (KKUH) in Riyadh, Saudi Arabia. The periodontal status and the relative risk were also analyzed. The study consisted of 30 cases [infants <37 weeks and/or weighing ≥2.500 kilograms (kg)] and a daily random sample of 60 controls [≥ 37 weeks and/or weighing >2.500 kg]. Clinical periodontal indices were measured on the labor wards. Associated risk factors for periodontal disease and PLBW were ascertained by means of a structured questionnaire and maternal notes. The prevalence of the PLBW was found to be 11.3%, and the prevalence of periodontal disease was high among the study population. The risk of PLBW remained high with increasing periodontal disease (odds ratio [OR] 4.21, 95% confident interval [CI] 1.99-8.93) despite controlling the other risk factors such as age, smoking, and social class. In conclusion, there is a correlation between periodontal disease and PLBW in KKUH.

Keywords: Periodontal disease, pre-term low birth weight

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Introduction

Recent progress in identification and characterization of periodontal pathogens, as well as elucidation of potential systemic mechanisms of action of bacterial products and inflammatory cytokines, have opened the way for a more realistic assessment of the systemic importance of periodontal disease. Epidemiological and microbiological studies have lent credence to the concept periodontal disease may be a separate risk factor for cardiovascular disease, cerebrovascular disease, respiratory disease, as well as pre-term delivery of low birth weight infants.[1]

Low birth weight (LBW), defined as birth weight less than 2.500 kilograms (kg), continues to be a significant public health issue in both developed and developing countries. This obstetric complication is usually a direct result of pre-term labor, in which case it is referred to as pre-term delivery (less than 37 weeks) of low birth weight infants (PLBW).[2,3]

The prevalence of LBW in the United State is about 7.3%.[4] In the United Kingdom 6% of all live births are classified as LBW and 6.7% as PLBW.[5] In Africa the average LBW is around 12% and around 15% in Asia.[6] Globally, about 16% of the infants born in the world are LBW infants.[7]

Various factors have been associated with the delivery of PLBW infants. Maternal risk factors include: age, height, weight, socioeconomic status, ethnicity, smoking, nutritional status, and stress.[8] In addition parity, birth intervals, previous complications, pre- and ante-natal care, maternal hypertension, generalized infections, localized infections of the genital and urinary system, and cervical incompetence may also be important.[9,10] However, a significant proportion of LBW is of unknown etiology.

The major factor among all of these is infection, whose role is increasingly receiving more attention. The first evidence involved the increased prevalence of maternal lower genitourinary tract infections with pregnancy complications such as pre-term labor (PTL) and LBW. Other investigators have looked at the effects of subclinical urinary tract infections on pregnancy outcomes. One study showed a 40% increase in pre-term delivery rates in mothers who where colonized with cervical *Bacteroides* at their initial prenatal visit.[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 mechanism plays an integral role in the pathogenesis of periodontal disease. Tissue destruction in periodontitis is mainly due to the activation of immune cells by the cell wall component of microorganisms, such as lipopolysaccharide, which potently stimulate the production of host derived enzymes, cytokines, and other pro-inflammatory mediators resulting in connective tissue distruction.[12,13]

The possibility periodontal infections may constitute remote maternal infections that may adversely influence the birth outcome was raised for the first time in the late 1980s.[14,15] A study conducted by Offenbacher and colleagues suggested maternal periodontal disease could lead to a seven fold increased risk of delivery of PLBW infants.[11] In a case-control study of 124 pregnant or postpartum mothers, in which cases were defined either as mothers who currently or previously delivered PLBW infants or as primiparous mothers delivering PLBW infants, showed these cases had significantly worse periodontal disease than controls. After controlling other risk factors, the study concluded periodontal disease is a statistically significant risk factor for PLBW. Moreover, it has been observed in animal models infection with Gram-negative periodontitis associated micro-organisms may adversely affect pregnancy outcomes.[11]

