Assessing the association between periodontitis and preterm birth: A case control study

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Abstract

**Background:** Premature delivery is among the leading causes of perinatal mortality and morbidity in developed societies which is an important problem in obstetrics. Maternal periodontitis is a prevalent condition that has been suspected to be associated with adverse pregnancy outcomes such as preterm birth. However, there are still conflicting results which this study aims to address by examining the association between periodontitis and preterm birth. This study provides necessary information to inform decisions on the screening tool to be recommended for use by nurses and midwives to screen for periodontal diseases during antenatal consultations in order to improve mothers’ and children's health.

**Methods:** A case control study was conducted at 12 health facilities in the Southern Province of Rwanda from February to August 2018. A total of 555 women in the postpartum period were enrolled in the study. Cases and controls were enrolled in a ratio of 1:2, each enrolled case of preterm birth was followed by 2 control cases delivered at term gestation that were next on the register. There were 185 cases of preterm deliveries and 370 controls of term delivery. Multivariate regression analysis was done and the variables were hierarchically grouped into three groups: The first group involved demographic variables that were put in the regression model as Step 1. The second group was made up of other potential factors that were put in the regression model as the second step. The third group was periodontitis, as it was hypothesized to be a major predictor variable and this constituted the third step of the regression model.

**Results:** Significant association was found between periodontitis and preterm birth. Women who had periodontitis had 6 times the odds of giving birth to preterm birth babies compared to women who had no periodontitis (p<0.001) (95% CI 3.9, 10.4).

**Conclusion:** Periodontitis is a risk factor for preterm birth and preventive solutions such as having a periodontitis screening tool for nurses and midwives during antenatal care consultations is highly recommended.

**Background**

Premature births are among the leading causes of perinatal mortality and morbidity globally. In the United States, preterm births and associated complications, such as immature lung development, reduced feeding ability and inferior weight gain, results in longer hospital stays and a higher cost of health care, and are responsible for up 70% of prenatal and infant mortality. Almost a quarter of prematurely born babies required hospitalization at least once during their first year, mostly associated with a reduced birth weight.

Neonatal delivery before 37 weeks of gestation is the main cause of low birth weight. Preterm birth is one of the major healthcare challenges and is associated with many potential consequences like lifelong disabilities and high health care costs. Preterm birth is the leading cause of neonatal mortality in low
Premature deliveries are around 12.9 million births worldwide representing around 9.6% of all births with some regional discrepancies. Specifically, African nations reported a higher incidence of preterm births (18%) followed by the United states (12-13%) and Europe (5-9%). According to demographic health survey (DHS) 2014-2015 in Rwanda, the incidence of low birth weight deliveries was 6.3% and according to the Rwanda Population Reference Bureau, preterm birth complications are among the top ten causes of child mortality in Rwanda.

Studies have identified various risk factors related to preterm birth and they are categorized as a) extra gynecological causes: socioeconomic, malnutrition, early maternal age, short maternal stature, low maternal weight, small volume of the maternal heart, smoking, alcohol consumption, low prenatal care, stress, genitourinary tract infections and malaria, b) gynecological causes: uterine malformations, uterine adhesions and pregnancy with intrauterine devi-infection, c) obstetric causes: primiparity in both young and old mothers, small interval during gestations, grand multiparity, previous PTBs, previous still-birth, multiple gestations, low insertion of the placenta and chorioamnionitis. However, 25% of preterm birth cases were of unknown etiology. There is also increasing evidence of an association between periodontitis, a chronic infection of the supporting structures of the dentition, and preterm birth. In 1996, Offenbacher and colleagues described this relationship between maternal periodontitis and premature delivery. Based on biological plausibility, it is believed that periodontitis can contribute to preterm birth through bacteremia where toxins and their products derived from maternal periodontitis can reach the bloodstream and cause injury to the placenta unit and to the amniotic fluid, leading to chorio-amniotic infections, increasing risk preterm birth. Second, the dissemination of local inflammation throughout the body may contribute to preterm low birth weight. Studies suggest that inflammation in periodontal tissues due to periodontitis increases secretion of different inflammatory cytokines notably; interleukin B (IL-1β), interleukin IL-6, interleukin 8 (IL-8), interleukin 17 (IL-17), and tumor necrosis factors alpha (TNF-α).

