The Association of Stress and Periodontitis with Low Birth Weight and Preterm Delivery in Danish Pregnant Women: A Cohort Study.

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ABSTRACT

Introduction

Pregnancy-related hormonal changes may adversely affect oral health and increase the risk of periodontitis. Periodontitis has been associated with **preterm birth (PTB) and low birth weight (LBW).** Maternal stress has also been proposed as potential risk factor for adverse birth outcomes, but the combined effect of stress and periodontitis on such outcomes remains unclear.

Aim

To investigate the association between periodontitis and (PTB and/or LBW) and whether this association is influenced by perceived stress.

Methods

This **prospective cohort** study included 552 Danish pregnant women. Demographic data were collected via questionnaire. Stress was assessed using the Perceived Stress Scale (PSS-10), and periodontitis was diagnosed clinically by a trained dentist. Both the survey and clinical examinations were conducted between gestational weeks 11 to 20. Logistic regression and interaction tests estimated crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for PTB and LBW.

Results

Of the participants, 11% had healthy gums, 56.7% gingivitis, and 32.3% periodontitis. Smoking and lower education were significantly more common among those with periodontitis **($p < .001$).** Neither periodontitis (aOR for PTB = 0.95, CI: 0.28–3.17; LBW = 1.44, CI: 0.29–7.15) nor stress (aOR for high stress and PTB = 0.98, CI: 0.42–2.28; LBW = 1.09, CI: 0.39–3.03) was significantly associated with PTB or LBW. No significant interaction between stress and periodontitis was observed.

Conclusion

This study did not find statistically significant associations between maternal periodontitis, perceived stress, or their interaction and PTB or LBW. However, larger studies are needed to confirm these findings and investigate the possible relevance of dental health and stress during pregnancy.

CONTENT

1 ABBREVIATIONS

ACTH	Adrenocorticotropic Hormone
APOs	Adverse Pregnancy Outcomes
BMI	Body mass index
BOP	Bleeding on Probing
CAL	Clinical Attachment Loss
CI	Confidence Interval
CNS	Central Nervous System
CPITN	Community Periodontal Index of Treatment Needs
CRH	Corticotropin-Releasing Hormone
CRP	C-Reactive Protein
DALYs	Disability-Adjusted Life Years
FMBS	Full-Mouth Bleeding Score
IL-1	Interleukin-1
IL-6	Interleukin-6
IL-8	Interleukin-8
IOPA	Intra-oral periapical
LBW	Low Birth Weight
LDH	Lactate Dehydrogenase
LMICs	Low- and Middle-Income Countries
MMPs	Matrix Metalloproteinases

OR	Odds Ratio
PGE2	Prostaglandin E2
PLBW	Preterm low Birth Weight
PPD	Periodontal Pocket Depth
PTB	Preterm Birth
TNF-α	Tumor Necrosis Factor-Alpha
USD	United States Dollar
WHO	World Health Organization

2 INTRODUCTION

Global Health Perspective on Oral Health.

Oral health has a vital role in people's lives since the oral cavity is important for facilitating everyday functions and maintaining a good personal identity (Peres et al., 2019). According to Peres et al.(2019) oral health is multidimensional and includes elements ranging from the psychological, physical, and emotional to the social, all essential to overall well-being. Good oral health allows individuals to eat, speak, smile, and socialize comfortably and maintain oral hygiene throughout their lifespan (Peres et al., 2019). Despite its importance, oral diseases remain a significant global health problem. The Global Burden of Disease (2019), reported that around 44.5% of the world's population is affected by Oral diseases, which consist of various chronic conditions that impact teeth and mouth health (Peres et al., 2019; Tu et al., 2023). Oral diseases such as Periodontal, and dental caries are common but preventable. Although being largely preventable, these diseases significantly impact individuals and communities, increasing in prevalence with age (Peres et al., 2019).

Oral health disparities are more common among economically disadvantaged and marginalized communities, often linked to socioeconomic status and social determinants of health (Tonetti et al., 2017). These disparities result in higher rates of untreated oral diseases, causing pain, infections, reduced quality of life, and impaired daily productivity (Tonetti et al., 2017). The financial burden of dental treatments further intensifies these challenges for families and healthcare systems in low socioeconomic settings. Globally, oral diseases including periodontitis create substantial economic costs, estimated at $442 billion (USD) annually (Tonetti et al., 2017). Beyond direct healthcare costs, periodontitis significantly affects economic productivity, primarily through work absenteeism and reduced work capacity. Severe periodontitis alone accounts for an estimated $54 billion in global productivity losses annually (Tonetti et al., 2017). The burden of periodontitis is marked, contributing to 3.5 million disability-adjusted life years (DALYs) (Tonetti et al., 2017). In Denmark, oral diseases impose a significant economic burden. In 2019, total national expenditure for outpatient dental care for private and public sectors reached approximately $1.87 billion, averaging $322 per capita. Productivity losses due to five major oral diseases, including caries, periodontitis, and edentulism, were estimated at $1.68 billion (Jevdjevic & M. Listl, S, 2022; WHO, 2022).

Overview of Periodontitis

Komine-Aizawa et al. (2019) argue that there are two broad periodontal inflammation categories: acute and chronic, both affecting the supportive structures of the teeth. The earliest stage of periodontal inflammation is gingivitis, a reversible inflammatory state of the periodontal soft tissues characterized by swollen gums and bleeding (Peres et al., 2019). If gingivitis remains untreated, it may progress into periodontitis (Komine-Aizawa et al., 2019). Periodontitis is widely defined as a severe inflammatory disorder that leads to the loss of tooth-supporting tissues "including the alveolar bone, cementum, periodontal fibers, and gingiva," eventually resulting in tooth loss (Xu & Han, 2022) (see Figure 1). It develops from a combination of adjustable or unadjustable risk factors, and insufficient dental care practices. Adjustable factors include tobacco use, improper oral hygiene maintenance, uncontrolled diabetes, and obesity. While the unadjustable factors include aging, genetic predispositions, and hormonal changes during pregnancy, which typically return to normal levels after childbirth (Gasner & Schure, 2025; Genco & Borgnakke, 2013).

Periodontitis is known as a 'silent epidemic,' frequently progressing without noticeable symptoms. Untreated periodontal diseases also elevate the risk of developing a systemic condition such as heart disease, pneumonia, atherosclerosis, and type II diabetes mellitus (Bostanci, 2023; Komine-Aizawa et al., 2019). In 2017, the American Academy of Periodontology, in collaboration with the European Federation of Periodontology, updated the 1999 classification of periodontal diseases. The revised system includes three categories: necrotizing periodontal diseases, periodontitis, and periodontitis linked to systemic health disorders (Gasner & Schure, 2025).

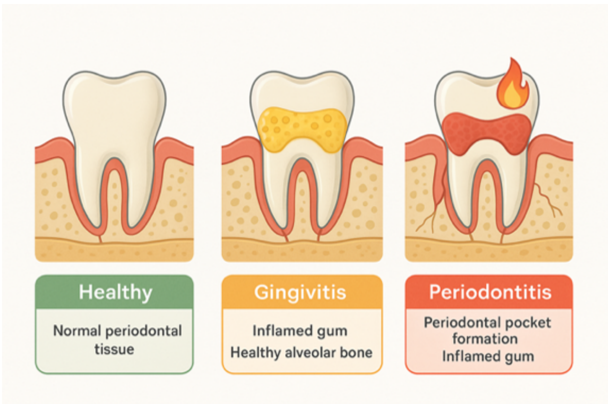


Figure 1: Illustrate the differences between the healthy tooth and tooth affected by gingivitis and periodontitis. Recreated by the author using (OpenAI, 2025) based on (Komine-Aizawa et al., 2019).

Etiology of Periodontitis

Unproper maintaining oral hygiene allows anaerobic pathogenic organisms, such as Porphyromonas gingivalis, Aggregatibacter Actinomycetemcomitans, to colonize subgingival periodontium regions. Bacterial accumulation initiates chronic inflammation by activating pro-inflammatory cytokines and host-derived defense responses. leading to rapid periodontal tissue destruction in susceptible individuals (Albandar, 2002; Gasner & Schure, 2025; Ridgeway, 2000). Key mediators in this inflammatory response include TNF-α, MMPs, IL-1, and IL-8 (Gasner & Schure, 2025).

Pregnancy and Oral Health Changes

Pregnant women face a significant hormonal fluctuation in estrogen and progesterone levels, which reach their highest levels during the second and third trimesters (Bostanci, 2023). By the third trimester, progesterone increase tenfold and estrogen thirtyfold compared to baseline menstrual-cycle levels (Amar & Chung, 1994; Bobetsis et al., 2020). These hormones bind to receptors in periodontal cells, priming tissues for inflammation (Vittek et al., 1982). Elevation in the hormonal levels during gestational weeks correlates with heightened gingival inflammation severity and frequency (Bobetsis et al., 2020). Pregnancy gingivitis is characterized by reddish, edematous gum that easily bleeds during flossing or brushing without damaging the surrounding periodontal tissues. Pyogenic granuloma is a rare, benign, and localized type of gingivitis that affects around 0.5% to 10% of pregnant women. More common is diffuse pregnancy-associated gingivitis, impacting 30% - 50% of pregnant women (Bobetsis et al., 2020; Bostanci, 2023). Christensen et al. (2003) assessed periodontal health among 1,935 pregnant women in Denmark and found that one-third experienced gingival inflammation. However, this was not fully reflected in the self-reported survey, where only 5% of pregnant women rated their gingival health as poor. Despite experiencing gingival inflammation, only 27% of affected women sought dental care (Christensen et al., 2003). Gingivitis during pregnancy is typically a temporary condition that resolves after childbirth. Nonetheless, oral health issues during pregnancy are common, with prevalence estimates ranging from 30% to 100%, depending on diagnostic criteria (Bostanci, 2023).

Adverse Pregnancy Outcomes (APOs)

Any consequences of fertilization that affect pregnant women between 28 weeks of gestation and the early postnatal period are known as Adverse Pregnancy Outcomes (APOs) (Tadese et al., 2022). These APOs differ from case to case and include preterm birth, miscarriage, stillbirth, abortion, or early neonatal death (Tadese et al., 2022). The wide range of complications that are caused by APOs that could happen either during pregnancy, delivery, and the postnatal period may affect both the pregnant woman and the baby, or either of them (Tadese et al., 2022). Complications such as persistent morning sickness, severe bleeding pre- or post-birth, stillbirth, low birth weight, premature labor, obstructed delivery, high blood pressure conditions, uterine rupture, and infections after childbirth (Tadese et al., 2022). The World Health Organization (WHO) claims that even if most of the APOs' complications are avoidable, approximately 810 women lose their lives every day worldwide (World Health Organization, 2019). Denmark is considered to have one of the lowest maternal mortality ratios globally, with only 4.7 maternal deaths per 100,000 live births reported in 2020 (World Health Organization, 2024).

Two of the most common APOs are low birth weight (LBW) and preterm birth (PTB). PTB refers to the baby's delivery before completing 37 weeks of gestation (less than 259 days). According to an Ohuma et al. (2023) study, around 13.4 million babies were born preterm globally in 2020, making up 9.9% of all live births. PTB is a major contributor to under-five mortality, and is associated with developmental disorders such as cerebral palsy, vision, and hearing impairments, particularly when the birth occurs before 34 weeks of gestation (Figuero et al., 2020). In 2019, PTB was responsible for 900,000 deaths among children under five, accounting for about 17.3% of the 5.2 million in that age group (World Health Organization, 2019). According to Norman et al. (2023), a study on PTB in Nordic countries found that Denmark had the highest PTB rate at 6.2% in 2021. While exact figures for Iceland and Norway were not provided, Finland (using 2020 data) had a lower PTB rate than Denmark and Sweden (Norman et al., 2023). Nearly two-thirds of PTB cases result from the spontaneous onset of labor or premature rupture of membrane (Figuero et al., 2020). PTB also imposes an economic burden. In the USA, it costs around $36 billion annually, mainly due to neonatal intensive care and long-term medical support needs (Figuero et al., 2020).

Low birth weight (LBW) was defined by the World Health Organization (WHO) as when a newborn baby's weight, measured within the first few hours of birth, is less than 2,500 grams (Diabelková et al., 2022). In general, birth weight is considered one of the good indicators of individual general health status. It also plays a crucial role in determining an infant’s physical and psychosocial development and survival chances (Diabelková et al., 2022). LBW has a significant impact on perinatal death and long-term impairment. It also has a significant economic impact due to the increased demand for newborn intensive care, long-term healthcare demands, and decreased productivity. U.S.A spends roughly $36 billion per year (Figuero et al., 2020). Annually, over 20 million babies are born with a LBW, accounting for approximately 15% to 20% of total births worldwide. For this reason, WHO focused on reducing this number by 30% before 2025 (WHO, 2014). In Denmark, the prevalence of LBW has gradually declined from 5.5% in 2000 to 4.8% in 2020, remaining under the global average of 15% to 20% (UNICEF & World Health Organization, 2023).

