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Relationship of Periodontal Disease to Pre-term Low Birth Weight Infants in a Selected Population - A Prospective Study.

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Objective*:** To assess effect of periodontal status of antenatal mothers on pregnancy outcomes in a selected population in Malaysia. ***Design: Prospective cohort study on a multi-ethnic convenient sample. ***Methods:*** 73 healthy pregnant women between 28 to 36 gestation weeks attending 5 ante-natal centres were recruited. Both Interviewer-administered Questionnaire and Periodontal examination, which included Plaque index, Gingival index, Papillary Bleeding index, probing pocket depth and attachment loss were conducted. ***Outcomes:*** Pregnancy outcome data which included gestational age at delivery, birth weight of newborn and delivery complications were collected after delivery. ***Results:*** Study sample of 73 mothers was approximately in 1:3 case:control ratio (21.9% & 78.1% respectively). Case was defined as those with preterm(PT) deliveries and low birth weight(LBW) infants whereas control was otherwise. 37 pregnant women were diagnosed with periodontal disease (minimum 2 teeth with $\geqslant$5mm periodontal pockets and $\geqslant$3mm attachment loss) and 36 without periodontal disease (PD). Of those with PD, 4 (10.8%) had PT delivery and 3 (8.1%) had LBW infants. None of the PD variable means or PD status associated significantly with either of the two groups ($P>0.05$). Logistic regression analysis to test the possible predictor (demographic and clinical) for PT or LBW status indicated only Plaque Index mean as a significant predictor ($P<0.03$). ***Conclusions:*** In this study population, PD was not shown to be a risk factor for PT delivery or LBW infant. Only mean Plaque Index was associated with PT deliveries and LBW infants.

Keywords: periodontal disease, pregnancy outcomes, prospective study, Malaysia.

Introduction

According to the World Health Organization (WHO), pre-term (PT) birth was defined as labour that begins before the gestational week of 37, and low birth weight (LBW) as delivery of an infant with a birth weight under 2.5kg. Approximately 11% of all pregnancies lead to PTLBW (Goldenberg & Rouse 1998) and despite considerable progresses in medical care, this rate is increasing in western countries. LBW has a higher incidence rate in Asia (15%) than in other areas of the world (Williams *et al.*, 2000). According to Health Facts 2007, Ministry of Health of Malaysia Preliminary Report indicated that 8.6% (32,991) LBW infants were born in the year 2006.

PTLBW is a significant cause for mortality and morbidity among infants (McCormick, 1985). More than 60% of the mortality that occurs among infants without anatomic or chromosomal congenital defects is attributable to PTLBW (McCormick, 1985). PTLBW infants who survive the neonatal period are at a significant risk of developing serious and lasting health problems such as asthma, upper and lower respiratory tract infections, ear infections and congenital anomalies. PT delivery is the cause of one-half of all serious long term neurological morbidities (McCormick, 1985).

Various risk factors have been associated with the delivery of PTLBW infants. Traditional known maternal risk factors include high (>34 years) or low (<17 years) maternal age, height, weight, ethnicity, socio-economic status, alcohol, tobacco and drug abuses, nutritional status and stress level. Low maternal bodyweight, birth interval, previous PTLBW, inadequate pre- and ante-natal care, maternal hypertension, diabetes mellitus, urinary and genital tract infections may also be important (Davenport, 1998). However, approximately 25% of PTLBW deliveries are of unknown etiology (Holbrook, 2001). Despite efforts in understanding and managing controllable risk factors, the incidence of PTLBW deliveries remains high which may be due to limited understanding of risk factors.

Several studies have demonstrated an association between infection and PTLBW e.g. genitourinary tract infections (Holbrook, 2001, Romero *et al.*, 1993). Offenbacher *et al.* in 1996 first demonstrated a statistically significant correlation between periodontal disease and PTLBW delivery.

