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ORAL HEALTH IN PREGNANT WOMEN AND OBSTETRIC COMPLICATIONS: A NARRATIVE REVIEW OF EVIDENCE ON PRETERM BIRTH, LOW BIRTH WEIGHT, PREECLAMPSIA, AND GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Background and Objectives: Periodontitis affects approximately 40% of pregnant women worldwide, although prevalence estimates vary considerably depending on diagnostic criteria and population characteristics [7]. Periodontal disease is considered a potentially modifiable risk factor for adverse pregnancy outcomes (APOs). This narrative review examines the current evidence linking maternal periodontal disease to four major obstetric complications: preterm birth (PTB), low birth weight (LBW), preeclampsia (PE) and gestational diabetes mellitus (GDM). A secondary aim was to assess the clinical evidence for periodontal treatment as a preventive strategy during pregnancy.

Methods: A narrative synthesis of literature published between January 2015 and April 2025 was conducted using PubMed/MEDLINE, Cochrane Library, Google Scholar, Embase and Web of Science. Systematic reviews, meta-analyses, randomised controlled trials (RCTs), prospective cohort studies and case-control studies were included. Quality appraisal was performed using AMSTAR-2, the Newcastle-Ottawa Scale and the Cochrane Risk of Bias 2.0 tool.

Results: Consistent epidemiological associations were identified for all four outcomes. Effect sizes ranged from OR 1.67–4.28 for PTB, OR 1.82–2.53 for LBW and OR 1.83 for GDM, whereas the evidence for preeclampsia was classified as suggestive. Two mechanistic pathways were characterised: direct hematogenous translocation of periodontal pathogens to the fetoplacental unit and an indirect systemic inflammatory cascade mediated by IL-1 β , IL-6, TNF- α and prostaglandin E2. Intervention trials demonstrated that non-surgical scaling and root planing (SRP) is safe for pregnant women but does not produce a consistent, statistically significant reduction in APO rates.

Conclusions: Maternal periodontitis is significantly associated with PTB, LBW, GDM and PE through biologically plausible mechanisms. However, causal inference is hampered by heterogeneous disease definitions, residual confounding and inconsistent RCT results. Integration of oral health screening into antenatal care protocols and standardisation of periodontal diagnostic criteria in obstetric research are priority recommendations.

KEYWORDS

Oral Health, Pregnancy Complications, Preterm Birth, Low Birth Weight, Preeclampsia, Gestational Diabetes Mellitus

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1. Introduction

1.1 Global Burden of Adverse Pregnancy Outcomes

Adverse pregnancy outcomes (APOs) represent a leading cause of perinatal morbidity and mortality worldwide and constitute a major public health priority. Preterm birth (PTB), defined as delivery before 37 completed weeks of gestation, is the most prevalent and clinically consequential of these outcomes. According to the most recent systematic analysis by the World Health Organization (WHO) and UNICEF, an estimated 13.4 million babies were born preterm in 2020, representing approximately 9.9% of all live births globally [1]. Despite decades of research and investment, global preterm birth rates have not meaningfully declined over the preceding decade and preterm complications remain the leading cause of death among children under five years of age, accounting for approximately one million neonatal deaths annually [2].

Low birth weight (LBW), defined as a birth weight below 2 500 grams regardless of gestational age, frequently co-occurs with PTB, but also arises from intrauterine growth restriction (IUGR) in term pregnancies. LBW is a critical predictor of neonatal mortality and long-term developmental impairment. Preeclampsia (PE), characterised by new-onset hypertension and evidence of end-organ damage after 20 weeks of gestation, affects an estimated 2-8% of pregnancies worldwide and is a leading cause of maternal death, severe maternal morbidity and iatrogenic preterm delivery [3]. Its global burden is disproportionately concentrated in low- and middle-income countries (LMICs), where access to antenatal monitoring remains limited. Gestational diabetes mellitus (GDM), defined as glucose intolerance first recognised during pregnancy, affects approximately 14% of pregnancies globally when assessed by International Association of Diabetes in Pregnancy Study Group (IADPSG) criteria, with prevalence rising in parallel with the global obesity epidemic [4].