The association between periodontitis and Adverse Pregnancy Outcomes

The association between periodontitis and APOs operates through two primary mechanisms: (1) direct pathways — migration of oral bacterial remnants to the placenta and fetus, and (2) indirect pathways — alteration of placental function through inflammatory biomarkers such as IL-1, IL-6, TNF-α, and PGE2 (Bobetsis et al., 2020; Xu & Han, 2022). The first study, published in 1996, suggested that periodontitis is a possible risk factor for APOs. Since then, numerous investigations have emphasized the role of poor oral hygiene and complications during pregnancy, shedding light on the importance of periodontitis in APOs (Xu & Han, 2022).

Direct Pathways

The direct transmission hypothesis is supported by several studies demonstrating the presence of oral pathogens such as Bergeyella and Fusobacterium identified in placental compartments, amniotic fluid, and umbilical blood (Han et al., 2006, 2010; Wang et al., 2013; Xu & Han, 2022). Bergeyella and Fusobacterium originate exclusively in the oral cavity and are not found in vaginal microbiota, other bacteria implicated in uterine infections are detectable in both oral and vaginal ecosystems (Xu & Han, 2022). To investigate oral-utero microbial translocation, researchers injected subgingival plaque from periodontitis patients into the bloodstream of pregnant mice. Diverse oral bacteria, such as Aggregatibacter, F. nucleatum, and Streptococcus, were later identified in placental tissue, confirming their ability to migrate from the maternal bloodstream to the uterus (Xu & Han, 2022) (Fig.2).

Indirect Pathways

Beyond direct bacterial migration, systemic inflammation due to periodontal disorders may also contribute to pregnancy complications. Inflammatory molecules, like cytokines and prostaglandins, may enter the bloodstream and influence the placenta and fetal tissues. This can intensify uterine contractions that can lead to premature labor or rupture of the placental membrane (Xu & Han, 2022). Furthermore, pregnant women with periodontitis have higher inflammatory markers, such as IL-1, IL-6, C-reactive protein, fibrinogen, and neutrophils, than those without periodontitis (Xu & Han, 2022). These high levels of pro-inflammatory cytokines help produce prostaglandin in the bloodstream and the placental tissues. Elevated C-reactive protein intensifies inflammation in the amniotic environment, heightening the likelihood of complications such as PTB and preeclampsia (Xu & Han, 2022). It is critical to understand that systemic inflammation and direct bacterial invasion are linked processes. Pathogens often associated with periodontitis, including Fusobacterium nucleatum and Porphyromonas gingivalis, can reach the blood circulation, activating immune responses, promoting toxin production, and contributing to systemic inflammation (Xu & Han, 2022) (see Figure 2). A recent study by Raaj et al. (2024) compared 30 pregnant women with chronic periodontitis to 30 healthy controls. The results showed significantly higher levels of IL-6, lactate Dehydrogenase (LDH), and CRP in the periodontitis group, indicating a systemic inflammatory response associated with periodontal disease during pregnancy.

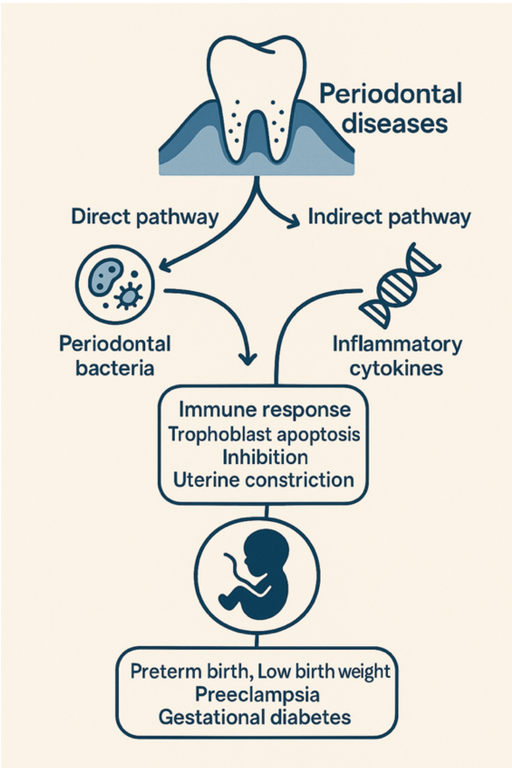


Figure 2: Direct and indirect pathophysiology pathways of periodontitis contributing to adverse pregnancy outcomes. Recreated by the author using (OpenAI, 2025), based on (Komine-Aizawa et al., 2019).

Stress

Nowadays, Stress has become an integral part of people's daily lives, impacting people psychologically and physically. Selye first defined it in 1936 as a “nonspecific response of the body to any demand made upon it.” Abera et al. (2024) summarized Selye's definition as a complex physiological and psychological response to diverse challenges. Stress cannot be eliminated because the body requires energy to function and can adapt to the surrounding environment. Whether the person is awake or asleep, stress remains present. For instance, stress plays a role in essential functions such as breathing, digestion, circulation, and even dreaming, as the brain remains constantly active. The idea that we should understand is that the only state free from stress is death. Despite the common belief that stress is entirely negative, it is necessary for survival. Instead of trying to avoid it, it is more important to focus on understanding how it works and how it is possible to manage to enhance people's lives (Selye, 1973).

In modern societies, stress has become a common issue that has significantly increased in self-reported stress levels. Recent global data shows that 31% of individuals surveyed in 2024 named stress as the top health concern in their country, while around 284 million people worldwide are affected by anxiety disorders (SingleCare Team, 2025). In Denmark, statistics showed a significant increase in reporting high stress during 2013, 2017, and 2021 by 21%, 25%, and 29%, respectively. In 2021, 34% of women reported high stress compared to 25% of men (Sundhedsstyrelsen, 2022, translated using Google Translate). In addition, Stress levels vary by employment status in Denmark, with 23% of employed individuals, 47% of unemployed individuals, 55% of early retirees, and 57% of those outside the labor market reporting high stress (Sundhedsstyrelsen, 2022, translated using Google Translate).

For a better understanding of the stress philosophy, Selye defines “stressors” as biological or psychological agents that disrupt an organism's homeostatic balance (Bathla & Chandna, 2010). Stress can have either positive (eustress) or negative (distress) effects (Bathla & Chandna, 2010). Several **taxonomies** for stress have been developed. One of these classifications divides stress based on duration and impact into two types: (1) acute stress, which is a short-term response to a stressor that occurs suddenly and has a clear beginning and end; and (2) chronic stress, which is a prolonged condition with minimal relief between stressful events (Abera et al., 2024). According to Genco et al. (1998), prolonged stress can impact the human body via biological and behavioral pathways. To explain its impact on periodontal health, Genco et al. (1998) offered two models: the psychological model and the behavioral model.

The physiological model (explains the biological role of stress on periodontal health)

Genco et al. (1998) demonstrate how stress activates the central nervous system (CNS), leading to a chain of hormonal reactions that affect periodontal health (see Figure 3). The pituitary gland produces adrenocorticotropic hormone (ACTH) as a response to the hypothalamus's production of corticotropin-releasing hormone (CRH). This process stimulates the adrenal cortex to produce cortisol. These immune components play a key role in protecting against periodontal infections. Thus, any reduction may promote the growth of pathogenic microorganisms through increased activity of inflammatory mediators such as IL-1 and tissue-degrading enzymes. Furthermore, stress activates the Autonomic Nervous System, stimulating the adrenal medulla to release catecholamines such as adrenaline. Stress-induced hormonal responses promote inflammation and tissue breakdown, which contributes to the advancement of periodontal disease (Genco et al., 1998).

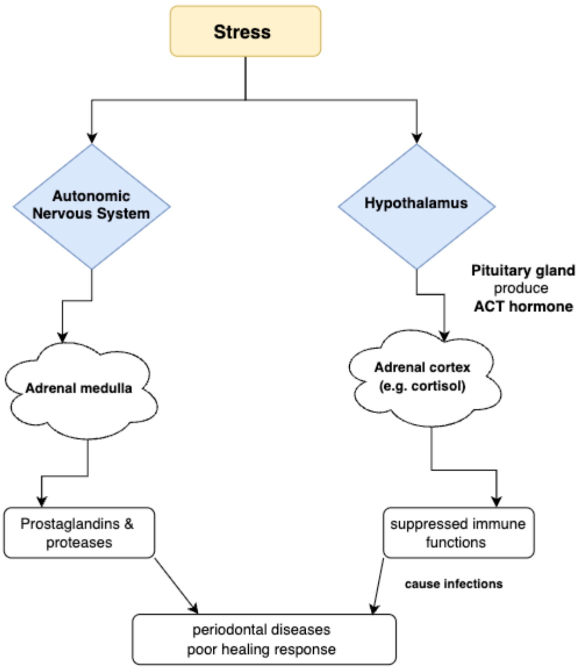


Figure 3: the biological role of stress on periodontal disease, adapted from (Genco et al., 1998).

The psychosocial model (explains the behavioral role of stress on periodontal health)

This model examines how psychosocial stress influences behavioral patterns that contribute to periodontal disease and deterioration of oral health. According to Genco et al. (1998), stress induced behavioral changes, for instance, smoking, neglecting oral hygiene, and failing to follow dental care, can significantly increase the risk of periodontal disease over time (Gunepin et al., 2018). Stress may also lead to emotional and dietary changes, such as excessive consumption of high-fat foods. An unhealthy diet may weaken the human body's immunity by raising cortisol levels, making the body more susceptible to infections, including periodontal diseases. Stress-induced conditions such as depression and distress may further decrease self-care motivation, worsening oral health. Since stress can influence various lifestyle factors, it is essential to consider these behaviors when studying their role in periodontal disease progression (Bathla & Chandna, 2010; Genco et al., 1998; Gunepin et al., 2018). (See Figure 4)

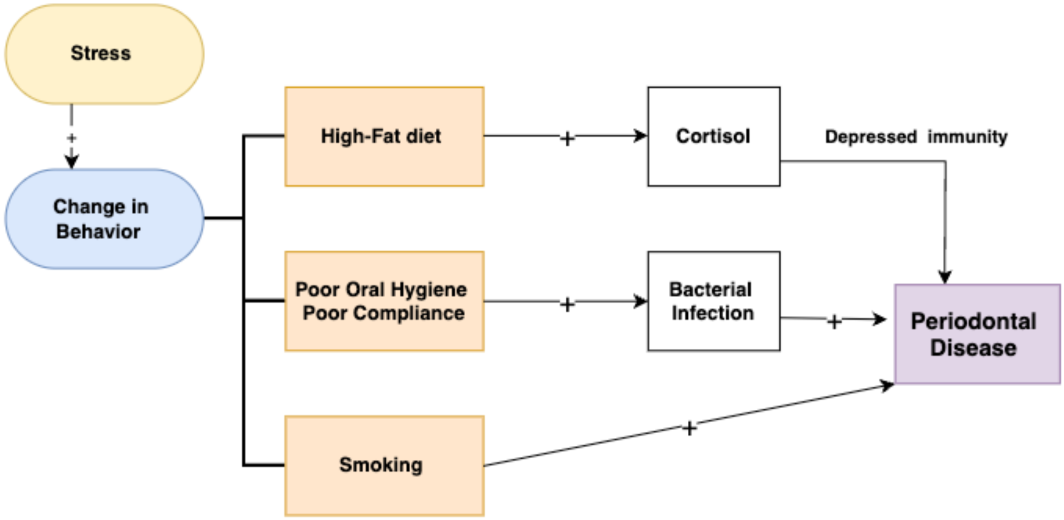


Figure 4: the Behavior role of stress on periodontal disease, adapted from (Genco et al., 1998).

Smoking behavior

Among all stress-related oral habits, smoking is considered to have the most harmful impact on periodontal health. Abu-Ta'a (2014) states that smokers are 7 to 8 times more likely to develop periodontal diseases than non-smokers. Although smokers have an increased risk of periodontal disease, they often exhibit less bleeding on probing due to nicotine's vasoconstrictive effect, which reduces blood flow to the gums. This indicates a reduction in blood flow to the gums due to the release of adrenaline and noradrenaline, which prevents essential nutrients from reaching periodontal tissues. Additionally, smoking weakens immune function by suppressing antibody responses and inhibiting neutrophil activity, making it harder for the body to fight infections in the oral cavity (Gunepin et al., 2018).

