Associations Between Maternal Periodontitis, Periodontal Treatment and Pregnancy Complications – Part 2: Analytical Epidemiology

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Possible links between maternal periodontitis and adverse pregnancy outcome have been proposed, and appear to be supported by experimental models based on data from animal studies, in vitro work and human obstetric studies. This paper aims to review the current literature on human clinical investigations into such a relationship, based on current knowledge and in light of proposed mechanisms.

Key words: periodontitis, pregnancy, complications, periodontal treatment, epidemiology

INTRODUCTION

Experimental Models for Periodontal-Pregnancy Associations

Potential relationships between periodontal disease and adverse pregnancy outcomes have been investigated for a number of years. It is widely believed that parturition is a process involving a range of proinflammatory mediators, modulated by hormonal changes and potentially influenced by local or distant infections (reviewed in previous paper, Farrell and Ide, 2005). The aim of this paper is to critically review the available epidemiological evidence for the relationship between periodontitis and adverse pregnancy outcome.

PREGNANCY COMPLICATIONS AND PERIODONTITIS: INITIAL HUMAN STUDIES

The first clinical investigation into putative links between periodontitis and pregnancy outcome in humans was published by Offenbacher et al in 1996. In this case control study, 124 women from a Prenatal Care Clinic completed questionnaires, had medical histories reviewed and underwent a full periodontal examination either during prenatal care (at undefined times) or up to 3 days post partum. Pregnancy outcomes were followed up and subjects allocated to case and control groups. The authors reported that the presence of maternal periodontitis was one of a number of risk factors (the rest being established obstetric risk factors) for preterm labour or low birth weight, and that the odds ratio for pregnancy complications in the presence of severe periodontitis was in the order of 7.5 to 8. It is interesting that whilst approximately 57% of the women recruited to the study with preterm and/or low birth weight babies were African American, this group made up 45% of the total women attending who experienced pregnancy complications. It is unknown whether this difference was significant, but this may limit the generalisability of the results to a broader population. Periodontitis was assessed between groups as a covariate in a regression model and despite the relatively low age of the subjects, the mean levels

of periodontitis were higher than reported elsewhere (probing depth 3.13 mm, attachment loss 3.03 mm). In developing the regression model, this group devised a dichotomous score described as 'extent 3:60', that is, 60% of sites with 3 mm or more loss of attachment, as a means of defining the presence of significant periodontitis. This seems to be a high threshold and heavily in excess of the case definition for chronic periodontitis agreed at the recent European workshop on periodontal diseases (5th European Workshop, Ittigen, Switzerland 2005). Moore et al (2001, 2004a) described a population representative of pregnant women with a range of ethnicity and with levels of periodontitis consistent with the UK population overall, yet only 1 woman in 2000 had the "extent 3:60" level of periodontitis, even though they were older than the population described here. Again this suggests that the odds ratios reported by this group relate to severe levels of periodontitis, which may not be seen in other populations. Indeed, the high specificity and low sensitivity of such a case definition may explain why no other groups have managed to replicate such large odds ratios in similar studies.

SUBSEQUENT HUMAN STUDIES

Several studies have followed the pioneering work of Offenbacher et al (1996). Dasanayake (1998) found, using CPITN as a means of assessing periodontal health in a case-control study of 110 Thai women, that low birthweight was related to maternal height and socio-economic status, as well as to gingival bleeding and the presence of calculus, but not to pocket probing depth. However, when a regression analysis was carried out (not strictly appropriate since subjects were recruited on a case-control basis), the associations with periodontal disease were lost, an indication of the confounding effects of other variables.

Relationships between maternal disease and pregnancy outcome were further investigated prospectively by Offenbacher et al and interim results described in 2002. These data related to 812 women, of which 188 (23.1%) went on to have preterm deliveries. In this paper the relatively high rate of complications is described as representative for the population locally, both in terms of complication rate, ethnicity and complications by ethnicity. Despite the case group being younger than controls and having the same proportion of first time deliveries, there was still a higher incidence of a history of previous prematurity for cases. In addition, the cases exhibited a much greater incidence of chorioamnionitis and a greater incidence of advanced periodontitis. However, the incidence of chorioamnionitis was still considerably lower in the cases (6.4%) than that seen in many other studies of this type, where the incidence is often as high as 50-60%. This may again reflect ethnic differences in susceptibility to local inflammation, since 50% of women recruited were African-American, or it may suggest that other distant inflammatory conditions are involved in the pathogenesis. Smoking was not associated with an elevated case risk. As birth weight and gestation fell, there was a greater percentage of mothers with more severe periodontitis (defined by pocket probing depths), but attachment loss was not reported. The authors also reported a tendency towards greater neonatal mortality with more severe maternal periodontitis, but like Moore et al (2004), the numbers were small and so the association was not statistically significant.

