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Periodontal Disease and Adverse Birth Outcomes: A Study from Pakistan

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Abstract

OBJECTIVES—Periodontal disease may increase the risk of adverse birth outcomes; however, results have been mixed. Few studies have examined periodontal disease in developing countries. We describe the relationship between periodontal disease and birth outcomes in a community setting in Pakistan.

METHODS—Enrollment occurred at 20–26 wks. A study dentist performed the periodontal examination to assess probing depth (PD), clinical attachment level (CAL), gingivitis index (GI) and plaque index (PI). Outcomes included stillbirth, neonatal mortality, <32 wk preterm birth (PTB), 32–36 wk PTB, and low birthweight (LBW), and are presented for increasing periodontal disease severity by quartiles (Q1–4).

RESULTS—Dental examinations and outcome data were completed for 1152 women. 81% were multiparous with a mean age of 27 yrs. 33% had no education. Dental caries were present in 47%, missing teeth in 27%, and 92% had no dental care in the last year. Periodontal disease was common: 87% had 4 teeth with a PD of >3mm, 54% had 4 teeth with a PI = 3, and 58% had 4 teeth with a GI = 3. In general, as the measure of periodontal disease increased, stillbirth, PTB <32 wks and neonatal mortality also increased. Late PTB and LBW were not related to measures of periodontal disease. Adjustment for demographic characteristics did not significantly change the relationships.

CONCLUSION—Pregnant Pakistani women have high levels of moderate to severe dental disease. Both stillbirth and neonatal mortality increased with the severity of periodontal disease.

Keywords

periodontal disease; preterm birth; stillbirth; neonatal death

INTRODUCTION

Periodontal disease affects approximately 90% of the population worldwide. It is characterized by the accumulation of plaque around the tooth and the gum line. Dental plaque, comprised of bacteria and its by-products, toxins, food debris, and dead cells, causes an inflammatory and immunological response that result in the breakdown of periodontal

tissue. If untreated, advanced periodontal disease can result in premature tooth loss. It is most often associated with alcohol and tobacco use, stress, poor oral hygiene, poor access to health care, a family history of periodontal disease and low socioeconomic status. (1)

The prevalence of periodontal disease varies between countries as well as among different populations within the same country. Severe periodontal disease is present in approximately 5–20% of most adult populations worldwide. (2) In recent years, several industrialized nations have reported a reduction in the proportion of adults with periodontal disease. However, limited access to health care and poor oral health practices have prevented similar reductions in developing countries (2).

Increasing evidence suggests that the inflammatory changes seen during periodontal disease may have repercussions beyond the oral cavity through damage related to systemic inflammation. These data have stimulated further investigation of periodontal disease and its association with cardiovascular problems and diabetes. (3–7) Several studies have also reported a positive association between periodontal disease and adverse pregnancy outcomes, including low birth weight, preterm birth, fetal growth restriction and preeclampsia (8–12). However, results have been mixed and several studies have not found associations between periodontal disease and preterm birth or low birthweight. (13–15) Systematic reviews of published studies tend to confirm a relationship between periodontal disease and preterm birth with an overall relative risk approaching 3. (16)

Few studies on periodontal disease have examined women in developing countries, with very limited data available from Pakistan. The National Health Survey of Pakistan found that an indicator of dental health, the DFMT (Decayed Missing Filled Teeth) index to be twice as high for women (mean = 2.8) compared to men (mean = 1.2) at 15–24 years, with the DMFT index increasing with age. (17) In a recent study, almost 17% of women aged 18–24 had advanced periodontal disease. (18)

Given the potential association of periodontal disease with poor pregnancy outcomes, in countries such as Pakistan with high rates of stillbirth, low birth weight and premature birth, further study of the relationship between periodontal disease and pregnancy outcome is needed. The aim of this study was to investigate the association between periodontal disease and birth outcomes in a peri-urban setting in Pakistan.

METHODS

The dental health study was conducted as one component of a prospective pregnancy outcomes study conducted in four units of Latifabad, in the Hyderabad District of Pakistan, from September 2003 to August 2005. Pregnant women at 20 to 26 weeks gestation were identified for enrollment in their homes by the Lady Health Workers (LHW) of the Ministry of Health's National Program for Primary Health Care and Family Planning. LHWs are female residents from the community with a minimum of eight years of formal schooling who provide basic maternal and child health services and counseling by visiting assigned households monthly.