Mothers with periodontal infection had more than 7 times the risk of delivering a PTLBW infant and 18.2% of the PTLBW deliveries occurring might be attributable to PD (Offenbacher *et al.*, 1996). In another study, women with progressive PD were 5 times more likely to give birth before 37 weeks (Madianos *et al.*, 2002). Hence the American Academy of Periodontology recommended that all women who are pregnant or planning pregnancy undergo periodontal examinations in order that appropriate preventive or therapeutic services are provided (Mitchell-Lewis *et al.*, 2001).

However, a number of recent studies (Davenport *et al.* 1998, Noack *et al* 2005) found no association between periodontitis and pregnancy outcomes. Davenport *et al.* (1998) did not find periodontitis more severe among mothers with PTLBW deliveries in a predominantly Bangladeshi population living in East London. Hence association between PD and PTLBW may vary among the different studied populations.

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The objective of this investigation was to assess the effect of periodontal status on the delivery of preterm low birth weight infants in a selected population in Malaysia.

Materials and Methods

Study Design and Population

Two ante-natal Clinics in Selangor (Kuala Lumpur General Hospital and National University of Malaysia Hospital) and three ante-natal Clinics in Perak (Gunung Rapat Health Clinic, Jelapang Health Clinic and Waller Courp Health Clinic) provided an accessible community of pregnant women comprising of a multi-ethnic population, namely Malays, Chinese and Indians.

A prospective cohort study design was chosen as the most appropriate as it could demonstrate temporal relationship between PD (exposure) and PTLBW infants (outcome). It also allowed direct measurement in exposed and non-exposed population. The study group was defined as mothers with PD while the control group was defined as mothers without PD.

Approval was granted for the study by the Ethics Committee, Faculty of Dentistry, University Malaya (DF OP0702/0016(L)) prior to the study. Approval to conduct the study was also obtained from the Department of Obstetrics and Gynecology of all the hospitals and health centres involved.

Study population

Participation from pregnant women who attended routine ante-natal care at the Prenatal Care Clinics was requested. Only those who were in the 28 to 36 gestational weeks were included in this study. Exclusion criteria included systemic conditions like severe anaemia, diabetes, cardiovascular disorders, hepatic deficiency, high blood pressure, venereal diseases, urinary tract infections, bacterial vaginitis and viral infections. This study was based on convenience and volunteer sampling methods. Potential participants were identified through checking folders at the prenatal care clinic. All of the patients' folders available on the selected days for periodontal examination were checked. A total of 127 mothers met the criteria and were selected but only 76 of them who attended the Prenatal Clinic agreed to volunteer for the study. An informed consent was obtained from the subjects. However, only 73 participants' complete data could be collected.

Maternal data including results of blood test, urine test and MGTT were obtained from the patients' folders and recorded.

Questionnaire administration

Before the periodontal examination, an interviewer-administered questionnaire was completed for each participant. The questionnaire was designed to gather personal data, demographic details including age, gender, race, socio-economic status, and habits including oral hygiene habits, tobacco use, parafunctional habits and regularity of dental visits. The maternal general health during and prior to pregnancy, and history of previous PTLBW babies were recorded as well.

Clinical periodontal examination

Clinical periodontal examination included Plaque index (Silness and Löe, 1964), Gingival index (Löe and Silness, 1963), Papillary Bleeding index (Saxer and Muhlemann, 1975), probing pocket depth (PPD), probing attachment loss (PAL) and total number of missing teeth. Probing pocket depth and attachment level were measured with William's periodontal probe for selected teeth at 4 sites, disto-buccal, mesio-buccal, mid-buccal and mid-palatal. Partial mouth recording (16 teeth) was conducted and the selected teeth were central incisors, canines, first premolars and first molars (or alternative teeth) in each quadrant.

The examinations were conducted using a portable dental chair under a portable dental light source at all centres except at the General Hospital Kuala Lumpur where the examination was conducted using a fixed dental chair and light sources available in the hospital dental clinic. An assistant recorded the dental and periodontal findings on a customized examination form.

All the periodontal examinations were conducted by both authors who are experienced periodontists. A standardized procedure was used.