Not maintaining oral hygiene, oral habits, and parafunction

Goyal et al. (2013) emphasize that mental health plays a crucial role in maintaining oral hygiene, as psychological stress and emotional disorders can lead to neglect of dental hygiene and may increase plaque accumulation in the oral cavity, which threatens periodontal health integrity (Gunepin et al., 2018). Johannsen et al (2010) found that academic stress negatively impacts the student's oral health, which links exam-related anxiety to both declining oral health behaviors and rising interleukin-1b levels in gingival crevices, highlighting stress as a modifiable risk factor for periodontal inflammation. Parafunction happens due to unusual oral habits such as thumb-sucking and infantile swallowing, though these are less common and may also be related to the Stress effect. Goyal et al. (2013) note that stress can lead to habits such as nail-biting, object-sucking, or pressing the tongue against the teeth. Over time, the repetition of these actions can result in dental displacement and occlusal trauma, both of which increase the risk of periodontal disease (Goyal et al., 2013; Gunepin et al., 2018).

Dietary behavior

Gunepin et al. (2018) explain that emotional well-being directly influences eating habits, such as food consumption and regularity. Stress often leads to cravings for soft, starch-rich foods that require minimal chewing, which can increase dental plaque buildup. Chronic stress also leads to an excessive consumption of fatty foods, which raises cortisol levels and weakens immune responses. These dietary shifts not only exacerbate stress but also raise susceptibility to gum diseases like periodontitis.

The association between stress and APOs (low birth weight and preterm birth)

Globally, between 15 and 25% of pregnant women experience stress during pregnancy (Abera et al., 2024). Research indicates that experiencing stress over short or long periods (Acute or Chronic stress) may lead to allostatic overload, which disrupts hormonal and immune functions in pregnant women and babies (Traylor et al., 2020). These disturbances in homeostasis may increase the risk of APOs, such as LBW, PTB, preeclampsia, maternal mental health disorders, and inflammation-associated depression (Gokoel et al., 2021; Traylor et al., 2020). Many pregnant women face mental health challenges, with anxiety and depression being particularly common during pregnancy (Traylor et al., 2020). Everyday stressors include financial struggles and relationship difficulties, which may worsen due to the biological, psychological, and social changes that occur throughout pregnancy (Traylor et al., 2020). Pregnancy-related stress affects 5.5–15% of women in high-income countries, whereas in low-resource settings, the prevalence is significantly higher, ranging from 33% to 52.9% (Gokoel et al., 2021). Vulnerable groups include socioeconomically disadvantaged individuals, those lacking social networks, younger pregnant women (<20 years), and those with lower educational attainment (Ahmed et al., 2017; Engidaw et al., 2019; Gokoel et al., 2021). Beyond individual concerns, external stressors, such as natural disasters (hurricanes, tornadoes, floods) and global crises like the COVID-19 pandemic, can further elevate stress levels in expectant pregnant women (Traylor et al., 2020).

A study in Denmark used data from over 80,000 pregnancies in the Danish National Birth Cohort (1996-2002) to assess maternal stress at 31 weeks of gestation. Stress was evaluated by using two self-reported scales: one for life stress (including daily burdens and pregnancy-related worries) and another for emotional distress (focusing on anxiety and depressive symptoms) (Bergeron et al., 2023). Primary findings showed that life stress and emotional distress were associated with shorter gestational length. However, this association disappeared after excluding pregnancy-related worries and concerns about the pregnant woman's health from the analysis. This finding raises reverse causality, where stress may be a response to early indicators of pregnancy complications rather than the cause of PTB (Bergeron et al., 2023)

To the best of our knowledge, no prior prospective cohort has tested whether maternal stress modifies the periodontitis and birth outcomes in Danish pregnant women. This study aims to address existing gaps by focusing on Danish pregnant women, measuring stress between gestational weeks 11 and 20, and formally examining whether stress modifies the association between periodontitis and adverse birth outcomes. Although previous research has explored the relationship between stress, periodontitis, and pregnancy outcomes, further studies are needed to clarify whether stress interacts with periodontal disease in influencing birth outcomes.

3 AIM

To investigate the relationship between periodontitis and adverse birth outcomes, PTB and LBW, to assess whether the relationship is stronger in Danish pregnant women experiencing perceived stress compared to those without perceived stress.

RESEARCH QUESTIONS

1- What is the relationship between periodontitis and adverse birth outcomes (PTB and LBW) among Danish pregnant women?

2- Is there an interaction effect between stress and periodontitis on adverse birth outcomes (PTB and LBW) among Danish pregnant women?

3- What is the relationship between perceived stress and adverse birth outcomes (PTB and LBW) among Danish pregnant women?

4 METHODS

The source of the data and study procedures:

This prospective cohort study was based on secondary data originally collected by Prevention of Adverse Pregnancy Outcomes by Periodontal Treatment (PROBE) controlled intervention study, titled “The Prevention of Adverse Pregnancy Outcomes by Periodontal Treatment During Pregnancy (PROBE) A Controlled Intervention Study”. 'Secondary data' refers to data obtained by the PROBE study team for their own research purposes, which were then evaluated here to address the specific aims of this thesis. Recruitment took place in Holbæk and Nykøbing Falster Hospitals in Region Zealand, Denmark. This study used baseline data gathered from pregnant women who participated in the first trial prior to the conclusion of enrollment and follow-up.

Study population:

This cohort study included 552 pregnant women, recruited during a nuchal translucency scan at 13-14 weeks of gestation. All participants had completed their oral examinations by March 25, 2024, which marked the end of recruitment and data inclusion. Baseline data were collected before this point, and participants were followed up accordingly. Data collection involved a periodontal examination conducted by a licensed dentist and self-administered questionnaires. The questionnaires covered socioeconomic, demographic data, general and oral health habits, medical and dental history, and the Perceived Stress Scale (PSS-10). The dataset utilized for this investigation did not include information on whether the pregnancies were singletons or multiples. Moreover, the survey and examinations were conducted during gestational weeks 11 to 20. This time window was selected primarily for logistical and practical reasons related to scheduling routine prenatal visits in the clinical setting, rather than based on a specific scientific rationale. As a result, all pregnancies were included, regardless of plurality status. Inclusion criteria were: pregnant women aged 18 years or older, receiving prenatal care at Holbæk and Nykøbing Falster Hospitals in the Region of Zealand, Denmark, who could speak and understand Danish, and who planned to give birth in one of the previously mentioned hospitals. Exclusion criteria were: diagnosed with stage

IV periodontitis or having fewer than 20 remaining teeth.

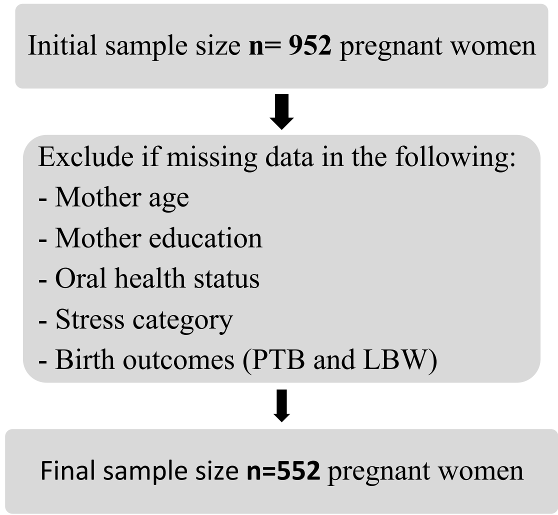


Figure 5. Participant Flow Diagram for Inclusion in the Final Analytic Sample

Data collection:

Clinical and Periodontal examination:

Pregnant women had a complete periodontal examination by a licensed dentist. To ensure measurement validity, the following periodontal parameters were assessed: plaque index (PI), bleeding on probing (BOP), probing pocket depth (PPD), and clinical attachment loss (CAL). These measurements were taken at baseline between gestational weeks 11 and 20. All teeth, except third molars, were examined at six sites per tooth. The plaque index was assessed by examining four sides per tooth (Heitz-Mayfield, 2024). The periodontal examination was conducted by using an American Eagle P2-12B probe.

The diagram shows the American Eagle P2-12B probe, adopted from plandent.dk

A. Probing pocket depth examination (PPD):

Probing pocket depth is used as an indirect measure of inflammation, as periodontal tissues affected by inflammation become more susceptible to probing, resulting in increased depth readings. PPD was measured on six sites per tooth and recorded in millimeters (mm). It was calculated by measuring the distance between the free gingival margin (FGM) and the base of the gingival pocket using an American Eagle P2-12B probe, with readings rounded to the nearest millimeter (Heitz-Mayfield, 2024).

B. Bleeding on probing (BOP)

Bleeding on probing is a common sign of gingivitis and is used as one of the periodontal examination parameters. Using the same periodontal probe, BOP was measured by averaging the gingival bleeding across the six tested sides per tooth. The clinical test was done by implementing a gentle probing force of 0.25 N, and bleeding was evaluated within 10 seconds of probing. The average number of bleeding points was calculated using the full-mouth bleeding on probing score (FMBS) formula (Heitz-Mayfield, 2024).

$$FMBS\ (\%) = (\text{Number of bleeding sites} / \text{Total number of sites examined}) \times 100$$

C. Plaque Index (PI)

This index, developed by Silness and Löe, assesses the amount of dental plaque at the cervical margin of the teeth. A disclosing agent was used to stain the plaque, making it easier to identify plaque sites and calculate the average of the present plaque (Heitz-Mayfield, 2024).

D. Clinical Attachment Loss (CAL)

Clinical Attachment Loss evaluates tissue destruction caused by periodontists. It was calculated at six sites per tooth using the distance between cementoenamel junction (CEJ), the free gingival margin (FGM), and the base of the periodontal pocket. The CEJ served as a fixed reference point to determine the extent of attachment loss (Heitz-Mayfield, 2024).

The definition of periodontal health

Healthy periodontium is characterized by no bleeding or the percentage of FMBS below 10%, PPD of 3 mm or less, and no clinical attachment loss. Gingivitis was defined as the FMBS of at least 10% and no signs of clinical attachment loss. Periodontitis is identified by the presence of CAL of at least 1 mm at two or more non-adjacent teeth, or buccal/lingual CAL of 3 mm or more on at least two teeth, which may include adjacent teeth (Heitz-Mayfield, 2024). The periodontal health variables will be treated as categorical variables (Healthy = 1, Gingivitis = 2, Periodontitis = 3).

Perceived Stress Scale (PSS):

Cohen, S et al. (1983) invented the PSS, a self-report tool for evaluating how unpredictable, uncontrollable, or overwhelming a person perceives their life circumstances. Since its invention, the PSS test has been referenced over 30,000 times and extensively used to examine the effects of stress on healthy individuals and those with medical conditions (Harris et al., 2023). Furthermore, PSS assesses recent stress levels by asking respondents to rate their thoughts and feelings during the past month. It also helps evaluate whether a person feels that their experiences have surpassed their capacity for adaptation. According to Harris et al. (2023), PSS has shown that stress is linked to a variety of health consequences, including delayed wound healing, increased infection susceptibility, and cardiovascular disease. Similarly, it has helped to pinpoint the physiological and behavioural processes that mediate the link between stress and general health (Harris et al., 2023). The PSS is available in three versions: 14-item (PSS-14), 10-item (PSS-10), and 4-item (PSS-4). Research has shown that all three versions are helpful tools for assessing perceived stress (Harris et al., 2023).

PSS-10 Questionnaire:

Scoring guidelines produce one overall stress score. Research on the PSS-10 and PSS-14 indicates that stress may be measured in perceived helplessness and self-efficacy. The PSS-10 and PSS-14 have strong internal reliability (Cronbach's $\alpha \geq 0.75$), while the PSS-4 is less reliable due to its fewer items (Cronbach's $\alpha = 0.60$) (Harris et al., 2023). In the present study, the PSS-10 demonstrated good internal reliability, with a Cronbach's alpha of 0.84, confirming its reliability for use in this cohort.