In another case-control study Dasanayake et al. studied 55 pairs of women; logistic regression indicated mothers with healthy gingiva were at lower risk for LBW infants (odds ratio=0.3).[16] Collins and coworkers reported there was a 25% reduction in birth weight in pregnant hamsters challenged subcutaneously in the dorsal region with periodontal pathogen *porphyromonas gingivalis* (PG), compared with normal healthy pregnant hamsters.[17,18] In 2002 Davenport et al. conducted a case-control study of 236 cases and 507 controls; he found no evidence for an association between PLBW and periodontal disease.[19]

Not until this study was conducted and published has there been data on this subject in Saudi Arabia. The objective of this study was to examine the prevalence and the relationship between PLBW and periodontal disease among Saudi mothers delivering at King Khalid University Hospital in Riyadh, Saudi Arabia (KKUH). The periodontal status and relative risk were also analyzed.

Materials and Methods

The study population was comprised of a group of Saudi mothers from Riyadh, Saudi Arabia, who gave birth at KKUH (December 2002 – January 2003). The study received ethical approval from the College of Dentistry Research Center (CDRC) and from KKUH. An un-matched case-control study with a selection ratio of (1:2) was performed using 30 cases and 60 controls derived from among 415 Saudi mothers who were interviewed.

Inclusion Criteria

All Saudi mothers with a singleton gestation were included. Any mother who delivered a live infant whose birth weight was less than 2.500 kg and/or before 37 weeks gestation was considered a potential case. Potential controls were mothers who delivered live infants who weighed 2.500 kg or more and/or 37 weeks gestation and after were selected randomly from eligible mothers present on the ward.

Exclusion Criteria

The exclusion criteria included a history of medications or medical problems that may affect the study outcome, such as, current use of systemic corticosteroids, antibiotics, congenital heart disease, existing hypertension and diabetes before pregnancy, asthma, and chronic renal disease. Moreover, those who had multiple deliveries, whose infants were stillborn, whose labor was induced, and whose infants did not fit either the "control" or the "case" definitions or mothers who refused to participate were also excluded.

The subjects were selected by inspection of KKUH birth records each weekday. They were seen within 24 hours of delivery. The subjects were then invited to participate in the study and informed signed consent was obtained. A structured questionnaire was administered to the participants. The contents of the questionnaire are listed in Table 1. Information from maternal notes were obtained (maternal age, weight, sex of infants, and method of delivery).

Table 1. Contents of the questionnaire.

Content of the Questionnaire		
Age	Previous Miscarriages	Previous LBW
Height	Medical History	Prenatal Care
Weight	Smoking Habit	Genitourinary tract infection
Nationality	High Coffee Intake	Weight Gain
Social Class	Medications	Dental History
Educational Level	Stress	Last Dental Visit
No. of Children	Placental Problems	Periodontal Infection
Previous Pregnancies	Previous Pre-term	Periodontal Treatment

Inter-examiner reliability in using the dental examination criteria was tested (pilot test) by performing duplicate examination on 10 randomly selected mothers on two consecutive days. Inter-examiner reliability was determined using Kappa statistic. Ninety-five percent agreement on criteria for pocket depth was obtained.

The same investigators who had been calibrated prior to the study carried out all periodontal examinations, blinded to case-control status. Periodontal disease was assessed by using the following:

1. Probing depth (PD) in millimeters was made at the mesiobuccal, buccal, distobuccal, disto-lingual, lingual, and mesiolingual positions of every tooth with the exception of third molars.
2. Bleeding on probing (BOP) on the six sites at which PD was determined and deemed positive if it occurred within 15 seconds after probing. BOP was expressed as the percentage of sites showing bleeding.
3. Presence or absence of calculus was obtained.
4. The Community Periodontal Index of Treatment Needs (CPITN) ranged from 0-4:

   0 = Healthy
   1 = Bleeding on probing
   2 = Supra and sub-gingival calculus
   3 = Shallow pockets (3.5-5.5 mm)
   4 = Deep pockets (>6mm), using a calibrated periodontal probe was quantified.

The contents of the clinical examination and information about oral hygiene are shown in Table 2.

The examination was conducted with the subject supine in the hospital bed. A head external lamp (Headband Magnifier S with lamp) was used to facilitate a calibrated periodontal examination.

Table 2. Contents of clinical examination and the information about oral hygiene.