The severity and progression of periodontal disease during pregnancy in women in North Carolina was reported by Lieff et al (2004). It is assumed that the 903 subjects involved in this study would be a similar population to those investigated by Offenbacher et al (1996). However they had relatively low mean probing depths (mean 1.6 mm, rising to 1.7 mm postpartum) and mean attachment loss (0.9 mm rising to 1.0 mm postpartum). At 26 weeks, around 24% of sites bled on probing. The authors reported that there were no clinically significant changes in periodontal status during pregnancy. However they did identify that some women with moderate periodontitis midterm did experience further attachment loss during pregnancy. Women were more likely to have disease, or disease progression if they were African-American, smoked during pregnancy or were of lower socioeconomic status.

López et al (2002b) investigated a group of 639 Chilean pregnant women. Of these 406 had gingivitis and received treatment before 28 weeks' gestation, and 233 with untreated periodontitis were monitored. The incidence of preterm low birth weight deliveries (PLBW) was 2.5% in periodontally healthy women, and 8.6% in women with perio-

dontitis (p = 0.0004, relative risk = 3.5, 95% CI, 1.7 to 7.3). Complications were associated with a previous history of adverse pregnancy outcome, periodontitis, antenatal care and maternal weight gain. A second group in South America (Romero et al 2002) have reported a potential relationship between birth weight for gestational age and maternal periodontitis in 69 women with a range of periodontal diseases. In this small study, Russell's periodontal index was used as a mean score for the whole mouth, and subjects were grouped accordingly: 13 were deemed healthy, 17 had gingivitis, 33 had early periodontitis, and 6 had established periodontitis. Women were not recruited if they had other obstetric complicating factors, including smoking. Although the authors report significant correlations between periodontal status (a categorical variable) and both birth weight and gestational age, there were only significant differences for these outcome variables between the periodontally healthy and severely diseased subjects, perhaps a reflection of the low numbers in the study. Even so, these data do support Offenbacher et al's (1996) original findings.

Jeffcoat et al (2001) published interim results from an ongoing study in Alabama and reported that their population was made up of 83% African Americans, and that these subjects had significantly more periodontal disease: unfortunately they did not report how much more. They characterised their subjects into no periodontitis, periodontitis and severe periodontitis, and reported odds ratios for preterm birth by periodontal disease severity. Unfortunately we do not know how many subjects were in each category, although the large confidence intervals reported suggest that the numbers with severe disease out of a population of 1313 were relatively low. The authors reported odds ratios of 4.45 to 7.07 for preterm birth of varying severity based on the presence of generalised periodontitis (90+ sites with 3 mm or more attachment loss). These analyses were also performed without controlling for important obstetric risk factors such as previous pregnancy history and history of infections during pregnancy (although these were investigated). Furthermore, they did not attempt to analyse solely the never-smokers recruited, the most reliable way to exclude the confounding effects of smoking.

Later work from Alabama (Goepfert et al 2004a, 2004b) compared women who had either spontaneous preterm birth or indicated preterm birth for planned reasons. Again the majority of the subjects in this study were African American. Examinations were not carried out at the same time in pregnancy on all women, some being seen before delivery at 24 weeks, and some post-delivery. Disease severity was assessed using a WHO probe and recording the greatest probing depth and attachment loss value for all teeth in each sextant, generating six scores for each variable per subject. Those experiencing spontaneous preterm birth were marginally older than term subjects and were more likely to have a history of previous complications. This group then reported the percentage of subjects in each group with sextants containing teeth with either 3 mm or more or 5 mm or more loss of attachment. They reported an association with gestational age, but did not allow for any other factors such as smoking or previous history, and so such an association could be misleading. When multivariate analysis was performed controling for age, ethnicity, education, socioeconomic status, smoking and pregnancy history, the odds ratio of 2.5 for spontaneous preterm birth associated with severe periodontal disease was not statistically significant. The presence or absence of periodontal disease did not affect the incidence of placental or umbilical cord positive cultures, chorioamnionitis or elevated levels of IL-6, in either the overall population or those with periodontitis. It is interesting to note that some periodontal organisms were identified in placental cultures of 5 women, with 2 case women and 3 term controls carrying these organisms. Hence it appears possible for these organisms to become established locally (confirming Dixon et al, 1994), but the numbers of infected subjects are too small to draw any meaningful conclusions. However, this does not refute the possibility of an underlying shared genetic susceptibility to the two conditions of interest.

