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Taiwanese Journal of Obstetrics & Gynecology 52 (2013) 71–76

www.tjog-online.com

Original Article

Association between maternal periodontal disease and preterm delivery and low birth weight

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Accepted 19 March 2012

Abstract

Objective: It has been suggested that periodontal disease is an important risk factor for preterm low birth weight (PLBW). The purpose of this study was to determine the association of maternal periodontitis with low birth weight (LBW) and preterm birth (PB).
Materials and Methods: Pregnant women ($n = 211$) aged 22–40 years were enrolled while receiving prenatal care. Dental plaque, probing depth, bleeding on probing, and clinical attachment level were used as criteria to classify three groups: a healthy group (HG; $n = 82$), a gingivitis group (GG; $n = 67$), and a periodontitis group (PG; $n = 62$). At delivery, birth weight was recorded.
Results: Mean infant weight at delivery was 3084.9 g. The total incidence of preterm birth and LBW infants was 10.4% and 8.1%, respectively. The incidence of LBW infants was 4.2% for term and 40.9% for preterm gestations. Maternal height was not correlated with infant birth weight ($p = 0.245$). Significant differences in mean infant birth weight were observed among the HG, GG, and PG groups ($p = 0.030$). No significant relationship was found between periodontal disease and PB, but the association between periodontal disease and LBW was significant.
Conclusion: After appropriately controlling for confounding variables, our results do not support the hypothesis of an association that was observed in previous studies of maternal periodontal disease and infant PB, but the association between periodontal disease and LBW is significant.

Keywords: low birth weight; periodontitis; pregnancy; preterm birth

Introduction

Periodontal diseases are a group of infectious diseases caused predominantly by Gram-negative, anaerobic, and microaerophilic bacteria that colonize the subgingival area. In 1931 Galloway first suggested that periodontal disease may "provide sufficient infectious microbial challenge" to have "potentially harmful effects on the pregnant mother and developing fetus" [1].

Preterm birth is defined as delivery at a gestational age < 37 weeks and is the main cause of low birth weight (LBW) in pregnancy outcomes. Preterm and LBW infants are at higher risk of death, neurodevelopmental disabilities, cognitive impairment, and behavioral disorders [2]. The determination of risk factors for the delivery of preterm LBW infants represents a major public health priority.

Various factors have been associated with the delivery of preterm and/or LBW infants. Maternal risk factors include age, height, weight, socioeconomic status, ethnicity, smoking, alcohol, nutritional status, and stress [3,4]. However, a significant proportion of LBW is of unknown etiology. The association between periodontitis and LBW has been studied since the mid-1990s [5]. As indicated by Offenbacher et al these findings have enormous potential significance for risk assessment of preterm LBW (PLBW), oral healthcare during pregnancy, and healthcare costs associated with PLBW [5].

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1028-4559/$ - see front matter
http://dx.doi.org/10.1016/j.tjog.2013.01.011

Periodontal disease and preterm birth are complex conditions with multifactorial etiologies that can be influenced by environmental (e.g., smoking and socioeconomic status) and genetic factors (e.g., polymorphisms in inflammatory genes) [6]. A number of risk factors exist for PLBW, including a maternal age of <17 years or >35 years, low socioeconomic status, alcohol and/or drug abuse, smoking, multiple pregnancies, and poor general health. These factors can be referred to as traditional risk factors [7], but in approximately 25% of preterm births (PB) these risk factors are absent [8].

The relationship between periodontal disease in pregnancy and PB and LBW has been increasingly investigated, but the results are inconclusive. Clinical periodontal disease has been associated with PLBW in some studies [5,9–11], whereas other studies have failed to observe such an association [12–14]. Therefore, further study is required to determine if maternal periodontal disease is an independent risk factor for PB and LBW.

In a systematic review of 12 studies, Scannapieco et al concluded that periodontal disease may be a risk factor for PB and LBW, but it was unclear if the association was causal [15]. This investigation involved pregnant women who received an oral examination on enrollment and a second examination on delivery. Periodontal disease was measured clinically during these examinations and laboratory assays were used to assess inflammatory mediators in maternal serum.

