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**Review article****Impact of Maternal Periodontitis on Preterm Birth and Low Birth Weight in Babies: Results of a Scoping Review**

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**Abstract****Background**

Periodontitis has been documented as public health concern but its association with preterm and low birth weight remains uncertain, thus the objective of this scoping review is to summarize the most recent published evidence related to the impact of periodontitis on preterm birth and low birth weight in order to improve public awareness and to inform policies for oral health during pregnancy.

**Methods**

Hinari, PubMed, and Google Scholar were searched to acquire the published literature. The retrieved studies included cross-sectional, case control studies and randomized controlled trials with available full text published in English from 2008 to 2019.

**Results**

After combining the key words, 333 articles were identified with only 133 eligible

articles published from 2008 to 2019. After reviewing the available 50 full text articles, duplicates were removed and 15 studies fully met the inclusion criteria. There were 13 articles that supported the association between maternal periodontitis and preterm low birth weight while 2 found no evidence to support the association.

### **Conclusion**

The results of this scoping review contribute to an increasing body of evidence to support the hypothesis that maternal periodontal disease may be a risk factor for preterm delivery and low birth weight.

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**Keywords:** Periodontitis, Periodontal disease, Preterm birth, Low birth weight, pregnancy

### **Background**

Periodontitis is a highly prevalent inflammatory and infectious disease of tooth-supporting tissues that can result in oral disability.[1] Periodontal diseases are commonly caused by gram-negative anaerobes that colonize the sub-gingival area. Periodontal diseases are reported to be the most common disease of mankind whereby severe periodontitis is the 6<sup>th</sup> most prevalent disease worldwide.[2,3] The global burden of periodontitis is reported to have increased by 57.3% between 1990 and 2010.[3] A recent study on the global burden of diseases estimated that oral diseases affect 3.5 billion people worldwide and severe periodontitis was estimated to affect nearly 10% of the population.[4] Periodontitis, as a chronic non-communicable disease shares risk factors with the major non-communicable diseases (NCD's) that cause around two-thirds of deaths worldwide, such as heart disease, diabetes, cancer and chronic respiratory disease.

Periodontitis prevalence rates varied greatly across the European continent where by 13% was reported in Norway, 12% in the UK, 82% in Sweden, 25% in Switzerland and 80% in France.[5,6] The National Health and Nutrition Examination Survey (NHANES) conducted in the United states between 2009-2010, estimated prevalence rates of periodontitis in the U.S. population to be as high as 50%,[7] while in Latin America, the prevalence of periodontitis was estimated to range between 40-80% over the period of 20 years between 2009-2010.[8] Shewale and colleagues in India reported the prevalence rate of periodontitis to be 85% in the general population and recommended the government as well as the dental council to develop and promote interventions in order to improve oral health and thus the quality of life.[10] Similarly, Bansal and colleagues found that 96.3% of the population in India had periodontal diseases.[12]

Periodontitis was reported to be very high in many African countries by

Houshmond and co-authors. [13-14] In East Africa, high prevalence of periodontitis has also been reported; in Uganda, Margret and colleagues conducted a study on determinants of periodontal health in pregnant women and the results showed that 67% of women presented with periodontal problems. [15] A high prevalence of periodontal diseases was also reported by Janviere and colleagues in Rwanda, [16] and Baelum et al in Kenya. [17]

Huck and colleagues have suggested that periodontitis might be linked to increased risk of preterm birth, but the evidence to support this association remains uncertain and debate about the association persists in the published literature. [18] Previous research has suggested that, periodontal infections can serve as a reservoir of inflammatory mediators, and thus may be a threat to the fetal-placental unit and therefore are associated with adverse pregnancy outcomes like preterm birth and low birth weight babies. [19] These inflamed periodontal tissues produce pro-inflammatory cytokines and host the bacteria that can cause inflammation once they get into the blood stream, where they are reported to possibly affect the fetus and result in low birth weight babies. [19] This connection is believed to originate with the deleterious effects of endotoxins released from the Gram-negative bacteria responsible for periodontitis. [19] The potential impact of periodontitis as a risk factor for low birth weight (LBW) requires further studies and also suggests a need for possible preventive measures for pregnant

women as well as better collaboration between the obstetrical and dental professions. [20]

Given the controversy in the literature about the association of periodontitis with preterm low birth weight, a scoping review is an appropriate approach to assess the published evidence testing the association between maternal periodontitis and preterm birth and low birth weight in babies. Therefore, this scoping review was conducted to synthesize the evidence relating to the impact of periodontitis on preterm low birth weight. The results of this review could help to improve public awareness and to inform policies for oral health during pregnancy.