A similar study from the USA (Jarjoura et al, 2005), compared 83 preterm cases with 120 controls from a largely Hispanic population. Periodontal health (partial recording), oral flora and circulating maternal antibodies were assessed within 48 hours of delivery. Cases and controls did not differ for demographic factors, although the cases included more smokers. Chorioamnionitis affected 19.3% of cases and 2.5% of controls, which also differed for attach-

ment loss (greater in cases, 1.7 vs 1.5 mm) but not for other indicators of periodontal disease, tooth number or oral hygiene. These subjects had similar levels of disease and age distribution to other studies with the exception of Offenbacher et al (1996). Regression analysis indicated that gestational age was related to previous pregnancy history, chorioamnionitis and attachment loss, and birth weight was also related to these factors and to maternal body mass. However attachment loss was only a significant factor when outcomes were treated as continuous variables: when patients were categorized into presence or absence of preterm delivery or low birth weight, significance disappeared. Only chorioamnionitis and pregnancy history were explanatory variables. Results for never smokers were not reported. There were no differences in the oral flora or in maternal antibody levels, although these findings could have been affected by the use of antenatal amoxicillin in those with chorioamnionitis.

EUROPEAN AND OTHER STUDIES

The first European study to find an association between preterm birth and maternal periodontitis in an ethnically homogenous group was published in 2004 (Radnai et al, 2004). Interestingly, the group's definition of periodontal disease was less severe than in previous studies in this field: one site or more with 4 mm or greater probing depth and bleeding on probing at more than 50% of sites. The number of subjects in each group was small: 41 cases with preterm labour or 'threatened' preterm labour and 44 controls with birth at full-term. The subjects had a wide range of educational and socio-economic backgrounds. There was also a large disparity between smokers in the case and control groups with 17% of case subjects, but no control subjects, reporting smoking during pregnancy. The group performed logistic regression on this small number of subjects after the seven smoking case subjects were excluded. The case subjects demonstrated an odds ratio of 5.46 for having the defined level of periodontal disease. The researchers did not find an association between preterm birth and loss of periodontal attachment but hypothesised that probing depth and bleeding on probing were more important markers of current infection.

The problems of defining the level of periodontal disease were addressed in a recent study from Austria (Dörtbudak et al, 2005). In this study 36 women were assessed at between 15 and 20 weeks of pregnancy; all were undergoing amniocentesis for medical reasons. A sample of amniotic fluid was taken and assayed for the presence of several cytokines, cultured for bacteria and analysed by polymerase chain reaction (PCR) for the presence of orange and red cluster bacteria as defined by Haffajee et al (2003). The women also underwent a periodontal examination and general health questionnaire. Two subgingival plaque samples were collected from the deepest periodontal pockets from each subject and analysed similarly to the amniotic fluid. Periodontal disease was defined as the presence of a periodontal pocket of at least 5 mm in each quadrant and if 60 or more colony forming units (CFUs) of orange and red clusters were present in these pockets. Six subjects later experienced a preterm birth, defined by the research group as birth at less than 37 weeks gestation and/or a birth weight of less than 2,500 g. The study population had a low level of smoking (one subject) but a mean age over 30 years. Of the six preterm birth subjects, five (83%) had the defined level of periodontitis whereas 6 of 30 "normal" term births (20%) had periodontitis. Amniotic fluid from the preterm group had higher levels of interleukin-6 (IL-6) and prostaglandin E_2 (PGE_2) whereas the levels of IL-8 were higher in the normal birth group. IL-6 and PGE_2 correlated with the number of subgingival CFUs. None of the amniotic fluid samples gave a positive bacterial culture. This small study appears to provide evidence for an association between periodontitis and preterm birth, but this is a selected population undergoing amniocentesis for other, undefined reasons with a high rate (20%) of adverse pregnancy outcome. The periodontal health was also generally poor, with 11 of the 36 women having a probing depth of at least 5 mm in each quadrant.