Collectively, case–control and cohort studies indicate that women with periodontitis are approximately two to three times more likely than healthy women to experience PB or deliver an LBW infant [16]. Nonetheless, inconsistencies among studies make it unclear whether periodontal diseases play a causal role in adverse pregnancy outcomes. These conflicting findings may reflect methodological differences related to bias introduced by sample size, heterogeneity of the criteria to define periodontitis, and inadequate assessment of confounding factors and interactions [17,18]. Thus, the association should be further explored in observational and interventional studies to establish whether it is causal in nature or incidental, and to determine the possible benefits of intervention and the potential to generalize the findings in diverse populations.

The objective of the present study was to measure the effect of maternal periodontitis on the incidence of PB and LBW in a population delivering at Taipei Chang Gung Memorial Hospital. As in another study [19], instead of correlating maternal periodontal status with LBW incidence, we analyzed the influence of maternal periodontal status on infant birth weight, considered as a continuous variable.

Materials and methods

According to the World Health Organization (WHO), premature delivery is defined as labor beginning before the 37th gestational week [20]. A randomized, clinically controlled trial was performed on pregnant women with periodontitis selected from patients at the Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital, Taipei. Participants were enrolled in the study from September 2009 to September 2010. After obtaining institutional approval and consent from the participants, they were assigned to three groups according to their periodontal condition. All participants signed an Ethics Committee-approved informed consent form before entering the study, which was approved by The Research Ethics Committee of Chang Gung Memorial hospital.

Inclusion and exclusion criteria

Inclusion criteria were as follows: (1) pregnant and <5 months gestation at the time of oral examination; (2) >20 teeth; (3) aged 18–40 years; and (4) single gestation. Exclusion criteria were as follows: (1) multiple births, a positive history of HIV or AIDS, diabetes (gestational diabetes was acceptable), chronic hypertension, any medical contraindication to periodontal probing (i.e., congenital heart disease), and use of phentermine or fenfluramine for weight loss; (2) currently undergoing periodontal treatment; and (3) chronic regimen of aspirin or non-steroidal anti-inflammatory drugs (NSAIDs), chronic use of medications that cause gingival enlargement such as phenytoin, cyclosporine A, or calcium channel antagonists.

A total of 222 volunteer mothers were enrolled. After exclusion of 11 patients because of missing data, the final study group consisted of 211 women.

Recording of maternal characteristics

Whenever possible, an oral examination was conducted at the enrollment visit. When this was not possible, an oral examination was performed during the next prenatal visit, always prior to 26 weeks of gestation. During the first visit, detailed data on previous pregnancies and outcomes and the current pregnancy were collected from the patient's medical record. The following variables were recorded for each woman: age, height, educational level, number of prenatal visits, previous pregnancy history, including number carried to full term and number of pregnancies aborted, tobacco consumption, alcohol consumption, use of illicit drugs, domestic violence, gestational age, and dental treatment.

Outcomes

During the post-delivery visit, the following variables were recorded: gestational age, birth weight, and total maternal weight gain during pregnancy. The primary outcome measurement was birth weight. Women were grouped according to birth weight and gestational age. If they delivered a baby with a birth weight <2500 g they were classified as the LBW group. If they delivered before 36 weeks of gestation they were classified as the PB group. Normal women delivered an infant with a birth weight >2500 g and after 36 weeks of gestation.