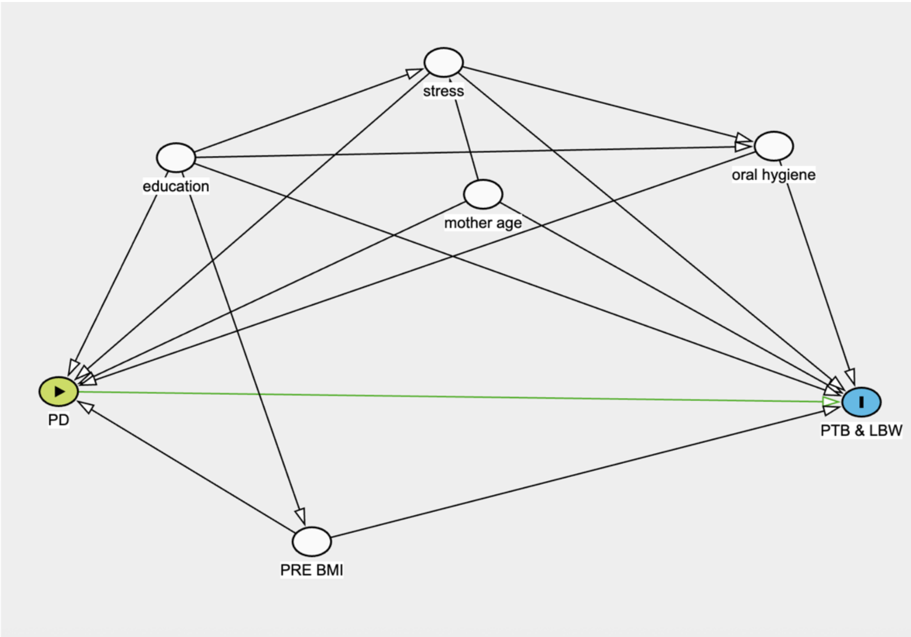
Sheldon Cohen & Gail Williamson, (1988) found that the PSS-10 is equally efficient in assessing perceived stress as the PSS-14. It has a more precise factors structure and better internal reliability (Sheldon Cohen & Gail Williamson, 1988). The PSS-10 is also considered to be unbiased across different demographic groups, making it a widely applicable stress assessment tool (Sheldon Cohen & Gail Williamson, 1988). Based on these findings, the Danish version of the PSS-10 was used in this study (see appendix). Perceived stress was measured at the baseline between gestational weeks 11 and 20. Perceived stress in this study was classified based on sample quartile into the following subcategories: Low stress (≤19), Moderate stress (20–26), and High stress (≥27). The pass-10 questions are divided into Negative Event Questions (1,2,3,6,9,10) and positive event questions (4,5,7,8). The negative item scoring uses the following scale: 0 = Never, 1 = Almost Never, 2 = Sometimes, 3 = Fairly Often, and 4 =

Very Often. The Positive items use a reverse scale: 0 = Very often, 1 = Fairly Often, 2 = Sometimes, 3 = Almost Never, 4 = Never.

Outcomes

The primary outcomes are the PTB (defined as giving birth before completing gestational week 37) and LBW (defined as the baby's weight at delivery being lower than 2500 grams). Both outcomes are treated as binary variables. Data on birth outcomes were obtained from medical records at Holbæk and Nykøbing Falster Hospitals.

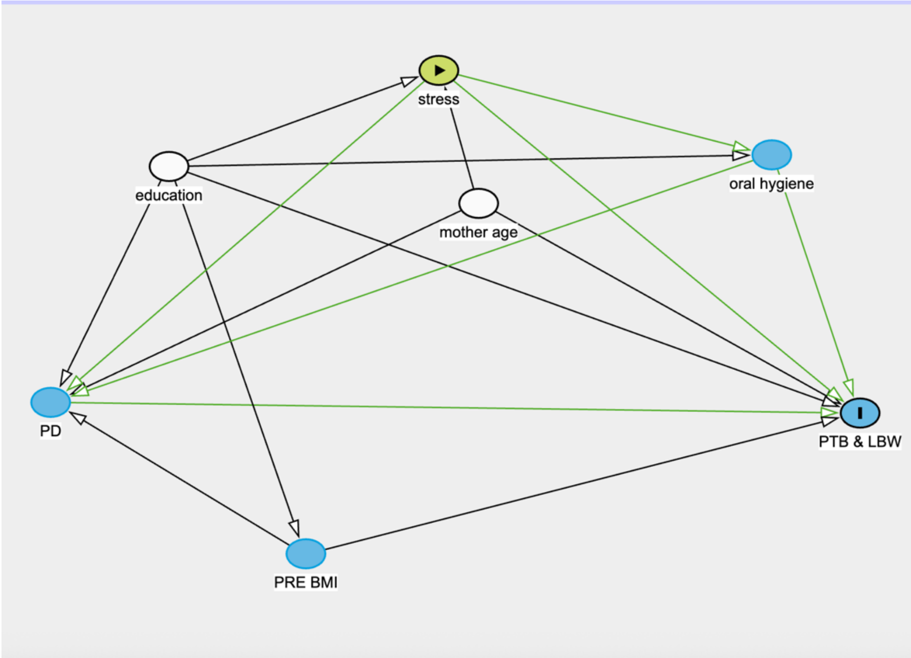
Figure 6. Directed Acyclic Graph (DAG) illustrating the hypothesized relationships between periodontitis, and adverse birth outcomes.



***Note**: Colored nodes indicate exposure and outcome variables→ Yellow: Exposure (Periodontal Disease – PD), blue: Outcome (Preterm Birth [PTB] and Low Birth Weight [LBW]), all other variables (in white) represent adjusted potential confounders. Arrows represent assumed directional relationships based on theoretical and empirical evidence. The green arrow represents the primary causal path of interest between the exposure periodontitis (PD) and the outcome (PTB & LBW).*

To answer the first research question in the study, A Directed Acyclic Graph (DAG) was used to determine the choice of the correct confounder and understand the causal pathway between periodontitis (PD) and adverse birth outcomes (PTB and LBW). The minimal adjustment to the potential confounders was maternal age, pre-pregnancy BMI, education, oral hygiene habits (dental visit within the last year), and perceived stress. BMI was collected pre-pregnant at the nuchal scan appointment, and the remaining variables were assessed between gestational weeks 11 and 20. Stress in this study was treated as a confounder and examined as a modifier. Other uncontrolled confounders, such as smoking and alcohol consumption, were excluded from this model due to the lower prevalence and insufficient variation in our sample. It is well known in the Danish maternal population that pregnant women avoid the consumption of alcohol and smoking.

Figure 7. Directed Acyclic Graph (DAG) illustrating the hypothesized relationships between stress, and adverse birth outcomes.



***Note**: Colored nodes indicate the primary exposure, outcome, and key variables under investigation→ Yellow: Exposure (Perceived Stress), blue: Outcome (Preterm Birth [PTB] and Low Birth Weight [LBW]), Light Blue: mediators (e.g., PD, oral hygiene, pre-pregnancy BMI), white: adjusted Confounders (e.g., education, maternal age). Arrow colors → Black arrows indicate assumed theoretical pathways. Green arrows highlight the primary hypothesized pathways being investigated in this model.*

To answer the third research question in the study, DAG was used to determine the potential confounders for estimating the total effect of perceived stress as exposure on adverse birth outcomes. This model treated periodontitis as a mediator in the causal pathway between stress and birth outcomes. The adjustment variable set included maternal age and education. Since this study assessed BMI before stress measurements, no arrows were drawn from stress to pre-BMI. Though related to both periodontitis and outcomes, oral hygiene was not included in the final adjustment set as it lies on the causal pathway and acts as an intermediate. Adjusting for the educational and maternal age ensured that the total effect of stress on PTB and LBW was estimated without overadjustment.

Potential Confounders:

This study adjusted for possible confounders, including demographic, behavioral, and lifestyle factors. Demographic confounders include maternal age (in years) and pre-pregnancy BMI (in kg/m²). Socioeconomic status was assessed based on the level of education, categorized as **low** (primary school or less, vocational education, upper secondary education, or short higher education ≤3 years), **medium** (3–5 years), **high** (≥5 years), and **unspecified**. last dental visit (within the past year or more than a year ago). Pregnancy lifestyle habit variables include smoking (non-smokers or smokers) and alcohol consumption (non-drinker or drinker).

Data Analysis and Statistical Software

Statistical analyses were performed using Stata 18 (StataCorp, College Station, TX, USA) and R version 4.4.1(R Core Team, 2024). Descriptive analyses were conducted in which the demographic data, socioeconomic status (education, visiting a dentist), habits (smoking and alcohol consumption), stress levels, and birth outcomes (PTB and LBW) were compared between the oral health status groups. PTB and LBW were further analyzed across different oral health and stress level groups using bivariate methods. Categorical variables were summarized, and the proportion and the relative frequencies were presented in a column percentage using Pearson's chi-square test.

The normality of continuous variables was assessed using histograms and the Shapiro-Wilk test. As the distributions were not normal distributed, continuous variables, including maternal age (years), and pre-pregnancy BMI (kg/m²), were summarized using medians and interquartile ranges (IQR). Median usage provides more robust estimates of central tendency in the presence of skewed data. Participants with missing data on the exposures and outcomes were excluded.

Crude and adjusted logistic regression were performed to analyze the relation between periodontitis and birth outcomes. The model was adjusted for potential confounders, including the pregnant women's age, BMI, education, stress, and dental visit history. Interaction analysis was conducted by using Firth logistic regression due to the small events observed in the subgroups. Firth logistic regression used to examine the crude and the adjusted potential effect modification between periodontitis and stress levels on birth outcomes (PTB and LBW). Another crude and adjusted model was applied to study whether there is an association between stress levels and birth outcomes. The model was adjusted for maternal age and education in this test. The results were reported as odds ratio (OR), 95% Confidence interval (CI), and a two-sided p-value of <0.05 was considered statistically significant.

Ethical consideration:

This study was based on secondary data obtained from the PROBE controlled intervention study. The PROBE study was approved by the Committees on Health Research Ethics in the Capital Region of Denmark and the Danish Data Protection Agency (Registration Number: H-20083249), and it was registered at ClinicalTrials.gov (NCT06110143). Since the data used in this thesis were anonymized and originally collected for the PROBE study, no additional ethical approval was required. Data access and analysis were conducted at the Parker Institute under appropriate data protection protocols, ensuring that participant confidentiality was maintained throughout. All procedures adhered to the ethical principles outlined in the Declaration of Helsinki.

5 RESULTS

This prospective cohort study analyzed 552 pregnant women in their 1st trimester of pregnancy. The demographic data, stress levels and birth outcomes as per oral health status represent by Table 1.

Table 1. Baseline Demographic characteristics, as per oral health status.

Characteristic	Healthy status	Un-healthy status		p-value
	Healthy gum (n=61)	Gingivitis (n=313)	Periodontitis (n=178)	
*** Demographic data, Median (IQR)**				
Age (years)	30.0 (26-33)	29.0 (24-34)	30.0 (23-37)	**0.25**
Pre-pregnancy BMI (kg/m²)	24.6 (18.6-30.6)	25.8 (18.9-32.7)	25.8 (17.3-34.3)	**0.72**
Socioeconomic status				
♣Education, n (%)				
Low educational level	22 (36.1)	133 (42.5)	108 (60.7)	
Medium educational level	31 (50.8)	125 (39.9)	46 (25.8)	
High educational level	7 (11.5)	51 (16.3)	19 (10.7)	
Unspecified	1 (1.6)	4 (1.3)	5 (2.8)	
p-value				**<0.001**
♣Visiting dentist, n (%)				
Within last year (6 months to a year)	41 (67.2)	205 (65.5)	72 (40.5)	
More than one year (> 1)	20 (32.8)	108 (34.5)	106 (59.5)	
p-value				**<0.001**
♣Habits				
Smoking status, n (%)				
Nonsmoker	60 (98.4)	291 (93.0)	133 (75.0)	
Smoker	1 (1.6)	22 (7.0)	44 (25.0)	
p-value				**<0.001**
Alcohol consumption during pregnancy, n (%)				
No	60 (98.4)	309 (98.7)	177 (99.4)	
Yes	1 (1.6)	4 (1.3)	1 (0.6)	

Characteristic	Healthy status	Un-healthy status		p-value
	Healthy gum (n=61)	Gingivitis (n=313)	Periodontitis (n=178)	
p-value				**0.34**
♣Stress Level, n (%) (PSS-10 scale)				
Low (≤19)	13 (21.3)	87 (27.8)	51 (28.7)	
Moderate (20–26)	34 (55.7)	134 (42.8)	70 (39.3)	
High (≥27)	14 (23.0)	92 (29.4)	57 (32.0)	
p-value				**0.28**

*Note: Un-healthy status split into gingivitis /periodontitis; BMI, body mass index; IQR, interquartile range; (pss-10), Perceived Stress Scale – 10 item version. * Data are presented as medians with interquartile ranges for continuous variables.♣ Data are presented as counts and percentages for categorical variables. P-values are based on chi-square tests for categorical variables and Kruskal–Wallis tests for continuous variables.*