Collectively, these four conditions impose an enormous burden on healthcare systems, families and societies. They share modifiable risk factors including nutritional deficiencies, smoking, low socioeconomic status, advanced maternal age and chronic infection that are targets for interdisciplinary preventive intervention. Periodontal disease has emerged as one such potentially modifiable, yet underrecognised, risk factor motivating a growing body of epidemiological and mechanistic research.

1.2 Periodontal Disease in Pregnancy: Prevalence and Hormonal Context

Periodontal disease encompasses a spectrum of inflammatory conditions of the supporting tissues of the teeth, ranging from reversible gingivitis to irreversible periodontitis characterised by clinical attachment loss (CAL), increased probing pocket depth (PPD) and alveolar bone destruction. According to the Global Burden of Disease study, severe periodontitis affects approximately 19% of the global adult population, making it the sixth most prevalent non-communicable disease worldwide [5].

Pregnancy profoundly alters the periodontal environment through several interacting mechanisms. Elevated concentrations of estrogen and progesterone increase gingival vascular permeability and reduce host immune surveillance, facilitating the proliferation of anaerobic periodontal pathogens within the subgingival biofilm [6]. The prevalence of pregnancy-associated gingivitis ranges from 36% to 100% across reported cohorts with peak severity observed in the second and third trimesters followed by postpartum resolution [5]. In contrast, periodontitis in pregnant women, a condition not fully reversible without treatment, has been reported in 14-67% of gestating women depending on the diagnostic criteria applied, the timing of examination and the population studied [5]. A systematic review and meta-analysis published in 2022 pooling data from 20 studies estimated the prevalence of periodontitis among pregnant women at 40% (95% CI: 0.15-1.00), underscoring the scale of this unmet clinical need [7].

The relationship between hormonal changes and periodontal susceptibility is bidirectional: preexisting gingivitis is exacerbated by pregnancy, while newly established periodontitis may in turn influence systemic inflammatory mediator profiles. This hormonal modulation renders pregnancy a window of particular vulnerability, during which subclinical periodontal disease may progress rapidly and exert systemic effects. Despite this, oral health screening and referral for dental care remain largely absent from routine antenatal care protocols in most healthcare systems globally.

1.3 Rationale and Objectives of the Review

The hypothesis that maternal oral infection could contribute to adverse pregnancy outcomes was first proposed in the early 1990s and has since generated an extensive body of observational research. Multiple systematic reviews and meta-analyses have confirmed associations between periodontitis and PTB, LBW, PE and GDM, however, intervention trials targeting periodontal disease during pregnancy have yielded inconsistent results. This disconnect between observational and interventional evidence constitutes the central unresolved scientific tension in the field.

No recent comprehensive narrative review covering all four major obstetric outcomes simultaneously and explicitly addressing this association-causation paradox, has been identified in the 2020-2025 literature. The present review therefore aims: (1) to synthesise the current evidence on the association between maternal periodontal disease and PTB, LBW, PE and GDM, (2) to characterise the biological mechanisms underpinning these associations and (3) to evaluate the clinical evidence for periodontal treatment as a preventive strategy during pregnancy.

2. Methodology

2.1 Search Strategy

This narrative was conducted in accordance with the principles of good practice for narrative synthesis of evidence. Electronic searches were performed in PubMed/MEDLINE, the Cochrane Library, Google Scholar, Embase and Web of Science, covering the period from 1 January 2015 to 30 April 2025. Landmark studies published prior to 2015 were included where essential for mechanistic context or as foundational references. The following MeSH terms and free-text keywords were employed, combined using Boolean operators: (“periodontal disease” [MH] OR “periodontitis” [MH]) AND (“premature birth” [MH] OR “infant, low birth weight” [MH] OR “preeclampsia” [MH] OR “diabetes, gestational” [MH]) AND (“pregnancy outcome” [MH]). Supplementary searches targeted specific bacterial species (“*Porphyromonas gingivalis*” [MH] OR “*Fusobacterium nucleatum*” [MH]) and treatment modalities (“periodontal diseases/therapy” [MH] AND “randomized controlled trial” [PT]). Reference lists of included reviews were hand-searched to identify additional relevant publications.

