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ORIGINAL ARTICLE

Oral health care patterns and the history of miscarriage

A Heimonen[1,2], S-J Janket[3], JH Meurman[2], J Furuholm[2], LK Ackerson[4], R Kaaja[5]

[1]*Institute of Dentistry, Oulu University and Hospital, Oulu, Finland;* [2]*Department of Oral and Maxillofacial Diseases, Institute of Dentistry, University of Helsinki, Helsinki, Finland;* [3]*Department of General Dentistry, Boston University, Boston, MA, USA;* [4]*Harvard School of Public Health, Boston, MA, USA;* [5]*Department of Gynecology and Obstetrics, Helsinki University Central Hospital, Helsinki, Finland*

OBJECTIVE: Oral infections can trigger the production of pro-inflammatory mediators that may be risk factors for miscarriage. We investigated whether oral health care patterns that may promote or alleviate oral inflammation were associated with the history of miscarriage in 328 all-Caucasian women.
MATERIALS AND METHODS: Of 328 women in this cross-sectional cohort, 74 had history of miscarriage (HMC). Medical, dental and sociodemographic data were collected through clinical examinations, medical record searches and structured questionnaires.
RESULTS: The multivariate regression analyses indicated that urgency-based dental treatment demonstrated a significant association [odds ratio (OR) = 2.54; 95% confidence interval (CI): 1.21–5.37; *P* = 0.01] and preventive dental treatment demonstrated a marginally significant inverse association (OR = 0.53; CI: 0.26–1.06; *P* = 0.07) with HMC. Self-rated poor oral health had a non-significant positive association with HMC (OR 1.60; CI: 0.88–2.90).
CONCLUSION: Our results provide sufficient evidence for hypothesis generation to test whether other precise measures of oral inflammation are associated with adverse birth outcomes.
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Keywords: spontaneous miscarriage; oral health care; oral infection

Introduction

Miscarriage is a prevalent adverse pregnancy outcome occurring in 15% of clinically recognized pregnancies (Rai and Regan, 2006) and in 30–50% of all conceptions (Stephenson and Kutteh, 2007). Sporadic miscarriage affects 25–50% of women, and recurrent miscarriage, defined as three or more foetal losses in a row, affects about 1% of women (Rai and Regan, 2006). Maternal age, previous poor pregnancy outcome, thrombophilia, and use of alcohol and tobacco are known risk factors for miscarriage (Regan *et al*, 1989; Chatenoud *et al*, 1998; Nybo Andersen *et al*, 2000; Rasch, 2003). In addition, infections such as *Chlamydia trachomatis*, cytomegalovirus and bacterial vaginosis have been linked with miscarriages (Oakeshott *et al*, 2002; Wen *et al*, 2002; Logan *et al*, 2005). Oral pathogens such as *Streptococcus* sp. and *Fusobacterium nucleatum* have been found in amniotic fluid by polymerase chain reaction (PCR), and the results of PCR for these micro-organisms was positively associated with adverse obstetrical outcomes including miscarriage (Bearfield *et al*, 2002).

Many studies have examined the association between oral health and preterm low birth weight, but the results have been inconsistent (Davenport *et al*, 2002; Lopez *et al*, 2002; Moore *et al*, 2004; Offenbacher *et al*, 2006; Vettore *et al*, 2008). Although miscarriage may be the strongest barometer of fetoplacental disruption resulting in early foetal loss, few have examined the association between dental health and miscarriages. Moore *et al* (2004) found a relationship between poor periodontal health and late miscarriage, but no association between maternal periodontal disease in the first trimester of pregnancy and preterm birth or low birth weight. Farrell(née Moore) *et al* (2006) found a weak relationship between poor periodontal health and late miscarriage in women who never smoked.

In pregnancy-associated gingivitis and periodontitis, bacterial products such as lipopolysaccharides stimulate the expression of pro-inflammatory cytokines such as interleukin-1, interleukin-6, tumour necrosis factor alpha (TNF-α) and prostaglandin E_2 (Lee *et al*, 1995; Offenbacher *et al*, 1998; Hasegawa *et al*, 2003). These cytokines and bacterial products may cause systemic inflammation that could affect the integrity of the feto-placental unit and threaten the welfare of the foetus.