Dental and periodontal examinations

Pregnant women ($n = 211$) aged between 22 and 40 years were enrolled while receiving prenatal care. Periodontal

examination was performed under infection control procedures. Clinical signs of inflammation and periodontal tissue destruction were assessed using bleeding on probing (BOP), probing depth (PD), and clinical attachment level (CAL). BOP was defined as the presence of bleeding from the gingival crevice after periodontal probing. PD was measured as the distance from the gingival margin to the bottom of the clinical sulcus or to the base of the probable gingival crevice. CAL was determined by measuring the distance from the cemento–enamel junction to the bottom of the clinical sulcus or to the base of the probable gingival crevice. The periodontal examination consisted of assessments at vestibular, lingual, mesial, and distal sites of all teeth present using the following parameters. (1) Plaque was assessed according to the O'Leary plaque index, with 0 = absence and 1 = presence of bacterial plaque [21]. The percentage of the tooth surface affected by plaque (+) was also assessed for all teeth. (2) BOP was recorded as present (+) or absent (−) using the index proposed by van der Velden for the most apical penetration of the probe [22], and the percentage BOP (+) was calculated for all teeth. (3) PD was measured from the gingival margin to the most apical penetration of the probe. A William probe was used to assess PD at six sites per tooth (mesiobuccal, mid-buccal, distobuccal, mesiolingual, mid-lingual, and distolingual). Results were rounded down to the nearest millimeter. (4) CAL was measured from the cemento–enamel junction to the most apical penetration of the probe. The patients were assigned to one of the following three groups according to their dental results.

The criteria used to determine the presence of periodontal disease were those established by Machtei et al [12]. Women with <5% gingival bleeding, without CAL > 6 mm in two or more sites, and without one or more sites with PD of 5 mm were assigned to the healthy group (HG). Women with >5% gingival bleeding but without CAL > 6 mm in two or more sites and without one or more sites with PD of 5 mm were assigned to the gingivitis group (GG). Finally, women with >5% gingival bleeding, with CAL > 6 mm in two or more sites and with one or more sites with PD of 5 mm were assigned to the periodontitis group (PG).

Statistical analysis

The continuous variables were analyzed by independent sample *t* test and ANOVA. In *post hoc* analysis for multiple comparisons of means, Bonferroni correction was used, depending on the normality of the data. The χ^2 test was used to analyze qualitative variables. Statistical significance was defined as $p < 0.05$. All statistical tests were conducted using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

Baseline demographic and periodontal data were collected for 222 participants. However, pregnancy outcome data were unavailable for 11 participants, who were thus excluded from analyses, yielding a study population of 211 women.

The questionnaire sheet shows clinical variables related to pregnancy. More than 50% of the women received dental treatment during the year previous to enrollment. All participants had a college education. No woman declared consumption of tobacco, alcohol, or illicit drugs during pregnancy. None of them reported domestic violence. Maternal height did not correlate with infant birth weight ($p = 0.245$). There was no significant difference in birth weight between mothers of <1.55 m in height (3016.4 ± 585.5 g) and those >1.65 m (3159.6 ± 618.3 g; $p = 0.245$). Maternal height did not correlate with infant birth weight ($p > 0.05$).

The mean maternal height was 159.4 cm, with the majority of the study population in the 156–159-cm (28.0%) or 160–164-cm (29.4%) categories (Table 1). The mean age of the women was 31.4 years, with a higher proportion older than 25 years (97.2%). The mean infant weight at delivery was 3084.9 ± 541.4 g. The total incidence of PB was 10.4% (22/211).

Table 2 shows infant birth weight in relation to gestational age. The LBW incidence was significantly lower in term (4.2%) than in preterm gestations (40.9%; $p < 0.001$). The mean infant weight on delivery was significantly lower in preterm (2356.4 ± 768.3 g) than in term gestations (3169.7 ± 438.3 g; $p < 0.001$).

Table 3 shows periodontal data for the HG, GG, and PG women. Plaque index did not significantly differ among the three groups; however, BOP was significantly lower in HG women (24.4%) than in GG (64.2%) and PG (61.3%) women ($p < 0.001$).

The data in Table 4 show a significant difference in mean age among the three groups (one-way ANOVA: $F = 3.972$, $p = 0.02$). According to *post hoc* analysis, mean age was significantly higher for PG than for GG women ($p = 0.0063$). The mean infant birth weight was 3175.5 ± 612.4 g for HG, 3109.4 ± 510.3 g for GG, and 2938.6 ± 442.5 g for PG

Table 1
Characteristics of the study population ($n = 211$).