Buduneli et al (2005) performed a case control study on a population from Izmir, Turkey. Their case subjects were defined as preterm and/or low birth weight when a mother delivered a baby preterm (less than 37 weeks gestation) and/or a low birth weight baby (less than 2500 g birthweight). In this study 53 case subjects and 128 controls were assessed for obstetric risk factors

and periodontal health within 72 hours of delivery. It is not evident whether the two examiners were blind to pregnancy outcome. Nevertheless the examination included subgingival plaque collection before a full mouth periodontal examination and subsequent analysis using a 'checkerboard' DNA-DNA hybridisation method. The periodontal examination included measurement of pocket probing depth but there was no assessment of loss of attachment. The population was young (mean age 25 years), of low socio-economic status and had a high level of smokers during pregnancy (approximately 45%). None of the classical obstetric risk factors such as socio-economic status, smoking, previous poor pregnancy history and low level of antenatal care were found to be associated with PLBW in this study. Likewise there were no differences between case and control subjects in the clinical periodontal parameters. The prevalence of periodontal disease (as defined by deep probing depths only) was low in this study. Microbiological analysis also failed to demonstrate relationships between the presence and loads of individual periodontal pathogens and PLBW. Occurrence rates of some bacterial species were found to be higher in the control subjects. Regression analysis on this small number of subjects found the combination of *Peptostreptococcus micros* and *Campylobacter rectus* to be associated with PLBW and the authors stated that this demonstrated that the complex actions of different bacteria were more important than the presence of individual pathogens.

The first published British study to introduce controversy into the field was by Davenport et al (2002) who performed a case-control study at the Royal London Hospital, Whitechapel. The periodontal health of 236 women who gave birth at less than 37 weeks gestation to a baby weighing less than 2500 g (preterm low birth weight, PLBW) was compared to that of 507 control women (birth at 38 weeks or over with a birth weight of 2500 g or more). The periodontal examination consisted of recording the maximum periodontal probing depth, bleeding on probing and Community Periodontal Index of Treatment Need (CPITN) (Ainamo et al, 1988) for each tooth. The examination was performed by a single examiner within 24 hours of the mother giving birth. In addition data were collected from the mother to assess for other obstetric risk factors. This included demographic details, smoking and alcohol consumption, medical and obstetric history. The demographic profile of the participants of this study demonstrated that the majority (53%) were Bengali in origin and the mean age was 27 years. One third of subjects were first-time mothers. Logistic regression revealed that factors associated with PLBW were hypertension during pregnancy, previous delivery of a low birth weight infant and smoking during pregnancy. The periodontal health of the study population was generally poor: 44% of subjects had at least one sextant with a CPITN score of 4 and mean probing depths were 3.72 mm and 3.85 mm for case and control mothers respectively. There was no association between poorer periodontal health and PLBW in this population. Bengali and White subjects were analysed separately and, again, there were no associations between periodontal disease and PLBW. Moreover, the authors state that increasing periodontal pocket depth was associated with an improved pregnancy outcome, but gave no hypothesis to explain this relationship.

The lack of an association between periodontal disease and adverse pregnancy outcome in a South East Asian population was shown by a study from Sri Lanka. Rajapakse et al (2005) performed a prospective study on a rural Sri Lankan population in the third trimester of their first pregnancy. This population were free of tobacco, alcohol and recreational drug use but were of a uniformly low socio-economic status. Periodontal assessment was a full-mouth analysis, four sites per tooth examined for the presence of plaque, bleeding on probing and pocket probing depth, with the periodontal 'exposure' defined as the mean of all three of the dental variables being greater than the median values for the population. Of the 227 subjects assessed, 66 women were in the exposed category. The pregnancy outcome of interest in this study was preterm low birth weight (PLBW, birth at less than 37 weeks gestation to a baby weight less than 2500 g). The rate of PLBW was 7.5% (17 subjects) in this study. This appeared to be a low rate of poor pregnancy outcome but may reflect the early antenatal care these subjects received. Logistic regression was performed to adjust for recognised risk factors, this demonstrated that, although the rate of PLBW was higher in the periodontal disease exposed group, the 95% confidence intervals for the odds ratios did not reach statistical significance.

