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Possible association between mother's periodontal status and preterm delivery

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Abstract

Background: A case–control study was undertaken to detect whether initial chronic localized periodontitis could be a risk factor for preterm birth (PB) and foetal growth restriction.

Methods: A PB case was defined if a patient had a threatening premature event during pregnancy pre-term premature rupture of membranes, or spontaneous pre-term delivery, before the 37th week of pregnancy, and/or the weight of the newborn was <2500 g. Into the PB (case) group, 77 women were allocated, while 84 were included in the control group, all of whom had delivery after the 37th gestational week and with a newborn weighing $\geqslant 2500$ g.

Results: A significant association was found between PB and initial chronic localized periodontitis, the criteria being bleeding at $\geqslant 50\%$ of the examined teeth and having at least at one site at $\geqslant 4$ mm probing depth ($p = 0.0001$). The adjusted odds ratio for initial chronic localized periodontitis was 3.32, 95% CI: 1.64–6.69. The average weight of newborns of mothers with periodontitis was significantly less than that of the women without periodontitis ($p = 0.002$).

Conclusions: The results support the hypothesis that initial chronic localized periodontitis of pregnant women could lead to PB, and birth-weight reduction.

Key words: newborn; periodontal disease; pregnancy; preterm birth; risk factors

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Even in historical times, people thought that diseases that affect the mouth and teeth, such as periodontal infection, could have an adverse effect on whole body health. In ancient documents from Egypt, Israel, Assyria, Greece and the Roman Empire, oral health was mentioned as an important factor in the overall heath (O'Reilly & Claffey 2000). During recent decades, a new area of periodontal research has emerged and new evidence collected referring to the connection between periodontal infection and systemic diseases. Recently, the concept of ''focal infection'' has re-emerged, based on new data, which suggest that periodontal infections contribute to the morbidity and mortality of certain systemic conditions (Slots 2003). Research demonstrates that oral diseases are not only markers of underlying health problems but also important determinants influencing the development of adverse chronic health conditions. Periodontitis, as a chronic oral disease, may serve as a risk factor for atherosclerosis, coronary heart disease, diabetes, respiratory infections and pre-term low-birth-weight infants (Lindhe 2003a).

The aim of this study was to investigate the relationship between initial chronic localized periodontitis and pre-term birth (PB) and to find the most important factor among demographic, socio-economic and periodontal factors, which influenced pregnancy outcome. The other aim was to examine whether initial chronic localized periodontitis of the mother during pregnancy influenced the birth weight of the newborn.

Materials and Methods

Population sample

The sample of this case–control study consisted of 161 systemically healthy Caucasian women who were informed about the aim of the study, and a detailed Ethics Committee Approved Consent Form for dental, obstetrical and microbiological investigation was signed by them. All subjects had delivery in the Department of Obstetrics & Gynecology, University of Szeged. The study population came from different social strata and had differing educational levels. In addition, those with systemic medical problems e.g. diabetes, asthma, cardiac problems, glomerulonephritis, hypertyreosis, ulcers, chronic infectious disease or multiple deliveries, were excluded from the

study, as were any who would required antibiotic cover for dental treatment, or those receiving antibiotics at the time of the dental examination. In view of the study aim, and the patients' situations (Offenbacher et al. 1996), all examinations, which were carried out by the same dental clinician blind to case–control status, were completed within 3 days post-partum.

Collection of demographic and socioeconomic data

Personal data, actual and previous general medical and obstetrical history, including the number of previous pregnancies, were recorded via a questionnaire. The women were interviewed about the socio-cultural status of both the patient and the father. Educational levels attained by both parents were defined as follows: primary school (8 years), technical school (3 years post-primary school), grammar school (4 years after primary school) and higher education (university or college). The occupation of the patient and father was categorized as manual worker, intellectuals/professionals or ''other occupation'', as e.g. shop assistant, housewife, unemployed person, etc. Socio-economic status was characterized by educational level and occupation of mother and father. Women were also grouped according to the place of residence i.e. as having urban or rural status. Adverse habits e.g. smoking and alcohol consumption were also recorded. Regarding these behaviours, there was a choice between ''Yes'' or ''No'' answers, although details regarding quantities consumed (or their frequencies) were not pursued.