Variable	Result
Age	
<18 y	0 (0.0)
19–25 y	6 (2.8)
>25 y	205 (97.2)
Mean (y)	31.4 ± 3.1
Height	
≤155 cm	52 (24.6)
156–159 cm	59 (28.0)
160–164 cm	62 (29.4)
≥165 cm	38 (18.0)
Mean (cm)	159.4 ± 5.1
Infant birth weight	
<2500 g	17 (8.1)
2500–3499 g	154 (73)
≥3500 g	40 (19)
Mean (g)	3084.9 ± 541.1
Gestational age at delivery	
Term	189 (89.6)
Preterm	22 (10.4)

Data are presented as *n* (%) or mean ± SD.

Table 2
Infant birth weight in relation to gestational age ($n = 211$).

Variable	Term (> 36 weeks)	Preterm (≤36 weeks)	p
Number	189	22	
Infant birth weight			
<2500 g	8 (4.2)	9 (40.9)	<0.001[a]
2500–3499 g	141 (74.6)	13 (59.1)	
≥3500 g	40 (21.2)	0 (0.0)	
Mean (g)	3169.7 ± 438.3	2356.4 ± 768.3	<0.001[b]

Data are presented as n (%) or mean ± SD.
[a] Data compared by χ^2 test.
[b] Data compared by independent sample t test.

women; the difference among the groups was significant (one-way ANOVA: $F = 3.566$, $p = 0.030$). There was a significant correlation between maternal periodontal disease and LBW. The rate of LBW was 7.3% (6/82) for HG women and 14.5% (9/62) for PG women and the difference was significant ($\chi^2 = 15.345$; $p = 0.005$). According to post hoc analysis, the mean infant weight was lower for PG than for HG women ($p = 0.009$). After Bonferroni correction, the p value should be <0.0167 (0.05/3) for a significant difference. Thus, the difference in infant birth weight between HG and PG women is significant (Table 4). The same conclusion was reached for women older than 25 years (one-way ANOVA: $F = 3.567$, $p = 0.033$); the infant birth weight significantly differed for PG and HG ($p = 0.0096$). Because only six women were younger than 25 years, these results are not presented in Table 4.

PG women had a higher frequency of LBW (14.5%) than GG women (3.0%) and the HG women (7.3%). PG women had the highest PB frequency, followed by GG women. More severe periodontitis is indicative of a higher percentage of PB. However, the differences in PB incidence among the groups was not clinically significant ($p = 0.080$; Table 4).

Table 5 shows that the maternal height is not related to pregnancy in women in relation to their age. The ≤25-years group is too small ($n = 6$) for meaningful discussion. No significant differences in birth weight or gestation period were observed between the two age groups ($p > 0.05$). There were 17 women (8.1%) with LBW (< 2500 g), with a mean age of 32.8 ± 2.6 years.

Discussion

No significant relationship was found between periodontal disease and PB, but the association between periodontal disease and LBW is significant. Differences between our results and those from previous studies may be due to differences in population for both periodontal health and the incidence of preterm delivery and LBW.

Nault supposed that LBW is very closely related to PB because it was estimated that approximately 50% of preterm infants but only 2% of full-term infants weigh less than 2500 g [23]. In our study, the incidence of LBW infants was 4.2% in term gestations and 40.9% in preterm gestations. Mean infant weight at delivery was significantly lower in preterm (2356.4 ± 768.3 g) than in term gestations (3169.7 ± 438.3 g; $p < 0.001$, Table 2). This result is in accordance with findings by Nault.

