Review Article

Evidence of oral health intervention during pregnancy for spontaneous preterm birth reduction: An integrative review

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Abstract

Oral health care is critical for overall well-being, which is associated with better obstetric outcomes. The aim of the present integrative review was to assess scientific reports to support the planning of effective oral health interventions to prevent preterm birth (PTB) and low birth weight (LBW), as a secondary target. Seven bibliographic bases were searched from 2013 to 2018. Studies including oral health interventions during antenatal care with measurable impact on PTB or LBW reduction were searched. Sixteen studies were included. The heterogeneity in the population of pregnant women, and the types of oral intervention as well as the lack of accurate gestational ages, made it difficult to summarize the evidence. Despite the early intervention in high-risk groups, there was not enough evidence to support a significant reduction in PTB rates. There was some evidence that untreated periodontal disease in pregnancy was associated with LBW. This review did not provide strong evidence that preventive oral interventions during pregnancy had a measurable impact on spontaneous PTB reduction. However, further research is needed to clarify the impact of oral health interventions on the general pregnant women population or on those with a high risk of PTB and LBW.

Keywords: Adult periodontitis, low birth weight, oral health, preterm birth, review

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INTRODUCTION

Adverse pregnancy outcomes, including premature birth (before 37 weeks of gestation,[1] represent a public health problem in both developed and developing countries.[2] According to the World Health Organization,[1] every year 30 million newborns are at risk due to preterm birth; 2.5 million die during the first 28 days of life and two-third of them were born prematurely.[3] In Brazil, the Ministry of Health stated that prematurity represented 11.2% of live births.[4] Brazil is one of the ten countries with the highest number of preterm births.[3] However,

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there are a multitude of reasons for preterm delivery, it is clinically classified as spontaneous or interventional due to life-threatening pregnancy situations.[5] Preterm prevention strategies require comprehensive approaches since public policies, educational programs, lifestyle adjustments, and actions improve the quality of obstetric health care.[6] Among these, oral diseases have been reported as a risk factor in preterm birth and low birth weight (LBW).[7]

Oral health is a key factor in overall health and WHO[1] estimates that oral diseases affect 3.58 billion people worldwide. Oral diseases, especially progressive periodontal disease (PD), can cause the destruction of the alveolar bones of the jaw and other supporting tissues.[8,9] Besides its effect on oral tissues leading to tooth loss, PD has been linked to systemic diseases including cardiovascular disease, diabetes mellitus, and preterm LBW.[8] PD is a group of infectious disorders with a high prevalence in the global population.[8] It can consist of gingivitis (reversible gingival inflammation) and periodontitis (gingivitis with gingival recession accompanied by loss of connective tissue and alveolar bone).[9] Studies have investigated the occurrence of PD during pregnancy, yielding a wide variation in prevalence.[10] Pregnant women with PD have been reported to be at increased risk of an adverse pregnancy outcome; however, the studies are controversial.[11] PD during pregnancy and the impact of oral hygiene and professional treatment as measures to reduce preterm birth rates are scarcely discussed or investigated. Considering the overall paucity of evidence regarding the effect of antenatal interventions in oral health on prematurity reduction, this integrative review aims to access scientific reports to support the planning of effective interventions in oral health to prevent spontaneous prematurity or LBW rates.

METHODS

An integrative review on evidence to respond to the primary research question: Are interventions to promote oral health during antenatal care associated with preterm birth (PTB) and LBW prevention? In an attempt to describe the background, objectives, design, methodology, and organization of this integrative review, it was online registered in Protocols. IO under DOI number dx. doi. org/10.17504/protocols. io. yyzfxx6. The complete search strategy is described in an additional file [Supplementary Material 1]. The databases searched included Spanish, Portuguese and English languages and were 'Bibliografía Nacional en Ciencias de la Salud', 'Biblioteca Virtual em Saúde, Indice Bibliográfico Espanhol de Ciências da Saúde', 'Literatura Latino-americana e do Caribe em Ciências da Saúde', 'Scientific Electronic Library Online', 'Segunda Opinião Informativa SOF', and 'MEDLINE via PubMed'. The literature study covered the last 5 years, until July 10, 2018. The review process was limited to this period of time to aim for latter evidences.

Study selection

Four reviewers screened the search output to identify potentially relevant studies, analyzing only titles and abstracts using the following predetermined eligibility criteria: human pregnancy, oral or dental health, oral health education, health promotion, and premature birth outcome. During the selection process, the prioritized studies were clinical trials (randomized/non-randomized/after-before), systematic reviews, and case–control studies. The exclusion criteria were nonhuman pregnancy, opinion of a specialist, literature review or recommendations without scientific evidence, no clinical approach, protocols of research without results, and no intervention in oral health.

Extraction and data analysis

Variables were extracted from all the selected and fully read studies, as planned in the review protocol. The primary outcome was the reduction in spontaneous PTB or LBW rates. The results were summarized according to the characteristics of the population (scenario), the moment of pregnancy for the approach, protocols of the PDs diagnosis, modality of the intervention, and the type of treatment or oral hygiene measures. Two senior specialists conducted the review process. They read the articles to confirm they were appropriate for the review and to decide between studies that disagreed. Standard data selection, extraction, and summarization were supported by software.[12]

RESULTS

Bibliographic searching retrieved a total of 317 articles. There were 95 full-text articles that were assessed for eligibility, 79 of which were deemed ineligible [a descriptive summary of the 79 full-text excluded studies is showed on Supplementary Material 2], and 16 met the inclusion criteria. Figure 1 presents the flow of identification, selection, and inclusion of studies, according to the PRISMA diagram.[13] No clinical approach or a lack of intervention during pregnancy was the primary reason for excluding the 79 studies (83.2%).