Content of Clinical Examination	Oral Hygiene
Probing Depth	Type of Tooth Brush
BOP%	No. of Brushing/day
Calculus	Brushing Technique
CPITN	Other Aids

Data Analysis

Data was entered into the computer and analyzed using Statistical Package for Social Sciences (SPSS) version 10 for Windows. Chi-square analyses and Fisher's exact test were used to test the group differences in categorical variables. A Student t-test was used to test the group differences in continuous variables. Logistic regression was performed to determine the risk model for PLBW. Statistical significance was defined as $P<0.05$.

Results

Results are summarized in Tables 3-8 and Figures 1-3. A total of 90 subjects (30 cases, 60 controls) were recruited into the study. The distributions of demographic features of the study population are shown in Table 3. The mean age of the cases was 30.8 years (S.D 6.90) and controls 28.60 years (S.D 6.40). The majority of mothers were of a high educational level. None of the mothers in either group reported stress or a habit of smoking. The distribution of all other variables showed no significant differences between the groups.

Distribution of pregnancy-related variables in the two groups is shown in Table 4. The majority of mothers had 5 or more previous pregnancies. Among the known risk factors for PLBW, a history of previous pre-term and previous LBW infants among case and control mothers approached statistical significance (P-value= 0.006, 0.011), respectively. The distribution of all other variables showed no significant differences between the groups.

The weight of the infants and the maternal age are shown in Table 5. The control group had a higher mean weight and maternal age than case group (P-value=0.00).

Table 6 shows dental history where the majority of mothers examined were subjected to dental treatment at least once in their lives. Thirty-one point seven percent of controls and 50% of cases indicated a history of periodontal disease, but only 3.3% of the controls and 10% of the cases stated they had periodontal treatment. Regarding oral hygiene habits, the majority of the mothers brushed twice a day using a soft toothbrush.

Table 3. Demographic details of cases versus controls.

	Case n=30	Control n=60	Odds Ratio (95% CI)	P-value
Age Group(yrs)				
18-24	5	21	1.687(0.568-6.129)	0.126
25-29	13	12	0.410(0.145-1.159)	
>30	12	27	1(reference)	
Social Class				
High	10	19	2.105(0.480-9.237)	
Medium	17	29	2.345(0.578-9.505)	0.475
Low	3	12	1(reference)	
Education				
Literate	1	3	1.44 (0.135-15.336)	
Elementary	4	6	0.720(0.171-3.040)	
Intermediate	6	8	0.640(0.181-2.262)	0.873
Secondary	7	18	1.234(0.406-3.752)	
College	12	25	1(reference)	
High Coffee Intake				
Yes	11	15	1.737(0.675-4.460)	0.250
No	19	45	1(reference)	
Medical Problem				
Yes	2	3	1.357(0.214-8.592)	1.00
No	28	57	1(reference)	
Medication				
Yes	2	3	1.357(0.214-8.592)	1.00
No	28	57	1(reference)	

Prevalence of PLBW

The prevalence of PLBW in all deliveries at KKUH over the period of this study was 11.3% (368 controls, 47 cases). Only 90 subjects were recruited into the study. The distribution of the birth weight and the maternal age of both control and case groups are shown in Table 7.

Periodontal Disease Evaluation

Based on CPITN scores, the prevalence of score 3 was 42.22%. Furthermore, none of the mothers examined were free of any periodontal disease. Figure 1 shows a summary of the scores by sextant which demonstrated that score 3 was most frequently recorded in the upper left sextant in this study population.

Table 8 shows the mean periodontal status for case and control mothers together with results of logistic regression analysis which examined the association between periodontal status and PLBW. The mean periodontal pocket depth for cases was higher than that of the controls (P-value=0.002). The mean percentage of sites with BOP was calculated. The data revealed a statistically significant difference between case

Table 4. Mothers-pregnancy related variables of cases versus controls.