The primary aim of this study was to investigate whether the history of miscarriage (HMC), a potential

Correspondence: Dr Aura Heimonen, Faculty of Medicine, Institute of Dentistry, University of Oulu, PB 5281, 90014 Oulu, Finland. Tel: +358 40 7444060, Fax: +358 8 5375560, E-mail: auro.heimonen@oulu.fi
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marker for the biological trait of exaggerated host response to pathogenic stimuli, was associated with dental care patterns that could increase these harmful stimuli. We hypothesized that preventive dental treatment would minimize systemic inflammation and thus lead to fewer adverse birth outcomes, namely miscarriage, while dental neglect, manifested by urgency-based dental treatment, would increase the probability of miscarriage. We thus tested the hypothesis that dental care patterns are associated with the HMC.

Materials and methods

Ethical consideration
The study was approved by the Ethics Committee of the Helsinki University Central Hospital (HUS 107/E6/2000, 25.10.2000) and Institutional Review Board (TYH 3245 10.2.2003, T1020Y0003 1.12.2006). The study was conducted according to the principles of the Declaration of Helsinki (2002).

Patient selection
A total of 482 women who gave birth at the Department of Gynecology and Obstetrics, Helsinki University Central Hospital (HUCH), Helsinki, Finland between September 2002 and May 2004 participated in the study. The Department of Gynecology and Obstetrics at HUCH is a tertiary referral centre serving a high proportion of women with complicated pregnancies. The women were randomly recruited twice a week by the study nurse. The women were informed about the aim of the investigation and those who agreed to participate signed a consent form. Exclusion criteria were drug abuse, infection with hepatitis B or C, and HIV infection. Four women dropped out for personal reasons and 25 mothers of twins were excluded. We were unable to examine 125 women within 2 days postpartum and these women were also excluded. Figure 1 describes the final study cohort of 328 women.

Data collection
For this cross-sectional study, clinical dental examination was made by two dentists within 2 days postpartum at the hospital of delivery to determine current oral health. The examiners were not calibrated but they both were employees of the City of Helsinki Health Department where regular diagnostic meetings served as calibration sessions according to the principles of oral diagnosis (Helsinki City Health Department, 1993). Each mother in the sample additionally provided information about oral hygiene and dental care habits in a structured questionnaire. For the purpose of validation, we randomly selected 40 maternity medical records and compared them with the questionnaire: 32 patients had the same report (alcohol use and smoking) in both questionnaire and maternity medical records. Eight patients reported 'no alcohol use during the pregnancy' in the maternity medical records, but in questionnaire they said that they drink less than once a month. This discrepancy might have been because of the different time frame these questions were asked. The maternity medical records were completed at the beginning of the pregnancy during prenatal care and the questionnaires were completed after the delivery. We also validated the infection frequencies reported by women against medical records and the reliability was 97.4%. Thus, reliability and validity appear to be satisfactory. A medical record search provided key sociodemographic characteristics and general health information.

Independent variables
The structured questionnaire provided information about self-rated oral health, preventive dental treatment and history of fillings without dental examination as a proxy for urgency-based dental care. Consistent with previous literature (Sanders *et al*, 2007), we considered those who had a dental examination in the previous 12 months as receiving preventive dental care. We considered those who had no dental examination but did have fillings when needed as utilizing urgency-based dental care. Those who had restorations after dental examination were excluded from the analyses. Self-rated poor oral health was assessed as a binary variable comparing those reporting moderate to poor oral health with those reporting good or very good oral health.