Definition of pregnancy outcomes

To aid the analysis of the data and result discussion, participants were grouped according to primary pregnancy outcomes into:

- PT birth group if they delivered before 37 weeks of gestation;
- LBW group if they delivered a baby with a birth weight under 2.5kg; and
- PTLBW group if they delivered a baby with a birth weight under 2.5kg before 37 weeks of gestation.
- Estimation of gestational age was based on the antenatal records.

Pregnancy outcome data collection

Collection of pregnancy outcome information was obtained using patients' postnatal records. The data were recorded on standardized data collection forms. Besides gestational age at delivery and birth weight of the delivered baby, data concerning delivery information and pregnancy complications such as type of delivery, onset of delivery, medication administered, total blood loss during delivery, and other complications such as genitourinary tract infections, were also collected.

Classification of periodontitis

A subject was categorized with PD if she had $\geq$ 2 teeth with $\geq$ 5mm probing pocket depth and loss of attachment $\geq$ 3mm. Subjects without these criteria were regarded as periodontally healthy.

Statistical analysis

The results were analyzed using SPSS and the statistical packages used were chi square test, independent sample t-test and logistic regression analysis.

Results & Discussion

Ethnicity and Age Profile of Study Population

Table 1 lists the ethnicity, age range and diseased/healthy subjects' distribution. The final study sample comprised of 73 pregnant mothers within the age range of 22-48 years and an average age of 29.1 years. Mother's age is a well known risk factor for PTLBW (Williams 2000). By including subjects who are not too young (younger than 18 years old) nor too old (older than 36 years old) it is easier to assess the true relationship between PD and PTLBW without interference from this risk factor.

According to Shiono (1986), ethnicity can affect the incidence of PT delivery which may contribute to higher incidence of LBW infants. The final study sample comprised of 42 Malays (57.5%), 19 Chinese (26%) and 12 Indians (16.2%). The ethnic composition for Malays and Chinese in this study is similar to the ethnic composition in the Malaysian population with the exception for the Indian group, which was higher in the study. However, there are no relevant studies done on ethnic differences between the Malay, Chinese and Indian ethnic groups in relation to PTLBW prevalence.

Distribution of disease and healthy subjects

37 (50.7%) pregnant women were diagnosed with PD and 36 (49.3%) without PD. This finding supports previous studies which reported that PD affects as many as 50% of pregnant women in the United States (Goepfert, 2004). Hence the present study group can be assumed to be fairly representative of the general population in Malaysia as well as others globally.

According to Health Facts 2007, Ministry of Health, Malaysia's Preliminary report, 8.6% infants were born with LBW in the year 2006. However only 6.8% infants were born with LBW in our study sample. This may be due to the removal of potentially interfering co-variables because pregnant mothers with systemic diseases were excluded.

Association between PD and its risk factors

There are many risk factors associated with PD, such as oral hygiene habits, smoking habit and regularity of dental visits. In this study, irregular dental visits showed a significant association ($p \leq 0.005$) with PD occurrence (chi-sq. test) as compared to other risk factors with an OR=7.7 (95% CI: 1.57, 37.82).

Association between PD parameters and PD prevalence

All the clinical periodontal parameters in this study show highly significant relationship with PD group as compared to the Healthy group (Table 2). Hence, these parameters can be excellent PD indicators and the results indicate the diseased sample was representative.

Table 1. Ethnicity, age ranges and diseased/healthy subjects' distribution

		Frequency (No. of Subjects)	*Percentage*
Ethnicity	Malays	42	57.5
	Chinese	19	26.0
	Indians	12	16.4
	Total	73	100.0
Age Ranges	20-29years	39	53.4
	30-39years	30	41.1
	40years	4	5.5
	Total	73	100.0
Group	Periodontally Diseased	37	50.7
	Healthy	36	49.3
	Total	73	100.0

Table 2. Comparison of PD Parameters in the diseased and healthy groups of the study using independent sample t-test