	Case n=30	Control n=60	Odds Ratio (95% CI)	P-value
Infection History				
Yes	7	17	1.299(0.471-3.586)	0.613
No	23	49	1(reference)	
Placental Problems				
Yes	2	2	2.071(0.277-15.478)	0.598
No	28	58	1(reference)	
Number of Previous Pregnancies				
1	5	18	2.100(0.639-6.903)	0.492
2	6	9	0.875(0.257-2.980)	
3-4	5	9	1.050(0.293-3.763)	
≥5	14	14	1(reference)	
Previous PTL				
Yes	10	6	4.500(1.447-13.996)	0.006
No	20	54	1(reference)	
Previous LBW				
Yes	11	8	3.763(1.315-10.769)	0.011
No	19	52	1(reference)	
Antenatal Care				
Yes	29	54	3.222(0.370-28.068)	0.417
No	1	6	1(reference)	
Method of Delivery				
Normal	19	47	2.093(0.799-5.487)	0.129
C-section	11	13	1(reference)	
Sex of Infant				
Girl	17	27	1.597(0.661-3.866)	0.297
Boy	13	33	1(reference)	

Table 5. Mean maternal age and weight of the infant of cases versus controls.

	Case n=30	Control n=60	Odds Ratio (95% CI)	P-value
Mean Maternal Age	34.63	39.35	3.391(2.041-5.632)	0.00
Mean Weight of Infant	2.140	3.240	147.06(16.74-1291.61)	0.00

Table 6. Distribution of dental history in cases versus controls.

	Case n=30	Control n=60	Odds Ratio (95% CI)	P-value
History of Dental Treatment				
Yes	28	59	4.214(0.367-48.46)	0.257
No	2	1	1 (reference)	
History of Periodontal Disease				
Yes	15	19	2.158(0.878-5.302)	0.091
No	15	41	1(reference)	
History of Periodontal Treatment				
Yes	3	2	3.222(0.508-20.42)	0.328
No	27	58	1(reference)	
Number of Brushing Times				
≤1	12	24	1.000(0.160-6.255)	0.967
2	16	32	1.000(0.165-6.052)	
≥3	2	4	1(reference)	
Type of Toothbrush				
No	1	1	2.667(0.123-57.62)	0.701
Soft	16	37	1.153(0.270-4.920)	
Medium	10	14	1.905(0.402-9.023)	
Hard	3	8	1 (reference)	

Table 7. The distribution of the birth weight and the maternal age of cases versus controls.

	Case	Control
Birth weight (kg)		
≤1.00	1	
1.01-1.49	2	
1.50-1.99	8	
2.00-2.49	14	
2.50-2.99	2	17
3.00-3.49	2	24
3.50-3.99	1	17
≥4.00		2
Total	30	60
Maternal Age (weeks)		
≤27	1	
28-30	3	
31-33	4	
34-36	16	
37-39	5	31
40-42	1	29
Total	30	60

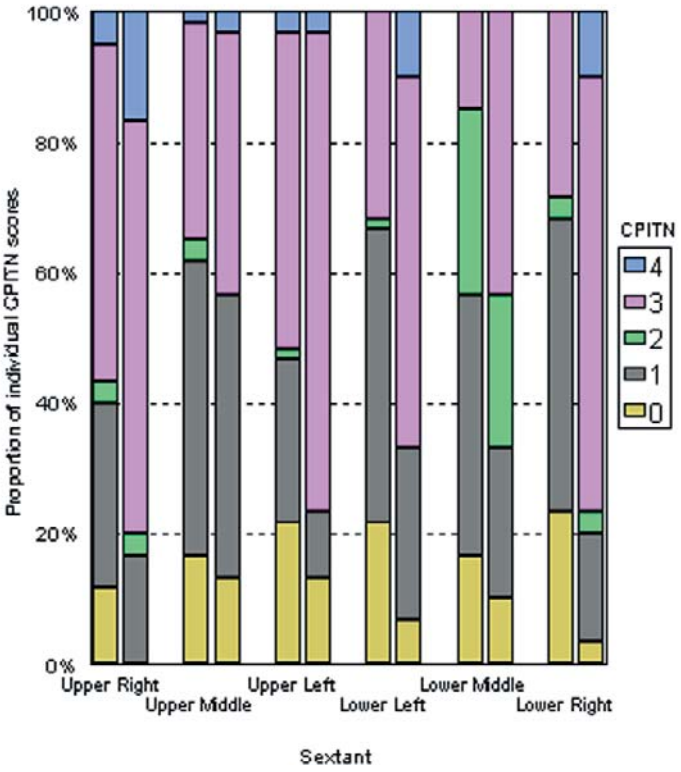

Figure 1. Proportion of sextants with various periodontal conditions as designated by CPITN score (controls versus cases).