2.2 Inclusion and Exclusion Criteria

Studies were eligible for inclusion if they: (1) examined the association between clinically diagnosed periodontal disease and at least one of the four target outcomes (PTB, LBW, PE, GDM), (2) involved adult pregnant women without restriction to specific subpopulations, (3) used validated periodontal diagnostic criteria (e.g., probing pocket depth, clinical attachment level, bleeding on probing) and (4) were published in English. Eligible study designs included systematic reviews, meta-analyses, RCTs, prospective cohort studies and case-control studies. Excluded were: animal studies, case reports, letters, editorials, expert opinion pieces and studies lacking reproducible periodontal diagnostic criteria. Grey literature and conference abstracts were not systematically searched, representing a potential source of publication bias.

2.3 Quality Assessment

Methodological quality was appraised using design-appropriate tools. Systematic reviews and meta-analyses were assessed using the AMSTAR-2 (A Measurement Tool to Assess Systematic Reviews) checklist. Observational studies (prospective cohort and case-control designs) were evaluated using the Newcastle-Ottawa Scale (NOS). Randomised controlled trials were appraised using the Cochrane Risk of Bias 2.0 (RoB 2.0) tool. Two reviewers independently screened titles and abstracts, followed by full-text review of eligible articles. Discrepancies were resolved by consensus. Given the narrative design of this review, formal statistical pooling of effect estimates was not performed. Instead, a qualitative synthesis was conducted with explicit attention to sources of heterogeneity and risk of bias.

3. Results

3.1 Biological Plausibility: Proposed Pathogenic Mechanisms

The biological plausibility of a causal link between maternal periodontal disease and adverse pregnancy outcomes rests on two well-characterised pathogenic pathways: direct bacterial translocation to the fetoplacental unit and an indirect, systemically mediated inflammatory cascade. Both pathways are not mutually exclusive and likely operate concurrently, amplifying each other's effects on the gestating host [8, 6].

Direct Pathway: Hematogenous Bacterial Translocation

The oral cavity harbours a diverse polymicrobial community in which periodontal pathogens, most notably

Porphyromonas gingivalis, *Fusobacterium nucleatum*, *Treponema denticola*, and *Prevotella intermedia*, reside within the subgingival biofilm. During periodontal inflammation, transient bacteremia may arise following routine activities such as tooth-brushing or chewing, enabling these organisms to disseminate hematogenously and colonise distant anatomical sites, including the decidua and placenta [9].

P. gingivalis is the most extensively studied periodontal pathogen in the context of pregnancy. Its principal virulence factors: gingipains (cysteine proteases), lipopolysaccharide (LPS) and fimbriae allow the bacterium to evade host innate immunity, degrade extracellular matrix components and directly impair trophoblast function [10]. *P. gingivalis* has been detected in placental tissue, amniotic fluid and umbilical cord stroma of women who delivered preterm, with placental colonisation density negatively correlating with gestational age at delivery (adjusted odds ratio 0.63, 95% CI 0.48-0.85 per additional gestational week) [11]. Once within the fetoplacental unit, the organism inhibits natural killer (NK) cell and T-cell activity, shifts the maternal-fetal immune response from a Th2-dominant tolerance profile toward pro-inflammatory Th1/Th17 phenotype and activates macrophage recruitment via monocyte chemoattractant protein-1 (MCP-1) patterns inconsistent with successful pregnancy maintenance [12].