In Africa, some studies have associated poor periodontal status with premature birth and low birth weight deliveries. For example, a study done in Nigeria by Umoh and colleagues concluded that the management of periodontal diseases reduced the prevalence of low birth weight deliveries. Although the studies highlighted the association between periodontal infection and the risk of low birth weight, the literature search conducted did not find any study that pointed to periodontal screening during pregnancy. Therefore, the aim of the current study is to assess the association between periodontitis and preterm birth with the long term goal of initiating the screening tool to be used by nurses and midwives for screening of periodontitis during antenatal consultations.
A case control study was conducted at 12 health facilities in the Southern Province of Rwanda from February to August 2018. A total of 555 women in the post-partum period were enrolled in the study. Cases and controls were enrolled in a ratio of 1:2 and each enrolled case of preterm birth was followed by 2 control cases delivered at term gestation that were next on the register. In total, there were 185 cases with preterm deliveries/ gestation age of 37 weeks or less and low birth weight/ weight of 2500g or less and 370 controls with term delivery/ gestation age >37 weeks and normal birth weight babies/ >2500g.

The study was done in the Southern Province of Rwanda in 6 districts namely; Kamonyi, Muhanga, Ruhango, Nyanza, Huye and Gisagara. Corresponding district hospitals and nearby health centers were selected for the study and one referral hospital in Huye. Participants were selected through hospital registers whereby researchers would verify daily to see the cases for preterm deliveries and the controls would be the next 2 on the register. An unmatched case control study design was used but a few key variables like age, smoking habits and presence or absence of systemic conditions were considered for matching. The sample was calculated using G-Power 3.1.9.6. The researcher used small effect size of 0.06, alpha of 0.05 and power of 0.95 with 10 predictors. The G-Power calculation gave the sample size of 182.

A structured clinical exam and standardized questionnaire was used to collect information regarding the presence of periodontal infection among the pregnant women attending antenatal care clinics in the Southern Province of Rwanda. The study adapted the questionnaire from the WHO Oral Health Assessment Tool for Adults of 2013 to the Rwandan context. The questionnaire was sent to experts for content validation and it was piloted to ensure that it captures all variables as well as ensuring that the questions are clear to the respondents.

The questionnaire was piloted in Nyamata District Hospital in the Eastern Province to ensure for cross-cultural validation and also to ensure that it captures all the information required and clarity of questions. After the pilot study, all the inputs from the participants were considered and questions that were not clear were corrected accordingly. The questionnaire was translated in Kinyarwanda using forward and backward translation whereby this questionnaire was translated in Kinyarwanda from English and it was again translated back to English by another translator to see if the meaning remains the same and the corrections were harmonized.

The questionnaire assessed the following variables: age of the respondent, education level, health and lifestyle behavior eg. Smoking, socio-economic status, mother’s weight, number of previous pregnancies, previous preterm or low birth weight and weight gain during pregnancy, illnesses during pregnancy and stress during pregnancy. “Ubudehe” categories in Rwanda are social classes put in place by the Rwanda Ministry of Local Government whereby “people in first category are very poor; do not have a house or cannot afford to pay rent, have a poor diet, cannot get basic household tools and clothes, the second category includes those who have their own houses, can afford to rent a house, mostly get food and earn
a wage from with others, the third category includes those who have at least one person in the family working in the government or the private sector and the fourth category includes people who earn high incomes, people who own houses, people who can afford a luxurious lifestyle.\(^{22}\)

A periodontal examination was also done on the women in the study. The trained and calibrated examiners used a calibrated William's periodontal probe to perform the periodontal clinical examination. Six examiners were calibrated by a qualified dentist on how to perform a periodontal examination to see that they all understood it in the same way to avoid having false results or different findings between patients. The examiners assessed bleeding on probing, probing depth and clinical attachment loss measured in mm at six different sites on each tooth (buccal-mesial, mid-buccal, buccal-distal, lingual-mesial, mid-lingual and lingual-distal). The mothers in the study group were asked about their dental care practices and their smoking habits. In additional, a full mouth periodontal screening was done by the researcher and calibrated dental therapists acting as research assistants.