Table 8. Measurements of periodontal status.

	Case n=30	Control n=60	Odds Ratio (95% CI)	P-value
Mean Probing Depth (mm)	2.559	2.367	12.877(2.27-72.95)	0.002
Mean BOP (%)	18.839	11.244	1.050(1.010-1.091)	0.028
Mean Calculus	0.70	0.40	3.300(1.372-8.926)	0.007
Mean CPITN	2.333	1.628	4.212(1.988-8.926)	0.000

and control mothers (P-value=0.028). Also, calculus was significantly higher in cases than in controls (P-value=0.007). The mean CPITN was higher in case mothers than in controls (OR 4.21 95% CI 1.99-8.93). In other words, case mothers with periodontal disease were found to have a 4.21 time higher chance of having PLBW than the mothers with healthy periodontal tissues.

The relationship between maternal periodontal disease status and the pregnancy outcome after adjustment of known risk factors are shown in Figures 2 and 3. In Figure 2, the prevalence of maternal periodontal disease is shown for each maternal age group using the CPITN. Only 10.6% of full-term mothers had deep probing depth (score 4), while 25% of maternal age 34-36 weeks had deep probing depth, indicating the prevalence of deep pockets was seen to increase among mothers delivering at lower maternal age. In Figure 3, a similar pattern was seen between prevalence of maternal periodontal disease and the infants' birth weight. The prevalence of deep probing depth was low (9.2%) among mothers with normal birth weight (≥2.500 kg), but a concomitant increase in the prevalence of deep probing depth was seen among mothers with birth weight deliveries of <1.5 kg (66.7%).

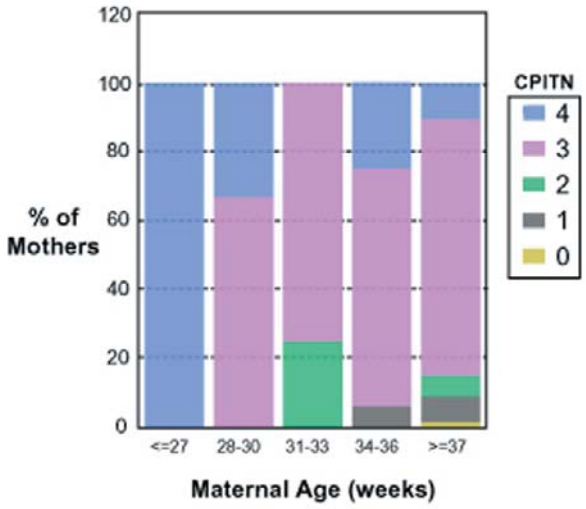

Figure 2. The rates of birth outcome within each maternal age group.

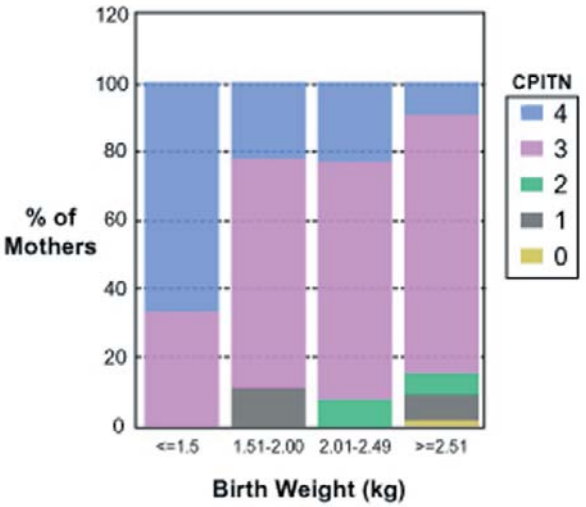

Figure 3. The rates of birth outcome within each birth weight group.