PD Clinical Parameters	*Periodontal Disease Group*		*Healthy Group*		*p value*
	Mean	*SD*	*Mean*	*SD*	
Probing pocket depth	2.54	0.67	1.65	0.45	<0.001**
Probing attachment loss	2.31	1.11	0.23	0.30	<0.001**
Papillary Bleeding Index	0.80	0.54	1.61	0.63	<0.001**
Plaque Index	0.68	0.38	0.43	0.21	0.004*
Gingival Index	0.56	0.55	0.86	0.38	0.027*

* Significant ** Highly Significant

Association between PD status and PT or LBW deliveries

Among the study subjects, 14 women had PT delivery and 5 had LBW infants. Out of these, only 3 pregnant women delivered PTLBW infants. Of those with PD, 4(10.8%) had PT delivery and 3 (8.1%) had LBW infants (Table 3). PD status was not significantly associated with PT delivery or LBW infants ($p>0.05$).

Clinical periodontal parameters as PT/LBW predictors

Table 4 shows that none of the PD parameter means associated significantly with either of the two groups ($p>0.05$) using independent samples t-test. The data was further analyzed using logistic regression analysis (Table 5). None of the PD parameter means associated significantly with PT or LBW status ($p>0.05$). Stepwise logistic regression analysis was used to further test these relationships (demographic and clinical) for PT or LBW status. Among all the clinical parameters, only Plaque Index mean was shown to be a significant predictor ($p<0.03$).

Comparison with other studies

This study addressed the question of whether pregnant women with PT contraction (risk for PT birth) or mothers with PTLBW deliveries have a periodontal status worse than women of the same age with risk-free pregnancies who give birth to normal weight healthy infants. PT and LBW infants present important health problems worldwide, as these factors are major causes of neonatal morbidity and mortality. LBW can result from PT birth or intrauterine growth restriction, or both. It is difficult to separate the PT component of LBW. It is estimated that approximately 50% of PT infants weigh less than 2.5 kg, whereas only 2% of full-term infants weigh below that threshold.

The results of this study are in contrast to the association between PD and a higher risk for PTLBW reported in other studies (Madianos *et al*., 2002; Offenbacher et al., 1996; Offenbacher *et al*., 1998). To examine the association between PD and PTLBW, regression models were used. Adjustment for potential confounding variables (maternal age, race, smoking, drug use, bacterial

Table 3. Association between PD Status and PT or LBW Deliveries using chi-square test

	PD n (%)	*Healthy n (%)*	*p-value*	*RR*	*95% CI for RR*
PT delivery	4 (10.8%)	10 (27.8%)	0.066	0.39	[0.13, 1.13]
LBW infant	3 (8.1%)	2 (5.6%)	0.66	1.46	[0.26, 8.23]

Table 4. Comparison of PD variables in the PT/LBW and normal delivery subjects using independent samples t-test

PD Variables	*Group*	*Mean*	*Std. Error*	*95% Confidence Interval*		*p-value*
PI	PT / LBW	.58	.04	.49	.67	0.17
	Normal (T & W)	.43	.08	.26	.60	
GI	PT / LBW	.71	.07	.58	.84	0.85
	Normal (T & W)	.74	.13	.49	.99	
PPD	PT / LBW	2.14	.10	1.94	2.33	0.20
	Normal (T & W)	1.87	.18	1.50	2.24	
PAL	PT / LBW	1.36	.18	1.01	1.71	0.10
	Normal (T & W)	.73	.33	.06	1.39	
PBI	PT / LBW	1.19	.10	.99	1.38	0.49
	Normal (T & W)	1.33	.19	.97	1.70	

Table 5. Clinical periodontal parameters as PTLBW predictors using logistic regression analysis

PD variables (mean)	*Model Fitting Criteria -2 Log Likelihood of Reduced Model*	*Likelihood Ratio Tests*		
		Chi-Square	*df*	*p value*
Intercept	53.15	0.41	1	0.52
PI	56.20	3.46	1	0.06
GI	53.72	0.99	1	0.32
PPD	54.10	1.37	1	0.24
PAL	53.13	0.40	1	0.53
PBI	53.13	0.40	1	0.53

vaginosis, socio-economic status) in these models is of great importance to avoid study bias (Madianos *et al.*, 2002). Thus the association between periodontitis and PTLBW supported in some studies may be due to inadequate adjustment or unknown confounding factors. Most studies did not control for potential confounding factors.