Seven studies selected for this review (43.8%) were systematic reviews[14-19] or meta-reviews.[14,20] Of the nine primary studies, eight were clinical trials with[15,16,19,21-25] or

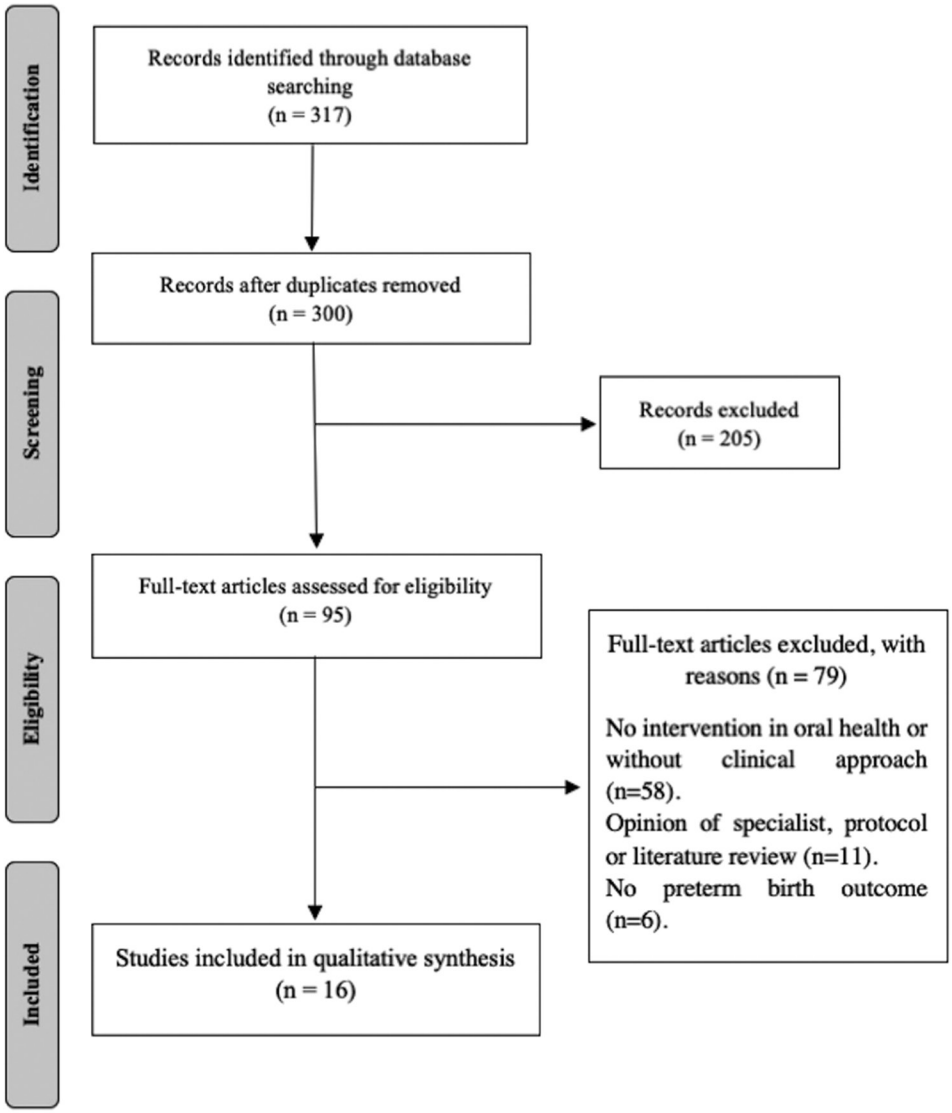

Figure 1: Flow diagram of the integrative review

without randomization[26-28] of the intervention and one was an experimental study.[29]

Characteristics of the reviewed studies

Table 1 summarizes the reviewed studies concerning the pregnancy scenario, schedule of intervention, and follow-up, as well as the study design and the quality of clinical data source.

Due to the impact of factors beyond the study design on the external validity of outcomes, the local health attention scenario, eligibility criteria, and the quality of clinical data are also detailed. The reports evaluated oral health interventions in different profiles of pregnant women, with varying levels of PD or gingivitis. Some of the studies enrolled pregnant women receiving prenatal care at a reference hospital[21,24,26,28] without the exclusion of maternal or fetal disease or only under vaginal delivery.[29] Most of the reports studied selected samples with moderate or severe disturbances in their oral health, PD or gingivitis, excluding maternal comorbidities.[15,22,23,25,27,29] Other studies were systematic reviews, with a heterogeneous scenario or a lack of sufficient details.[14,16-20] In most of the primary studies (62.5%), the gestational age (GA) was not confirmed with an obstetric ultrasound. Standardized reports of birth weight measurements were only mentioned in Soroye *et al*.[29]

Characteristics of the performed periodontal treatment

Concerning the intervention in PD, Table 2 presents results based on the time of intervention: ≤20 weeks of gestation, >20 weeks of gestation, or time not described. The criteria for PD diagnosis and the mode of treatment are highlighted.