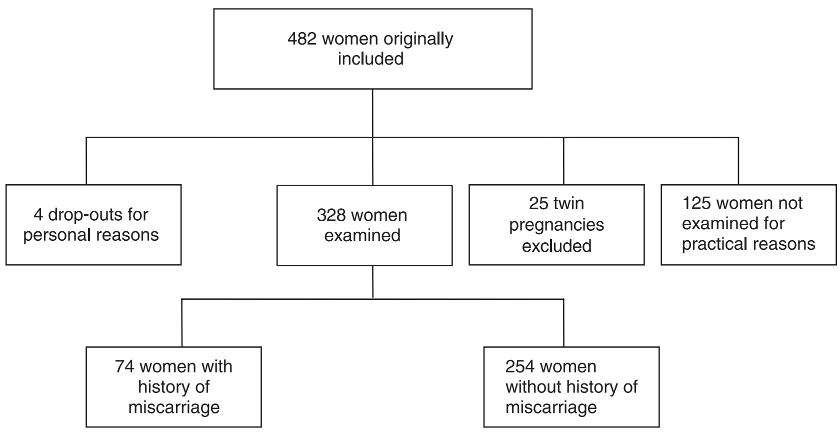

Figure 1 Evolution of the cohort

Dependent variable
A woman was considered to have a HMC if she reported pregnancy loss before 24 weeks of gestation in one or more former pregnancies (Rai and Regan, 2006) and was considered to have no history of miscarriage (NHMC) otherwise. HMC was validated by medical record search by a nurse⁄midwife and the agreement rate was 91%.

Potential confounders
The medical record search provided data about age, education, fertility, general health aspects such as having asthma and antimicrobial treatment during pregnancy. The structured questionnaire provided data about smoking and alcohol use. Smoking was recorded using three categories (current, past and non-smokers) and if current or previous, the number of daily cigarettes was recorded. Alcohol consumption was recorded as alcohol used daily, used less than a week, or less than a month, or not at all. Previously, the risk of adverse pregnancy outcomes were found to increase when maternal age is younger than 18 or older than 35 (Fraser *et al*, 1995). Our cohort did not have anyone younger than 18, therefore, we dichotomized age, analysing age >35 as a group at risk. Approximately 70% of our cohort had college or higher education and 7% had less than vocational school education. Thus, we assessed education in two categories; high school or less *vs* college and above education.

Statistical analyses
In univariate analyses, all demographic and behavioural factors were compared between the groups of HMC and NHMC by using a Student's *t*-test for the variables that were continuous with normal distribution and chi-squared tests for variables that were non-normal or categorical. In three separate models, we used multivariate logistic regression techniques to test whether history of preventive dental treatment, urgency-based dental treatment and self-rated oral health were associated with HMC after adjusting for all established risk factors for adverse pregnancy outcomes that were found to be statistically significant in unadjusted analyses, such as antimicrobial treatment, or considered theoretically necessary, such as alcohol consumption and smoking.

Because of the small sample size, multicategory variables were fitted as binary variables when appropriate to conserve power. Our power calculation indicated that we had power of 0.38–0.54 to observe significant results at the alpha level of 0.05, based on the proportions of the predictors in the two groups. Thus, we took special care to conserve power by adjusting our models for only the necessary confounding variables. Nevertheless, because SAS excludes any observation that has missing values in the predictor or confounding variables, the sample size decreased slightly for each analysis. Additionally, in assessing urgency-based treatment, we only considered those who had restorations without dental examination and excluded those who had restorations after dental examination (n = 20) from the analyses. Thus, the sample size decreased even further for the urgency-based dental treatment analyses (n = 308). All analyses were performed using SAS version 9.1 (SAS Institute Inc., Cary, NC, USA) as two-tailed tests and with alpha level of 0.05. All confidence intervals were set at 95%.

Results

Table 1 shows the demographic and behavioural characteristics and aspects of oral health of the mothers. Unadjusted analyses revealed that none of the demographic variables was statistically different between the HMC (n = 74) and NHMC (n = 254) groups, except age. Of HMC women, 21.1% had had urgency-based dental care within 12 months compared with 13.1% of NHMC women, and the difference was nearly significant (P = 0.09). Unlike other cohorts, in the crude analyses of our data, smoking and alcohol consumption were not significant risk factors for HMC: 85–90% of the cohort did not smoke during pregnancy and more than 90% drank alcohol less than once a month or not at all. However, the HMC mothers smoked less than mothers without HMC (P = 0.06). The HMC and NHMC groups were significantly different in term of antimicrobial treatment (19.4% *vs* 10.3%, $P < 0.05$) as well as infertility treatment (8.1% *vs* 2.4%, $P < 0.05$). Reports of infections during pregnancy were modest with 6.1%, 1.5% and 0.9% of all women reporting gynecological, urinary and respiratory infections, respectively. There were no statistically significant differences in mean body mass index between the HMC and NHMC groups, and frequency of infection or frequency of gynecological infection were not significant risk factors in this cohort. On the contrary, antimicrobial treatment was significantly different between the groups suggesting that the severity of the infections was greater among HMC women. Therefore, adjusting antimicrobial treatment in the multivariate model appears to be more appropriate.