Baseline characteristics for the 552 participants were presented according to their oral health status. In our sample, 61 pregnant women had healthy gums, while the remaining participants were categorized as having gingivitis (n=313) or periodontitis (n=178) based on their periodontal diagnosis. The median age of the participants in the healthy gum group and periodontitis group was 30 years (IQR: 26-33) and 29 years (IQR: 25-32) for the gingivitis group, with no statistically significant difference among the three groups (P= 0.25). Similarly, the median BMI in the healthy group was 24.6 kg/m² (IQR: 18.6-30.6); in gingivitis and periodontitis, it was 25.8 kg/m² (IQR: 18.9-32.7), and 25.8 kg/m² (IQR: 17.3-34.3) respectively (see Table 1). Although there were no statistically significant differences between the groups (P= 0.72), the periodontitis group had a slightly higher median BMI than the healthy gum group (25.8 kg/m² vs. 24.6 kg/m²). The educational level across the oral health status was statistically significant (P<0.001). Pregnant women with periodontitis had the highest proportion of low educational level (60.7%), followed by those with gingivitis (42.5%) and healthy gums (36.1%). Medium educational levels were more frequent among the healthy gum (50.8%) and the lowest among the periodontitis group (25.8%). The frequency of Visiting dentists differed significantly between oral health groups (P<0.001). Most women with healthy gum (67.2%) and gingivitis (65.5%) reported to dental clinics within the past year, while this was less common among those with periodontitis (40.5%). Smoking during pregnancy was statistically significant (P<0.001) and more prevalent among the periodontitis group, where (24.7%) of women reported smoking during pregnancy, compared to (7%) in the gingivitis group and only (1.6%) in the healthy group. No significant differences were found for alcohol use during pregnancy (P = 0.34), with nearly all participants in all groups reporting no alcohol consumption. Based on the PSS-10 scale, stress levels were not significantly different across groups (P= 0.28). Moderate stress was the most common across all groups. The proportion of women who had PTB and LBW did not differ significantly across oral health groups (P = 0.98 and P = 0.81, respectively; see Table 2)

Table 2. Distribution of PTB and LBW by oral health status

Birth outcomes	Healthy gum (n=61)	Gingivitis (n=313)	Periodontitis (n=178)	P-value
***PTB, n (%)**				
No	57 (93.4)	290 (92.7)	165 (92.7)	
Yes	4 (6.6)	23 (7.3)	13 (7.3)	
p-value				**0.98**
***LBW, n (%)**				
No	59 (96.7)	300 (95.9)	169 (94.9)	
Yes	2 (3.3)	13 (4.1)	9 (5.1)	
p-value				**0.81**

*Note: *PTB, preterm birth; LBW, low birth weight.*

PTB and LBW rates by different Maternal Stress Levels

Table 3 depicts the rate of the PTB and LBW by the stress levels. No clear trend was observed between maternal stress levels and birth outcomes. PTB rate was (7.9%) in the low-stress group (12/151), (6.7%) in the moderate group (16/238), and (7.4%) in the high-stress group (12/163), with no statistically significant difference (p = 0.90). LBW ranged from 3.8% to 4.9% (p = 0.85), showing no significant variation between stress categories.

Table 3. PTB and LBW Rates According to Maternal Stress Level

Stress Level	Total number	PTB (n/Total)	PTB Rate (%)	LBW (n/Total)	LBW Rate (%)
Low	151	12/151	7.9	7/151	4.6
Moderate	238	16/238	6.7	9/238	3.8
High	163	12/163	7.4	8/163	4.9
P-value	**p = 0.90**			**p = 0.85**	

Note: PTB, Preterm Birth; Distribution of PTB (<259 days) across different stress categories; LBW, Low birth Weight; Distribution of LBW (<2500 g) across different stress categories. Chi square test.

Crude logistic regression analysis revealed that neither PTB nor LBW was statistically associated with maternal oral health (see model 1 in Table 4). All confidence intervals crossed one, indicating no group was at an increased or decreased risk. In addition, model 2 was the adjusted logistic regression to examine the oral health status on the adverse birth outcomes, controlling for maternal age, BMI, oral health status, stress levels, maternal education, and dental visits. There was no statistically significant association between oral health status and the odds of PTB or LBW (Table 4). All adjusted odds ratios had confidence intervals that included 1, suggesting no meaningful effect of these exposures on birth outcomes. For instance, compared to women with healthy gums, those with periodontitis had an adjusted OR of 1.44 (CI: 0.29–7.15) for LBW, and those with gingivitis had an adjusted OR of 1.26 (CI: 0.27–5.79), both nonsignificant. Similarly, neither moderate nor high-stress levels significantly increased the odds of PTB or LBW. Additional detailed information on the adjusted results is in the Appendix (Table A4).

Table 4. Crude and adjusted Odds Ratios for Oral Health with PTB and LBW

Characteristic	PTB OR [95% CI]		LBW OR [95% CI]	
	Model 1	Model 2	Model 1	Model 2
Healthy (ref)	–	–	–	–
Gingivitis	1.13 [0.38 – 3.39]	0.96 [0.32–2.95]	1.28 [0.28 – 5.81]	1.26 [0.27–5.79]
Periodontitis	1.12 [0.35 – 3.58]	0.95 [0.28–3.17]	1.57 [0.33 – 7.48]	1.44 [0.29–7.15]

Note: Model 1is the crude logistic regression; Model 2 is the adjusted model for mother age, BMI, mother education, visiting dentist and stress levels. PTB, Preterm Birth; LBW, Low birth Weight. Exponentiated coefficients; 95% confidence intervals (CI) in brackets; $^{*}\ p < 0.05$, $^{**}\ p < 0.01$, $^{***}\ p < 0.001$.

Interaction between oral health status and perceived stress on PTB and LBW

On one hand, the interaction analyses were conducted to explore whether the interaction between oral health status and stress was associated with PTB and whether it varied by perceived stress levels. None of the interaction terms in the crude model (Model 1) showed statistically significant associations. This illustrates that, compared to the reference group (having healthy periodontal status and low stress), those with gingivitis and high stress had an OR of 4.97 (95% CI: 0.10–103.67, $p = 0.50$). Similarly, among women with periodontitis, those experiencing high stress had an OR of 3.85 (95% CI: 0.11–132.47, $p = 0.46$) compared to those with low stress (see Table 5).

Although the adjusted model (Model 2) included maternal age, pre-pregnancy BMI, education, and dental visit, the interaction terms remained non-significant. Gingivitis with high stress had an adjusted OR of 4.97 (95% CI: 0.15–167.18, p = 0.37), while periodontitis with high stress had an adjusted OR of 6.76 (95% CI: 0.19–246.57, p = 0.30) (see Table 5).

Table 5. Interaction term (oral health status x stress levels) on PTB and LBW

Characteristic	N	PTB OR [95% CI]				LBW OR [95% CI]			
		Model 1	P (M1)	Model 2	P (M2)	Model 1	P (M1)	Model 2	P (M2)
Gingivitis × Moderate Stress	134	0.88 [0.09 – 8.36]	0.91	0.92 [0.09 – 9.27]	0.94	2.93 [0.21 – 41.11]	0.43	2.88 [0.20 – 41.0]	0.44
Gingivitis × High Stress	92	4.97 [0.10 – 103.67]	0.50	4.97 [0.15 – 167.18]	0.37	1.78 [0.05 – 68.37]	0.76	1.88 [0.05 – 75.44]	0.74
Periodontitis × Moderate Stress	70	0.77 [0.07 – 8.81]	0.84	1.21 [0.09 – 14.90]	0.88	1.15 [0.05 – 26.10]	0.93	1.25 [0.05 – 29.50]	0.89
Periodontitis × High Stress	57	3.85 [0.11 – 132.47]	0.46	6.76 [0.19 – 246.57]	0.30	8.70 [0.25 – 324.33]	0.24	9.79 [0.25 – 379.24]	0.22

Note: *reference group (healthy x low stress). The main effects of stress levels (Moderate, High) represent the comparison within the healthy group. Interaction terms reflect differences among gingivitis or periodontitis groups relative to the reference.PTB, Preterm Birth; LBW, Low birth Weight Model 1 (M1) is the crude logistic regression model; Model 2 (M2) is the adjusted model for maternal age, BMI, maternal education, and recent dental visit. Exponentiated coefficients; 95% confidence intervals (CI) are shown in brackets. P: p-value.*

On the other hand, the Interaction analyses between oral health status and stress levels showed no statistically significant associations with LBW in either the crude or adjusted models. Compared to women in the reference group, those with gingivitis and high stress the crude model (model 1) had an adjusted OR of 1.78 (95% CI: 0.05 – 68.37), and while in the adjusted model (model 2) showed adjusted OR of 1.88 (95% CI: 0.05–75.44). Similarly, women with periodontitis and high stress showed an increased odds of LBW compared to reference group for the adjusted model (adjusted OR = 9.79, 95% CI: 0.25–379.24). However, this association was not statistically significant (see Table 5). It is important to note that several estimates showed very wide 95% confidence intervals (see Table 5). These wide intervals likely reflect the limited number of participants in some exposure subgroups, leading to imprecise effect estimates.

Table 6 shows the crude (model 1) and adjusted ORs (model 2) for the association between perceived stress levels and the odds of PTB and LBW. Compared to women with low stress levels, neither moderate nor high stress levels were significantly associated with PTB or LBW in either the crude or adjusted models. For PTB, the crude OR for high stress was 0.92 (95% CI: 0.40–2.12), and for LBW, the adjusted OR for high stress was 1.09 (95% CI: 0.39–3.03). Both crude and adjusted analyses showed no statistically significant associations between stress levels and birth outcomes. Additional detailed information on the adjusted results is in the Appendix (Table A6).

Table 6. Crude and adjusted Odds Ratios for Stress levels with PTB and LBW

Characteristic	**PTB OR [95% CI]**		**LBW OR [95% CI]**	
	Model 1	**Model 2**	**Model 1**	**Model 2**
Low Stress (ref)	–	–	–	–
Moderate Stress	0.83 [0.38 – 1.82]	0.84 [0.38–1.83]	0.81 [0.30 – 2.22]	0.83 [0.31–2.22]
High Stress	0.92 [0.40 – 2.12]	0.98 [0.42–2.28]	1.06 [0.38 – 3.00]	1.09 [0.39–3.03]

Note: Model 1is the crude logistic regression; Model 2 is the adjusted model for mother age, and mother education. PTB, Preterm Birth; LBW, Low birth Weight. Exponentiated coefficients; 95% confidence intervals (CI) in brackets; $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

6 DISCUSSION

The present study investigated whether maternal periodontitis and/or elevated self-reported stress during early pregnancy were associated with adverse birth outcomes, specifically preterm birth (PTB) and low birth weight (LBW). No statistically significant associations were found between periodontitis diagnosed in the first trimester and either PTB or LBW. Similarly, baseline stress levels measured between gestational weeks 11 and 20 were not significantly associated with these outcomes. The crude and adjusted interaction models testing whether stress modified the association between periodontitis and birth outcomes also yielded no statistically significant results.

These findings both align with and diverge from prior literature. For instance, the results are consistent with some cohort studies cited in the review by Bobetsis et al. (2020), including studies by Agueda et al. (2008) and Ercan et al. (2013), which also did not find significant associations between maternal periodontitis and PTB or LBW. In terms of psychosocial stress, while several studies suggest a positive association between stress and periodontal disease, the systematic review by Peruzzo et al. (2007) highlights inconsistencies. Studies such as those by Castro et al. (2006) and Solis et al. (2004), for example, found no significant results.

In contrast, many observational studies have reported a direct association between maternal periodontal disease and adverse pregnancy outcomes (Bobetsis et al., 2020; Karimi et al., 2023; Y.-L. Lee et al., 2022). Offenbacher et al. (1996) first highlighted this link, reporting significantly higher odds of PTB and LBW in women with clinical periodontitis. A recent meta-analysis by Karimi et al. (2023) demonstrated that pregnant women with periodontitis were about twice as likely to deliver a LBW infant (95% CI: 1.82–2.64). PTB showed a relatively modest connection, with a pooled relative risk of 1.10 (95% CI: 1.08–1.12). However, Karimi et al. (2023) also highlighted the significant variation in the definition and diagnosis of periodontitis between studies, making it more challenging to assess pooled effects estimates. Such diagnostic heterogeneity highlights the need for unified case definitions for future research and may assist in clarifying discrepancies among studies.

