

Periodontal Disease and Adverse Pregnancy Outcomes: A Prospective Study in a Low-Risk Population

Laurence Soucy-Giguère,^{1,2} Amélie Tétu, MSc,² Simon Gauthier, DMD, MSc, FRCD(C),³ Marianne Morand, DMD, MSc, FRCD(C),³ Fatiha Chandad, PhD,³ Yves Giguère, MD, PhD, FRCPC,^{2,4} Emmanuel Bujold, MD, MSc, FRCSC^{2,5}

¹Faculty of Medicine, Université Laval, Quebec QC

²Centre de recherche du CHU de Québec, Quebec QC

³Faculty of Dentistry, Université Laval, Quebec City QC

⁴Department of Molecular Biology, Medical Biochemistry and Pathology, Faculty of Medicine, Université Laval, Quebec QC

⁵Department of Obstetrics and Gynecology, Faculty of Medicine, Université Laval, Quebec QC

Abstract

Background: Periodontal disease has been associated with systemic inflammation and adverse pregnancy outcomes, including preeclampsia and preterm birth.

Objective: To examine the relationship between periodontal disease in early pregnancy and the risk of amniotic inflammation, preterm birth, and preeclampsia.

Methods: We performed a prospective cohort study of women undergoing amniocentesis for fetal karyotype between 15 and 24 weeks' gestation. Participants underwent periodontal examination by a certified dentist, and a sample of amniotic fluid was collected. Periodontal disease was defined as the presence of one or more sites with probing depths ≥ 4 mm and $\geq 10\%$ bleeding on probing. Matrix metalloproteinase-8 and interleukin-6 concentrations in the amniotic fluid were measured. Medical charts were reviewed for perinatal outcomes. Univariate and multivariate logistic regression analyses were used to assess the association between periodontal disease and adverse pregnancy outcomes.

Results: We recruited 273 women at a median gestational age of 16 weeks (range 15 to 24), and 258 (95%) agreed to undergo periodontal examination. Periodontal disease was observed in 117 of the participants (45%). We observed no significant association between periodontal disease and preterm birth (relative risk [RR] 2.27; 95% CI 0.74 to 6.96) or spontaneous preterm birth (RR 0.90; 95% CI 0.20 to 4.11). However, women with periodontal disease were more likely to develop preeclampsia, and this association remained significant after adjustment for potential confounders (adjusted RR 5.89; 95% CI 1.24 to 28.05). Periodontal disease was not associated with significant differences in the intra-amniotic concentration of matrix metalloproteinase-8 (13.0 ± 46.6 vs

5.7 ± 10.4 ng/mL, $P = 0.098$) or interleukin-6 (3.3 ± 20.3 vs 1.0 ± 1.6 ng/mL, $P = 0.23$), although a non-significant trend was observed.

Conclusion: Periodontal disease is associated with preeclampsia but not with spontaneous preterm birth. The current study cannot exclude an association between periodontal disease and intra-amniotic inflammation.

Résumé

Contexte : Les parodontopathies sont associées à l'inflammation générale et à des issues indésirables de la grossesse, dont la prééclampsie et l'accouchement préterme.

Objectif : Examiner le lien entre les parodontopathies en début de grossesse et les risques d'inflammation du liquide amniotique, d'accouchement préterme et de prééclampsie.

Méthodes : Nous avons réalisé une étude de cohorte prospective auprès de femmes ayant subi une amniocentèse aux fins de l'établissement du caryotype fœtal entre la 15^e et la 24^e semaine de grossesse. Un dentiste agréé a procédé à un examen parodontal des participantes et un échantillon de liquide amniotique a été prélevé. Nous avons défini les parodontopathies par la présence d'un ou de nombreux sites d'une profondeur de ≥ 4 mm, accompagnés de $\geq 10\%$ de saignements au sondage. Nous avons également mesuré les concentrations de métalloprotéinase matricielle-8 et d'interleukine 6 présentes dans le liquide amniotique. De plus, nous avons passé les dossiers médicaux en revue afin d'étudier les résultats périnataux. Des analyses de régression logistique univariées et multivariées ont permis d'évaluer le lien entre les parodontopathies et les issues indésirables de la grossesse.

Résultats : Nous avons recruté 273 femmes dont l'âge gestationnel médian était de 16 semaines (intervalle de 15 à 24 semaines). Parmi ce nombre, 258 femmes (95 %) ont accepté de se soumettre à un examen parodontal. Nous avons observé des parodontopathies chez 117 participantes (45 %). Toutefois, nous n'avons établi aucun lien significatif entre ces états pathologiques et l'accouchement préterme (risque relatif [RR], 2,27; IC à 95 %, 0,74 à 6,96) ou l'accouchement préterme spontané (RR, 0,90; IC à 95 %, 0,20 à 4,11). Cependant, les femmes qui présentaient une parodontopathie étaient plus susceptibles d'en venir à connaître une prééclampsie et cette association demeurait

Key words: Pregnancy, preeclampsia, periodontitis, amniotic fluid, preterm birth

Competing interests: None declared.