Fusobacterium nucleatum, a gram-negative anaerobe and bridging species within the oral biofilm, employs distinct molecular mechanisms to reach the intrauterine compartment. Its adhesin FadA binds vascular endothelial cadherin (VE-cadherin) on endothelial cells, increases vascular permeability and facilitates systemic dissemination not only of *F. nucleatum* itself but also of co-infecting oral species [13]. Additionally, the virulence protein Fap2 binds D-galactose- β (1-3)-N-acetyl-D-galactosamine (Gal-GalNAc), a receptor whose placental expression increases progressively across gestation, thereby promoting placental colonisation and suppressing TIGIT-mediated NK and T-cell activation [14]. Experimental murine models have demonstrated that intravenous inoculation with *F. nucleatum* isolates results in placental infection, chorioamnionitis and preterm birth or stillbirth [15].

Indirect Pathway: Systemic Inflammatory Cascade

Even in the absence of direct placental colonisation, periodontal infection can exert remote effects on pregnancy through chronic systemic inflammation. Periodontal LPS binds to LPS-binding protein and activates macrophages via the TLR4/MyD88/NF- κ B signalling axis, triggering systemic release of pro-inflammatory mediators including interleukin (IL)-1 β , IL-6, tumour necrosis factor-alpha (TNF- α) and prostaglandin E2 (PGE2) [16,6]. At sufficient concentrations, these mediators stimulate uterine smooth muscle contractility, promote membrane degradation by matrix metalloproteinases and induce premature rupture of membranes, thereby precipitating preterm labour [17, 18].

Secondary to the cytokine-mediated inflammatory response, periodontal disease generates a measurable systemic burden of reactive oxygen species (ROS). Oxidative stress, reflected by elevated levels of salivary 8-hydroxydeoxyguanosine (8-OHdG) and prostaglandin E2 (PGE2), has been independently associated with preterm birth in clinical studies [19]. In the context of preeclampsia, excessive ROS production contributes to trophoblast dysfunction, endothelial injury and activation of pro-inflammatory signalling pathways, thereby exacerbating placental oxidative stress and ischaemia [20]. Experimental evidence further suggests that

exposure of trophoblast cells to periodontal pathogens induces oxidative stress responses and molecular alterations consistent with mechanisms implicated in the pathogenesis of preeclampsia [20].

Furthermore, antibody-mediated mechanisms may contribute: elevated maternal IgM and IgG titres against periodontal pathogens have been proposed to cross-react with placental antigens and complement activation via TLR4-dependent pathways may independently injure the placental vasculature [9].

Saliva has been proposed as a clinically accessible proxy biomarker for this systemic inflammatory burden. In a nested case-control study, elevated salivary TNF- α and PGE2 were independently associated with preterm birth (OR 4.79, 95% CI 1.01-22.63 and OR 1.07, 95% CI 1.00-1.14, respectively), supporting the potential utility of salivary biomarker profiling for non-invasive periodontal risk stratification in antenatal settings [19]. Taken together, the two-pathway model provides a mechanistically coherent framework for the periodontal-obstetric association, though the relative contribution of each pathway likely varies by disease severity, microbial community composition and host immunogenetic factors.

3.2 Periodontal Disease and Preterm Birth

Preterm birth is the most extensively studied obstetric outcome in relation to maternal periodontitis and the one for which the epidemiological evidence is strongest. Multiple meta-analyses have consistently reported significantly elevated odds of PTB among women with periodontal disease, with pooled effect estimates ranging from OR 1.67 to 4.28 across different study designs and diagnostic criteria [21; 22]. An umbrella review that appraised 43 systematic reviews published up to February 2023 classified the association between periodontitis and PTB as “strong” based on convergent evidence across meta-analyses [22]. The fail-safe number analysis indicated that only 8.7% of significant estimates were likely to change upon the inclusion of future unpublished studies, suggesting relative robustness of the observed signal.