## Methods

### Study design

This scoping review was undertaken using the Arksey and O'Malley framework and was guided by The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extended for Scoping Reviews (PRISMA-ScR), [21] as discussed by Peterson and colleagues, [22] and recommended by Levac et al. [23] The study followed the stages of the Arksey and O'Malley framework which included: (1) identifying the research question, (2) identifying relevant studies, (3) study selection, (4) charting the data and (5) collating, summarising and reporting the results. [21] The main strengths of a scoping review lie in its ability to examine a broader study area to identify research gaps and document on types of evidence that

address and enlighten practice in the field under study. Therefore, the present scoping review is designed to synthesize the evidence on the impact of periodontitis on preterm low birth weight.

### **Data sources and search strategy**

Electronic databases were searched for relevant articles. These databases included Hinari, PubMed and Google Scholar. The search strategies were developed and refined through the discussion among the authors. Retrieved articles were exported into Mendeley where duplicates were removed. The research team screened the titles and abstract independently from each other and any disagreement was resolved by consensus. The same process was used to screen the references. A thorough reading of the full text articles was performed by both reviewers for the papers selected from the initial title review.

Key search terms pertaining to the topics of periodontitis, preterm birth, low birth weight and risk factors were used for literature search. For example, in each data base the following key terms were used and combined as follows; (Periodontal disease OR periodontal diseases OR periodontitis) AND (Preterm birth OR Premature birth OR Gestational age OR Premature labor) AND (Low birth weight OR extremely low birth weight OR very low birth weight) AND ( risk factor OR causality OR etiology).

### **Study selection**

Articles were included if they investigated periodontal disease in

pregnancy in relation to gestational period and infant weight. The review was limited to case-control, cross-sectional or randomized controlled trial designs conducted on human participants. Articles published between the periods of 2008-2019 and written in English were included. Reviews, case studies, editorials, magazine articles and commentaries were excluded.

### **Data charting**

The reviewers used a consensus agreement approach to validate the data extraction form for consistency of the results from title screening and abstract review. [22] The data that were abstracted included the authors, years of publication, country, type of study, sample size, definition of periodontal disease used in the study. We also reported the main outcome variables and a summary of the final conclusions.

## **Results**

### **Description of studies**

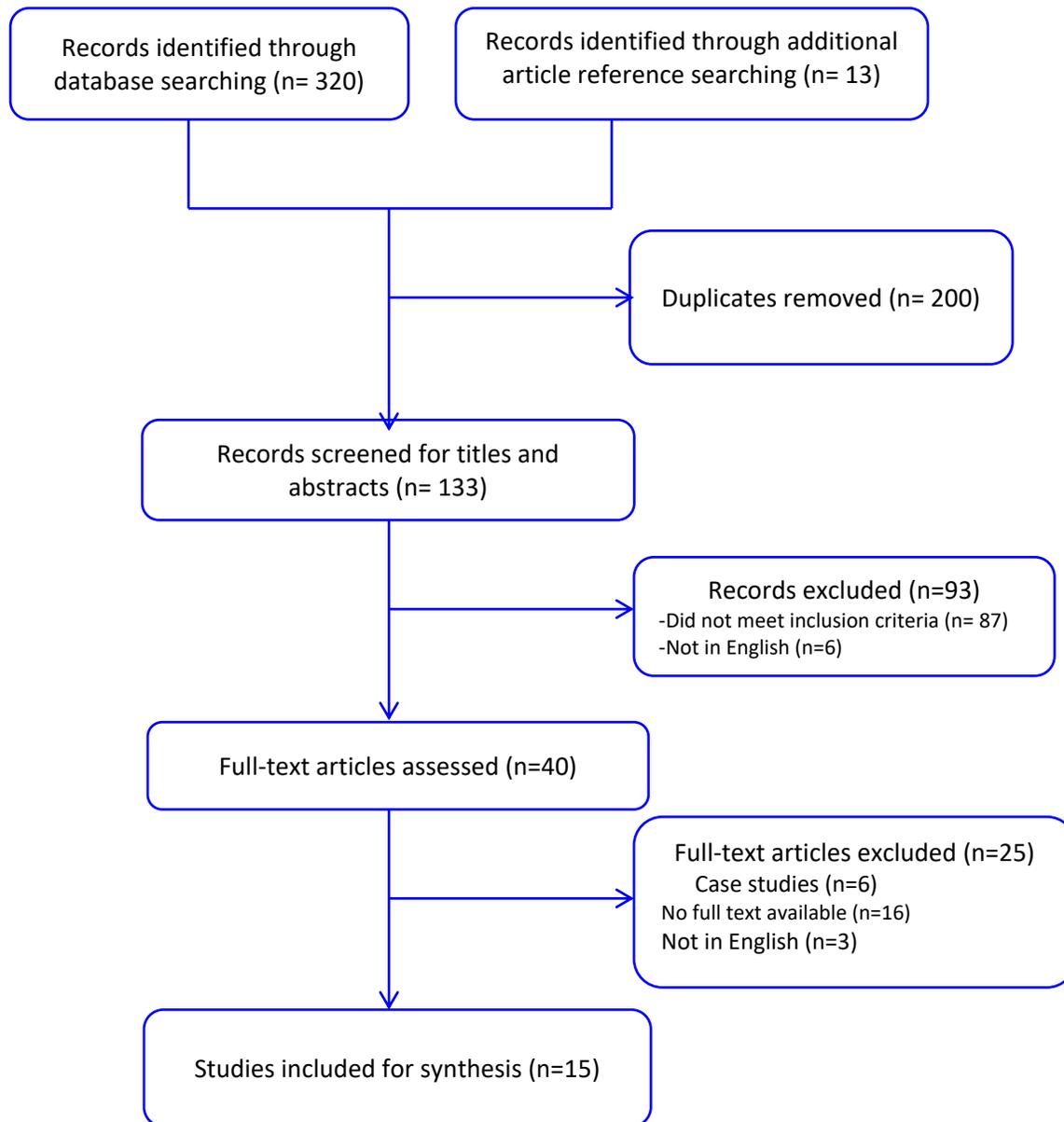
The search from the different databases retrieved 320 articles from the initial search. These articles were screened based on the titles, years of publication and types of studies. Additional 13 articles were located from the reference scans of the screened articles. After the screening and reviewing the key search terms, 333 articles remained of which 200 were deemed to be duplicates and thus were removed leaving 133 eligible articles. Of these 133 articles, a total of 93 articles did not meet the study inclusion criteria thus with a total of 40 articles were retained for