In studies investigating possible association between periodontitis and PB, the results can be controversial. Noack et al found that periodontitis was not a detectable risk factor for PLBW in Germany [24]. Mitchell-Lewis et al found no evidence to connect periodontitis and PB [13], in agreement with a 2002 study of 236 patient cases and 507 control individuals in a mixed-race population by Davenport et al [14]. Studies by Buduneli et al [25] and Lunardelli and Peres [26] could not establish a significant association between periodontitis and LBW. In our study, the relationship between maternal periodontal health and infant birth weight showed some correlation (Table 4). However, the sample size for women aged ≤25 years was very small ($n = 6$) compared to the group >25 years old ($n = 205$). No significant association between periodontal disease and PB in women >25 years old was observed in preliminary findings by Mitchell-Lewis et al [13] or in studies by Davenport et al [24,27], Noack et al [24], Buduneli et al [25], and Lunardelli and Peres [26].

The results of our investigation are different from those of some studies that reported significant associations of varying degrees between periodontal health and PLBW. Offenbacher et al suggested in 1996 that periodontal infection during pregnancy could lead to a sevenfold higher risk of PB [5]. In a further 814 participants, Offenbacher et al again demonstrated that maternal periodontal infection was significantly associated with a higher prevalence of PB [9]. Lopez et al found higher mean PD and CAL, a higher percentage of bleeding sites, higher units with redness, deeper PD (4–6 mm), and surfaces with plaque in women with PLBW infants [28]. Our study revealed no significant relationship between periodontal disease and PB, but the association with LBW was significant. This result is consistent with two previous studies [29,30]. In contrast to another study in which a significant difference in birth weight was observed between mothers of <1.55 m and ≥1.65 m in height [17], we found that maternal height did not correlate with infant birth weight ($p = 0.245$), in accordance with results reported by Berkowitz and Papiernik [31]. Dasanayake et al also found no significant difference in height between mothers of LBW infants and mothers with normal-weight infants, probably because birth weight was used as a dichotomized variable [32].

In recent years, a number of studies found a correlation between periodontal disease and adverse pregnant outcomes [33,34] while others did not [35,36]. After reviewing these reports, we found conflicting results that might or might not support the hypothesis that periodontal disease is a risk factor

Table 3
Indicators of periodontal disease ($n = 211$).

Variable	Healthy	Gingivitis	Periodontitis	p (χ^2 test)
Number	82	67	62	
Plaque index (+)	29 (35.4)	28 (41.8)	28 (45.2)	0.473
Bleeding on probing (+)	20 (24.4)	43 (64.2)	38 (61.3)	<0.001

Data are presented as n (%).

Table 4
Patient characteristics according to periodontal condition ($n = 211$).

Variable	Healthy (HG)	Gingivitis (GG)	Periodontitis (PG)	*p*	*Post hoc p*
Number	82 (38.9)	67 (31.8)	62 (29.4)		
Mean age (y)	31.6 ± 2.7	30.6 ± 3.1	32.1 ± 3.5	0.02[a]	0.0063 PG vs. GG
Infant birth weight				0.005[b]	
<2500 g	6 (7.3)	2 (3.0)	9 (14.5)		
2500–3499 g	52 (63.4)	55 (82.1)	47 (75.8)		
≥3500 g	24 (29.3)	10 (14.9)	6 (9.7)		
Mean ± SD (g)	3175.5 ± 612.4	3109.4 ± 510.3	2938.6 ± 442.5	0.030[a]	0.009 HG vs. PG
Gestational age at delivery				0.080[b]	
Term	77 (93.9)	61 (91.0)	51 (82.3)		
Preterm	5 (6.1)	6 (9.0)	11 (17.7)		

Data are presented as *n* (%) or mean ± SD.
[a] Data compared by one-way ANOVA, with post hoc analysis by Bonferroni correction.
[b] Data compared by χ^2 test.

for PB. Although we cannot explain the inconsistency between studies, our results exclude any significant association between clinical indices of periodontal disease and PLBW (Table 4). This may highlight the idiopathic nature of adverse pregnancy outcomes.