Table 1: Descriptive summary of the integrative review

Study	Study design	Scenario of the prenatal care	Time of intervention and follow-up	Standard of information: GA estimate, PTB and LBW
Rangel-Rincón *et al*.[14]	Meta-review of systematic review/meta-analyses of interventional studies	Pregnant women with PD	Not described	Heterogeneous
da Silva *et al*.[15]	Systematic review of RCT	Chronic PD with inflammatory biomarkers. Excluded: Existence of comorbidities and oral surgery	Not described. Follow-up: Until delivery	GA: Without reference for estimative; PTB <37 weeks; LBW ≤2500 g
Iheozor-Ejiofor *et al*.[16]	Systematic review of RCT	Pregnant women with PD	9-39.6±1.2 weeks. Follow-up: Until delivery	GA: Without reference for estimative; PTB <37 weeks; LBW ≤2500 g
Schwendicke *et al*.[17]	Systematic review of RCT	Pregnant women with PD: Mild <20% and high rate (≥20%)	Not described	Not mentioned
Shah *et al*.[18]	Systematic review of RCTs	Pregnant women with PD	21-32 weeks. Follow-up: Until delivery	GA: Not mentioned; PTB <37 weeks; LBW ≤2500 g
Boutin *et al*.[19]	Systematic review of RCTs	Pregnant women with several levels of PD	<28 weeks. Follow-up: Not mentioned	GA: Not mentioned; PTB <37 weeks
López *et al*.[20]	Meta-review of meta-analyses with RCT	Periodontal therapy versus no treatment	Not described	GA: Considered in each primary study; LBW: According to NIH[30]
Jiang *et al*.[21]	RCT	Pregnant women without sexually transmitted disease with mild PD	<20 weeks. Follow-up: 3rd trim/until delivery	GA: Medical records
de Farias *et al*.[22]	RCT	Healthy pregnant women, nonsmokers, with moderate/severe PD	<18 weeks. Follow-up: 0-90 and 150 days	Not mentioned
Khairnar *et al*.[23]	RCT	Healthy pregnant women, single pregnancy, nonsmokers, with mild PD. Absence of fetal or maternal disease	>11-20 weeks. Follow-up: Until delivery	GA: Last menstrual period, ultrasound, physical and postnatal examinations; LBW: <2500 g
Weidlich *et al*.[24]	RCT	Reference hospital; pregnant women with single pregnancy	<20 weeks (monthly and delivery). Control: After delivery	GA: Last menstrual period, and ultrasound; LBW: According to WHO[31]
Pirie *et al*.[25]	RCT	Healthy pregnant women, single pregnancy, and PD. Excluded: Comorbidities	<22 weeks review: 8 weeks. Follow-up: Until delivery	GA: Last menstrual period, confirmed by ultrasound±20 wog; SGA: <10%[32]
Miyoshi *et al*.[26]	Non-RCT	2 groups: PD rate of 47.7% and of 59.7%	<20 weeks. Follow-up: Until delivery	Not mentioned
Kaur *et al*.[27]	Non-RCT, single-arm. Pilot study	University Hospital; healthy pregnant women with PD. Excluded: Comorbidities	>16-<24 weeks; Follow-up: Until delivery	GA: Last menstrual period, confirmed by <20 weeks ultrasound; PTB: <37 weeks
Jeffcoat *et al*.[28]	Non-RCT	University Hospital. High-risk pregnant women with PD	>6-<20 weeks. Follow-up: Until delivery	GA: Not mentioned; PTB: <37 weeks
Soroye *et al*.[29]		UH; nonsmokers, single pregnancy, healthy pregnant women; vaginal delivery; PD rate: 33.38%	>10-28 weeks. Follow-up: Until delivery	GA: Interview; LBW: ≤2500 g

GA: Gestational age, LBW: Low birth weight, NIH: National Institutes of Health, PD: Periodontal disease, PTB: Preterm birth, RCT: Randomized clinical trial, SGA: Small-for-gestational-age, Trim.: Trimester, WHO: World Health Organization, Wog: Weeks of gestation

Only six of the studies (37.5%) clarified that there was an intervention at less than 20 weeks of gestation.[21-23,26,28] In five of these studies, oral hygiene education was offered and two mentioned that dental supplies (toothbrush and toothpaste) were also provided.[21,28] One report[24] added a structured and extensive questionnaire to investigate oral hygiene habits. The indices used to diagnose PDs varied among the six studies, ranging from one to three. Two studies used additional methods to diagnose the level of PD: detection of C-reactive protein (CRP) levels[23] in blood samples, and the association among genes recovered from saliva and the obtained results.[28] All but one study stated that periodontal scaling and root planing (PSRP) was the nonsurgical treatment offered.[21] Despite this apparent homogeneity in treatment, a different number of dental visits was observed among the studies. In four studies,[21,22,26,28] the periodontal treatment resulted in an improvement in the oral health indices. One study did not demonstrate any oral health progress, but it is important to emphasize that no local intervention was applied.[23] Another study showed that unsuccessful periodontal treatment group deteriorated their periodontal status.[28] There were five studies that investigated intervention after 20 weeks of gestation.[18,19,25,27,29] Oral hygiene education was part of the treatment in almost all studies, except for two systematic reviews of randomized controlled trial RCTs,[18,19] which included works that were not mentioned in the procedure. The studies cited several indices to achieve PD diagnosis. Two studies included the investigation of inflammatory mediators.[25,27] The number of dental visits to perform treatment was also dissimilar among studies.[25,27] All studies stated that periodontal treatment consisted

Table 2: Outcomes and results according to the moment of intervention, the consideration of oral hygiene measures, and the diagnosis and treatment of periodontal diseases