full text screening.

Twenty-five

articles further removed for a variety reasons including missing information, thereby leaving 15

articles as shown in Figure 1.



**Figure 1. Flowchart for article selection**

## Overview of studies

Among the 15 selected and included articles, there were 10 case control studies, three prospective cohort studies, one cross-sectional study and one randomized controlled trial, as shown in Table 1.

**Table 1. Characteristics of the selected studies.**

<b>Authors, publication year and Country</b>	<b>Type of study Sample size</b>	<b>Periodontitis definitions</b>	<b>Outcome variables</b>	<b>Conclusions</b>
Wang 2012 Taiwan	Randomised controlled trial N=211 HG= 82 GG= 67 PG= 62	Gingival bleeding >5%, CAL>6, PD of 5mm	Gestational age, birth weight and total maternal weight gain during pregnancy	The periodontitis group women had a higher frequency of preterm low birth weight (14.5%) than the healthy group 7.3% and the difference was significant (X <sup>2</sup> =15.345; p= 0.005)
Rakot et al 2010 Madagascar	Prospective cohort N=204		Preterm birth, low birth weight	Periodontitis was significantly associated with preterm birth (P<0.001), low birth weight (P<0.001) and preterm low birth weight (P<0.001)
Sindhu 2009 USA	Prospective cohort N=786	Not mentioned	Birth weight, preterm birth	This cohort study did not support the association between periodontitis and preterm birth.
Lohana et al 2016 India	Prospective cohort N=300	Slight perio CAL=1-2mm Moderate perio CAL=3-4mm Severe perio CAL ≥5mm	Gestational age, birth weight, BMI	As the level of periodontal disease severity increases, the proportion of preterm delivery also increases. (p<0.005 )
Davenport 2012 London, UK	Case control 236 cases, and 507 controls	CPITN =4mm	Birth weight, Premature deliveries	There is no association between periodontal diseases and PTLBW