The mean maternal age in our study was significantly greater in PG (32.1 ± 3.5 years) than in GG women (30.6 ± 3.1 years; $p = 0.0063$, Table 4). However, this is of limited clinical significance. We restricted the current study to a population of women with a high (~90% had completed college) or moderate (10% had completed high school or vocational school) level of education women. In addition, our sample was of homogenous ethnicity and high socioeconomic status, and thus we avoided additional confounding by racial and socioeconomic status. In a number of previous studies, the sample comprised a high percentage of African Americans (between 58% and 82%) [5,12,13]. Such racial and social homogeneity may limit the generalizability of our results to other populations. The strength of our study is that our results were finely adjusted for the most important confounders. Many previous studies were conducted among multiracial cohorts [12,13]; mothers of African American ancestry were mainly of low socioeconomic status [10–12]. These demographic factors are known to be associated with PTB. Marked racial differences exist in the prevalence of both PLBW [37] and severe forms of periodontitis. The patients in our study were homogeneous in terms of social, racial, and demographic factors, and could be considered representative of the normal pregnant female population in Taipei. We controlled for several well-known risk factors for LBW, including tobacco and alcohol use. Other authors used similar criteria to select study samples [11,15]. However, some studies used samples in which most of the mothers were African Americans [5,10,12,13], a racial group with a 2.4-fold higher risk of LBW (11.4%) than Caucasian mothers (4.7%) and a threefold higher risk of very LBW (<1500 g) than the Caucasian group [31]. In agreement with the data, in our study the incidence of preterm birth was 10.4% (22/211), and the incidence of LBW was 8.1% (17/211) (Table 1). Conversely, the relatively high level of PLBW found by other authors could be explained by the high percentage of African Americans in their samples [5,10,12].

Table 5
Maternal height and clinical variables related to pregnancy in relation to maternal age.

Variable	≤25 years	> 25 years	*p*
Number	6 (2.8)	205 (97.2)	
Height			
≤155 cm	1 (0.5)	51 (24.2)	0.338[a]
156–159 cm	1 (0.5)	58 (27.5)	
160–164 cm	1 (0.5)	61 (28.9)	
≥165 cm	3 (1.4)	35 (16.6)	
Mean (cm)	163.5 ± 7.6	159.3 ± 5.0	0.237[b]
Infant birth weight			
<2500 g	0 (0.0)	17 (8.1)	0.157[a]
2500–3499 g	3 (1.4)	151 (71.6)	
≥3500 g	3 (1.4)	37 (17.5)	
Mean (g)	3352.5 ± 287.8	3077.0 ± 545.4	0.220[b]
Gestational age at delivery			
Term	6 (2.8)	183 (86.7)	>0.999[a]
Preterm	0 (0)	22 (10.4)	

Data are presented as *n* (%) or mean ± SD.
[a] Data compared using χ^2 test.
[b] Data compared using an independent sample *t* test.

Inconsistent control of confounding factors thus likely underlies discrepancies among published results. Caution must be exercised in interpreting the applicability of the current data because of the unique study group. In addition, the lack of standardized criteria for periodontal disease has been described as an important limitation of different studies [38] and may explain differences in results. Offenbacher et al stated that periodontitis corresponds to an average attachment loss of >3 or 4 mm [5,39]. Lopez et al examined six sites for all teeth present in the dental arch and considered mothers who had sites with a probing pocket depth ≥4 mm and a probing attachment level of ≥3 mm to be suffering from periodontitis [28]. Dasanayake et al [10] and Davenport et al [14] used the Community Periodontal Index of Treatment Needs (CPITN) to diagnose periodontitis. A large prospective study performed in London examined two sites of all teeth present [40]. The decision to rely on CAL for diagnosis was based on the fact that this parameter is not seriously affected by pregnancy, and diagnosis based on attachment loss has higher sensitivity and specificity than diagnosis based on PD [41].

Conclusion

This study provides inadequate evidence to identify periodontal disease as a risk factor for preterm delivery. Conversely, the association between periodontal disease and LBW is significant. Differences between our results and those of previous studies may be due to population differences for both periodontal health and the incidence of PB or LBW. The current study group had vigorous prenatal care and most of the participants were also are in good oral care, which underlies the importance for healthcare workers to promote good oral health.

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