Table 2 shows the results of the multivariate logistic regression analyses of the three models with preventive dental care, urgency-based dental care and self-rated oral health as predictors, respectively. Age older than 35 years was not a significant risk factor for miscarriage although age was significantly different between the groups in the crude analysis. In fact, none of the previously reported risk factors were significant predictors of miscarriage history except antimicrobial and infertility treatments in current pregnancy.

Dental risk factors including urgency-based dental treatments and preventive dental treatment remained significant or nearly significant. Those utilizing urgency-based dental treatment experienced an increased likelihood of HMC (OR = 2.54; 95% confidence interval [CI]: 1.21–5.37; P = 0.01) compared with those who did not use this care. Receiving preventive dental care had a marginally significant inverse association with the HMC (OR = 0.53; CI: 0.26–1.06; P = 0.07) compared with not receiving preventive care. Those reporting poor or moderate self-rated oral health also experienced an increased odds of HMC compared with those reporting good or very good self-reported health (OR = 1.60; CI:

Table 1 Demographic, behavioural characteristics and dental parameters of the cohort

Parameter	*History of miscarriage (n = 74)*	*No history of miscarriage (n = 254)*	P-*value*
Age (mean ± s.d.)	32.2 ± 4.6	30.8 ± 5.1	<0.05
BMI (mean ± s.d.)	23.5 ± 4.8	23.4 ± 4.0	0.88
All infection *n* (%)	11 (14.9)	24 (9.5)	0.26
Gynecological infection *n* (%)	8 (11.0)	12 (4.7)	0.09
Antimicrobial treatment *n* (%)	13 (19.4)	25 (10.3)	<0.05
Infertility treatment *n* (%)	6 (8.1)	6 (2.4)	<0.05
Duration of gestation in days, current pregnancy (mean ± s.d.)	264.7 ± 16.1	266.2 ± 14.3	0.36
Education			
High education (university or higher)	50 (67.6)	178 (71.8)	0.49
Moderate education (vocational school)	19 (25.7)	54 (21.8)	0.48
No formal education	5 (6.8)	16 (6.5)	0.93
Smoking			
During pregnancy	7 (9.5)	29 (11.4)	0.64
Before pregnancy	6 (8.1)	43 (16.9)	0.06
Not at all	61 (82.4)	182 (71.7)	0.06
Alcohol consumption during pregnancy			
Not at all	56 (75.7)	184 (72.4)	0.58
Less than once a month	12 (16.2)	52 (20.5)	0.42
Less than once a week	6 (8.1)	18 (7.1)	0.77
Preventive dental visit within 12 months			
No	17 (23.3)	45 (17.9)	0.30
Yes	56 (76.7)	206 (82.1)	
Urgency-based dental treatment within 12 months			
No	56 (78.9)	206 (86.9)	0.09
Yes	15 (21.1)	31 (13.1)	
Self-assessed poor oral health (*n* = 324)			
No	40 (56.3)	163 (65.7)	0.15
Yes	31 (43.7)	85 (34.3)	

BMI, body mass index.
Due to missing values, some variables had $n < 328$.

0.88–2.90; $P = 0.12$), although this was only approaching statistical significance. Self-rated oral health was validated by the decayed, missing, or filled surfaces (DMFS) index and gingival bleeding and proved to be a significant predictor of both DMFS ($P = 0.0001$) and gingival bleeding ($P < 0.0001$). In contrast, in the unadjusted analysis, preventive dental treatment was not significantly associated with HMC ($P = 0.30$). However, after adjusting the analysis for smoking, age, asthma, antimicrobial treatment and infertility treatment the relationship was found to be marginally significant ($P = 0.07$).