Periodontal status measurements

The periodontal examinations were completed within 3 days post-partum (Offenbacher et al. 1996) at the Department of Obstetrics & Gynecology, where the subjects were seated in a comfortable chair with a head support, and a dental light-source was used. Third molar teeth were excluded, as they are often impacted (Saglam & Tuzum 2003), angulated or extracted for eruption problems (Schersten et al. 1989). Furthermore, because of the location of these teeth, difficulties occur in measuring the probing depth.

A detailed periodontal status was determined, which evaluated plaque, calculus, recession, tooth mobility, probing depth (PD) and bleeding on probing (BOP). The amount of plaque was recorded on a 0–3 scale at four surfaces per tooth, and the plaque index was then calculated according to the criteria of Silness & Löe (1964). The plaque index was calculated only on Ramfjord teeth (Ramfjord 1959), as these teeth adequately represent the dentition of the patients for epidemiologic purpose. The presence or absence of calculus was recorded dichotomously (''Yes'' *or* ''No'') and expressed in percentage of teeth per individual. The recession of buccal marginal gingivae was measured from the cemento-enamel junction to the marginal gingiva and recorded in millimeter. Tooth mobility was assessed on a 0–3 scale (Lindhe 2003c). For probing depth, disposable periodontal probes with a tip diameter of 0.5 mm were used. PD was measured from the gingival margin to the most apical penetration of the probe at six sites per tooth i.e. mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual and distolingual. Finally, BOP was regarded positive if it occurred within 15 s after measuring the probing depth at any site of the tooth and was recorded dichotomously (Mitchell-Lewis et al. 2001). The radiographic alveolar bone level was not assessed, because the actual degree of periodontitis is better shown by probing depth, and BOP (Rahardjo et al. 2005). Additionally, the examined persons were young; therefore, great bone loss was not expected. Furthermore, in relation to the association of periodontal infection with PB, the size of the surface area of the pocket (Slots 2003), through which bacterial products can invade the periodontal tissues, was found to be more important than bone levels *per se*, these indicating only the results of previous inflammation.

The examinations were completed by the same team-member, blind to case–control status. Reproducibility trials were performed on 20 subjects before the survey. The examiner, who was an experienced dental clinician, re-examined the patients over a 30 min. period. The intra-class correlation coefficient was 0.94 or greater, with respect to the different periodontal scores and indices.

Case definition

Premature delivery (WHO 1950) implies labour, that occurs at less than 37 weeks' gestation, and is generally accompanied by low birth weight i.e. a birth weight <2500 g. Mothers were included into the case group if the newborn's weight was less than 2500 g, or the mother had spontaneous pre-term labour, with pre-term premature rupture of membranes before the 37th gestational week. Women who had threatening pre-term labour were treated by a special protocol at the Department of Obstetrics & Gynecology to maintain their pregnancy as long as possible. As a result, in some cases labour was delayed until week 37, but these mothers were then allocated to the case group. Mothers whose delivery occurred after week 37 without any previous problem, and had a newborn with a weight ≥ 2500 g were included in the control group.