The mothers in the study group were examined at their bedsides by the researcher and calibrated research assistants using a periodontal probe, intra oral mirror and headlights. A gentle probing force was applied to guide the tip into the periodontal pocket until the resistance was felt. The pocket depth was measured using gingival margin as a reference point.

The current study defined periodontitis as presence of pocket depth greater than 3 mm on either maxilla or mandible or both and presence of interdental clinical attachment loss (CAL) on ether maxilla, mandible or both of 2mm or above and buccal or oral CAL of 3 mm or above.\(^{23}\) Clinical attachment loss was measured as follows: when the gingival margin was at the cemento-enamel junction and there was no recession, then the CAL was equal to the pocket depth; when the gingival margin was apical to the cemento-enamel junction, CAL was equal to pocket depth plus gingival recession; when the gingival margin was on the anatomical crown in case of gingival overgrowth, CAL was equal to pocket depth minus gingival recession. CAL was not considered in some of the specific cases that were of non-periodontal cause. For example, when gingival recession was of traumatic origin like in the case of poor brushing techniques, dental caries extending in the cervical area of the tooth and in the cases of recession by malposition of the tooth.\(^{23}\)

“Gingival recession was defined as apical migration of marginal gingiva and characterized by gradual displacement of gingiva away from the cemento-enamel junction that results in the root surface exposure to the oral environment.”\(^{24}\) The researcher and research assistants filled in the questionnaires until the required sample was reached.

Multivariate regression analysis was done and the variables were hierarchically grouped into three groups: the demographic variables of age and employment status were put first in the regression model as step 1, followed by the second group (regression model step 2) other potential factors of ever used tobacco, mother's weight, last pregnancy, whether premature delivery was experienced before, whether
stress was experienced before, malaria during pregnancy, urinary tract infection, physical and violence during pregnancy. On the third step of the regression model, the researcher put periodontitis as it was hypothesized as a predictor variable.

The current study defined some of the variables as follows; physical trauma as a wound on the body that was caused by a sudden physical injury for example an accident. Violence as any behavior or action that intends to hurt someone, physical or verbal and stress during pregnancy as anything that causes emotional strain or tension to the pregnant women.

The exclusion criteria were postpartum mothers aged 18-35 who delivered singleton babies within 1 to 5 days before recruitment in all selected health facilities. Mothers with twin babies, those with systemic conditions like uncontrolled diabetes, HIV infection and those without teeth in one or more sextants were excluded from the study. Also women whose conditions that could obviously lead to prematurity like abnormal placentation, eclampsia, uterine abnormalities and other pregnancy complications that may easily lead to prematurity were excluded from the study so that they do not bias the results. Other variables that were likely to cause prematurity were taken as covariates and were controlled during multivariate analysis.

Descriptive statistics, chi square analysis was conducted as part of the background to the main hypothesis testing analysis using multiple logistic regression. The study regression model was built using a hierarchical approach, where the demographic (control) variables were entered first followed by the proposed risk factors. The odds ratio was calculated with 95% confidence intervals and statistical significance was defined as p < 0.05.