Moment of OH intervention		
≤20 weeks of gestation	**>20 weeks of gestation**	**Not specified**
Jiang *et al*.[21] OH-measures: OH education+dental supplies PD diagnose: Rapid periodontal screening and recording tool- PD: ≥3 area scored ≥3, severe PD: ≥1 area scored 4. 2X: 0*/32-35 weeks; Follow-up: Until delivery Treatment: Control group: OH education+dental supplies/treatment group: OH education+dental supplies+registered 0.7 cetylpyridinium chloride mouthwash use Results: 3rd trim: Treatment group↓periodontal score (P=0.038)‡; PD severity: No differences between groups (P=0.41). 3rdtrim versus 0*: ↓scores between groups (P<0.001)‡	Shah *et al*.[18] OH-measures: OH education to treatment group (3 studies) PD diagnose: CAL and/or BOP and PPD. Moments: Various Treatment: Control group: Not treated; Treatment group: PSRP + chlorhexidine with or without maintenance therapy until delivery Results: Not mentioned separately	Rangel-Rincón *et al*.[14] OH-measures: OH education: 11 studies, 05 did not mention PD diagnose: 10 studies: BOP + CAL + PPD; 3 studies: PI + GI + BOP + CAL + PPD; 2 studies: PI + BOP + CAL + PPD/CAL + PPD/not mentioned; 1 study: BOP + PPD Treatment: Various Results: Treatment considered safe†
de Farias *et al*.[22] OH-measures: Control group/treatment group: OH education (3X) PD diagnose: PI, GI, BOP, PPD and CAL. Events: 3X: 0*, 90, 150 DOP Treatment: 0*: PSRP to control group/treatment group; 90/150 days: PSRP to treatment group Results: GI, PI, BOP (percentage presence/absence): Lowered between groups. PPD and CAL (mm): Lowered between groups (P<0.05)	Boutin *et al*.[19] OH-measures: OH education: 3 RCTs for control group; offered to treatment group in all, but 2 RCTs PD diagnose: CAL, BOP, and different number of PPD. 01 RCT did not mention the criteria Treatment: Control group: not treated; Treatment group: PSRP (<28 wog); 06 studies: Cointervention - 05 chlorhexidine Results: Not mentioned separately	da Silva *et al*.[15] OH-measures: OH education: 01 RCT (treatment group); 01 RCT (only to control group); 02 not mentioned PD diagnose: CAL+PPD (≠ number and % of sites); ≠ maximum PPD. Inflammatory biomarkers collected in (≠ moments from gingival crevicular fluid (2 RCTs) and serum cord and blood (2 RCTs) Treatment: Control group: Not treated. Treatment group: various +0.2% chlorhexidine Results: Treatment considered safe†
Khairnar *et al*.[23] OH-measures: Control group/treatment group: OHI-S PD diagnose: PI, GI, CAL: 1X: 0*; C-reactive protein levels: 2X: 0* and after-delivery (10 mL of blood: control group/treatment group) Treatment: Control group: PI, GI, OHIS -0*/treatment group: PI, GI and OHIS - 0*; 2nd trim: PSRP Results: No differences between groups: PI, GI, CAL, OHIS, PPD‡, (P>0.05); C-reactive protein levels: ↓After-delivery for treatment group versus 0* (P<0.05)	Pirie *et al*.[25] OH-measures: OH education: Control group/treatment group PD diagnose: Control group/treatment group: PI, GI, BOP, CAL and PPD (0*). During-Delivery: IL-1b, IL-6, IL-8 levels, from cord blood Treatment: Control group: Supragingival scaling. Treatment group: PSRP (≥2-1 h session). 8th weeks after: Same initial examinations Results: ↓After-Treatment: PI, BOP, CAL, PPD (P<0.001)	Iheozor-Ejiofor *et al*.[16] OH-measures: OH education: 13 studies; 02 reported only treatment procedures PD diagnose: PI, GI. PPD (≥-6 mm), CAL (≥2-≥4 mm), and BOP (≥25%-≥50% of teeth) Treatment: Control group: Not treated/alternative treatment/placebo. Treatment group: various Results: ↓After-treatment: PI, CAL, BOP, and PPD (P<0.05), except in one study
Weidlich *et al*.[24] OH-measures: OH education+OH habits questionnaire PD diagnose: PI, GI, BOP, CAL and PPD, supragingival calculus. 2X: 0*, 26-28wog Treatment: Treatment group: OH education+PSRP (unlimited sessions). After-Treatment: 01 monthly visit including OH education. Pain relief treatment Results: PI, GI, BOP, supragingival calculus, PPD: Differences between groups (P<0.001)	Kaur *et al*.[27] OH-measures: 0*: OH education (video) + dental supplies§ + OH habits questionnaire + DVD. 4th week: OH education + dental supplies. 8th week: 2nd questionnaire + dental supplies PD-D: 0*/4th week: PI, GI, BOP and CAL, PISA, PESA. 0*/8th week: Gingival crevicular fluid and blood samples. 3X: 0*, 4-8 weeks Treatment: PSRP Results: PD‡, PI‡, GI‡, CAL‡, PISA‡, PESA‡: ↓After-Treatment (P<0.0001); TNF-α, IL-1β levels: ↓After-Treatment (P<0.005)	Schwendicke *et al*.[17] OH-measures: OH education: Control group/treatment group PD diagnose: Not clearly described Treatment: Control group: Supragingival scaling; optional antimicrobial use. Treatment group: PSRP with or without use of antimicrobials Results: Not mentioned separately
Miyoshi *et al*.[26] OH-measures: OH education (2X); PD diagnose: 3-4 CPI index codes: periodontitis; 2X: 1st/2nd half of pregnancy Treatment: PSRP Results: OH status improved in the 2nd half of pregnancy for pregnant women who received both dental examinations	Soroye *et al*.[29] OH-measures: Control group: OH education, after-delivery/treatment group: oh education, during treatment PD diagnose: OHI-S, CPITN, BOP, PPGR; 3X: 0*/30/90 days. Treatment: Control group: I- PSRP, after-delivery/II: not treated; treatment group: PSRP <28 wog Results: OH status - Treatment group (%): ↑good oral hygiene, ↓poor oral hygiene, ↑code 0 CPITN (P<0.001)	López *et al*.[20] OH-measures: OH education: 14 RCTs and meta-analysis to treatment group and 3 studies also included control group PD diagnose: PPD: ≥4-≥5 mm (7 studies); BOP: ≥25%-50% of sites (4 studies); CAL: 1-≥4 mm (10 studies). Associated or not Treatment: Control group: not treated (7 RCTs); others: placebo, oral prophylaxis, and supragingival scaling. Treatment group: PSRP (9 RCTs), others: tooth polish, antimicrobials use Results: Not mentioned separately