The mechanistic plausibility of the PTB association is supported by clinical data demonstrating elevated concentrations of inflammatory mediators including IL-1 β , IL-6, TNF- α and PGE2 in the gingival crevicular fluid, serum and amniotic fluid of women with both periodontitis and preterm labour [17]. The indirect inflammatory pathway is considered the dominant mechanism in spontaneous preterm labour, while direct bacterial translocation is more relevant to infection-associated preterm premature rupture of membranes (PPROM) [23]. However, a critical methodological limitation affecting the entire observational literature is the absence of a universally applied definition of periodontitis prior to the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (AAP/EFP classification). Studies have employed heterogeneous thresholds for probing pocket depth (PPD), clinical attachment level (CAL) and bleeding on probing (BOP), limiting the comparability of findings across studies and contributing to substantial statistical heterogeneity in meta-analyses [22;24].

Findings from intervention trials differ substantially from those reported in observational studies. Evidence from randomized controlled trials does not support a significant reduction in PTB following periodontal treatment during pregnancy. A Cochrane systematic review including 15 randomized controlled trials involving 7,161 participants reported no statistically significant effect of periodontal therapy on PTB rates (RR 0.87, 95% CI 0.70–1.10; low-certainty evidence) [25].

A recent network meta-analysis of 20 randomized controlled trials reported heterogeneous effects across periodontal treatment strategies. Although some interventions appeared to reduce the risk of preterm birth, the overall certainty of evidence remained limited by methodological heterogeneity and variations in treatment protocols across studies [26]. Publication bias and substantial methodological heterogeneity should be considered when interpreting the available evidence [22]. This discrepancy between the strong associations observed in epidemiological studies and the predominantly null findings of randomized controlled trials remains a major unresolved issue in the field and is discussed further in Section 4.2.

3.3 Periodontal Disease and Low Birth Weight

The association between maternal periodontitis and LBW has been reported across multiple systematic reviews and meta-analyses with pooled odds ratios ranging from 1.82 to 2.53 [21;22]. An umbrella review evaluating systematic reviews published up to February 2023 classified this association as “strong”, consistent with the evidence reported for PTB [22]. However, several important caveats qualify this classification. Effect sizes are consistently larger in studies conducted in LMICs, where residual confounding by socioeconomic factors, including nutritional deficiencies, poor sanitation and limited healthcare access, is likely to be more pronounced and less fully adjusted for in statistical models.

Shared risk factors for both periodontitis and LBW, including tobacco smoking, low socioeconomic status, advanced maternal age and pre-pregnancy underweight, represent significant sources of potential confounding in observational studies. Several authors have noted that many published case-control and cohort studies fail to adequately control for these factors, raising concern about inflated observed effect sizes. When studies with more comprehensive confounder adjustment are isolated, effect estimates tend toward the lower end of the reported range.

Intervention data for LBW parallel those for PTB in demonstrating a lack of significant benefit. The Cochrane review reported low-quality evidence for a possible reduction in LBW (RR 0.53, 95% CI 0.30-0.95) but cautioned that confidence in this estimate was severely limited by methodological heterogeneity. A pooled RCT analysis reported a non-significant RR of 0.92 (95% CI 0.71-1.20) for LBW following periodontal treatment [22]. Notably, small for gestational age (SGA) was the only outcome among the assessed APOs that did not demonstrate a significant association with periodontal disease in the umbrella review, suggesting that the mechanistic pathway may be more relevant to gestational duration than to intrauterine growth velocity per se.

3.4 Periodontal Disease and Preeclampsia

The association between maternal periodontitis and preeclampsia is biologically plausible but supported by a smaller and methodologically less robust evidence base than PTB or LBW. A systematic review and meta-analysis published in *Maternal and Child Health Journal* confirmed a statistically significant association between periodontal disease and PE, with effect sizes that were consistently larger in studies conducted in lower-middle-income countries [27]. The mechanistic link is hypothesised to involve periodontal pathogen-driven endothelial dysfunction mediated by sustained elevations in circulating TNF- α and IL-6 [6].