Criteria of initial chronic localized periodontitis

The ''critical probing depth'' (Waerhaug 1978, Lindhe et al. 1982, Lindhe et al. 1984, Westfelt et al. 1985, Bergström & Eliasson 1989) and frequency of BOP were used for categorizing a mother with chronic periodontitis (Armitage 1999, 2002), as these parameters of periodontal status reflect mostly the current inflammation burden. A woman had periodontitis if she had $\geqslant 4$ mm probing depth at least at one site and BOP at $\geqslant 50\%$ of teeth. These criteria for initial chronic localized periodontitis were chosen because a 4 mm pocket depth represents a disease level that permits less post-treatment attachment gain than can be achieved with a depth of 3 mm (Lindhe 1995). Furthermore, probing depth values <4 mm can be regarded as normal variations (Lindhe 2003b). The other criterion of chronic periodontitis was BOP, as a great number of studies showed that it was a reliable sign of the activity of periodontitis and inflammation (Davenport et al. 1982, Greenstein 1984, Lang et al. 1986, 1990, Haffajee et al. 1991). Additionally, Lang & Tonetti (2003) have stated that these two parameters should be taken into consideration as important factors in a patient's risk assessment for recurrence of periodontitis. Subjects having no $\geqslant 4$ mm pockets, or BOP occurring at $<50\%$ of teeth were regarded as periodontally healthy.

Statistical analysis

Descriptive statistics were used to assess the demographic and socio-economic

data. For comparison of mean values, Student's *t*-test (age, comparison between birth weight in the periodontitis and healthy periodontium group) and Mann–Whitney tests were used in case of non-normality. The normal distribution of samples was tested using the Kolmogorov–Smirnov test. Univariate dependence of PB on categorical data was analysed using the χ^2 test and Fisher's exact test. The multivariable dependence of PB on both categorical (age, educational level, profession, place of residence) and continuous data (PB 4 mm and BOP 50%) was analysed using logistic regression with stepwise (forward) model selection, based on the likelihood ratio criterion ($p_{in} = 0.05$, $p_{out} = 0.10$). The predictors were age, educational level, profession, place of residence, smoking and initial chronic localized periodontitis (at least one PD >4 mm and BOP $>50\%$). SPSS 13.0 statistical software was used for statistical analysis (SPSS Inc., Chicago, IL, USA).

Results

Demographic and periodontal data of 161 women were analysed statistically (Table 1), with 77 in the case group, and 84 in the controls, their socio-economic variables and connection with PB (χ^2 test; *p*-values) being described in Table 1. The mean age was 27.7 years, and the age distribution was found to be normal, with no significant difference between the mean age of the case and control groups ($p = 0.589$). The youngest mother was 16.7 years and the oldest 41.1 years, with 66.5% aged between 20 and 30 years, only 5.6% being <20 and 27.9% >30 years of age.

With respect to educational data, 26 (16.2%) patients had only completed primary school, 41 (25.5%) attended a technical school, 59 (36.6%) had completed a grammar school course and 35 (21.7%) had a university or college degree. As shown in Table 2, the participants represented all categories of education in Hungary. There were 57 (35.4%) manual workers and 59 (36.6%) professionals among the patients. The number of mothers belonging to the ''other'' category was 45 (28.0%), i.e. housewives, shop assistants, unemployed persons, etc. Regarding similar paternal data (Table 3), which, together with the educational status and occupation of the mother, characterize the socio-economic grade of the pregnant women, it was found that only 23 (14.7%) had primary school education, 56 (35.9%) technical school, while grammar school was completed by 46 (29.6%) fathers, and higher education by 31 (19.8%). The fathers were also divided according to their occupation into three categories: manual workers (76; 48.7%), office workers (46; 29.5%) and ''other'' persons (34; 34%). In the last group, shop assistants, professional drivers, unemployed persons, etc. were included. Not all mothers gave data about the father; therefore, such calculations were possible for 156 men. However, neither of these data were significantly different between case and control groups (see Tables 2 and 3). Nonetheless, PB occurred more frequently if mothers and fathers were less educated.

Among participants, slightly more patients were urban (87; 54.0%) than rural dwellers (74; 46.0%), although the difference was not significant between case and control participants (Fisher's test, $p = 1.000$). There was no patient who admitted either regular or excessive alcohol consumption, but 17 admitted smoking during pregnancy, 14 belonging to the case and three to the control groups (Fisher's test, $p = 0.004$).