Contd...

Table 2: Contd...

Moment of OH intervention		
≤20 weeks of gestation	>20 weeks of gestation	Not specified
Jeffcoat *et al*.[28] OH-measures: OH education+dental supplies PD diagnose: BOP and CAL; 2X-0*, 20 weeks later. DNA sample: buccal swab to investigate the allele pairs (AA, AB, and BB) for each SNPs associated to each outcome (successful/unsuccessful treatment, and full-term/PTB) Treatment: PSRP before the end of the 1st trim; BOP at ≤5 sites at the 2nd exam: Successfully treated Results: BOP‡: successful/unsuccessful: (*P*=<0.0001). CAL‡: Successful (*P*=<0.0001), unsuccessful (*P*=<0.004)		

*At baseline, †Treatment was considered safe and effective during pregnancy, enhancing oral and general health conditions, ‡Mean±SD, §Tooth brush, dental floss, 0.454% stannous fluoride toothpaste, and 0.07% alcohol-free mouthrinse, ≠Different, ↓Reduced, ↑Increased. BOP: Bleeding on probing, CAL: Clinical attachment loss, CI/CPITN: Community periodontal index of treatment needs, DOP: Days of pregnancy, GI: Gingival index, IL: Interleukin, LBW: Low birth weight, OH: Oral health, OHI-S: Oral hygiene index simplified,[33] PD: Periodontal diseases, PESA: Periodontal epithelial surface area, PI: Plaque index, PSRP: Periodontal scaling and root planing, PPD: Periodontal probing depth, PISA: Periodontal inflamed surface area, PPGR: Periodontal pocket and gingival recession, RCTs: Randomized controlled trials, PT: Premature birth, PTLBW: Premature low birth weight, SNPs: Single-nucleotide polymorphism, Trim: Trimester, VLBW: Very low birth weight, Wog: Weeks of gestation

of PSRP. In three of the five studies, the periodontal treatment resulted in an improved oral health status, and the remaining two did not provide the results.[17,18] The time of oral health intervention was not mentioned in the last 5 of 16 studies.[14-17,20] A miscellaneous group of indicators, combined or alone, were used to diagnose and treat PD. A single study[16] provided some evidence about the existence of potential factors that influence the severity of PD, such as who gave the treatment (e.g., periodontists, hygienists, and therapists). The results of periodontal treatment were not clearly demonstrated in two reports.[17,20] The other three studies[14-16] demonstrated that treatment was safe and effective during pregnancy, enhancing oral and general health conditions.

Subgroups of the reviewed studies considering the moment of oral health intervention

Subgroups of early, late, or unspecified temporal approaches are organized in Table 3 to clarify the lessons learned when planning antenatal interventions in oral health to reduce prematurity and LBW.

Subgroup one is comprised four studies[22,23,25,26] where approaches, treatment, or prophylaxis were introduced at less than 20 weeks of gestation in women with a higher than normal severity of PD. Even with the early intervention in high-risk groups, there was not enough evidence of a significant reduction in PTB rates. However, there was little evidence that untreated PD in pregnancy was associated with LBW.[22] Regarding the relevance of early intervention by modulating levels of inflammatory mediators, the adverse pregnancy outcome was lower when traced by the CRP.[23] However, the following RCT in a reference center for pregnant women had no success in demonstrating that the reduction of periodontal inflammation, up to the second trimester of gestation, affected preterm birth LBW (PTLBW) rates.[24] Subgroup two is comprised studies which investigated late interventions (>20 weeks of gestation) and the evidence is inclusive concerning the effect in PTB and LBW.[18,25,27,29] Inconclusive outcomes are not useful for planning oral health approaches. However, the systematic review of Boutin *et al*.[19] stated that pregnant women with PD should receive periodontal therapy, adding that PTB is reduced by the use of an antimicrobial mouth rinse.[19] Subgroup three includes studies that fail to clarify the time of oral antenatal intervention, standardize the severity of the PD, state the source of variables (e.g., GA), or state confounders (e.g., obstetric risks associated with adverse results of pregnancy). Systematic reviews that do not specify the time of intervention, despite the low quality of evidence, suggest that periodontal treatment may reduce PTB and LBW.[14-16,20] Concerning high-risk PTB populations, when periodontal treatment was properly performed and adequate criteria for periodontitis were used, the elimination of PD was potentially an effective way to prevent PTB and LBW.[17]

DISCUSSION

Strengths and limitations of the study

The strength of this study was the vast critical review of the impact of oral health treatment during pregnancy and the possible improvements in PTB and LBW rates. This integrative review contains several periodontal treatments, such as oral health education and the use of a mouth