The prevalence of gingivitis in our sample (56.7%) was comparable to that reported among pregnant women in general. For example, an estimated 60–75% of pregnant women experience gingivitis (CDC, 2024). Likewise, the periodontitis rate in our cohort (32.3%) was slightly below the approximately 40% prevalence observed in pregnant populations globally (Chen et al., 2022)

In terms of psychosocial factors, our participants exhibited relatively high perceived stress. In this cohort study, stress categories were defined using sample quartiles, which created specific cutoffs that distributed participants evenly across stress levels. Using quartiles may explain why the proportions were approximately 27.4% for low stress, 43% for moderate stress, and 27% for high stress. Since Sheldon Cohen did not define a specific cutoff for the PSS-10, it is challenging to directly compare our findings with those of other studies, as researchers such as Arteaga-Guerra et al. (2010), Coelho et al. (2020), and Cohen and Williamson (1988) employed different classification methods and cutoffs. It should be noted that direct national data on periodontal health and stress in pregnant Danish women are limited, which constrains precise comparisons. These findings underscore the need for more comprehensive Danish surveillance of prenatal oral health and stress levels among pregnant women.

Discrepancies between the present results and prior studies may stem from differences in study design, stress measurement tool, timing, populations studied, confounder control, and definitions of periodontal disease. Arteaga-Guerra et al. (2010) for example, used a case-control design assessing both periodontal disease and stress retrospectively, increasing the risk of recall bias. In contrast, the current prospective cohort design reduced such biases by assessing both exposures during early pregnancy. This approach better preserves temporality and reduces the risk of recall bias.

Regarding stress measurement, this study used the PSS-10 scale as other studies (Ahmed et al., 2017; Arteaga-Guerra et al., 2010; Coelho et al., 2020). According to E.-H. Lee (2012), the PSS-10 scale is more favorable for use because it showed higher internal reliability, reliable test-retest scores, and a more transparent factorial structure over the PSS-14. Moreover, the timing of stress measurement is crucial. In the present study, the stress was measured once at weeks 11 and 20. In, stress was measured at two different times: at gestational weeks 24 and 28, and then it was remeasured at weeks 32 and 36 before the delivery. The results show that the stress increased more at the time of delivery than at the first time measured.

This study concentrated on the Danish pregnant women, and not stratify the population based on different ethnic groups (white, black, Asian, etc.), as many studies include various ethnic groups. In the United States, Vianna et al. (2011) found that racism and discrimination based on skin color may increase stress levels and may play a role in discrepancies in adverse birth outcomes. If a similar case had happened and not been detected in the present study, it may have impacted the result of our analysis. Consequently, results may underestimate the associations between stress, periodontitis, and birth outcomes in more heterogeneous individuals.

Based on the DAG, we adjusted for a selected set of key confounders such as maternal age, pre-pregnancy BMI, education level, and dental visit history, based on theoretical relevance and data availability. In contrast, it did not control for smoking or alcohol habits, oral hygiene habits (brushing and flossing) diseases such as hypertension, diabetes, autoimmune diseases, pulmonary diseases and vaginal infections as in (Coelho et al., 2020; Y.-L. Lee et al., 2022). Evidence supporting the negative impact of smoking on pregnancy outcomes and oral health comes from large-scale and systematic research. For instance, a cross-sectional study involving over 20,000 pregnancies by Tarasi et al. (2022) reported that maternal smoking was associated with an increased risk of several adverse perinatal outcomes, including low birth weight (adjusted OR = 1.78; 95% CI: 1.53–2.08) and a 16% higher odds of preterm delivery compared to non-smoking pregnant women. Similarly, a systematic review by Leite et al. (2018) demonstrated that tobacco use significantly increases the risk of developing periodontitis, with smokers having an 85% higher risk than non-smokers. Together, these findings underscore the dual role of smoking in affecting both oral and reproductive health, making it a critical variable in studies examining these outcomes. Although smoking is a known confounder for both periodontal disease and birth outcomes, it was not included in the adjusted models in this study; the rationale and implications for this decision are discussed in the limitations section.

This study classified "oral health status" into healthy gum, gingivitis, and periodontitis based on different definitions. The study by Manau et al. (2008) emphasizes that different periodontitis case definitions may shape the observed associations between periodontitis and adverse pregnancy outcomes. The definition used by López et al. (2002) was the nearest to the one used in the study. It requires at least four teeth, each with at least one site exhibiting probing pocket depth (PPD) ≥4 mm and clinical attachment loss (CAL) ≥3 mm at the same site, showed significant associations with PTB and LBW, with adjusted odds ratios around 1.8 for PTB and LBW together. Goepfert et al. (2004), which categorized CAL ≥3 mm as a disease (capturing mild cases), did not consistently yield significant associations. Notably, the severe subset in Goepfert's definition (CAL >5 mm) did produce significantly elevated odds for adverse outcomes (e.g., OR = 2.17, CI (1.15–4.09) for PTB). In addition, Cruz et al. (2005) used the CAL as the only criterion in the periodontitis definition that requires four teeth with a high level of attachment loss and identified it as an increased risk of LBW, OR = 3.98, CI(1.58–10.10). In contrast, definitions focusing only on pocket depth, like Holbrook et al. (2004), failed to find meaningful links to pregnancy outcomes.

The Danish healthcare system covers all dental treatment until the age of 18. Approximately 20% of dental care costs for patients over 18 are reimbursed by the Danish healthcare system (Winckler et al., 2024). The present study demonstrates that around 60% of the pregnant women classified with periodontitis did not visit the dentist for more than a year. Despite the availability of recommendations, national data from the Danish Dentist Association show that up to 40% of all women of reproductive age do not regularly visit a dentist. A recent study conducted in Denmark by Winckler et al. (2024) identified 38 different barriers that had a role in preventing pregnant women from seeking regular dental care. Economic and low prioritization were rated the most significant barriers (Winckler et al., 2024). These barriers help explain our null findings. If a large proportion of women do not receive dental checkups or treatment during pregnancy, milder or progressing cases of periodontitis may go undiagnosed or untreated. This could have attenuated the observed association between periodontitis and adverse outcomes, especially if disease severity varied and was not adequately captured in our baseline assessment.

The absence of an observed association in this study may also reflect Denmark's robust prenatal care system. According to the Danish Health Authority (2022), pregnant women in Denmark are eligible for comprehensive, publicly funded prenatal care, which includes ultrasounds and frequent professional consultations focused on early identification and management of health hazards. This may explain why there was no associaion between oral health status and on birth outcomes.

Strengths and limitations

This study has several strengths. Periodontal health and psychosocial stress during pregnancy were assessed by a trained dentist and via validated inventories, respectively, and birth outcomes were obtained from medical records. To our knowledge, few studies have incorporated periodontitis and stress when assessing birth outcomes and including both factors in our research is a key strength. Another strength of the study was the use of a detailed questionnaire to collect information on demographics, stress, and dental and medical history. In addition, periodontal examinations were conducted on six sites per tooth, rather than on index teeth alone as in the CPITN. This comprehensive approach combined multiple periodontal parameters, BOP, PPD, and CAL, to support a more accurate diagnosis and reduce misclassification of periodontal status, which helps increase the internal validity of the periodontal status assessment. The same trained dentist conducted the periodontal examination in all four public dental clinics. In this way, the study reduced the risk of measurement bias associated with inter-examiner differences. This consistency is critical in periodontal assessments, which are prone to variability due to differences in probing force or the technique used among examiners. Regarding sample size, compared to earlier studies with smaller samples, such as Ahmed et al. (2017) with 438 women and Arteaga-Guerra et al. (2010) with 46, the sample size in our study is relatively larger, which strengthens the reliability of our findings. However, the number of observations in each subgroup remained sparse. In the statistical analysis, we used Firth logistic regression. This likelihood approach improved the stability and reliability of estimates, enhancing the robustness of our findings.

Despite these strengths, several limitations must be acknowledged first. However, we adjusted for important confounders such as age, BMI, education, and whether participants had visited a dentist within the past year. There could be residual confounding, likely from unmeasured variables such as oral hygiene behaviors (e.g., brushing and flossing frequency), undiagnosed systemic conditions like gestational diabetes or hypertension, which were unavailable in our dataset. Data on brushing and flossing were not provided for the whole cohort by the Parker Institute. For this reason, we did not control flossing and brushing behaviors in our analysis. Our study would have been more robust if it had adjusted for oral hygiene practices, as they may be an important factor in improving periodontal health and decreasing the prevalence of periodontitis. A recent study by Lee et al. (2025) emphasizes the importance of pre-pregnancy dental cleaning in reducing the risk of PTB, particularly among women who maintain good oral hygiene practices such as daily brushing, flossing, rinsing, and a healthy diet. When combined with professional dental cleaning, these behaviors may have an additive protective effect. We also collected data on smoking and alcohol consumption. However, most pregnant women self-reported as non-smokers and non-drinkers, as it is well known among the Danish community that pregnant women try to avoid such behaviors. In preliminary models, including smoking and alcohol status did not materially change the results. While the overall smoking prevalence in the cohort was 12.1%, it was considerably higher among women with periodontitis, with 25% reporting smoking during pregnancy. This shows that smoking could act as a confounder in the relationship between periodontitis and adverse birth outcomes, so excluding it may have introduced residual confounding. Alcohol intake remained uncommon across all categories and, unlike smoking, did not show a trend based on oral health condition. Furthermore, both variables were self-reported, raising the possibility of underreporting due to social desirability bias during pregnancy. This bias may be more prominent for smoking, which has a greater connection with periodontal health and birth outcomes.

Second, stress was measured only once at baseline using a self-reported questionnaire, which may not reflect changes throughout pregnancy, as stress levels can vary across trimesters. Additionally, both stress and pre-pregnancy BMI were self-reported, which may introduce reporting or measurement bias. Additionally, stress was measured as experienced psychological stress rather than physiological stress. Biological indicators such as cortisol in saliva or blood may have offered further information about the body's hormonal stress response. BMI was included as an adjustment variable in the regression models. Inaccurate height and weight reporting resulted in a fictitious BMI, which would have limited its capacity to appropriately account for confounding. Third, this study focused on pregnant Danish women. The recruitment was limited to Danish speakers due to the language of the survey and consent documents. This restricts generalizability regarding behavioral, cultural, or access-related factors. However, the primary focus of the study was on biological associations between periodontitis, stress, and birth outcomes—mechanisms that are not population-specific. Therefore, while generalizability to non-Danish-speaking populations may be limited regarding sociodemographic profiles, the biological relationships examined are likely broadly applicable.

Additionally, the study was conducted in four public health dental clinics in the region of Zealand and not at the national level, which also affected the generalizability. Fourth, periodontal measurement was measured in the first trimester. We did not reassess later, so we assumed periodontal status remained the same. In reality, some women with gingivitis could have progressed to periodontitis (or received treatment) during pregnancy. In addition to the clinical, we would prefer to use the radiological examination, such as bitewing and intra-oral periapical (IOPA), which may help assess the interdental bone and give a more accurate diagnosis for periodontitis. Hence, without radiographs, mild or early bone loss might not be detected, potentially leading to misdiagnosis of periodontal status and diluting any true association with birth outcomes.

7 CONCLUSION

This cohort study examined whether there was an association between periodontitis and stress during the first trimester, and later birth outcomes (PTB and /or LBW) among Danish pregnant women living in the Zealand region of Denmark. While previous literature has highlighted possible links between these factors, our results showed no statistically significant association between either periodontal disease or stress and adverse birth outcomes. No interaction effect was observed between stress and periodontitis. Although some trends suggested increased odds of PTB and LBW among women with periodontitis or high-stress levels, these did not reach statistical significance. These findings contrast with several observational studies and meta-analyses reporting positive associations. This difference may be explained by variations in periodontitis definitions, population characteristics, and study design. Specific limitations in this study included residual confounding and self-reported bias due to the data collected through surveys and questionnaires for stress and BMI, as well as a single time-point assessment of periodontal status and stress. While no clear causal link was established, maintaining good periodontal health and addressing maternal stress remain important aspects of prenatal care. Although the overall sample size in this study was relatively large, future research should also incorporate repeated measurements of both periodontal status and stress across pregnancy. Doing so would improve the capacity to capture sustained versus transient exposures and strengthen subgroup analyses, such as the interaction between stress and periodontal health, by ensuring more accurate and temporally sensitive exposure assessments.