The oral health and periodontal status of the women was described by the plaque index, frequency of calculus, probing depth and frequency of BOP (Table 4). As the patients were mostly young women, gingival recession and tooth mobility were found only in very few cases, and it was thus not possible to analyse these data statistically. The plaque index was 0–1 in 133 patients (82.6%) and 1–2 in 28 patients (17.4%). The mean plaque index was 0.72 in the case, and 0.62 in the control groups i.e. the difference was insignificant (Mann–Whitney test, $p = 0.198$).

Table 1. Mean age of mothers in case and control groups

	Years case ($N = 77$)	Years control ($N = 84$)	Years all ($N = 161$)	*t*-test *p*-value
Mean	28.2 ± 5.4	27.2 ± 4.2	27.7 ± 4.8	0.589
Minimum	16.7	18.3	16.7	
Maximum	41.1	39.2	41.1	

Table 2. Educational level and occupation of patients

	Case $N = 77$ (100%)	Control $N = 84$ (100%)	All $N = 161$ (100%)	χ^2 test *p*-value
Educational level of mothers				
Primary school	17 (65.4%)	9 (34.6%)	26	
Technical school	23 (56.1%)	18 (43.9%)	41	
Grammar school	23 (39.0%)	36 (61.0%)	59	
Higher education	14 (40.0%)	21 (60.0%)	35	0.069
Occupation of mothers				
Manual worker	29 (50.9%)	28 (49.1%)	57	
Intellectual	24 (40.7%)	35 (59.3%)	59	
Other	24 (53.3%)	21 (46.7%)	45	0.381

χ^2 test shows the association between the socio-economic data and preterm birth.

Table 3. Educational level and occupation of fathers

	Case $N = 74$ (100%)	Control $N = 82$ (100%)	All $N = 156$ (100%)	χ^2 test *p*-value
Educational level of fathers				
Primary school	15 (65.2%)	8 (34.8%)	23	
Technical school	27 (48.2%)	29 (51.8%)	56	
Grammar school	18 (39.1%)	28 (60.9%)	46	
Higher education	14 (45.2%)	17 (54.8%)	31	0.244
Occupation of fathers				
Manual worker	35 (46.1%)	41 (53.9%)	76	
Intellectual	20 (43.5%)	26 (56.5%)	46	
Other	19 (55.9%)	15 (44.1%)	34	0.517

χ^2 test shows the association between the socio-economic data and preterm birth.

Table 4. Means of plaque index, frequency of calculus, probing depth and bleeding on probing (BOP) in the case and control groups

	Mean ± SD			Mann–Whitney *p*-value
	case	control	all	
Plaque index	0.72 ± 0.42	0.62 ± 0.33	0.67 ± 0.37	0.198
Calculus freq. (%)	23.35 ± 25.6	18.98 ± 21.4	21.07 ± 23.5	0.303
Probing depth (mm)	1.72 ± 0.51	1.62 ± 0.45	1.67 ± 0.48	0.305
BOP (%)	43.30 ± 34.36	32.76 ± 30.60	37.80 ± 32.78	0.060

Table 5. Results of the univariate analyses between the different signs of periodontitis and preterm birth one by one and pair-wise

	Case ($N = 77$)	Control ($N = 84$)	Total ($N = 161$) (100%)	Fisher's exact test *p*-value	Odds ratio
PD 4 mm*				0.041	1.961
No	33 (39.8%)	50 (60.2%)	83		
Yes	44 (56.4%)	34 (43.6%)	78		
BOP 50%†				0.004	2.688
No	36 (37.9%)	59 (62.1%)	95		
Yes	41 (62.1%)	25 (37.9%)	66		
PD 4 mm+BOP 50%				0.0001	3.763
No	38 (36.5%)	66 (63.5%)	104		
Yes	39 (68.4%)	18 (31.6%)	57		

*PD 4 mm = Probing depth ⩾4 mm at least at one site.
†BOP 50% = Bleeding on probing at ⩾50% of the teeth.