During routine home visits, LHWs identified the pregnant women and provided them a brief orientation to the study. Women who indicated interest were seen at a local research clinic to confirm eligibility. For those who consented, demographic and health data and laboratory tests were collected on pre-tested study forms by trained research staff including two female doctors, one female dentist, two female health visitors, one midwife and a laboratory technician. Gestational age was determined by ultrasound examination and a physical examination was performed. The survey of oral health care practices and a dental examination were performed at this visit.

Dental Methodology

All the dental examinations were conducted by one of two trained dentists with periodontology expertise. The dentists were given one-week research-related teaching session on calibration to ensure intra-examiner agreement, supervised by a consultant dentist (NB). The WHO standard data collection tool was used for the oral examination.(19) All dental examinations were conducted using standard dental collection tools, a dental chair, and periodontal probes that meet WHO specifications. (20) To ensure a high level of hygiene, an autoclave and sufficient numbers of instruments were provided.

The dental examination assessed dental caries, quantitative periodontal disease measures and clinical evidence of other oral infection. No radiographs were taken. A full mouth periodontal examination was performed, assessing the plaque and gingival indices. The values at six sites per tooth were measured for clinical attachment loss, probing pocket depth and recession and the worst score per tooth was recorded. The measures used are summarized below (21, 22):

- Probing Depth (PD): the distance between the gingival margin and the base of the pocket in mm.
- Clinical Attachment Loss (CAL): the distance from the cemento-enamel junction to the base of the pocket in mm.
- Gingival Index (GI): a score from 0 (normal appearance, no bleeding, no inflammation) to 3 (marked redness, hypertrophy, edema, ulceration, spontaneous bleeding and severe inflammation)
- Plaque Index (PI): measure of the degree of dental plaque accumulation ranging from no plaque to severe with scores ranging from 0 to 3.

The examination also recorded the number of teeth with caries, missing teeth, and teeth with fillings [the DMFT index (19)].

To ascertain birth outcomes, we developed liaisons with the local delivery facilities and the home birth attendants. Once a delivery was reported to the study clinic, the study physician and a nurse visited the woman at home or at the health facility within 48 hours to collect the delivery, birth outcome and postnatal data. A second postnatal visit was completed on day 28. Stillbirth was defined as birth of an infant with no sign of life (breathing, crying, heart beat); low birthweight (LBW) as an infant weighing < 2.5 kg at delivery; preterm birth as a live birth < 37 weeks and early preterm birth as one occurring at < 32 weeks; and neonatal death as a liveborn infant dying at 28 days of age.

The study was conducted under the auspices of the Global Network for Women's and Children's Health Research, a multi-country research network supported by the U.S. National Institutes of Health. The study was approved by the Aga Khan University Ethical and Review Committee and the Institutional Review Boards at the University of Alabama at Birmingham, Drexel University and the Research Triangle Institute. All women provided informed consent prior to study participation.

Data Management and Analyses—All data were entered centrally; data edits, including inter and intra-form consistency checks, were performed at entry with additional edits performed by an independent data center. Data were analyzed using SAS 9.1.3 (SAS Institute Inc, Cary, NC). Descriptive analyses were calculated (frequencies, percentages, means and standard deviations) to describe demographics, pregnancy information, economics and dental examination data.

Individual scores for each of the measures of periodontal disease (i.e. PD, CAL, PI and GI) were created by summing the highest score of this measure for each tooth (maximum 28 teeth). Disease severity was calculated for each periodontal measure by determining quartiles (25%, 50%, and 75% of the data were less than or equal to that score). The quartiles were not equally distributed because many women had the same score. The relationship between periodontal disease (i.e. PD, CAL, PI and GI) measured in quartiles of disease severity, and the adverse birth outcomes were evaluated using the Cochran-Armitage test for trend. Chi-square and Fisher's exact tests were completed, and relative risks (RR) were calculated for the measures of periodontal disease and pregnancy outcomes. For early preterm birth, exact CMH procedures in StatXact, version 7 (Cytel, Inc., Cambridge, MA, 2005) were used because the binary outcomes were sparse, yielding odds ratios (OR) instead of risk ratios.