Discussion

In this study conducted among 328 Finnish women, neglectful dental care patterns were found to be positively associated with HMC while preventive dental care patterns were inversely associated with HMC. These results partially supported our study hypothesis suggesting that poor oral health might be associated with increased risk of HMC while preventive dental treatment might be associated with diminished risk of HMC.

Our results can be explained in three possible ways. Firstly, poor oral health may indeed trigger biological processes generating pro-inflammatory responses which could influence birth outcomes. These biological processes linking oral health and obstetrical outcomes may include inflammatory mediators such as TNF-α, interleukins and prostaglandins (Lee *et al*, 1995; Offenbacher *et al*, 1998; Hasegawa *et al*, 2003). As we did not have data on systemic and oral inflammation and could not test this mediating pathway, the results we present cannot be considered definitive, but provide sufficient basis for hypothesis generation.

Secondly, the observed association may be the result of reverse causation. That is to say, women who have had an adverse birth outcome may be more prone to neglect other health issues in the future, including oral care. Previous research has found that mothers who have suffered a miscarriage are often depressed (Stephenson and Kutteh, 2007), and this depression may lead to the neglect of one's own oral health.

Finally, it is theoretically possible that the observed association may be a result of uncontrolled confounding by a third variable. One possible candidate for this is medical utilization patterns which are associated with both dental utilization patterns and miscarriage. In this study, however, this connection is unlikely because 99.7% of the women had over six prenatal care visits, indicating good utilization of preventive medical care.

To our knowledge, this study is the first investigation to examine the association between oral healthcare patterns and an adverse birth outcome. Furthermore, our study is the first to control for asthma, the systemic infection assessed by antimicrobial treatment and infertility treatment in dental research. We believe that this

Table 2 Multivariate logistic models to explain the history of miscarriage

	Model 1			Model 2			Model 3		
	Preventive dental treatment (n = 324)			*Urgency-based dental treatment (n = 308)*			*Self-rated poor oral health (very good, good vs moderate, poor) (n = 325)*		
Variable	*OR*	*95% CI*	P-*value*	*OR*	*95% CI*	P-*value*	*OR*	*95% CI*	P-*value*
Main predictor									
No (*n* = 62)	1.00			1.00			1.00		
Yes (*n* = 262)	0.53	0.26–1.06	0.07	2.54	1.21–5.37	0.01*	1.60	0.88–2.90	0.12
Covariates									
Smoking status									
Never smoked	1.00			1.00			1.00		
Current smoker	0.57	0.21–1.57	0.28	0.57	0.21–1.57	0.28	0.58	0.20–1.64	0.30
Past smoker	0.37	0.13–1.04	0.06	0.38	0.14–1.08	0.07	0.41	0.15–1.13	0.08
Age									
< 35	1.00			1.00			1.00		
≥ 35	0.79	0.40–1.54	0.49	0.81	0.41–1.60	0.50	0.78	0.40–1.55	0.48
Alcohol use during pregnancy									
No	1.00			1.00			1.00		
Yes	0.99	0.51–1.94	0.98	0.99	0.50–1.99	0.98	1.09	0.55–2.14	0.81
Asthma									
No	1.00			1.00			1.00		
Yes	0.91	0.23–3.57	0.89	0.79	0.22–3.38	0.74	3.80	0.24–3.80	0.95
Antimicrobial treatment									
No	1.00			1.00			1.00		
Yes	2.72	1.24–5.97	0.01*	2.53	1.15–5.57	0.02*	2.37	1.06–5.29	0.04*
Infertility treatment									
No	1.00			1.00			1.00		
Yes	4.21	1.32–15.5	0.02*	3.50	0.95–12.8	0.06	4.73	1.37–16.63	0.01*
Education									
≤ High school	1.00			1.00			1.00		
College and above	0.93	0.57–1.53	0.79	0.91	0.54–1.46	0.72	1.04	0.62–1.76	0.88

OR, odds ratio.
*Significant at $\alpha = 0.05$.

contribution is important as these covariates are powerful risk factors for adverse birth outcomes.