**Results**

There were 555 women in their postpartum period that were screened and all questionnaires were filled in using a structured interview until the sample was accumulated. The participants were from 6 districts of the Southern Province of Rwanda and from 12 health facilities. The participants were distributed with respect to age, education level, employment status, social economic status. The mean age was 27.35 (SD=5.2) ranging from 18 to 35 years. Most participants (n=338, 60.9%) were in the age range of 26-35 years, 47.6% had primary education, 38.7%, had secondary education, 7% had tertiary education and 6.7 % had no formal education. The majority of the study participants, (n=513, 92.4%) are from a rural setting, 63.2% are farmers and 55.5% are in category 3 of the “Ubudehe”/ social economic status as categorized by Rwanda national categories. **Table 1**

**Table 1: Demographic characteristics of participants**
### Variables

| Variables          | Frequency (n) | Percent (%) |
|--------------------|---------------|-------------|
| **Age category**   |               |             |
| 16-25              | 217           | 39.1        |
| 26-35              | 338           | 60.9        |
| **Education level**|               |             |
| No formal education| 37            | 6.7         |
| Primary            | 264           | 47.6        |
| Secondary          | 215           | 38.7        |
| Tertiary           | 39            | 7           |
| **Residence**      |               |             |
| Urban              | 42            | 7.6         |
| Rural              | 513           | 92.4        |
| Farmers            | 351           | 63.2        |
| **Employment status** |             |             |
| Employed           | 71            | 12.8        |
| Students           | 32            | 5.8         |
| Not employed       | 101           | 18.2        |
| Category 1         | 56            | 10.1        |
| **Economic status**|               |             |
| Category 2         | 191           | 34.4        |
| Category 3         | 308           | 55.5        |

**Factors associated with preterm birth among pregnant women attending antenatal care clinics**

To assess if there is a relationship between periodontitis and premature birth, we enrolled 370 women who delivered at term gestation (controls) and 185 women who delivered prematurely (cases). Baseline characteristics between preterm and term groups were compared. Upon univariate analysis, we found that periodontitis, maternal low birthweight, interconception period between previous and present pregnancy, previous preterm delivery, stress during pregnancy, some illnesses such as malaria and urinary tract infection, violence during pregnancy and tobacco use were associated with preterm delivery.
During bivariate analysis using chi square test, 11 variables namely: employment status, ever used tobacco, periodontitis, mother's weight, last pregnancy, malaria during pregnancy, urinary tract infection during pregnancy, previous premature delivery, stress and violence during pregnancy were associated with preterm birth and therefore eligible for multivariate logistic regression. Multivariate regression analysis was done and the variables were hierarchically grouped into three groups: whereby demographic variable of employment status was put first in the regression model as step 1 and followed by other potential factors of ever used tobacco, mother's weight, last pregnancy, previous premature delivery, previous stress, malaria during pregnancy, urinary tract infection during pregnancy, physical trauma during pregnancy and violence during pregnancy. On the third step of the regression model, the researcher put periodontal diseases as it was hypothesized as a predictor variable.

After controlling for other variables, logistic regression revealed strong association between periodontitis and preterm birth where periodontitis could lead to a six-fold higher risk of delivering preterm birth babies compared to women who had no periodontitis (p<0.001) (95% CI 3.9, 10.4). **Table 2**