RESULTS

Of the 1369 women enrolled, dental examinations were completed for 1245 (90.9%). (Figure 1) Of these, 1,152 (92.5%) had a birth outcome recorded and 1,037 (90.0%) also had a 28-day outcome. Table 1 describes the socio-demographic characteristics of the study participants. The mean age of the respondents was 26.5 years (SD± 5.1) and 88.2% were housewives. Thirty-three percent of the women had no formal schooling. Of those with schooling, 6% completed grade five, 42% completed grades 5–10 and 17 % completed grade 10 or higher (data not shown). For those with income recorded, the mean monthly household income was 6155 Rs (SD 6598) or approximately \$100 US. Most (81.3%) were Urdu-speaking followed by Punjabi (8.4%), Pushto (4.2%), and Sindhi (3.8%). The majority of the women were multiparous, with a mean number of previous pregnancies of 3.6 (SD 2.3). Of those with previous pregnancies, 13.3% reported a previous miscarriage or abortion and 2.7% reported at least one previous stillbirth.

Table 2 presents dental history and dental examination characteristics of the participants. About half (58.0%) brushed their teeth with toothpaste and 30.7% used their finger with manjun to clean their teeth. Most women (91.2%) had no dental care in the past year. Nearly 47% had at least one decayed tooth at the time of the exam and 27.2% had at least one missing tooth (mean of 0.6, SD 1.4). Only 4.0% had any filled teeth (mean = 0.1 ± 0.5 filled teeth per woman). Less than half (43.7%) of the women had no decayed, missing or filled teeth. In data not shown, the DMFT Index was not associated with any adverse pregnancy outcome.

Table 2 also presents the periodontal disease examination results based on defined criteria: moderate periodontal disease defined by a probing depth of ≥ 3mm for at least 3 teeth, a clinical attachment level (CAL) of ≥ 3mm for 4 teeth, a plaque index (PI) of 3 for at least 4 teeth, and a gingival index (GI) of 3 for at least 4 teeth. Periodontal disease was common using these criteria: 75.9% met the criteria for moderate periodontal diseases with a probing depth of 3 mm or greater on ≥ 3 teeth. 87.0% had ≥ 4 teeth with a CAL of ≥ 3mm, 55.6% had ≥ 4 teeth with a PI = 3, and 60.2% had ≥ 4 teeth with a GI = 3. None of these measures was significantly associated with any of the adverse pregnancy outcome measures.

To determine whether increasing levels of periodontal disease were associated with adverse perinatal outcomes, we evaluated the association between the measures of periodontal disease in quartiles with adverse birth outcomes, presented as rates per 1000 total births for stillbirth and rates per 1000 live births for neonatal deaths and <32 wk preterm births (Table 3). The stillbirth rates increased with increasing severity of periodontal disease: from 19 per 1000 to 41 per 1000 (p=0.069) between the first and the fourth probing depth quartiles, from 26 per 1000 to 42 per 1000 (p=0.131) with the increasing severity of clinical attachment

measures, from 22 per 1000 to 50 per 1000 ($p=0.033$) with increasing severity of PI measures, and from 24 per 1000 to 51 per 1000 ($p=0.019$) with increasing severity of the GI measures. The rate of 28-day neonatal death also increased with the severity of periodontal disease: from 41 per 1000 to 96 per 1000 ($p=0.011$) for increasing probing depth; from 49 to 99 per 1000 live births ($p=0.019$) for increasing severity of CAL; from 62 to 116 per 1000 live births ($p=0.010$) with increasing PI; and from 48 to 105 per 1000 live births ($p=0.005$) for increasing GI. While the <32 week PTB rate increased in a linear fashion as the measure of periodontal disease increased from the 1st to the 4th quartile, none of the differences were statistically significant. Late preterm birth and low-birth-weight were not related to measures of periodontal disease (data not shown).