Further European studies have failed to demonstrate any associations between poor periodontal health and pregnancy outcome. Holbrook et al (2004) from Iceland reported the results of a prospective pilot study in a short communication. 96 women were recruited and assessed in their third trimester of pregnancy. The population was predominantly Caucasian, of a high socio-economic status and had quite a high rate of smoking during pregnancy (23%). Clinical examination included a partial mouth periodontal examination with no assessment of loss of attachment, subgingival plaque collection and vaginal swabs for the presence of bacterial vaginosis (BV). Periodontal disease was defined as any site probing 4 mm or greater. Unsurprisingly, given this definition in a pregnant population, 89% had a least one pocket of 4 mm. One third of women had some markers of BV. 6 (6%) of subjects subsequently experienced a PLBW birth, all of which had some markers of BV. There were no associations between pregnancy outcome and periodontitis or periodontal pathogens, however no statistical analysis was performed on this small number of subjects.

Noack et al (2005) performed a case control study in Dresden, Germany. The study population was Caucasian, the majority of which were of middle to high socio-economic status, with a mean age between 27 to 30 years (depending on the study subgroup) and there was a low prevalence of smoking during pregnancy. The control subjects were assessed within three days of delivery but the case subjects were seen before they gave birth (the exact time during gestation was not stated) and were defined as women at high risk of PLBW as demonstrated by preterm contractions. The case subjects were divided retrospectively after delivery into those that experienced a PLBW birth and those that had a baby weighing more than 2500 g (but perhaps a preterm birth) possibly due to medical intervention. The periodontal examination was a full-mouth (six sites per tooth) assessment of plaque, bleeding, probing depth and loss of attachment. In addition gingival crevicular fluid (GCF) samples were taken from the mesio-buccal sites of each of the first or second molars and were analysed for the presence of interleukin-1β (IL1β). Subgingival plaque samples were taken from the deepest sites and were analysed for the presence of periodontal pathogens by a commercial assay kit. There were two examiners who were not blind as to whether the subject was a case or control subject. The control group contained 42 women, there were 59 in the case group. Of these 59 subjects, 16 had a PLBW delivery. Classical obstetric risk factors such as previous adverse pregnancy outcome and systemic infection during pregnancy were associated with PLBW. The population had relatively good periodontal health and there was no association between any of the periodontal variables and pregnancy outcome, even when risk factors were controlled for in regression models on this small number of subjects. There were no statistically significant differences in the concentration of GCF-IL1β between study groups nor were there any associations between the presence of periodontal pathogens and pregnancy outcome.

Most recently, Moreu et al (2005) have reported data from a population of 96 Spanish women delivering 89 infants: this included multiparous women, who would have a greater risk of preterm and small babies. Women were examined several times during the pregnancy, and it was apparent that there was no direct association between any of: severity or extent of periodontal pocketing, oral hygiene or gingival inflammation, and pregnancy outcome. However, the subjects were relatively periodontally healthy, with disease levels consistent with other European populations of a similar age. Regression analysis also failed to identify any significant associations, even though no attempt was made to incorporate other established risk factors such as maternal age, ethnicity, previous obstetric history and smoking into their model.

The majority of the previously published papers in this field have described case-control studies, many being of modest volunteer numbers. These lack the power of prospective studies. Our own group therefore undertook a prospective study at Guy's and St Thomas' Hospital Trust to ascertain if there was an association between mothers with periodontal disease during pregnancy and a subsequent adverse pregnancy outcome, such as preterm birth, low birth weight or late miscarriage (Moore et al, 2004). 3738 subjects were assessed at 12 weeks of pregnancy for periodontal health and obstetric risk factors. The periodontal examination was a full-mouth, two-sites-per-tooth assessment for plaque, bleeding on probing, probing depth and loss of attachment. Their pregnancy outcomes were collated by a Research Midwife and the data analysed.