### Table 2: Multivariate analysis of preterm birth and associated factors
| Variables                    | Categories     | Wald | p-value | Odds  | 95% C.I  |
|------------------------------|----------------|------|---------|-------|----------|
| Employment status            | Farmers        | 2.9  | 0.403   | 0.7   | 0.3-1.2  |
|                              | Employed       | 1.6  | 0.203   | 0.7   | 0.3-1.2  |
|                              | Students       | 1.9  | 0.169   | 0.6   | 0.2-1.3  |
|                              | Not employed   | 1.5  | 0.218   | 0.5   | 0.1-1.6  |
| Ever used tobacco            | No             |      |         |       |          |
|                              | Yes            | 1.4  | 0.233   | 2.8   | 0.5-15.8 |
| Mother's weight              | 30-50          | 12.9 | 0.002   | 6.4   | 1.5-27.9 |
|                              | 51-75          | 6.3  | 0.012   | 6.4   | 1.5-27.9 |
|                              | 76 & above     | 1    | 0.299   | 2     | 0.5-7.7  |
| History of Malaria           | Yes            | 2.8  | 0.096   | 1.5   | 0.9-2.5  |
|                              | No             |      |         |       |          |
| History of UTI               | Yes            | 1.2  | 0.271   | 1.4   | 0.8-2.8  |
|                              | No             |      |         |       |          |
| History of RTI               | Yes            | 0.4  | 0.522   | 1.6   | 0.3-6.3  |
|                              | No             |      |         |       |          |
| Other illnesses              | Yes            | 0.09 | 0.761   | 0.7   | 0.1-5.0  |
|                              | No             |      |         |       |          |
| Previous premature delivery  | Yes            | 14.3 | <0.001  | 12.4  | 3.4-45.9 |
|                              | No             |      |         |       |          |
| Stress during pregnancy      | Yes            | 0.1  | 0.723   | 0.8   | 0.2-3.0  |
|                              | No             |      |         |       |          |
| Physical trauma              | Yes            | 0.9  | 0.332   | 0.5   | 0.1-1.9  |
|                              | No             |      |         |       |          |
| Violence                     | Yes            | 7.2  | 0.007   | 5.6   | 1.6-20.0 |
|                              | No             |      |         |       |          |
| Other causes of stress       | Yes            | 0.5  | 0.457   | 1.6   | 0.4-6.2  |
|                              | No             |      |         |       |          |
| Last pregnancy               | 12-24 Months   | 7    | 0.008   | 2.1   | 1.2-3.6  |
Discussion

Preterm birth is a major healthcare challenge and is associated with many potential consequences such as lifelong disabilities and high healthcare costs\(^4\). Premature delivery is defined as any delivery within a period of less than 37 weeks which accounts for almost 15 million neonates born prematurely worldwide mostly and in particular in low and middle income countries\(^25\). Various risk factors were identified to be related to preterm birth and these maternal risk factors include age, weight, socio-economic status, smoking, multiple pregnancies, low prenatal care, nutrition, stress, genito-urinary tract infections and malaria. Similarly, some studies have reported on the possible relationship between periodontitis and preterm birth.

Many studies have reported the association between maternal age and preterm birth; both extreme ages either under 18 years or above 40 years are considered to be risk factors for preterm birth\(^26, 27, 28, 29\). Though the majority of the studies concluded that the older maternal age was associated with higher risk of preterm birth, Ambrogio and colleagues in their study observed that both extreme ages that is, maternal age under 17 and advanced age over 40 were independent factors for preterm birth (OR 2.97; 95% CI 1.24, 7.14, P<0.005)\(^26\). This was echoed by Florent and co-authors who also found that both advanced age and lower age were risk factors for preterm birth\(^28\).

On the other hand, Mumghamba in Tanzania compared mothers who had PTB babies and those with normal weight babies and reported that PLBW had a lower mean age\(^30\). Our study shows no association between maternal age and preterm birth. In this study, most of the mothers were young whereby the mean age was 27.35 (SD 5.2) ranging from 18 to 35 years and may be the reason why there was no statistical association between maternal age and preterm birth in this study. Similarly, the study done in Uganda by Muwazi who also worked on a young population which led to low prevalence of periodontitis and later led to reduced statistical power and therefore no association was found\(^31\).
Maternal weight was also reported to be associated with preterm birth whereby in our study the logistic regression revealed that mothers with less weight had higher chances of pre-mature deliveries and low birthweight babies as opposed to mother with normal weight whereas the odds of having preterm birth baby was 6 times for underweight compared to those with normal weight mothers (p = 0.002) (95% CI 1.5, 27.9). Our study findings were echoed by Zhen and colleagues who revealed that neonates born to underweight mothers had higher chances of preterm delivery (95% CI 1.14, 1.25, RR 1.21) 32. Many other variables were found to be associated with preterm birth in this study; for example: the interval between last pregnancies and the current, previous preterm birth, stress and illnesses during pregnancy. However, 25% of the cases of preterm birth was of unknown etiology 8.