The relative risks (RR) or odds ratios (OR) and 95% confidence intervals (CI) for the relationship between the quartile measures of periodontal disease and stillbirth, neonatal death and early preterm birth before and after adjustment for maternal age, education and employment status are shown in Table 4. In general, the RR or OR for the adverse outcome increased as the severity of the periodontal disease measure increased, with the RR or OR for the outcome for quartile 4 compared to quartile 1 generally in the range of 1.2 to 1.35 with approximately 30% of the adjusted 95% CIs excluding 1, suggesting that the relationships were significant. The relationships were more frequently significant for neonatal mortality where the number of outcomes was larger ($N = 83$) than for either stillbirth ($N = 37$) or early preterm birth ($N = 27$), where the number of adverse events in the individual quartiles was often 5 or less. Nevertheless, in almost every relationship evaluated, the RR or OR for an adverse outcome was greater than one.

DISCUSSION

Periodontal disease has been identified as a risk factor for heart disease, rheumatoid arthritis and other medical conditions. Offenbacher et al, in 1996, reported a strong association between periodontal disease and risk of preterm birth. (8) Subsequent reports have found mixed results. (9–16) The reasons for the differences in study findings are unclear, but the associations have appeared stronger and more consistent in US black populations and among women with severe periodontal disease. While nearly all of the observational studies have examined the relationship between periodontal disease and all preterm births, several have suggested that the strongest relationship is between periodontal disease and early preterm births. (11,13,23) The largest interventional study reported to date suggested that periodontal treatment consisting of scaling and root planning to prevent preterm birth, if effective at all, was only effective against preventing very early preterm births, in a sense corroborating the observational data. (24)

Periodontal disease has rarely been studied in developing country settings, especially in relationship to birth outcomes. In this study, carried out in a peri-urban setting among a group of relatively middle class Pakistani women, dental care was used infrequently and periodontal disease was very common. A significant increase in both stillbirth and neonatal mortality, as well as a non-significant increase in early preterm birth, was associated with several measures of severe periodontal disease. These results are consistent with the existing observational studies from developed countries that suggest a stronger relationship between periodontal disease and late miscarriage and early neonatal death, stillbirth, and early spontaneous preterm birth than with all preterm birth. (11,13,23) As noted above, the one large treatment study published to date from a developed country had suggestive evidence that treatment of periodontal disease reduced adverse events early in pregnancy. (24)

It is unknown if the observed association between periodontal disease and adverse pregnancy outcomes reflect cause and effect (periodontal disease leading to preterm birth) or

simply an association. Confounding by genital tract infections, low socioeconomic status, smoking or other factors associated with both periodontal disease and preterm birth is a possible explanation, although positive results have persisted in some studies after adjustment for multiple maternal characteristics. (11) In this population of Muslim women with family incomes of approximately US \$100 per month, virtually none of the women smoked, used alcohol, or had genital tract infections (data not shown). Adjusting for several demographic conditions had little impact on the observed relationship. Periodontal disease may lead to preterm birth via seeding of the placenta or amniotic fluid by oral pathogens; however, in the published studies only a very small percentage of preterm births are associated with intrauterine infection with oral flora. (25) Alternatively, systemic inflammation initiated by periodontal disease might contribute to both the increase in stillbirth and neonatal mortality noted in this study. (25–28)

In both developed and developing countries, periodontal disease is an attractive candidate for intervention, especially because it is readily identified and treated. Periodontal disease treatment has included antiseptic mouthwash, several antibiotics, and periodontal cleaning and plaque removal (scaling and root planing). The latter treatment is believed to be the most effective for periodontal disease. In addition to the interventional study described above, (24) two smaller studies (29, 30) have suggested that treatment of periodontal disease in pregnancy is feasible and may reduce preterm birth. At least two other large studies evaluating periodontal disease treatment to reduce preterm birth are underway, and the results from those trials should help determine the efficacy of periodontal disease treatment in improving birth outcomes. (31, 32)