The rate of preterm birth at less than 37 weeks gestation in this population was approximately 8%, similar to national maternity statistics for the UK. Likewise the levels of periodontal attachment loss appeared to be similar for the same age group in the latest UK Adult Dental Health Survey (Morris et al, 2001). Our population did have a higher proportion of deeper periodontal pockets than the UK national survey however that may have reflected the pregnant status of our population who may be expected to demonstrate an increase in false pocketing (Cohen et al, 1971). Although our population ostensibly appeared to represent our general UK population in terms of periodontal health, it is important to note that the level of periodontal disease was higher in several studies from the USA (Offenbacher et al, 1996; Jeffcoat et al, 2001; López et al, 2002b) and in the Royal London Hospital case-control study (Davenport et al, 2002). For instance, only 1.4% of our population had loss of attachment of 3 mm or greater in over 25% of sites, whereas one-third of Jeffcoat's study population had this level of disease. Likewise there were differences in the demographic profile of our study compared to others. The USA studies had high proportions of Black (African-American) subjects (Offenbacher et al, 1996; Jeffcoat et al, 2001), and the primary ethnic group in the other UK study was Bengali (Davenport et al, 2002).

We found that classical obstetric risk factors such as non-White ethnicity, low socio-economic status and smoking during pregnancy were associated with adverse pregnancy outcome. There were no associations between either preterm birth or low birth weight and periodontal disease. Likewise there appeared to be no relationship between extreme preterm birth (at less than 32 weeks gestation) and periodontal disease. However, in the regression model employed, the outcome of late miscarriage demonstrated associations with increased interproximal probing depth (odds ratio 2.54, 95% confidence interval 1.20 – 5.39, p = 0.015). We postulated that the difference in outcome between our study and those from parts of North America was likely to be due to differences in demographics, and case definitions of periodontitis. Limitations of this study included the use of self-reporting for risk factors and the use of multiple examiners for the periodontal assessments, necessitated by the large sample size.

As outlined above, studies of periodontal and systemic disease associations tend to be poorly controlled for smoking, which is an important potential confounding factor between periodontal disease and adverse pregnancy outcome (Hujoel et al, 2002). Hujoel proposes that further studies should improve the quality of smoking data collected and its analysis and include 'never smokers'. As our prospective study (Moore et al, 2004) had a large number of subjects, we performed a subanalysis for never smokers in our population (Farrell et al, submitted for publication). We found similar associations between poor pregnancy outcome and recognised obstetric risk factors, but again no associations between periodontal disease and preterm birth or low birth weight. The relationship between increased interproximal probing depth and late miscarriage was still present in regression models for the never smokers (odds ratio 3.84, 95% confidence interval 1.68 – 8.75, p = 0.001).

There was also a potential selection bias in our prospective study, as not all pregnant women attended our hospital early enough in pregnancy to be potentially recruited to the prospective study. Therefore we undertook a case-control study to address this (Moore et al, 2005), but women were recruited postpartum. Case subjects were defined as those that delivered a singleton infant less than 37 weeks of gestation, whereas control subjects delivered at, or around, term. A careful protocol was utilised to ensure that the periodontal exam was performed blind with the Research Midwife administering the questionnaire and separating the examiner from the baby and medical records. The periodontal examination was performed by a single examiner. Sixty-one case subjects and 93 control subjects were assessed. Only five (7.6%) potential case subjects refused consent when approached by the research midwife. The demographic factors of age, ethnicity, socio-economic status and the proportion of women who had just experienced their first pregnancy differed between case and control subjects. However there were a higher proportion of subjects of Black ethnic origin, of lower socio-economic groups and a lower proportion in their first pregnancy in this population compared with the prospective study population. There were no significant differences in periodontal health between the case and control subjects apart from the proportion of sites probing

5 mm or greater, which was lower in case subjects (2% versus 4%, p = 0.016). In addition, there was a tendency to a lower proportion of sites probing 4 mm or greater in the case subjects (8% versus 11%, p = 0.074). Potentially, the lower proportion of deeper periodontal pockets in the case group could be caused by the observed differences in the administration of antibiotics during pregnancy. Of the case subjects 53% had antibiotics before delivery compared with 28% of the control subjects (p = 0.002). This was despite no difference in the rate of urinary tract infection between the study groups. The level of periodontal disease was similar to our prospective study meaning the differences in periodontal health between our studies and those from the USA, as previously discussed, are also an issue in this case-control study.