8 GLOBAL HEALTH PERSPECTIVES/IMPLICATIONS

Although our research did not show a significant association between periodontitis and adverse birth outcomes, several prior studies have reported the opposite. Moreover, PTB and LBW are a significant economic burden on health systems worldwide. For instance, the standard care in Denmark for premature infants delivered below week 32 of gestation costs around 14,300 euros, while in Canada, the cost for a premature birth between 29 and 32 weeks is around $30,572 (Y.-L. Lee et al., 2022). At the individual level, women of preterm infants often require up to three years to stop working to care for their babies compared to women of normal infants (Y.-L. Lee et al., 2022).

Based on our findings, we recommend encouraging women to attend early dental checkups and periodontal evaluations when they plan pregnancy. Improving oral health among pregnant women diagnosed with periodontal inflammation may help reduce adverse birth outcomes and the economic burden. Periodontal treatment during pregnancy, such as scaling and root planing, is considered safe and may improve periodontal health (H. Lee et al., 2025).

In our opinion, prenatal checkups should also include screening for psychosocial stress and the mother's mental health. Stress management programs, counseling, or referrals to mental health services are examples of therapies that may be beneficial for pregnant women who are under much stress. A review by Traylor et al. (2020) showed that non-pharmacological interventions may improve maternal health and pregnancy outcomes. Interventions like mindfulness, yoga, expressive writing, and biofeedback have been demonstrated to effectively reduce perceived stress and anxiety during pregnancy (Traylor et al., 2020). Although direct evidence linking stress reduction to PTB and LBW is still under investigation, it is plausible that stress reduction benefits maternal and fetal health.

9 DECLARATION OF AI AND AI-ASSISTED TECHNOLOGIES

During the preparation of this work, I used [ChatGPT, Grammarly, Quillbot] for [checking and evaluating the grammar, vocabulary, and punctuation, and giving suggestions to improve some of the paragraph flow and order of the idea, summaries and paraphrase some of the content, also in generating pictures]. After using the tools, I reviewed and edited the content as needed and took full responsibility for the content of the work.

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REFERENCES

Abera, M., Hanlon, C., Daniel, B., Tesfaye, M., Workicho, A., Girma, T., Wibaek, R., Andersen, G. S., Fewtrell, M., Filteau, S., & Wells, J. C. K. (2024). Effects of relaxation interventions during pregnancy on maternal mental health, and pregnancy and newborn outcomes: A systematic review and meta-analysis. *PLOS ONE*, *19*(1), e0278432. https://doi.org/10.1371/journal.pone.0278432

Abu-Ta'a, M. (2014). The effects of smoking on periodontal disease: An evidence-based comprehensive literature review. *Open Journal of Stomatology*, *4*(1), Article 1. https://doi.org/10.4236/ojst.2014.41007

Ahmed, A. E., Albalawi, A. N., Alshehri, A. A., AlBlaihed, R. M., & Alsalamah, M. A. (2017). Stress and its predictors in pregnant women: A study in Saudi Arabia. *Psychology Research and Behavior Management*, *10*, 97–102. https://doi.org/10.2147/PRBM.S131474

Albandar, J. M. (2002). Global risk factors and risk indicators for periodontal diseases. *Periodontology 2000*, *29*, 177–206. https://doi.org/10.1034/j.1600-0757.2002.290109.x

Amar, S., & Chung, K. M. (1994). Influence of hormonal variation on the periodontium in women. *Periodontology 2000*, *6*(1), 79–87. https://doi.org/10.1111/j.1600-0757.1994.tb00028.x

Arteaga-Guerra, J. J., Cerón-Souza, V., & Mafla, A. C. (2010). Dynamic among periodontal disease, stress, and adverse pregnancy outcomes. *Revista de Salud Pública*, *12*(2), 276–286. https://doi.org/10.1590/S0124-00642010000200011

Bathla, M., & Chandna, S. (2010). Stress and Periodontium: A Review of Concepts. *Journal of Oral Health and Community Dentistry*, *4*(Spl), 17–22. https://doi.org/10.5005/johcd-4-Spl-17

Bergeron, J., Cederkvist, L., Fortier, I., Rod, N. H., Andersen, P. K., & Andersen, A.-M. N. (2023). Maternal stress during pregnancy and gestational duration: A cohort study from the Danish National Birth Cohort. *Paediatric and Perinatal Epidemiology*, *37*(1), 45–56. https://doi.org/10.1111/ppe.12918

Bobetsis, Y. A., Graziani, F., Gürsoy, M., & Madianos, P. N. (2020). Periodontal disease and adverse pregnancy outcomes. *Periodontology 2000*, *83*(1), 154–174. https://doi.org/10.1111/prd.12294

Bostanci, N. (2023). Periodontal health and pregnancy outcomes: Time to deliver. *Acta Obstetricia et Gynecologica Scandinavica*, *102*(6), 648–651. https://doi.org/10.1111/aogs.14548

CDC. (2024, November 4). *Talking to Pregnant Women about Oral Health*. Oral Health. https://www.cdc.gov/oral-health/hcp/conversation-tips/talking-to-pregnant-women-about-oral-health.html

Chen, P., Hong, F., & Yu, X. (2022). Prevalence of periodontal disease in pregnancy: A systematic review and meta-analysis. *Journal of Dentistry*, *125*, 104253. https://doi.org/10.1016/j.jdent.2022.104253

Christensen, L. B., Jeppe-Jensen, D., & Petersen, P. E. (2003). Self-reported gingival conditions and self-care in the oral health of Danish women during pregnancy. *Journal of Clinical Periodontology*, *30*(11), 949–953. https://doi.org/10.1034/j.1600-051X.2003.00404.x

Coelho, J. M. F., Miranda, S. S., Da Cruz, S. S., Trindade, S. C., Passos-Soares, J. D. S., Cerqueira, E. D. M. M., Costa, M. D. C. N., Figueiredo, A. C. M. G., Hintz, A. M., Barreto, M. L., Seymour, G. J., Scannapieco, F., & Gomes-Filho, I. S. (2020). Is there association between stress and periodontitis? *Clinical Oral Investigations*, *24*(7), 2285–2294. https://doi.org/10.1007/s00784-019-03083-9

Cohen, S, Kamarck, T, & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior*, *24*(4), 385–396. https://doi.org/10.2307/2136404

Cruz, S. S. da, Costa, M. da C. N., Gomes Filho, I. S., Vianna, M. I. P., & Santos, C. T. (2005). [Maternal periodontal disease as a factor associated with low birth weight]. *Revista De Saude Publica*, *39*(5), 782–787. https://doi.org/10.1590/s0034-89102005000500013

Danish Health Authority. (2022). *Pregnancy and birth in Denmark* (p. 4). Danish Health Authority. https://www.sst.dk/-/media/Udgivelser/2022/Ukraine/Gravid/Ukraine-gravid-EN.ashx

Diabelková, J., Rimárová, K., Urdzík, P., Dorko, E., Houžvičková, A., Andraščíková, Š., Drabiščák, E., & Škrečková, G. (2022). Risk factors associated with low birth weight. *Central European Journal of Public Health*, *30*(Supplement), S43–S49. https://doi.org/10.21101/cejph.a6883

Engidaw, N. A., Mekonnen, A. G., & Amogne, F. K. (2019). Perceived stress and its associated factors among pregnant women in Bale zone Hospitals, Southeast Ethiopia: A cross-sectional study. *BMC Research Notes*, *12*(1), 356. https://doi.org/10.1186/s13104-019-4383-0

Figuero, E., Han, Y. W., & Furuichi, Y. (2020). Periodontal diseases and adverse pregnancy outcomes: Mechanisms. *Periodontology 2000*, *83*(1), 175–188. https://doi.org/10.1111/prd.12295

Gasner, N. S., & Schure, R. S. (2025). Periodontal Disease. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK554590/

Genco, R. J., & Borgnakke, W. S. (2013). Risk factors for periodontal disease. *Periodontology 2000*, *62*(1), 59–94. https://doi.org/10.1111/j.1600-0757.2012.00457.x

Genco, R. J., Ho, A. W., Kopman, J., Grossi, S. G., Dunford, R. G., & Tedesco, L. A. (1998). Models to evaluate the role of stress in periodontal disease. *Annals of Periodontology*, *3*(1), 288–302. https://doi.org/10.1902/annals.1998.3.1.288

Goepfert, A. R., Jeffcoat, M. K., Andrews, W. W., Faye-Petersen, O., Cliver, S. P., Goldenberg, R. L., & Hauth, J. C. (2004). Periodontal disease and upper genital tract inflammation in early spontaneous preterm birth. *Obstetrics and Gynecology*, *104*(4), 777–783. https://doi.org/10.1097/01.AOG.0000139836.47777.6d

Gokoel, A. R., Abdoel Wahid, F., Zijlmans, W. C. W. R., Shankar, A., Hindori-Mohangoo, A. D., Covert, H. H., MacDonald-Ottevanger, M.-S., Lichtveld, M. Y., & Harville, E. W. (2021). Influence of perceived stress on prenatal depression in Surinamese women enrolled in the CCREOH study. *Reproductive Health*, *18*(1), 136. https://doi.org/10.1186/s12978-021-01184-x

Goyal, S., Gupta, G., Thomas, B., Bhat, K. M., & Bhat, G. S. (2013). Stress and periodontal disease: The link and logic!! *Industrial Psychiatry Journal*, *22*(1), 4–11. https://doi.org/10.4103/0972-6748.123585

Gunepin, M., Derache, F., Trousselard, M., Salsou, B., & Risso, J.-J. (2018). Impact of chronic stress on periodontal health. *Journal of Oral Medicine and Oral Surgery*, *24*(1), Article 1. https://doi.org/10.1051/mbcb/2017028

Han, Y. W., Fardini, Y., Chen, C., Iacampo, K. G., Peraino, V. A., Shamonki, J. M., & Redline, R. W. (2010). Term stillbirth caused by oral Fusobacterium nucleatum. *Obstetrics and Gynecology*, *115*(2 Pt 2), 442–445. https://doi.org/10.1097/AOG.0b013e3181cb9955

Han, Y. W., Ikegami, A., Bissada, N. F., Herbst, M., Redline, R. W., & Ashmead, G. G. (2006). Transmission of an uncultivated Bergeyella strain from the oral cavity to amniotic fluid in a case of preterm birth. *Journal of Clinical Microbiology*, *44*(4), 1475–1483. https://doi.org/10.1128/JCM.44.4.1475-1483.2006

Harris, K. M., Gaffey, A. E., Schwartz, J. E., Krantz, D. S., & Burg, M. M. (2023). The Perceived Stress Scale as a Measure of Stress: Decomposing Score Variance in Longitudinal Behavioral Medicine Studies. *Annals of Behavioral Medicine*, *57*(10), 846–854. https://doi.org/10.1093/abm/kaad015

Heitz-Mayfield, L. J. A. (2024). Conventional diagnostic criteria for periodontal diseases (plaque-induced gingivitis and periodontitis). *Periodontology 2000*, *95*(1), 10–19. https://doi.org/10.1111/prd.12579

Holbrook, W. P., Óskarsdóttir ,Ásta, Fridjónsson ,Theódór, Einarsson ,Hrólfur, Hauksson ,Arnar, & and Geirsson, R. T. (2004). No link between low-grade periodontal disease and preterm birth: A pilot study in a healthy Caucasian population. *Acta Odontologica Scandinavica*, *62*(3), 177–179. https://doi.org/10.1080/00016350410001522

Jevdjevic & M. Listl, S. (2022). *Economic impacts of oral diseases in 2019 – data for 194 countries* (Version v1.0) [Dataset]. https://doi.org/10.11588/data/JGJKK0

Johannsen, A., Bjurshammar, N., & Gustafsson, A. (2010). The influence of academic stress on gingival inflammation. *International Journal of Dental Hygiene*, *8*(1), 22–27. https://doi.org/10.1111/j.1601-5037.2009.00397.x

Karimi, N., Samiee, N., & Moradi, Y. (2023). The association between periodontal disease and risk of adverse maternal or neonatal outcomes: A systematic review and meta-analysis of analytical observational studies. *Health Science Reports*, *6*(10), e1630. https://doi.org/10.1002/hsr2.1630

Komine-Aizawa, S., Aizawa, S., & Hayakawa, S. (2019). Periodontal diseases and adverse pregnancy outcomes. *Journal of Obstetrics and Gynaecology Research*, *45*(1), 5–12. https://doi.org/10.1111/jog.13782

Lee, E.-H. (2012). Review of the psychometric evidence of the perceived stress scale. *Asian Nursing Research*, *6*(4), 121–127. https://doi.org/10.1016/j.anr.2012.08.004

Lee, H., Hong, N., & Janevic, T. (2025). Prenatal Dental Visits, Perceived Benefits of Oral Health, and Preterm Birth Outcome, 2009-2021. *JDR Clinical and Translational Research*, 23800844251318698. https://doi.org/10.1177/23800844251318698