The major strength of this study is the prospective intensive dental evaluation of pregnant Pakistani women drawn from a well described community during the prenatal period and the independent collection of perinatal outcomes by staff unfamiliar with the results of the dental examination. The use of dentists trained in periodontal disease evaluation using standardized data collection instruments is an added strength of this study. Its major weakness is the relatively small number of adverse outcomes, specifically stillbirths and early preterm births, in some of the periodontal disease quartiles, likely leading to some of the relationships appearing to lack statistical significance. Nevertheless, in a population with a high prevalence of periodontal disease, it appears that the likelihood of an adverse pregnancy outcome increases as the degree of periodontal disease worsens. In general, for stillbirth, neonatal mortality and early preterm birth, the RR for quartile 4 compared to quartile 1 is about 1.3. While a number of these relationships are statistically significant, the magnitude is often less than the 2 to 8-fold differences in preterm birth described in some studies from developed countries (8–11) One potential explanation for this discrepancy is the very large difference in the rates of adverse outcomes between Pakistan and the US. For example, in the US, the stillbirth and neonatal mortality rates are in the range of 5/1000 births, while in this Pakistani population, the stillbirth rates were > 30/1000 total births and the neonatal mortality rates > 50/1000 live births. This suggests that because of the high all-cause perinatal mortality in Pakistan, periodontal disease may make a smaller relative contribution to adverse pregnancy outcomes in Pakistan than in developed countries.

In summary, in this prospective community based study of pregnant Pakistani women, periodontal disease was extremely common. As various measures of the severity of the periodontal disease increased, both stillbirth and neonatal death increased, accompanied by a non-significant increase in early preterm birth. It is unknown if treatment of the periodontal disease either before or during pregnancy would improve these adverse pregnancy outcomes.

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Figure 1.
Enrollment Diagram

Table 1
Socio-demographic Characteristics of the Participants

Socio-demographic characteristic	Women (n = 1,152)
Age, mean (SD)	26.5 (5.1)
Level of education	
No education (%)	33.4
If education, number of years, mean (SD)	8.7 (3.3)
Employment status	
Employed (%)	11.8
Housewife (unemployed) (%)	88.2
Ethnicity (mother tongue)	
Urdu (%)	81.3
Punjabi (%)	8.4
Pushto (%)	4.2
Sindhi (%)	3.8
Other (%)	2.3
Monthly household income (Rupees), mean (SD)	6,155 (6598)
Number of pregnancies, mean (SD)	3.6 (2.3)
Previous miscarriage/abortion (%)	13.3
Previous stillbirth (%)	2.7

Table 2
Dental History and Examination of the Participants

Dental History and Examination	Women (n = 1,152)
Method of cleaning teeth, n, (%)	
Brushing with toothpaste	666 (58.0)
Using finger with manjun	353 (30.7)
Brushing with manjun	44 (3.8)
Other (miswak)	88 (7.6)
Dental treatment in past year, n, (%)	101 (8.8)
Decayed teeth	
Have decayed teeth, n %	538 (46.7)
Number of decayed teeth, mean (SD)	1.3 (1.9)
Missing teeth	
Have missing teeth, n (%)	313 (27.2)
Number of missing teeth, mean (SD) ¹	0.6 (1.4)
Filled teeth	
Have filled teeth, n (%)	46 (4.0)
Number of filled teeth, mean (SD)	0.1 (0.5)
DMFT,	
DMFT = 0, n (%)	504 (43.7)
DMFT = 1, n (%)	193 (16.8)
DMFT = 2, n (%)	134 (11.7)
DMFT >2, n (%)	320 (27.8)
Periodontal disease by probing depth	
< 3 teeth with a probing depth 3mm (%)	277 (24.1)
3 teeth with a probing depth 3mm (%)	875 (75.9)
Clinical Attachment	
< 4 teeth with a CAL of 3mm (%)	150 (13.0)
4 teeth with a CAL of 3mm (%)	1,002 (87.0)
Plaque Index	
< 4 teeth with a PI = 3 (%)	511 (44.4)
4 teeth with a PI = 3 (%)	641 (55.6)
Gingival Index	
< 4 teeth with a GI = 3 (%)	458 (39.8)
4 teeth with a GI = 3 (%)	694 (60.2)