PE is characterised pathophysiologically by impaired spiral artery remodelling due to defective extravillous trophoblast (EVT) invasion, leading to placental ischaemia and the systemic release of antiangiogenic factors including soluble fms-like tyrosine kinase-1 (sFlt-1) and soluble endoglin, with concomitant reduction in placental growth factor (PlGF [28]). Periodontal LPS, acting through TLR4 on trophoblast and endothelial cells, has been shown in experimental studies to activate NF- κ B signalling pathways and promote inflammatory responses [29;30]. This is associated with increased ROS production, oxidative stress and impaired trophoblast migration and function, mechanisms consistent with the pathophysiology of PE [29;30;31].

Despite this mechanistic plausibility, an umbrella review classified the level of evidence for the association between periodontitis and PE as only “suggestive to weak” [22]. This lower grade reflects the small number of randomized controlled trials available for the specific outcome, in contrast to the PTB literature, and the high heterogeneity observed across studies. PE is therefore the least evidenced of the four outcomes reviewed, representing a clear gap for future prospective trials and mechanistic studies.

3.5 Periodontal Disease and Gestational Diabetes Mellitus

The association between periodontitis and GDM has received growing research attention, paralleling well-established bidirectional relationships between periodontitis and type 2 diabetes mellitus (T2DM). A meta-analysis published in *Primary Care Diabetes* reported a pooled odds ratio of 1.83 (95% CI 1.25-2.69; $p=0.0017$) for GDM among women with periodontitis [32]. The observed association appears consistent across geographically and clinically diverse study populations.

The mechanistic overlap between the periodontitis-GDM and periodontitis-T2DM relationships is substantial. Chronic periodontal inflammation sustains elevated systemic concentrations of IL-6 and TNF- α , which promote peripheral insulin resistance through inhibition of insulin receptor substrate-1 (IRS-1) phosphorylation and downregulation of glucose transporter type 4 (GLUT-4) expression [8]. Additionally, increased ROS production during active periodontal disease contributes to pancreatic β -cell dysfunction, potentially impairing the adaptive insulin secretory response required to meet increased metabolic demands during pregnancy.

A bidirectional component characterises this relationship: GDM-induced hyperglycaemia and the associated advanced glycation end-products (AGEs) may in turn worsen periodontal conditions by promoting gingival inflammation, impairing neutrophil function and altering the subgingival microbiome toward a more dysbiotic profile, a dynamic analogous to the well-documented periodontitis-T2DM bidirectional cycle [33; 8]. This bidirectionality has important clinical implications: periodontal disease may both predispose to GDM and be exacerbated by it, creating a compounding cycle of systemic and oral inflammatory burden that requires concurrent management.

3.6 Periodontal Treatment During Pregnancy: Clinical Evidence

Non-surgical periodontal treatment, primarily scaling and root planing (SRP), with or without adjunctive chlorhexidine gluconate mouthwash, is considered safe throughout all trimesters of pregnancy, with the second trimester conventionally preferred for elective procedures. No iatrogenic risks associated with SRP during pregnancy have been documented in published RCTs or observational studies [25].

Despite its established safety profile, the evidence that periodontal treatment during pregnancy reduces the incidence of adverse birth outcomes remains inconclusive. A Cochrane systematic review encompassing 15 randomized controlled trials ($n = 7,161$) found no statistically significant effect of periodontal therapy on preterm birth (RR 0.87, 95% CI 0.70-1.10; low-certainty evidence) and only limited, uncertain evidence regarding the reduction of low birth weight [25]. A systematic review of systematic reviews synthesising 17 eligible umbrella reviews reached similarly inconclusive conclusions, reporting inconsistent findings across the included studies and concluding that evidence supporting the prevention of adverse pregnancy outcomes through periodontal treatment remains unclear [34]. Nevertheless, the authors consistently recommended treatment because of its established safety profile and its effectiveness in reducing periodontal inflammation and bacterial burden [34].

A recent network meta-analysis including 20 randomized controlled trials and evaluating five periodontal intervention strategies reported heterogeneous effects across treatment modalities [26]. Although some interventions were associated with favourable outcomes, no approach demonstrated consistent superiority across all assessed outcomes, including PTB, LBW, preterm low birth weight (PTLBW), SGA and PE [26]. The authors identified substantial heterogeneity in treatment timing, participant characteristics and outcome assessment as major limitations affecting the interpretation of pooled estimates [26].