Table 3: Obstetric outcomes, limitations on the evidence, and the lessons learned for planning oral health intervention during prenatal care

Moment of OH intervention		
Subgroup 1	**Subgroup 2**	**Subgroup 3**
de Farias *et al*.[22] 95% CI outcomes: GA: treatment group 38.3±1.52 weeks versus control group 39.5±1.28 weeks; *P*=0.99). Birth weight: Treatment group 3.43±0.41 versus 3.15±0.54 kg; *P*<0.05 Limitations: Limited generalizability due to the sample size: research protocol: Not registered Lessons learned: There is not enough evidence for significant reduction of PTB in pregnant women receiving periodontal treatment. Untreated PD in pregnant women was associated with LBW	Shah *et al*.[18] 95% CI outcomes: 4 studies found↓PTB-rate associated with periodontal treatment (*P*<0.05), and 2 trials did not. 2 studies found ↓LBW-rate associated with periodontal treatment (*P*<0.05) and 1 study did not Limitations: Lack of the definition of PD in the primary studies. Periodontal treatment was given at ≠phase of pregnancy in ≠studies Lessons learned: Inconclusive to plan prevention. Pregnant women with PD should receive periodontal treatment	Rangel-Rincón *et al*.[14] 95% CI outcomes: no significant difference of PTB-rate and LBW-rate in meta-analysis reviews. Sociodemographic conditions modified the effect of interventions Limitations: No standardization of PD classification, indicators, and variables of reviews Lessons learned: There was no significant reduction of PTB-rate/LBW-rate in pregnant women receiving periodontal treatment
Khairnar *et al*.[23] 95% CI outcomes: ↓PTB-rate: Treatment group 32% versus control group 72%, *P*<0.05. ↓LBW-rate: Treatment group 36% versus 52%, *P*<0.05. Significant C-reactive protein reduction (*P*<0.001) Limitations: Limited generalizability due to the sample size and high PTB-rate/LBW-rate; research protocol: not registered Lessons learnt: PTB can influence the adverse pregnancy outcome by modulating levels of inflammatory mediators	Boutin *et al*.[19] 95% CI outcomes: PTB-rate <35 weeks: RR=1.00 (0.73-1.38), I^2=22%. PTB-rate <32 weeks: RR: 0.85 (0.53-1.34), I^2=13%. LBW-rate: RR=0.83 (0.60-1.16), I^2=62%. VLBW rate: RR=0.98 (0.53-1.79), I^2=29%. Chlorhexidine used by the treatment group: LBW-rate: RR=0.44 (0.31-0.65), I^2=0% GA, mean difference: 0.53 weeks (0.29-0.78), I^2=31%. Birth weight, mean difference: 122 g (73-172), I^2=0%) Limitations: Substantial heterogeneity among primary studies. Lack of a unanimous definition of chronic periodontitis in primary studies Lessons learned: PSRP alone initiated during pregnancy is not effective in reducing PTB-rate. Antimicrobial mouthwash could help reducing PTB	da Silva *et al*.[15] 95% CI outcomes: PTB-rate: RR=0.54 (0.38-0.77); I^2=32%. LBW-rate: RR=0.78 (0.50-1.21); I^2=41% Limitations: Lack of the definition of PD in the primary studies. There is no universally accepted consensus for PD definition. Scarce data for LBW as primary outcome in the primary studies Lessons learned: Periodontal treatment, during pregnancy, decreased periodontal inflammatory biomarkers levels. The approach did not consistently reduce adverse gestational outcomes
Weidlich *et al*.[24] 95% CI outcomes: PTB-rate <37 weeks: Treatment group 11.72% versus control group 9.09%, *P*=0.57. VPTB rate<35 weeks: Treatment group 5.52% versus control group 5.84%, *P*=0.99. VPTB rate <32 weeks): Treatment group 3.45% versus control group 4.55%, *P*>0.77. LBW-rate: Treatment group 5.63% versus control group 4.05%, *P*>0.59 PTLBW rates: Treatment group 4.15% versus control group 2.60%, *P*=0.53 Limitations: Limited generalizability due to the sample size and the enrolment criteria did not select high-risk sampling of PD Lessons learned: The reduction of periodontal inflammation up to the 2nd trim of gestation did not affect PTLBW-rate	Pirie *et al*.[25] 95% CI outcomes: PTB-rat e<35 weeks: RR=1.00 (0.73-1.38, I^2=22%). PTB-rate <32 weeks: RR=0.85 (0.53-1.34), I^2=13%. LBW-rate: RR=0.83 (0.60-1.16), I^2=62%. VLBW-rate: RR=0.98 (0.53-1.79), I^2=29%. Chlorhexidine in the treatment group: LBW-rate: RR=0.44 (0.31-0.65) I^2=0%; GA: Mean difference: 0.53 weeks (0.29-0.78), I^2=31% Limitations: Limited generalisability due to the sample size and the enrollment criteria did not select high-risk sampling of PD Lessons learned: Inconclusive to plan prevention. It is possible that late intervention in PD does not improve the birth outcomes	Iheozor-Ejiofor *et al*.[16] 95% CI outcomes: PTB-rate <37 weeks: RR=0.87 (0.70-1.10). PTB-rate <35 weeks: RR=1.19 (0.81-1.76), PTB-rate <32 weeks: RR=1.35 (0.78-2.32) Limitations: Imbalance in baseline characteristics of participants, in different stages of pregnancy; low number of events studied. Substantial heterogeneity among primary studies Lessons learned: There is low-quality evidence that periodontal treatment may reduce PTB-rate
Miyoshi *et al*.[26] 95% CI outcomes: ↓PTB-rate: 2.7%; ↓LBW-rate: 3.4%; ↓ELBW rate: 0.27%. Both in comparison with historical rates from hospital-based records Limitations: Multifaceted prophylactic intervention for chorioamnionitis and PD without control group. Small PTB-rate Lessons learned*: There is not enough evidence for significant reduction of PTB in pregnant women receiving periodontal treatment	Kaur *et al*.[27] 95% CI outcomes: PTB-rate cohort 6.7% vs historic controls 9.5%, *P*=0.113. LBW-rate: Cohort 10.2% versus historic controls 9.5%, *P*=1.00 Limitations: Limited generalisability due to the sample size. No controlled randomized group. High loss of follow-up rate; PISA was used to assess the amount of periodontal inflamed tissue, but it is not a very precise criterion. Errors related to observer, instruments, teeth, patients, and their combination could be possible Lessons learned: Inconclusive to plan prevention. Pregnant women with PD should receive periodontal treatment	Schwendicke *et al*.[17] 95% CI outcomes: PTB-rate: OR=0.79 (0.57-1.10). LBW-rate: OR=0.69 (0.43-1.13). Subgroup with high rate of PD (≥20%): Periodontal treatment may reduce the risk of PTB OR=0.42 (0.24-0.73), and LBW OR=0.32 (0.15-0.67) Limitations: Potential bias of selection due to update of existing review. Possible confounders were not extensively analyzed Lessons learned: Only for high-risk populations periodontal treatment appeared potentially effective to prevent PTB and LBW. The main indication for periodontal treatment, during pregnancy, should be PD itself