In this study, the presence or absence of periodontitis disease was a major predictor of preterm delivery and low birth weight. After controlling for other variables, logistic regression revealed strong association between periodontitis and preterm birth where periodontitis could lead to a six-fold higher risk of giving birth to preterm birth babies compared to women who had no periodontitis (p<0.001) (95% CI 3.9, 10.4). Nevertheless, our study results are controversial in comparison to other studies, for example, the study done in Germany by Noack and colleagues who did not find any association between periodontitis and preterm birth 33. Similarly, Davenport in 2002 in his case control study did not detect any association between periodontitis and preterm birth 34 and also Mumghamba in Tanzania in 2017 did not find any evidence to support periodontitis to be associated with preterm birth 30.

However, our study is echoed by several other studies that supported the association between periodontitis and preterm birth. Offenbacher et al., 1996 reported for the first time that there is a possible relationship between maternal periodontitis and delivery of a preterm infant where they reported that periodontitis during pregnancy could lead to seven times more risk of preterm birth 8. A systematic review by Teshome in 2016 revealed the association between periodontitis and preterm birth 35. Lopez and colleagues also assessed the risk of preterm birth and low birth weight in women with periodontitis in the USA and found that pregnant women with periodontitis were at a high risk of giving birth to premature babies with low birth weight (p=0.0004; RR=3.5) 36. Several other studies also confirmed the association 37, 38, 39, 40, 41, 42, 14, 43. Also in Africa, some studies have been done on preterm birth and low birth weight deliveries and these were significantly associated with poor periodontal status; for example a study done in Nigeria by Umoh and colleagues revealed that periodontal treatment was effective in preventing low birth weight deliveries 20. In Uganda, Wandera and colleagues also found that mothers with periodontal problems and poor oral hygiene during pregnancy had a greater risk of preterm birth as opposed to mothers who did not have periodontitis during pregnancy 44 and Muwazi in Uganda in his cross-sectional study revealed the association between gingival recession and preterm birth 31.

Conclusion:
Periodontitis is a risk factor for preterm birth and prevention solutions such as having a periodontitis screening tool for nurses and midwives during antenatal care consultations are highly recommended.

**Abbreviations**

DHS  
Demographic health survey  
LBW  
low birth weight  
PTLBW  
Preterm low birth weight  
TNF-α  
Tumor necrosis factor-alpha  
IL-6  
Interleukin-6  
PD  
Pocket depth  
CAL  
Clinical attachment loss  
TSAM  
Training Support Access Model  
WHO  
World Health Organization  
SD  
Standard deviation  
CI  
Confidence Interval

**Declarations**

**Ethics approval and consent to participate:** Permission to conduct the study was sought from the ethics committee of the University of Rwanda, College Medicine and Health Sciences and approval from study sites. Also, permission from the Ministry of Health to conduct the study in the selected health facilities was sought and granted. Informed consent forms were given to the participants. Participants were informed of their right to withdraw at any time and that their participation was entirely voluntary. The participants were given the information sheet containing all the information about the study and was read to those who did not know how to read. After understanding the study's risks and benefits along with the details involved in the study, those who agreed were given the consent form to sign that they have
voluntarily agreed to participate in the study. Information from the participants was kept confidential and used for study purposes.

**Consent for publication:** This manuscript contains no individual person's data in any form and consent for publication is not applicable for this section.

**Availability of data and materials:** The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

**Competing interests:** All authors declared no competing interests.

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**Authors’ contributions:** All authors made a significant contribution to the work reported that is; conception, study design, execution, acquisition of data, analysis and interpretation, have critically reviewed the article, have agreed on the journal to which the article will be submitted, gave approval of the final version to be submitted and agree to be accountable for all the content of the article.

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