Discussion

The assumption poor oral health of the pregnant woman is associated with PLBW of the newborn was tested by using an un-matched case-control study. Designing a case-control study insures (1) the controls are representative (by avoiding selection bias) and (2) all potential confounding factors are measured.

The examination was conducted specifically at KKUH. The selection of this hospital was based on the fact it provides a large accessible

community of child bearing women from diverse groups. The examination was carried out within 24 hours post delivery coinciding with a study conducted by Davenport et al.[20] as this indicates the previous disease condition and insures the mothers were recruited prior to their discharge from the hospital.

Differences between the study populations in the present study and that of Offenbacher and colleagues include ethnic mix and age. The North Carolina study consisted of 124 women who were slightly younger on average, especially the cases (22 years old) and 58% were black.[11] In the present study the sample size was slightly smaller (90 subjects) with the mean age of the cases (30.8 years old), and mothers were recruited from a 100% Saudi community. Most of the mothers examined were of medium to high socioeconomic status and probably contributed to their position as families of the university staff.

In an earlier study by Davenport et al. multiple gestation were included.[18]

However, it was well established in previous studies multiple gestation has a significant relationship with PTL.[20] For this reason, only mothers with singleton gestation were included.

The relationship between periodontal disease and several systemic diseases such as coronary heart disease was well documented.[21] Therefore, mothers with medical problems were excluded in most of the earlier studies.[13,16,18] However, in the present study five mothers were not excluded since their medical problems did not impact the study outcome (two of the cases used topical cortisone to treat their skin allergy and three of the controls used Iron tablets to treat their anemia).

The number of case mothers interviewed over the period of this study was 47. Seventeen of them were excluded due to different reasons; some had multiple deliveries, some with medical problems, and others refused to participate leaving only 30 cases to be included. Based on the selected ratio of (1:2), the number of controls was limited to 60 mothers.

PLBW was subdivided in the beginning of the study into three groups: PTL, LBW, and both. However, the sample size of each group was very small (PTL=5, LBW=6, PLBW=19) compromising the data analysis. Therefore, they were combined into one group (PLBW).

The risk factors for PLBW were established by examination of the hospital records and by questionnaire. The analysis was controlled for known confounding variables which confirmed several of the well known risk factors for PLBW, including previous pre-term and previous LBW, and disconfirmed some, such as smoking which was not significant in this study population due to the area customs.

It is not known why a woman with a previous PLBW has a higher risk to have a subsequent one. It is possible in a woman with a positive history of PLBW, the cause of the subsequent PLBW may be the same factor that caused the previous. Genitourinary tract infections are well known risk factors of PLBW.[22] There was a significant proportion of mothers in the present study who presented genitourinary tract infections, but no association was found between these variables and PLBW probably due to the adequate treatment of these infections.

In studying periodontal disease clinically there are a lot of potential measures of the disease severity available. The most accurate measure is the clinical attachment level. However, it was not used in this study similar to other previous studies[16,18] because it was considered impractical to collect these data under the conditions of the clinical exam as the comfort of the subject was a paramount. The choice in this study was to use the CPITN (Ainamo et al.).[23] Several studies reported the use of this index because it is a quick screening system which can be carried out easily on the ward.[16,18,19] Moreover, Davenport et al. compared the outcome from using CPITN and another alternative measure such as concentrating on the deepest pockets or the most inflamed sites, which gave a conclusion similar to those presented by the use of CPITN.[19] No radiographs were taken in

the interest of patients' safety and due to the limitation of the facilities.

It is likely CPITN scores are significantly influenced by pregnancy. In a study of 121 pregnant women, Loe and Silness observed all showed signs of gingival inflammation.[24] This is being confirmed in the present study in which no scores of 0 have been recorded. Furthermore, the high prevalence of score 3 may also reflect elevations in gingival inflammation leading to enlarged gingiva and, hence, an increase in probing depth.

The present study demonstrated a 42.22% prevalence of CPITN score 3, corresponding to shallow pockets. Miyazaki et al. reported 31% of the pregnant women in a Japanese population had periodontal pockets of 4 or 5 mm, results similar to the data in the present work.[25] CPITN score 3 was most frequently recorded in the upper left sextant in this study. While Davenport et al. stated score 4 was most frequently recorded in the upper right sextant.[18] A possible explanation would be the habitual preference of chewing on the left side in this population.