Table 6. Mean weight of newborns of mothers with and without periodontitis*

	With periodontitis ($N = 57$)	Without periodontitis ($N = 104$)	Total ($N = 161$)	*t*-test *p*-value
Weight (g)	2834.5 ± 725.6	3180.3 ± 621.2	3057.9 ± 678.4	0.002
Minimum	950.0	990.0	950.0	
Maximum	4100.0	4370.0	4370.0	

*Periodontitis = ⩾4 mm probing depth at least at one site and BOP at ⩾50% of the teeth.

Table 7. Result of the logistic regression analysis between PLBW and initial chronic localized periodontitis

Variables in the model	Odds ratio e^B	Coefficient *B*	Standard error	Wald-test *p*-value	CI 95% minimum	CI 95% maximum
PD 4 mm + BOP 50%*	3.32	1.1987	0.3586	11.1722	1.64	6.69
Smoking	4.55	1.5150	0.6784	4.9872	1.20	17.19
Constant		− 0.6430	0.2100	9.3779		

*PD 4mm + BOP 50% = Probing depth ⩾4 mm at least at one site and bleeding on probing at ⩾50% of the teeth.
Overall prediction rate: 66.46%.
Sensitivity: 55.84%.
Specificity: 76.19%.
CI, confidence interval.

There were slight differences in the frequency of calculus and probing depth between case and control groups, these parameters being worse in the case group, although not significantly ($p = 0.303$; $p = 0.305$). While a greater difference was found in the frequency of gingival bleeding, this was also insignificant ($p = 0.060$).

Preliminary univariate analysis was performed using Fisher's exact test to find the association between the signs of initial chronic periodontitis and PB. Table 5 shows that having ⩾4 mm probing depth at least at one site (4 mm) and BOP at ⩾50% of the teeth (BOP 50%) had a significant relationship with PB and low birth weight in this study group. The total number of mothers with periodontitis was 57, among them 39 (68.4%) women being in the case group and only 18 (31.6%) in the controls; the difference was significant ($p = 0.0001$). The mean weight of periodontitis newborns was 2834.5 g, while in the control group it was higher at 3180.3 g. The comparison between the weight of newborns of mothers with and without periodontitis was significant ($p = 0.002$; Table 6).

Table 7 presents the findings of the logistic regression analysis with a stepwise model-building procedure, based on the likelihood ratio selection criterion. As a result, the adjusted odds ratio for initial chronic localized periodontitis was 3.32, 95% CI: 1.64–6.69, i.e. the second most important factor for PB was the initial chronic localized periodontitis of the mother. The other most important influencing factor of PB in this study proved to be smoking, with an adjusted odds ratio of 4.55, 95% CI: 1.20–17.19. With respect to smoking, the minimum and maximum of CI differed more, because the number of smokers was only 17 in the whole study sample.

Discussion

In a preliminary study by the same authors (Radnai et al. 2004), among all periodontitis-related criteria, the existence of at least one PD ⩾4 mm and POB at ⩾50% of teeth in the same patient was found to be the most important predictor of PB, the odds ratio being 5.46, 95% CI 1.72–17.32. In the present investigation, in a sample of 161 systemically healthy but otherwise non-selected women, where the number and mean age of cases and controls was similar, a significant association between initial chronic localized periodontitis and PB was found. Among the demographic, socio-economic and periodontal factors examined, only smoking, which is a well-known risk factor for PB, was more important (OR 4.55) than initial chronic localized periodontitis (OR 3.32).

Another important finding of this study was that birth weight was also influenced greatly by the periodontitis status of the pregnant women, there being a significant difference between the mean weight in those mothers with and without periodontitis, in spite of prenatal treatment received by women

having a threatening pregnancy event ($p = 0.002$).

As per the results of Moss et al. (2005), it was found that probing depths $\geqslant$4mm and a concomitant greater frequency ($\geqslant$50% of teeth) of gingival bleeding were the most important periodontal parameters in connection with PB in the group of pregnant women ($p = 0.0001$, OR 3.76 univariate analysis).