Received on November 25, 2015

Accepted on December 22, 2015

<http://dx.doi.org/10.1016/j.jogc.2016.02.012>

significative à la suite de la neutralisation des effets des facteurs parasites potentiels (RR corrigé, 5,89; IC à 95 %, 1,24 à 28,05). Par ailleurs, les parodontopathies n'ont pas été associées à des différences significatives en ce qui concerne les concentrations intra-amniotiques de métalloprotéinase matricielle-8 ($13,0 \pm 46,6$ vs $5,7 \pm 10,4$ ng/ml, $P = 0,098$) et d'interleukine 6 ($3,3 \pm 20,3$ vs $1,0 \pm 1,6$ ng/ml, $P = 0,23$); toutefois, une tendance non significative a été constatée.

Conclusion : Bien que les parodontopathies soient associées à la prééclampsie, elles ne sont pas associées à l'accouchement préterme spontané. Cette étude n'a pas permis d'exclure la présence possible d'une association entre les parodontopathies et l'inflammation du liquide intra-amniotique.

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J Obstet Gynaecol Can 2016;38(4):346-350

INTRODUCTION

Periodontal disease is a group of inflammatory diseases of the periodontal tissues, the tissues supporting the teeth, and encompasses gingivitis and periodontitis.¹ It is one of the most common chronic infectious diseases; worldwide, its prevalence varies between 10% and 90%, depending on the population studied and the diagnostic criteria used.^{2,3} Although the disease is localized to the periodontal tissues, it has been reported to have a role in several systemic conditions and chronic diseases, such as atherosclerotic disease and diabetes.^{4,5} Periodontal disease has also been associated with adverse pregnancy outcomes, including preterm birth and preeclampsia.^{6,7} However, most studies have been limited by their retrospective design and analyses, the presence of uncontrolled or inadequately reported confounders, or by the fact that periodontal examinations were performed after delivery.^{6,8-12} Physiologic changes during pregnancy include an increase in maternal serum estrogen and progesterone levels, increased vascular permeability, and changes in the immune system, and these are believed to contribute to the progression of periodontal disease to a more severe state during pregnancy.^{13,14}

The specific pathogenesis explaining the association between periodontitis and adverse perinatal outcomes is still unknown. It has been hypothesized that preterm birth

could be the result of direct translocation of pathogens from the oral flora to the placenta or to the amniotic cavity.¹⁵⁻¹⁷ This could result in intrauterine infection and inflammation, which have been established as major risk factors for preterm birth.¹⁸ Indeed, increased intra-amniotic interleukin-6 has been associated with a 4.5-fold increase in the risk of spontaneous preterm delivery.¹⁹ Moreover, Yoon et al. found that elevated intra-amniotic IL-6 and matrix metalloproteinase-8 levels at the time of mid-trimester amniocentesis are associated with spontaneous preterm birth before 32 weeks of gestation.²⁰ Periodontal disease could also result in the production of pro-inflammatory cytokines; these cytokines, originating from the crevicular fluid, can gain access to the systemic circulation and cause endothelial lesions and systemic inflammation, resulting in an increased risk of developing preeclampsia and preterm birth.^{4,21,22}

In this context, we aimed to evaluate the association between periodontal disease and preterm birth, preeclampsia, and the intra-amniotic pro-inflammatory markers MMP-8 and IL-6.

METHODS

This was an ancillary study of a prospective cohort of pregnant women recruited at the CHU de Quebec between December 2006 and June 2010. Women between 15 and 24 weeks' gestation who were undergoing amniocentesis for fetal karyotype were invited to participate. The exclusion criteria for the prospective study were the presence of regular uterine contractions, premature rupture of membranes, multiple pregnancies, lethal congenital anomalies, fetal aneuploidy, and maternal age under 18 years. All women who were recruited gave written, informed consent before amniocentesis. At the time of amniocentesis, a sample of amniotic fluid was collected for research purposes in addition to amniotic fluid sampling for clinical testing. Eligible women were invited to participate in the ancillary study that involved periodontal examination by two certified dentists in the seven days following amniocentesis. The examination included full mouth probing (except wisdom teeth) with an automated periodontal probe (Florida Probe Corp., Gainesville, FL) at six sites per tooth. For the purpose of the current study, periodontal disease was defined according to the Offenbacher criteria for moderate to severe periodontal disease: these include the presence of at least one site with probing depths ≥ 4 mm and $\geq 10\%$ bleeding on probing.²³ Amniotic fluid MMP-8 and IL-6 concentrations were measured using a specific immunoassay according to the manufacturer's instructions (R&D Systems Inc., Minneapolis, MN). The

ABBREVIATIONS

aOR	adjusted odds ratio
IL-6	interleukin-6
MMP-8	matrix metalloproteinase-8
RR	relative risk

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