Table 3

The Relationship Between Level of Periodontal Disease* and Birth Outcomes

Measure of Periodontal Disease	Level of Periodontal Disease*	Stillbirths /1000	Neonatal Deaths/1000	< 32 week Preterm Births/1000	Total N (%)
By Probing Depth					
Quartile 1	0 – 83	19	41	11	269 (23.2)
Quartile 2	83 – 101	32	83	25	281 (24.2)
Quartile 3	101 – 120	34	94	34	292 (25.2)
Quartile 4	120	41	96	22	318 (27.4)
P-value		0.069	0.011	0.161	
By Clinical Attachment					
Quartile 1	0 – 94	26	49	15	267 (23.0)
Quartile 2	94 – 114	27	79	27	292 (25.2)
Quartile 3	114 – 131	31	88	24	292 (25.2)
Quartile 4	131	42	99	26	309 (26.6)
P-value		0.131	0.019	0.240	
By Plaque Index					
Quartile 1	0 – 75	22	62	13	231 (19.9)
Quartile 2	75 – 88	27	63	23	299 (25.8)
Quartile 3	88 – 104	26	70	36	308 (26.6)
Quartile 4	104	50	116	19	322 (27.8)
P-value		0.033	0.010	0.284	
Gingival Index					
Quartile 1	0 – 90	24	48	8	249 (21.5)
Quartile 2	90 – 108	18	65	22	276 (23.8)
Quartile 3	108 – 122	31	92	38	321 (27.7)
Quartile 4	122	51	105	22	314 (27.1)
P-value		0.019	0.005	0.086	

*. Score for each category of periodontal disease for each woman is defined by the sum of the score for each tooth.

Table 4
Unadjusted and Adjusted* Risk for Various Pregnancy Outcomes by Increasing Severity of Periodontal Disease

	Stillbirth n=37		Neonatal death n = 83		<32 wk Preterm Birth n = 27	
	RR (95% CI)	Adj* RR (95% CI)	RR (95% CI)	Adj* RR (95% CI)	RR (95% CI)	Exact OR* (95% CI)
Probing Depth						
Quartile 1 **						
Quartile 2 – 3	1.17 (0.95, 1.44)	1.17 (0.93, 1.46)	1.23 (1.08, 1.41)	1.22 (1.07, 1.40)	1.26 (1.04, 1.52)	1.81 (0.64, 6.27)
Quartile 4	1.35 (1.00, 1.81)	1.31 (0.95, 1.81)	1.40 (1.13, 1.74)	1.37 (1.09, 1.72)	1.30 (0.86, 1.97)	2.25 (0.74, 2.25)
Clinical Attachment						
Quartile 1 **						
Quartile 2 – 3	1.03 (0.80, 1.34)	1.02 (0.78, 1.34)	1.17 (1.01, 1.35)	1.18 (1.01, 1.37)	1.16 (0.91, 1.46)	1.11 (0.43, 3.22)
Quartile 4	1.22 (0.88, 1.70)	1.23 (0.87, 1.73)	1.35 (1.07, 1.69)	1.29 (1.03, 1.62)	1.25 (0.83, 1.88)	1.63 (0.59, 4.90)
Plaque Index						
Quartile 1 **						
Quartile 2 – 3	1.05 (0.83, 1.34)	1.07 (0.84, 1.36)	1.02 (0.86, 1.22)	1.04 (0.87, 1.24)	1.19 (0.99, 1.42)	1.22 (0.42, 4.32)
Quartile 4	1.32 (1.03, 1.70)	1.29 (0.98, 1.69)	1.27 (1.05, 1.54)	1.25 (1.03, 1.51)	1.15 (0.72, 1.83)	2.36 (0.81, 8.36)
Gingival Index						
Quartile 1 **						
Quartile 2 – 3	1.01 (0.77, 1.33)	0.99 (0.75, 1.32)	1.14 (0.99, 1.32)	1.15 (0.99, 1.33)	1.28 (1.10, 1.50)	1.04 (0.38, 3.32)
Quartile 4	1.32 (1.01, 1.72)	1.32 (1.01, 1.73)	1.35 (1.10, 1.66)	1.35 (1.10, 1.64)	1.40 (0.98, 2.01)	2.17 (0.79, 6.88)

* Adjusted for maternal age, education and employment status

** Referent quartile