An ongoing multicentre randomized controlled trial registered under UMIN000057519 is investigating whether the combination of scaling and root planing (SRP) and chlorhexidine gluconate mouthwash initiated during the first trimester can reduce adverse pregnancy outcomes among high-risk pregnant women in Bangladesh [35]. The study is expected to provide more definitive evidence regarding the impact of periodontal treatment on adverse pregnancy outcomes. Importantly, its focus on first-trimester intervention addresses a potential limitation of earlier trials, most of which initiated treatment during the second trimester, possibly after critical stages of placentation and spiral artery remodelling had already occurred [35]. Early periodontal intervention may therefore be more effective in modifying inflammatory pathways implicated in adverse pregnancy outcomes.

4. Discussion

4.1 Synthesis of Evidence: Strength and Consistency

The body of evidence reviewed in this paper reveals a consistent epidemiological signal linking maternal periodontitis to all four adverse pregnancy outcomes examined. Across meta-analyses conducted over the past decade, the direction of association is uniformly positive (periodontitis increases the odds of APO) and the magnitudes of effect are clinically meaningful. A comprehensive umbrella review classified the associations between periodontitis and PTB, LBW and GDM as “strong”, whereas the association with PE was classified as “suggestive”, based on evidence synthesized from 43 systematic reviews [22].

The biological mechanisms proposed to mediate these associations, hematogenous translocation of oral pathogens and systemic inflammatory cytokine elevation, are supported by experimental animal data, in vitro studies and human clinical evidence demonstrating the presence of periodontal pathogens in placental tissue, elevated inflammatory mediators in amniotic fluid and salivary biomarker signatures associated with preterm labour. The two-pathway model thus provides a mechanistically coherent, multi-level explanation for epidemiological findings.

Nonetheless, mechanistic plausibility does not equal causation and the evidence base has important limitations, that preclude definitive causal inference. The graded evidence hierarchy, PTB and LBW as “strong”, GDM as “strong” but with fewer studies, PE as “suggestive”, reflects both the volume of published research and the consistency of estimated rather than the quality of individual studies. Many contributing meta-analyses incorporate observational data with heterogeneous diagnostic criteria, inadequate confounder adjustment and variable outcome ascertainment.

4.2 The Association-Causation Gap

The most clinically and scientifically significant finding of this review is the persistent disconnect between robust observational associations and null or near-null RCT intervention effects. Strong epidemiological odds ratios (1.67-4.28 for PTB) have not been replicated by periodontal treatment trials, which consistently report risk reductions in the range of RR 0.87-0.90, not statistically significant and insufficient for public health recommendations. This paradox is not unique to the periodontitis-pregnancy literature. Analogous gaps have been documented in the periodontitis-cardiovascular disease field, where observational associations have similarly not been confirmed by intervention trials.

Several explanatory mechanisms have been proposed. First, residual confounding by shared risk factors, most importantly low socioeconomic status, smoking, poor nutrition and chronic stress, may inflate observational effect estimates even in studies claiming multivariate adjustment. These factors influence both periodontal disease, susceptibility and pregnancy outcomes through multiple overlapping biological pathways and their simultaneous measurement and adjustment remain methodologically challenging. Second, the timing and adequacy of periodontal treatment in existing RCTs may be insufficient to interrupt the relevant biological cascade. Most trials initiate SRP in the second trimester (14-20 weeks), potentially after the critical first-trimester window of implantation and spiral artery remodelling during which placentation is established. Earlier intervention, preconceptionally or during the first trimester, has not been adequately tested. Third, the heterogeneity of periodontal disease definitions across studies renders meta-analytic pooling unreliable as studies addressing different severity thresholds may be estimating associations for fundamentally different patient populations. Fourth, publication bias, confirmed by funnel plot asymmetry in both observational and RCT meta-analyses, inflates observational estimates and may suppress null RCT results, distorting the apparent evidence base.