Lee, Y.-L., Hu, H.-Y., Chou, S.-Y., Lin, C.-L., Cheng, F.-S., Yu, C.-Y., & Chu, D. (2022). Periodontal disease and preterm delivery: A nationwide population-based cohort study of Taiwan. *Scientific Reports*, *12*(1), 3297. https://doi.org/10.1038/s41598-022-07425-8

Leite, F. R. M., Nascimento, G. G., Scheutz, F., & López, R. (2018). Effect of Smoking on Periodontitis: A Systematic Review and Meta-regression. *American Journal of Preventive Medicine*, *54*(6), 831–841. https://doi.org/10.1016/j.amepre.2018.02.014

López, N. J., Smith, P. C., & Gutierrez, J. (2002). Higher risk of preterm birth and low birth weight in women with periodontal disease. *Journal of Dental Research*, *81*(1), 58–63. https://doi.org/10.1177/002203450208100113

Manau, C., Echeverria, A., Agueda, A., Guerrero, A., & Echeverria, J. J. (2008). Periodontal disease definition may determine the association between periodontitis and pregnancy outcomes. *Journal of Clinical Periodontology*, *35*(5), 385–397. https://doi.org/10.1111/j.1600-051X.2008.01222.x

Norman, M., Padkær Petersen, J., Stensvold, H. J., Thorkelsson, T., Helenius, K., Brix Andersson, C., Ørum Cueto, H., Domellöf, M., Gissler, M., Heino, A., Håkansson, S., Jonsson, B., Klingenberg, C., Lehtonen, L., Metsäranta, M., Rønnestad, A. E., & Trautner, S. (2023). Preterm birth in the Nordic countries—Capacity, management and outcome in neonatal care. *Acta Paediatrica*, *112*(7), 1422–1433. https://doi.org/10.1111/apa.16753

Offenbacher, S., Katz, V., Fertik, G., Collins, J., Boyd, D., Maynor, G., McKaig, R., & Beck, J. (1996). Periodontal infection as a possible risk factor for preterm low birth weight. *Journal of Periodontology*, *67*(10 Suppl), 1103–1113. https://doi.org/10.1902/jop.1996.67.10s.1103

Ohuma, E. O., Moller, A.-B., Bradley, E., Chakwera, S., Hussain-Alkhateeb, L., Lewin, A., Okwaraji, Y. B., Mahanani, W. R., Johansson, E. W., Lavin, T., Fernandez, D. E., Domínguez, G. G., de Costa, A., Cresswell, J. A., Krasevec, J., Lawn, J. E., Blencowe, H., Requejo, J., & Moran, A. C. (2023). National, regional, and global estimates of preterm birth in 2020, with trends from 2010: A systematic analysis. *Lancet (London, England)*, *402*(10409), 1261–1271. https://doi.org/10.1016/S0140-6736(23)00878-4

Peres, M. A., Macpherson, L. M. D., Weyant, R. J., Daly, B., Venturelli, R., Mathur, M. R., Listl, S., Celeste, R. K., Guarnizo-Herreño, C. C., Kearns, C., Benzian, H., Allison, P., & Watt, R. G.

(2019). Oral diseases: A global public health challenge. *The Lancet*, *394*(10194), 249–260. https://doi.org/10.1016/S0140-6736(19)31146-8

Peruzzo, D. C., Benatti, B. B., Ambrosano, G. M. B., Nogueira-Filho, G. R., Sallum, E. A., Casati, M. Z., & Nociti Jr., F. H. (2007). A Systematic Review of Stress and Psychological Factors as Possible Risk Factors for Periodontal Disease. *Journal of Periodontology*, *78*(8), 1491–1504. https://doi.org/10.1902/jop.2007.060371

Raaj, V., Bhardwaj, A., Singh, P. K., Sinha, K., Raaj, V., Bhardwaj, A., Singh, P. K., & Sinha, K. (2024). Comparative Evaluation and Correlation of Periodontal Status With Inflammatory Markers in Pregnant Women With or Without Chronic Periodontitis: A Clinico-Hematological Study. *Cureus*, *16*(3). https://doi.org/10.7759/cureus.55868

Ridgeway, E. E. (2000). Periodontal disease: Diagnosis and management. *Journal of the American Academy of Nurse Practitioners*, *12*(3), 79–84. https://doi.org/10.1111/j.1745-7599.2000.tb00171.x

Selye, H. (1973). The evolution of the stress concept. *American Scientist*, *61*(6), 692–699.

Sheldon Cohen & Gail Williamson. (1988). Perceived stress in a probability sample of the United States. In *The social psychology of health: Claremont* (pp. 31–67). Sage.

SingleCare Team. (2025, April 8). *Stress statistics 2025: How common is stress, and who's most affected?* SingleCare. https://www.singlecare.com/blog/news/stress-statistics/

Sundhedsstyrelsen. (2022, December 6). *Tal og fakta om stress*. Sundhedsstyrelsen. http://www.sst.dk/da/Fagperson/Forebyggelse-og-tvaergaaende-indsatser/Mental-og-digital-sundhed/Mental-sundhed/Stress/Tal-og-fakta

Tadese, M., Dagne, K., Wubetu, A. D., Abeway, S., Bekele, A., Misganaw Kebede, W., & Baye Mulu, G. (2022). Assessment of the adverse pregnancy outcomes and its associated factors among deliveries at Debre Berhan Comprehensive Specialized Hospital, Northeast Ethiopia. *PLOS ONE*, *17*(7), e0271287. https://doi.org/10.1371/journal.pone.0271287

Tarasi, B., Cornuz, J., Clair, C., & Baud, D. (2022). Cigarette smoking during pregnancy and adverse perinatal outcomes: A cross-sectional study over 10 years. *BMC Public Health*, *22*(1), 2403. https://doi.org/10.1186/s12889-022-14881-4

Tonetti, M. S., Jepsen, S., Jin, L., & Otomo-Corgel, J. (2017). Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action. *Journal of Clinical Periodontology*, *44*(5), 456–462. https://doi.org/10.1111/jcpe.12732

Traylor, C. S., Johnson, J. D., Kimmel, M. C., & Manuck, T. A. (2020). Effects of psychological stress on adverse pregnancy outcomes and nonpharmacologic approaches for reduction: An expert review. *American Journal of Obstetrics & Gynecology MFM*, *2*(4), 100229. https://doi.org/10.1016/j.ajogmf.2020.100229

Tu, C., Wang, G., Hu, Z., Wang, S., Yan, Q., & Liu, X. (2023). Burden of oral disorders, 1990–2019: Estimates from the Global Burden of Disease Study 2019. *Archives of Medical Science*, *19*(4), 930–940. https://doi.org/10.5114/aoms/165962

Vianna, P., Bauer, M. E., Dornfeld, D., & Chies, J. A. B. (2011). Distress conditions during pregnancy may lead to pre-eclampsia by increasing cortisol levels and altering lymphocyte sensitivity to glucocorticoids. *Medical Hypotheses*, *77*(2), 188–191. https://doi.org/10.1016/j.mehy.2011.04.007

Vittek, J., Hernandez, M. R., Wenk, E. J., Rappaport, S. C., & Southren, A. L. (1982). Specific estrogen receptors in human gingiva. *The Journal of Clinical Endocrinology and Metabolism*, *54*(3), 608–612. https://doi.org/10.1210/jcem-54-3-608

Wang, X., Buhimschi, C. S., Temoin, S., Bhandari, V., Han, Y. W., & Buhimschi, I. A. (2013). Comparative microbial analysis of paired amniotic fluid and cord blood from pregnancies complicated by preterm birth and early-onset neonatal sepsis. *PloS One*, *8*(2), e56131. https://doi.org/10.1371/journal.pone.0056131

Winckler, K., Rasmussen, M. U., Laugenborg, J., Bukkehave, K. H., Fischer, H., Heitmann, B. L., & Wæhrens, E. E. (2024). Barriers for why pregnant women do not visit a dentist on a regular basis: Using group concept mapping methodology. *Acta Odontologica Scandinavica*, *83*, 40286. https://doi.org/10.1080/00016357.2023.2283198

World Health Organization. (2019). *Trends in maternal mortality 2000 to 2017: Estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division*. World Health Organization. https://iris.who.int/handle/10665/327595

World Health Organization. (2022). *Oral health country profile: Denmark.* https://cdn.who.int/media/docs/default-source/country-profiles/oral-health/oral-health-dnk-2022-country-profile.pdf

World Health Organization. (2024). *Sexual, reproductive, maternal, newborn, child and adolescent health policy survey 2018–2019: Denmark country profile*. World Health Organization. https://platform.who.int/docs/default-source/mca-documents/policy-documents/policy-survey-2018/country-profiles/policy-country-profile-2018-denmark.pdf

Xu, B., & Han, Y. W. (2022). Oral bacteria, oral health, and adverse pregnancy outcomes. *Periodontology 2000*, *89*(1), 181–189. https://doi.org/10.1111/prd.12436

APPENDIX

PSS-10 questionnaire

♣ **PSS-10 Questions**	**Likert scale**				
	(0)	(1)	(2)	(3)	(4)
1. In the last month, how often have you been upset because of something that happened unexpectedly?					
2. In the last month, how often have you felt that you were unable to control the important things in your life?					
3. In the last month, how often have you felt nervous and 'stressed'?					
*4. In the last month, how often have you felt confident about your ability to handle your personal problems?					
*5. In the last month, how often have you felt that things were going your way?					
6. In the last month, how often have you found that you could not cope with all the things you had to do?					
*7. In the last month, how often have you been able to control irritations in your life?					
*8. In the last month, how often have you felt that you were on top of things?					
9. In the last month, how often have you been angered because of things that were outside your control?					
10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?					

♣ *perceived stress scale- 10 item.*
* *Positive event questions.*

Table A4. Detailed Adjusted Multivariable logistic regression of Oral Health with PTB and LBW

Characteristic	PTB (OR [95% CI])	LBW (OR [95% CI])
Oral status		
Healthy (ref)	1.00 [1.00–1.00]	1.00 [1.00–1.00]
Gingivitis	0.96 [0.32–2.95]	1.26 [0.27–5.79]
Periodontitis	0.95 [0.28–3.17]	1.44 [0.29–7.15]
Stress levels		
Low Stress (ref)	1.00 [1.00–1.00]	1.00 [1.00–1.00]
Moderate Stress	0.81 [0.36–1.84]	0.89 [0.32–2.47]
High Stress	1.02 [0.43–2.43]	1.17 [0.40–3.41]
Maternal age		
Age (years)	0.93 [0.86–1.02]	1.00 [0.91–1.16]
Pre-BMI		
BMI (kg/m2)	1.01 [0.95–1.07]	0.97 [0.90–1.05]
Mother education		
Low educational level (ref)	1.00 [1.00–1.00]	1.00 [1.00–1.00]
Medium education	1.06 [0.46–2.44]	1.09 [0.40–2.93]
Higher education	2.46 [0.91–6.65]	1.39 [0.39–4.99]
Visiting dentist		
Within past year (ref)	1.00 [1.00–1.00]	1.00 [1.00–1.00]
More than one year	1.59 [0.79–3.20]	1.35 [0.57–3.22]

Note: PTB, preterm birth; LBW, low birth weight; Adjusted for mother age, BMI, oral health status, stress levels, mother education, visiting dentist. The "unspecified" category was excluded from the model due to small cell size and unstable estimates. Exponentiated coefficients; 95% confidence intervals in brackets* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table A6. Detailed Adjusted Multivariable logistic regression of Stress with PTB and LBW

Characteristic	PTB (OR [95% CI])	LBW (OR [95% CI])
Stress levels		
Low Stress (ref)	1.00 [1.00–1.00]	1.00 [1.00–1.00]
Moderate Stress	0.84 [0.38–1.83]	0.83 [0.31–2.22]
High Stress	0.98 [0.42–2.28]	1.09 [0.39–3.03]
Maternal age		
Age (years)	0.94 [0.87–1.02]	1.00 [0.91–1.10]
Mother education		
Low educational level (ref)	1.00 [1.00–1.00]	1.00 [1.00–1.00]
Medium education	1.03 [0.48–2.23]	0.96 [0.38–2.41]
Higher education	2.19 [0.86–5.58]	1.34 [0.41–4.39]

Note: PTB, preterm birth; LBW, low birth weight; Adjusted for mother age, and mother education. The "unspecified" category was excluded from the model due to small cell size and unstable estimates. Exponentiated coefficients; 95% confidence intervals in brackets * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$