The prevalence of PLBW in this study was (11.3%) close to the global range (16%)[7], and higher than the finding reported by Davenport et al. in East London 1998, where the prevalence of PLBW was 4%.[18] This could be due to the small sample size (415 mothers) compared to their 800 mothers.

The present study supports the earlier findings regarding the risk of having PLBW in mothers with periodontal disease.[11,13,16,18] Periodontal disease showed the strongest association in the univariate analysis with an odds ratio of 4.21 (95%CI 1.988-8.926). This can be explained by the fact periodontal disease may influence pregnancy outcome by the direct and/or indirect effect of periodontal pathogens on the developing fetus. Explaining the biologic mechanism begins with endotoxins resulting from Gram-negative bacterial infections such as periodontal disease. These endotoxins stimulate the production of cytokines and prostaglandin. It is known prostaglandin and certain cytokines (interleukin-1ß, interleukin-6, and TNF-α), in appropriate quantities, stimulate labor (Figure 4). However, this biologic mechanism was beyond the scope of this study.

The limited aspect of this case-control study was that it does not enable broad generalizations regarding the potential healthcare impact of these findings. Caution must be taken in interpreting the applicability of the current data until these findings can be confirmed by larger, prospective multi-center investigations.

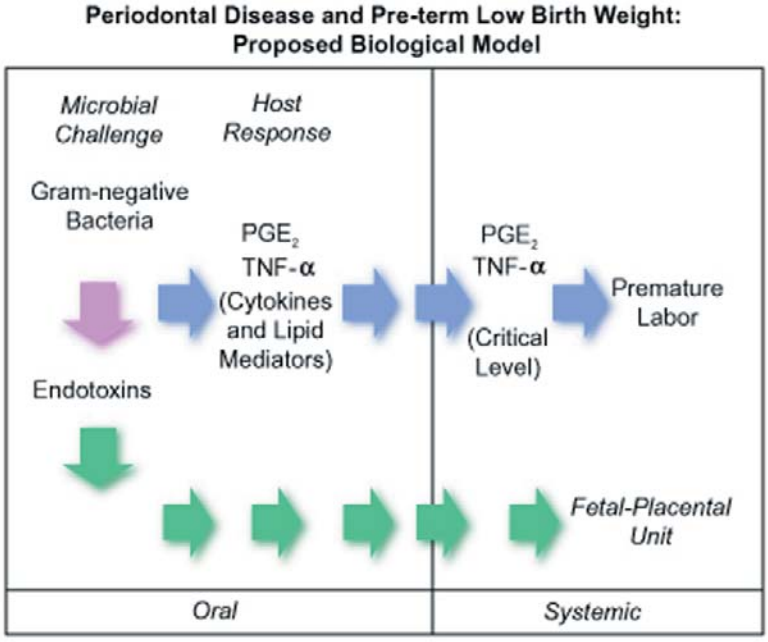

Figure 4. Proposed biological model of periodontal disease and pre-term low birth weight. [26]

Conclusions

Within the limitations of this study, the following conclusions may be drawn:

- The prevalence of periodontal disease was high among the study population.
- The prevalence of PLBW was 11.3% in KKUH.
- There was a correlation between maternal periodontal disease and PLBW infants among Saudi mothers in KKUH with a four fold increased risk of PLBW.

The following are recommendations resulting from this study:

- Additional epidemiological studies are needed including a larger number and wider spectrum of participants from different hospitals in different areas.
- Future studies in which the direct measurement of specific periodontal pathogens in the fetal environment and the measurement of the resulting inflammatory mediator levels are made would be helpful in either approving or disapproving the hypothesis.
- The use of clinical attachment level and gingival crevicular fluid as a clinical parameter.
- The use of the Decayed, Missing, or Filled Teeth Index (DMFT) as an extra measure to indicate the total number of decayed, missing, or filled teeth as a result of dental caries.
- Further studies are needed to address the question whether pre-term births can be reduced by treating the periodontal disease.

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