As in the study of Dörtbudak et al. (2005), women in the current study were of European descent and represented all socio-economic classes in a Middle-European country, as distinct from other investigations where the samples were mostly of Afro-American or Hispanic origins, often of low socio-economic status (Dasayanake et al. 2001, López et al. 2002a), and having poor oral hygiene and periodontal conditions (Machuca et al. 1999, Yalcin et al. 2002).

In studies dealing with a possible association of periodontitis and PB, the results can be controversial, with some authors finding no such association. Thus, Lunardelli in Brazil (Lunardelli & Peres 2005) and Noack et al. in Germany (2005) found that periodontitis was not a detectable risk factor for preterm low birth weight. Similarly, Holbrook et al. (2004), in Iceland, found that none of 96 pregnant women with more than four gingival pockets of depth >4 mm delivered preterm. Likewise, Mitchell-Lewis et al (2001) reported no evidence to connect periodontitis and PB, as did Davenport et al. in a case–control study in 2002 of 236 cases and 507 controls in a mixed-race population. In a recent study group of 54 women (Skuldbøl et al. 2006), a relation between PB and periodontitis was not revealed. Farrell et al. (2006) found an association between some measures of periodontal disease and late miscarriage; however, there was no association between periodontitis and PB. On the other hand, Offenbacher et al. (1996) suggested in 1996 that periodontal infection during pregnancy could lead to a seven-fold risk of PB. They found that attachment loss was significantly higher in mothers who had pre-term delivery in a study group of 124 predominantly white women. In a further 814 subjects, Offenbacher et al. (2001) demonstrated again that maternal periodontal infection was significantly associated with a higher prevalence rate of PB. Following analyses relating to 1313 women, Jeffcoat et al. (2001) claimed a 4.4-fold greater risk of PB with generalized periodontitis. In 2002, López et al. (2002a) reported a significant association between probing depth, PB and low birth weight, independent of other risk factors. Furthermore, more recently, Jarjoura et al. (2005) compared the periodontal status of 83 PB mothers and 120 controls and found that PB was associated with attachment loss (adjusted odds ratio 2.75, 95% CI: 1.01–7.54). Other more recent studies also found evidence for an association between periodontitis of the pregnant woman and PB (Marin et al. 2005, Moliterno et al. 2005), and Urbán et al. (2006) demonstrated that the number of anaerobic flora of the crevicular sulcus was significantly higher, and the composition of the flora was more complex, among those women associated with PB and/or low birth weight, than in their control group. Finally, intervention studies have also been published that showed the benefits of periodontal treatment to pregnant women on their pregnancy outcome, with such therapy significantly reducing their PLBW rate (López et al. 2002b, Jeffcoat et al. 2003, López et al. 2005, Sadatmansouri et al. 2006).

The present results have demonstrated that initial chronic localized periodontitis of pregnant women was associated with adverse pregnancy outcome, namely preterm delivery and growth restriction of the fetus. Hence, as poor oral hygiene and periodontal status can be improved easily via dental hygienists and patient collaboration, there is a need to develop preventive programmes for pregnant women in coordination with the gynaecological and dental professions, and to provide professional oral hygiene measurements during pregnancy, especially in case of threatening PB.

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Clinical Relevance

Scientific Rationale: Concerning the proposed association between periodontal infection and PB and low birth weight, more evidence is necessary to reveal whether this hypothesis may be sustainable in a Middle-European Caucasian population.

Principal Findings: The findings of this case–control study showed that initial chronic localized periodontitis, with a diagnostic level of $\geqslant 4$ mm probing depth at least at one site, together with $\geqslant 50\%$ BOP, meant a more than threefold risk for both PB and low birth weight.

Practical Implications: It would be necessary to develop preventive programmes for pregnant women in cooperation with the gynaecological and dental professions and to provide preventive professional oral hygiene measurements, or treatment, on a regular basis during pregnancy.