In previous work using these data (A. Heimonen, H. Rintamäki, J. Furuholm, S-J. Janket, R. Kaaja, J.H. Meurman, unpublished data), we have observed that periodontitis assessed by pocket depth was not a significant predictor of adverse birth outcome (OR = 1.46; CI: 0.62–3.45; $P = 0.38$) similar to the report of Vettore *et al* (2008). This may be ascribed to several reasons. First, periodontal pocket depth is not a precise measure of oral inflammation because it includes the results of past infection. Second, other infections besides periodontitis, such as gingivitis, pericoronitis and mucositis, can also contribute to inflammation burden indicating that periodontal pocket depth necessarily underestimates total oral inflammation. Vettore and co-workers stopped their assessment of this link at the crude analyses and we have no way of knowing the true association from their study. Stopping an analysis when the unadjusted association is not statistically significant is as biased as presenting significant unadjusted results as a final model. Only when an analysis has been adjusted for all pertinent covariates can a valid assessment of the relationship between an explanatory variable and the response variable be possible.

Contrary to previous research (Chatenoud *et al*, 1998; Rasch, 2003), we found that smoking and alcohol consumption appeared to be inversely associated with HMC. Although these findings are surprising, this phenomenon could be explained as 'confounding by indication.' The doctor's order to avoid these known risk factors might have been well heeded by those who were at a higher risk and particularly those who had a history of foetal loss in the past, and hence these parameters appeared to have an inverse relationship in the statistical analyses.

Only two previous studies have examined the association between oral health and miscarriage (Moore *et al*, 2004; Farrell *et al*, 2006). Both studies were conducted among racially and socioeconomic heterogeneous groups of women. Interestingly, the association between periodontitis and miscarriage reported by Moore *et al* (2004) (OR = 2.54; CI = 1.20–5.39; *P*-value = 0.01) was almost identical to the association we found between our urgency-based treatment and miscarriage (OR = 2.54; 95% CI: 1.21–5.37; $P = 0.001$). We interpret this to mean that although oral health has been measured by different instruments (periodontitis *vs* oral care pattern), there might be aspects of oral health that influence pregnancy outcomes.

Thus, strength of our study is that it was conducted among socially and ethnically homogenous Finnish women with high to moderately high education allowing us to avoid confounding by these factors. A further strength of our study comes from the high prevalence of the HMC in this cohort. The Department of Gynecology and Obstetrics at HUCH is a tertiary referral centre. Most women in the region who anticipate problem pregnancies will come to this hospital, which explains the unusually high prevalence of HMC in our study.

A weakness of this study is that the analyses modelled the HMC as an outcome. Thus, the temporal ordering of the exposure and outcome is not ideal. As our outcome occurred before the predictors, it is possible that dental predictors may be the result of the adverse outcome. However, our results provide a logical basis for hypothesis generation so that future study would elucidate if this relationship is causal. Although the causality is not yet proven, the recommendation that proper oral health should be a part of total health care for those women who are planning to become pregnant is prudent (Task Force on Periodontal Treatment of Pregnant Women, 2004).

In conclusion, the results of this study showed that receiving urgency-based dental treatment was associated with increased probability, and preventive dental treatment was associated with a trend towards a lower probability, of a history of pregnancy loss. Thus, this study partially confirmed our hypothesis that oral health care patterns affect birth outcomes. However, future prospective investigations utilizing biomarkers of inflammation are warranted to establish whether this observed association is a causal relationship.

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Author contributions

Dr. A. Heimonen was responsible with study design, clinical examination, data analysis and reporting, Drs. S-J Janket and L.K. Ackerson are epidemiologists and biostatisticians and had integral roles at the planning, data analysis and reporting, Drs. J.H. Meurman and R. Kaaja are senior investigators and were responsible for study hypothesis and design, study group leadership, data analysis and reporting, and Dr. Furuholm is junior investigator and took part in all phases of the study.

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