Grandi 2010 Argentine	Case control 53 cases 79 controls	Bleeding index of 0-3, CAL>1, PPD>30% of involved sites	Preterm birth	Bleeding index and periodontal pockets depths were associated with preterm birth (odds ratio = 4.19; 95% CI: 1.28 – 13.69, p = 0.018)
Cruza et al. 2013 Brazil	Case control 102 cases 200 controls	CAL 4 mm at least 4 teeth	Birth weight	Periodontal disease is a risk factor for low birth weight (LBW)
Satheesh 2011 India	Case Control 52 cases 52 controls	PD≥4mm, CAL ≥3mm at the same site in atleast 4 teeth	Birth weight, Preterm birth	There is strong evidence showing that maternal periodontitis is an independent risk factor for preterm low birth weight (P<0.001)
Haerian et al 2013 IRAN	Case control n=88 44 cases 44 controls	CPITN grade III and IV	Birth weight	Mothers of LBW infants had less healthy areas of gingiva (p=0.042), and more deep pockets (p=0.0006, Mann-Whitney test). Maternal periodontitis is therefore a potential independent risk factor for LBW.
Vettore et al 2008 Brazil	Case control N=542 Cases 149 Controls 393		Birth weight	Periodontitis is not a risk factor for preterm low birth weight.
Marakoglu I. et al 2008 Turkey	Case control n=48 20 cases 28 controls	3 or more sites with 4mm or more pocket depth, bleeding on probing, alveolar bone loss	Preterm birth, and low birth weight	The study results indicated that periodontitis is independent risk factors of a preterm low birth weight. (OR= 3.6; 95% CI: 1.06 -12.18).
Karimi et al 2016 Iran	Case control N=264 132 cases	CPITN	Preterm, and low birth weight	Women with periodontal diseases were 10 times more likely to deliver low

	132 controls			birth weight infants and 8 times more likely to have premature infants that women with no periodontal diseases.
Kukkamalla et al 2014 India	Case control N=200 100 cases 100 controls	Not mentioned	Preterm delivery	There was significant association between gingival inflammation, probing depth to preterm delivery and low birth weight.
Khadem et al 2012 Iran	Case control N=70 35 cases 35 controls	CAL >3 mm, PPD>3mm	Preterm birth, low birth weight	Gum diseases was found to be a risk factor for preterm delivery.
MUWAZI et al. 2014 Uganda	Cross sectional N= 400	Bleeding on probing, probing pocket depth, calculus with plaque deposits and gingival recession	Birth weight, Gestational age	Approximately 26% and 29% of the post-partum mothers had gingival bleeding and periodontal pockets of 4mm or above. Gingival recession was associated low birth weight (p<0.005)

N: B: List of abbreviations used in Table 1

CAL: Clinical attachment loss, PD: Probing depth, PTB: Preterm birth, LBW: Low birth weight, PTLBW: Preterm birth and low birth weight, CPITN: Community periodontal index of treatment need, PPD: Probing pocket depth, HG: Healthy group, GG: Gingiva group, PG: Periodontal group.

## Discussion

The aim of the present review was to synthesize the evidence relating to the possible association between periodontitis and birth outcomes, including preterm delivery and low birth weight. This scoping review focused on the results of 15 different studies retrieved from the literature that were conducted to test these associations between periodontitis and birth outcomes. Despite the variability in the case definitions, 13 out of 15 included studies reported

an association between periodontal disease and either prematurity, low birth weight or both outcomes. Out of the 13 studies that showed an association, some found an association between periodontal disease and low birth weight only (n=5), some reported an association between periodontal disease and preterm birth (n=3), and others reported association between periodontal disease and preterm low birth weight (n=5).

Kastroit and colleagues reported that women with periodontal disease were 3.2 times more at risk (OR=3.2, 95% CI 1.5-6.8) for delivering a low birth weight baby and 3.4 times more likely to deliver premature babies (OR= 3.4, 95% CI 1.6-7.3) than women without periodontal disease. [24] Also the findings from Karimi and co-authors reported that women with periodontal disease in their study were 10 times more likely to deliver low birth weight infants and 8 times more likely to deliver premature infants than women without periodontal disease. [25] The findings of this review are consistent with a recent systematic review of case-control studies only done by Teshome, which reported that periodontal disease may be a risk factor for preterm birth, low birth weight or preterm low birth weight and the odds ratio ranged from 2-4. [26] Studies show that the inflammatory cytokines such as tumor necrosis factor- alpha (TNF- $\alpha$ ) and interleukin-6 (IL-6) which can reach high concentrations in periodontitis cases, stimulate increased prostaglandin production from the amnion and decidua,

leading to the onset of preterm labor. [12] This is evidenced by the presence of increased cytokines and prostaglandin levels in preterm birth patients with no other infections like genitourinary tract infections. This supports the hypothesis that preterm low birth weight are associated with infections of unknown origin and possibly with periodontitis. [27-29]

One key challenge in reviewing the literature was dealing with the inconsistencies in the definitions of preterm birth, low birth weight and periodontitis used in the studies. Different authors used different definitions of the key terms under study. Almost all the authors considered bleeding on probing, pocket depth, calculus and clinical attachment loss (CAL) but the measurements for these parameters for defining periodontal disease varied depending on the authors. For example, some authors considered bleeding on probing, pocket depth and CAL, while others considered bleeding on probing, pocket depth, calculus and CAL and others only considered only pocket depth, and CAL.