The net effect of these factors is a literature in which the epidemiological signal is real but the causal architecture remains opaque. This does not preclude clinical action, periodontal treatment during pregnancy is safe, beneficial for oral health and entails no evidence of harm, but it does prevent the stronger recommendation that treating periodontitis will meaningfully reduce adverse pregnancy outcomes at a population level.

4.3 Clinical Implications for Interdisciplinary Prenatal Care

The evidence reviewed supports several clinically actionable recommendations, even in the absence of definitive causal proof. First, oral health assessment should be integrated into routine antenatal care protocols. Pregnant women should be screened for signs of periodontal disease at their first antenatal visit, with referral to dental services where indicated. This recommendation is consistent with the principle that treating an active infectious and inflammatory condition during pregnancy is beneficial for maternal health independent of its effect on birth outcomes. Second, bidirectional communication between dental professionals and obstetricians requires strengthening. Current clinical pathways in most healthcare systems operate with minimal coordination between dental and maternity care, leaving periodontal disease largely unaddressed during pregnancy. Third, the burden of periodontitis is disproportionately concentrated in LMICs and in socially disadvantaged populations within high-income countries, the very populations at highest risk of adverse pregnancy outcomes. Resource allocation and public health strategies must therefore prioritise these groups.

The emergence of teledentistry as a scalable tool for periodontal screening in resource-limited settings represents an area of potential innovation for antenatal care delivery. Remote periodontal assessment using photographic documentation and validated patient-reported symptom tools could facilitate earlier identification of high-risk pregnant women without requiring face-to-face dental consultation, enabling more targeted referral pathways and reducing barriers to care access.

4.4 Limitations of This Review

This review has several limitations that must be acknowledged. As a narrative rather than systematic review, it is susceptible to selection bias in the choice and weighting of included literature. A formal PRISMA-compliant systematic search with duplicate independent screening was not conducted and grey literature was not searched. The evidence base itself carries substantial limitations: heterogeneity in periodontal disease definitions prior to the 2017 AAP/EFP classification system reduces comparability across studies, and publication bias has been confirmed across multiple meta-analyses, with likely inflation of observational effect sizes and suppression of null RCT results. The evidence base for PE is particularly thin at the RCT level, limiting conclusions about this outcome. Finally, adequately powered RCTs in European high-income settings remain scarce, restricting the generalisability of existing evidence to LMICs and North American populations.

5. Conclusions

5.1 Summary of Key Findings

Maternal periodontal disease is significantly associated with preterm birth, low birth weight, gestational diabetes mellitus and preeclampsia across a large body of epidemiological literature spanning multiple study designs and geographical settings. The biological mechanisms underpinning these associations, direct hematogenous translocation of oral pathogens and indirect systemic inflammatory cascade, are increasingly well-characterised at the molecular level. However, current evidence does not establish causality: intervention trials testing non-surgical periodontal treatment during pregnancy have not consistently demonstrated reductions in adverse birth outcomes and the association-causation paradox remains the field's most important unresolved question.

5.2 Recommendations and Future Directions

Four priorities emerge from this review. First, standardisation of periodontal disease diagnostic criteria in obstetric research, ideally adoption of the 2017 AAP/EFP classification system across all future studies, is essential to enable reliable meta-analytic synthesis. Second, adequately powered RCTs testing early (first trimester or preconceptional) periodontal intervention, including adjunctive antimicrobial therapies, are urgently needed to determine whether current null results reflect genuine absence of effect or suboptimal treatment timing and intensity. Third, integration of oral health screening into WHO antenatal care guidelines should be evaluated as a low-cost, scalable public health intervention, justified by the high prevalence of periodontitis among pregnant women and the demonstrable oral health benefits of treatment. Fourth, investigation of teledentistry as a feasible screening and monitoring tool for periodontal disease in high-risk pregnant population in LMICs represents a promising research direction consistent with the interdisciplinary and digital health framing of contemporary perinatal care.

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