The definition of PT birth used in our study includes births that followed spontaneous labour or spontaneous rupture of membranes, because there is considerable evidence that the risk factors for both are similar, and the distinction is artificial. The determinants of PT birth and intra-uterine growth restriction appear to differ (Kramer, 1987), we analyzed the data evaluating the risk factors for LBW and PT delivery together. The only risk factor in the present study that showed significant association with PT and LBW was Plaque Index.

PD has been identified as a potential risk factor for PTLBW (Offenbacher *et al.*, 1996), and it might be one of the factors associated with some of the approximately 50% of PT births that occur in women without established risk factors (Kramer, 1987).

Some obvious differences between the present study as compared to others are the differences in our study population, study design and sample size. Their populations included very high percentages of Afro-Americans, up to 58-82% (Mitchell-Lewis *et al*., 2001: Offenbacher *et al*., 1996). In addition, the subjects in these mentioned studies were of low socio-economic status. There are marked racial differences in the prevalence of both PTLBW infants (Hogue *et al.*, 1995; Kleinman *et al.*, 1987) and in the prevalence of severe forms of periodontitis (Brown *et al.*, 1996). In our study, the pregnant women who participated were from the Malay, Chinese and Indian ethnic groups and mainly of middle socio-economic status (67.3%). The ethnic distribution of the Malay and Chinese groups reflected the general Malaysian population although the percentage of Indian subjects was slightly higher. Study design, whether prospective or retrospective, may influence the results of these studies (Offenbacher *et al.*, 1996). The present study design was prospective whereas the other studies are mainly retrospective. Differences in the sample sizes may also influence the results of these studies.

The findings of the present study are consistent with a number of recent studies e.g. Holbrook *et al.* (2001), Sundell *et al.* (2002), Davenport *et al.* (1998) which also failed to find an association between PD status and PTLBW deliveries. Indeed, the British case-control study showed a general tendency for decreasing odds ratio of PTLBW with increasing mean probing pocket depth (Sundell *et al.*, 2002). The results of this British study and the previous reports as well as the present study, in fact indicate there may be no association; the differences may reflect differences in the study populations; and finally, PD may be associated with PTLBW but only in the presence of other specific environmental or genetic risk factors.

In the present study, where most of the data collection was conducted before the deliveries, show that PD was evaluated as an independent risk factor for PTLBW. However some of these adverse pregnancy outcomes are frequently associated with potentially correctable lifestyles like tobacco abuse, or with infectious diseases, that, like PD, can be eliminated prior to or during pregnancy prior to delivery.

Limitation of the study

Due to the logistic restrictions and some patients' refusal to participate, the final study sample comprised of only 73 pregnant mothers. A larger sample size would have made it amenable to subject the data to more statistical packages. A larger sample size would have also contributed to greater power of the study, which would directly influence the representation of the study sample to the general population.

Being a pilot study, the present investigation was conducted in Selangor and Perak only. Assumption was made that the study population in Selangor and Perak can represent the total ante-natal population in Malaysia. The sample size was not sufficient to further discuss the relationship of PD in ethnic groups to PTLBW babies in the Malays, Chinese and Indians individually.

Clinical Implications

Although the present study shows no significant association between PD and PTLBW deliveries in Malaysia, oral hygiene instructions, prophylactic scaling and polishing of teeth of pregnant women is recommended to prevent adverse pregnancy outcome as indicated by the positive relationship in some studies as well as the fact that pregnant women are prone to develop PD. The present study has revealed that PD affected as many as 50% of pregnant women and the possible need for the health delivery system to address the needs of the ante-natal mothers.

Conclusions

In this study population, PD was not shown to be a risk factor for PT delivery or LBW infants. Only the mean Plaque Index showed an association with the outcome of PT deliveries and LBW infants.

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