The variability in these case definitions likely contributed to the heterogeneity of the study results and thus contributes to the overall uncertainty of the validity of the association. There is a need to have a calibrated definition of periodontal disease so that the researchers can have the same understanding of what is being studied. Also the variability in the results could also be impacted by differences in the study settings, the sample size, the

duration of the study as well as the different periodontitis definitions.[2]

Some studies done in urban settings differed to studies done in rural settings because in urban settings, people may tend to have more advanced knowledge on oral health and better socio economic status both of which are known to have a positive influence on periodontal disease. For example the prospective study in this review done by Sindhu and colleagues, was conducted in an urban setting. This may have influenced the results of no association between periodontal disease and preterm low birth weight.

This is simply because the prevalence of periodontal disease tends to be lower and this may have reduced the study's statistical power.[29] This study by Sindhu was also testing for improvements in perinatal outcomes following periodontal treatment during pregnancy but it failed to show any association between periodontitis and preterm birth low birth weight . [29] This lack of association was in agreement with Bansal and colleagues who stated that providing periodontal treatment during pregnancy may be too late to reduce the local and systemic inflammations and may be ineffective in preventing the preterm birth.[30]

The case control study in Uganda conducted by Muwazi and colleagues also did not find any association between periodontitis and preterm birth and this could have been due to the use of small sample size in a

short period of time that could have led to loss of some data resulting in inadequate statistical power and imprecise results.[31]

### **Limitations of the study:**

The conclusions to be drawn from this scoping review are limited by the number and nature of the reviewed studies, because there was only one randomized controlled study and the majority were case control studies. While this review revealed inconsistencies regarding the association of periodontal disease and preterm low birth weight, there are different reasons among reviewed studies that may contribute to limited evidence.

The definitions of preterm birth and low birth weight were relatively consistent but the literature does not clearly point out the definition of periodontitis in periodontal research. A consensus on a definition of periodontitis is important to optimize the interpretation, comparison, and validation of research data. Also clinical markers of periodontal disease, such as clinical attachment loss, bleeding on periodontal probing and periodontal pocket depth were defined considering different measurements.

Another potential reason for different findings among the included studies is the differences in the study settings. One of the studies that did not find any association between periodontal disease and preterm low birth weight in this review was conducted in urban setting which

may have impacted the findings. [29] Finally, the study design was also among the factors for consideration as most of the studies were case control studies and these are limited in their ability to demonstrate causality. Lastly, it is also possible that some articles were missed in the review. Despite the above limitations, based on the fifteen articles reviewed, the scoping review provides evidence that periodontitis is associated with preterm birth and low birth weight outcomes.

## Conclusions

In conclusion, the review has supported the existence of an association between maternal periodontitis and prematurity and low birth weight. The present scoping review highlights the need for further research that will enable the development of a screening tool to be used by nurses and midwives during antenatal consultations for early detection and referral of periodontitis during pregnancy. Also further research using more robust study designs, like controlled clinical trials should be done to confirm the impact of periodontitis on preterm low birth weight.

## Recommendations

Although evidence supports this association between periodontitis and preterm birth and low birth weight, it is important in future research that scholars clearly specify exactly how they are defining their independent and dependent variables so that the inconsistencies

observed in case definitions, study designs and findings can be minimised. Also more detailed and rigorous studies are needed with stronger, and ideally prospective randomized trial designs, using more calibrated (i.e. consistent) definitions of periodontal diseases. This more rigorous designs could more directly address the possible cause and effect relationship between periodontitis and preterm low birth weight.

## Implication of this study

The results from this study may help to improve awareness about periodontitis and its possible association with preterm birth and low birth weight. It can also be used to inform the development of new public health policies relating to periodontal screening in the antenatal care package for early detection of periodontitis and to proactively promote periodontal health during pregnancy.

## Authors' contributions

PU Searched for articles and participation in manuscript preparation.

PU and AN developed search strategies and refined through the discussion among the rest of the authors. CM, SR, MK and HS have made substantial contributions to the design and critical reading of manuscript. All authors read and revised critically and approved the final manuscript

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## Conflict of interest

All authors declared no conflict of interest and no competing financial interest.

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