Contd...

Table 3: Contd...

Moment of OH intervention		
Subgroup 1	**Subgroup 2**	**Subgroup 3**
Jeffcoat *et al*.[28] 95% CI outcomes: The allele pair (BB) variation - SNP rs2817864 (PTGER3) was related to 16.7% probability of successful periodontal treatment, OR 11.09. Allele pair (BB) was associated with the "disadvantageous" outcome: OR=11.1:1 favoring treatment failure *P*<0.0002, and an OR of 6.9:1, favoring PTB, *P*<0.0032 Limitations: Limited generalisability due to the sample size and very high-risk-group of women: at baseline all pregnant women had ≥5 sites with BOP Lessons learned: Inconclusive to plan prevention. Pregnant women with PD should receive periodontal therapy Jiang *et al*.[34] 95% CI outcomes: GA: Treatment group 39.5±1.52 weeks versus control group 39.5±1.28 weeks; *P*=0.99. PTB-rate <37 weeks: OR=1.59 (0.51-4.92). LBW: OR=3.50 (0.72-17.05) Limitations: Limited generalizability due to the sample size for secondary outcomes, poor areas without standard therapy for PD. The study analyzed only one isolated OH- measures: Antimicrobial mouthwash use Lessons learned: The improvement of periodontal conditions with a mouthwash intervention in pregnant women with PD had no effect on PTB-rate or LBW-rate	Soroye *et al*.[29] 95% CI outcomes: ↓PTB-rate: Treatment group 5.0% versus control group 31.2% and ND 1.4%, *P*<0.05. LBW-rate: Treatment group 7.8% versus control group 28.4%, *P*<0.05 Limitations: Limited generalizability due to the sample size; research protocol: not registered Lessons learned: Inconclusive to plan prevention. pregnant women with PD should receive periodontal treatment	López *et al*.[20] 95% CI outcomes: Periodontal treatment did not reduce PTB-rate (except in 01 meta-analysis), for groups with a high risk of PTB Limitations: The majority of the RCTs failed to control confounding factors for PTB. The inconsistency in PTB has made it difficult to interpret the data. There were many different criteria used to diagnose PD and also in the types of administered treatment Lessons learned: Studies with low risk of bias concluded that periodontal treatment did not reduce the PTB rate

≠: Different, ↓: Lower, *Lessons learned to plan antenatal interventions. BOP: Bleeding on probing, ELBW: Extreme low birth weight, LBW: Low birth weight, ND: No disease, OH: Oral health, PD: Periodontal diseases, PSRP: Periodontal scaling and root planing, PISA: Periodontal inflamed surface area, RCTs: Randomized controlled trials, PTB: Premature birth, PTLBW: Premature low birth weight, SNPs: Single-nucleotide polymorphism, Trim: Trimester, VLBW: Very Low birth weight, CI: Confidence interval, GA: Gestational age, RR: Relative risk, VPTB: Very preterm birth

rinse, along with surgical and nonsurgical therapy. Our integrative review was registered online (Protocols. IO) and was performed by following a strict methodological approach. The limitations of our study are in part due to the primary articles. The source of GA calculation at birth and the number of periodontal indices to diagnose PD were not carefully considered in these studies and could be considered potential sources of prejudice in the analyses. There is a gap between these indices to diagnose PD and obstetric outcomes. In the present review, it was difficult to establish a correlation between them due to the large number of indices used and the variability in the combinations. This review should be interpreted with some caution due to these limitations.

Periodontal therapy, pregnancy, and neonatal outcomes

Periodontal therapy during pregnancy seems to decrease periodontal inflammatory status by providing a healthier oral environment.[17,18,23,24,34] In addition, treatment was considered safe and effective if performed during pregnancy.[14,15,17,27,29] Nonetheless, the reduction of periodontal inflammation itself[24] and the decreasing of all PD indices[16,21,22,24-27,29] were not enough to affect the neonatal outcomes, although untreated PD was associated with higher LBW levels.[22] Another perspective came from a study performed in the first half of pregnancy.[28] The authors found an interesting relation among PD treatment failure, spontaneous PTB, and a gene associated with inflammatory response. Despite the small sample size, the authors encouraged periodontal therapy in pregnant women.