SUMMARY: RELATIONSHIP BETWEEN PERIODONTITIS AND PREGNANCY OUTCOME

The vast majority of published studies are of a case-control design and of varying size, in various populations, and generating conflicting results. No study has repeated the degree of association originally reported by Offenbacher et al in 1996, but this may be related to the ethnicity and the severity of periodontitis in study subjects. Results may be compromised by the recruitment of smokers. It does appear harder for researchers to establish a link in populations where periodontal disease is not severe and common. However, perhaps the largest variable that blights meaningful comparisons between studies was identified at the 5th European workshop on Periodontics (Ittigen, February 2005) and that is the lack of any consistency in case definition between studies.

IS PERIODONTAL TREATMENT DURING PREGNANCY PROTECTIVE OR DAMAGING?

It is apparent that clinical studies are contradictory on potential relationships between periodontitis and pregnancy outcome. One way to try to establish if a cause-and effect relationship exists would be to perform intervention studies on pregnant women with periodontitis. These would also help establish the cost benefit of such treatment, and ensure that bacteraemias caused by instrumentation do not adversely affect pregnancy.

Several reports have been published investigating the possible effects of periodontal treatment during pregnancy on birth outcome.

Mitchell-Lewis et al (2001) studied a population of 213 teenage pregnant women, who were either African American (the majority) or Hispanic. Around half the subjects were recruited during pregnancy, the rest being examined within three months of delivery. They were described as having poor oral hygiene and generalised gingivitis but minimal attachment loss. There were no differences between those recruited pre- and post-partum for plaque index (mean 1.4) or sites bleeding on probing (mean 54%), but those seen pre-partum had mean probing depth greater than those recruited later (2.7 versus 2.4 mm). There were no differences for these variables between women with pregnancy complications and controls. However those women recruited pre-partum were given periodontal treatment, and it is possible that this may have influenced the effect of periodontitis in those women with disease who were recruited during pregnancy, when compared to those without disease or those who were untreated. When those with disease were considered based on their time of assessment (and hence whether they had periodontal care during pregnancy), no differences were found for risk of preterm birth or low birthweight. Plaque samples for those with preterm birth or low birthweight contained higher levels of *Bacteroides forsythus*, and *Campylo bacter rectus*. No other established risk factors were considered in this report.

In a larger Chilean study, López et al (2002a) recruited 400 pregnant women with periodontal disease, and randomly assigned these to either a treatment group (treated before 28 weeks gestation), or to an untreated control group. Of the 400 women enrolled, 49 were excluded from the analyses for different reasons. Those who were treated were 5.5 times less likely to have a preterm or small baby (1.8 vs 10.1%), and the presence of periodontitis, pregnancy history and maternal health and care were relevant associated factors.

More recently, the largest study from the USA investigating such an effect was carried out in Alabama, in which 366 women were recruited at between 21 and 25 weeks gestation (Jeffcoat et

al, 2003). All subjects had at least three sites with more than 3 mm loss of attachment, and were known not to have bacterial vaginosis. Data presented within this paper suggests that these women were the 10% most affected by periodontal disease who were screened for a larger longitudinal study, especially since the mean age was 22 years, suggesting significant attachment loss for such an age. Subjects were stratified and allocated to one of three regimes: dental prophylaxis and placebo drug for one week, root surface instrumentation (no limitation on timing and duration of visits) and placebo drug for one week, or instrumentation (no limitation on timing and duration of visits) and oral metronidazole 250 mg three times daily for one week. There were no differences between groups for established obstetric risk factors, and the population was 85% African American. Despite involving relatively large groups, results showed that instrumentation, with or without metronidazole, had no protective effect for the risk of preterm birth. The lack of effect for metronidazole may not be unexpected if no subjects were experiencing vaginosis at recruitment, and if there were no cause-and-effect relationship between periodontitis and pregnancy outcome. However, it was also apparent that the women willing to be recruited to this study had lower rates of complications compared to a reference population, perhaps because of different health or lifestyle factors which may have an influence on outcome (unfortunately no data on the reference population were presented for such a comparison).

The limited published data from intervention studies to date would tend to suggest that periodontal treatment during pregnancy, whilst not causing damage, does not seem to offer great benefits in terms of reducing pregnancy complications. However, there are currently other larger ongoing studies which will help to answer this question more definitively. In particular, we await the results of the ongoing Oral Conditions and Pregnancy study in North Carolina with interest.

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