The principle of periodontal treatment, including non-surgical therapy, is to re-establish and maintain periodontal health and function.[34] There was a consensus about PD treatment among studies that specified the time of oral health interventions. PSRP was the prevailing treatment among studies whose oral interventions were performed before[22-24,26,28] and after 20 weeks[18,19,25,27,29] of gestation. The study of Khairnar *et al*.[23] included an evaluation of CRP levels, in addition to periodontal indices at baseline and after delivery. Their results demonstrated that a reduction of CR*P* values after delivery only occurred for the treatment group who received PSRP. The study of Aljateeli *et al*.[35] demonstrated that PSRP led to a considerable reduction in PD and also eliminated the need for surgery for one patient.[35] Hence, PSRP was considered a very important

initial phase of periodontal therapy. In studies where the time of oral health intervention was not defined, several treatments were provided, sometimes a combination of treatments, including oral surgery. Among these reports, some mentioned the use of topical or systemic antimicrobial therapy.[14-17,20]

Oral health preventive measures and pregnancy

Oral health during pregnancy is receiving more attention and is being recognized as an integral part of preventive health care for pregnant women and their newborns. Prevention measures include providing information promoting oral health, which should be incorporated into prenatal visits.[36] Most studies in this review mentioned preventive measures, such as oral hygiene instructions/education, including a video.[27] Six systematic or meta-reviews did not homogeneously inform about these procedures to the control and test groups. Only Khairnar *et al*.[23] did not mention their approach. Some reports mentioned a statistically significant decrease in plaque index with one or more sessions of oral health education.[22,24,25,27,29] Several indices, both associated and unassociated, were used to diagnose PD. Clinical attachment loss and bleeding on probing were the most commonly used indices among the studies that specified the time of intervention (37.5%). As this is an integrative review congregating primary and secondary studies, a multiple publication bias of research is possible. Notwithstanding, we did not consider excluding primary studies, even those used in systematic reviews, because they provided detailed analyses. For instance, Pirie *et al*.[25] was included by Rangel-Rincón *et al*.,[14] Iheozor-Ejiofor *et al*.,[16] da Silva *et al*.,[15] and Schwendicke *et al*.[17] Similarly, including systematic reviews may present some intersection of the primary base of the articles. Performance bias related to a lack of random allocation of intervention,[26] pilot analysis,[27] and small samples,[22,23,25] as well as fragile methodology based on interview[29] is to be expected.

Periodontal therapy and spontaneous prematurity

PTB is considered a multifactorial disorder with different causes in assorted scenarios. It is a big challenge, the rate is growing globally, reflecting racial, ethnic, and socioeconomic disparities, and it is a leading cause of death in children below 5 years of age.[37] In this study, we focused our question on spontaneous prematurity to avoid iatrogenic pregnancy interruptions related to maternal and/or fetal diseases. Many current methods for the diagnosis of prematurity are inadequate, and little is known about how PTB can be prevented.[30] Preterm neonate identification depends on reliable pregnancy dating, which can be challenging in low- and middle-income countries. A lack of concern about the source of GA calculation at birth was present in most of the selected studies. The last menstrual period, early or late ultrasounds, or maturity score references result in uncertainties of 5 to 40 days, directly affecting the rates of prematurity.[38] An early crown–rump length measurement of an embryo, obtained by obstetric ultrasound, currently offers the best due date.[39] However, none of the reports used this consensual reference.

Periodontal therapy and low birth weight

The birth weight is much easier to obtain than GA. We chose this outcome due to the lower uncertainty with this classification. Nevertheless, an LBW newborn needs specific attention to survive.[3] Thirteen articles mentioned LBW or PTLBW outcomes, there was a lack of evidence to support a plan concerning oral health prevention to improve birth outcomes. Specific treatment may reduce the risk of LBW in groups with a high rate of PD disease[17] or for those in poor, rural areas[23] or when chlorhexidine is added to the intervention.[19,25] In contrast, the use of 0.7 cetylpyridinium chloride to treat PD was not effective in reducing PTB or LBW.[21]

Final comments

Future studies will need to address various challenges to better understand the impact of poor oral health on pregnancies. For example, the way the severity of PD is classified needs to be addressed. Furthermore, more reliable markers are needed to measure the effectiveness of the different types of intervention. Regarding the outcomes, the impact of oral health promotion during pregnancy for PTB reduction will remain hard to robustly quantify if pregnancy dating continues to be viewed as a trivial task. An early enrolment of pregnant women confirming GA references with an obstetric ultrasound and implementing a thoroughly planned, large RCT that investigates the multifactorial environment of PTB pathogenesis could provide better answers.

This integrative review did not provide conclusive evidence to plan effective interventions in oral health to prevent spontaneous prematurity and LBW occurrence. There remains uncertainty about the best way to approach oral health during pregnancy to prevent PTB. These results did not support the absence of actions that promote oral health during pregnancy since a comprehensive view of integral health is a fundamental element of antenatal care. This review did not provide strong evidence to show that the implementation of preventive oral intervention during prenatal care had a measurable impact on spontaneous PTB reduction or LBW occurrence.

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Ethical clearance

This integrative review did not require Ethical approval since it did not collect participants' personal, sensitive, or confidential information. The authors affirm that the manuscript is an honest, accurate, and transparent account of the reported study.

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Conflicts of interest

There are no conflicts of interest.

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