Relationship between periodontal disease in pregnant women and premature birth: a comprehensive review

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Abstract
Initially, it should be noted that the birth of premature babies constitutes the fundamental cause of morbidity and mortality soon after birth. There are several factors that imply risks and are directly related to its development, such as the use of psychoactive substances, infections of the genito-urinary tract and tobacco smoke and other infections at a distance. Periodontal disease is considered an independent risk factor for premature low birth weight babies, which places active periodontal disease as an independent risk factor for the birth of premature and low birth weight babies. In this perspective, the objective of this work is to analyze periodontal disease as a risk factor for prematurely born babies. The methodology used in the development of the work is the literature review, with the use of articles from reference periodicals for the theme. It can be stated that in cases of periodontal disease, inflammatory stimuli can induce hyperirritability of the uterine smooth muscle, causing contraction of the uterus and cervical dilation, triggering premature birth. By constituting a chronic infection, it can influence the occurrence of premature birth indirectly or directly. However, it is important to understand that the treatment of periodontal disease is effective, reducing the incidence of premature birth.

Keywords: Periodontal disease. Premature birth. Low weight at birth.

Introduction
Initially, it should be considered that the delivery of premature babies, that is, those below 37 weeks of gestation and with low birth weight (below 2,500 g) is still an important public health problem, both in developed and developing countries, being related to the high rate of postnatal mortality (28 days to 11 months of age), as well as the higher risk of death as a result of sequelae such as cerebral palsy, blindness, and learning difficulties, which can lead to partial or total disability [1].

Effectively, the low birth weight of newborns (NB) is associated with premature birth, representing around 70% of infant deaths. Children who are born weighing less than 2,500 g have a greater chance of mortality than those with normal weight [1]. 95% of newborns with low birth weight in the world occurred in developing countries, and Brazil, 10% of children born in the 1990s were underweight [1,2].

Some factors are traditionally linked to premature and low birth weight babies, such as maternal genitourinary infections at any time during pregnancy, maternal short stature (below 150 cm), parents’ lower occupational level and absence of prenatal care. Given these factors, some studies led to the improvement of information on the pathophysiological characteristics related to prematurity and low birth weight, with the development of advanced techniques to investigate pathological processes and specific phenomena. In this perspective, several concepts about diseases were modified and made more complete [3].

Periodontal disease was understood as a phenomenon located in the periodontium, involving the tooth and its underlying tissues, becoming a more complex problem involving the health of the pregnant woman, making it possible to understand that there is
an association between periodontal disease and premature babies with low birth weight to be born. This association can be verified by traditional clinical signs found in periodontal disease, which makes the study of the subject of great relevance for Dentistry [4].

Therefore, the present study analyzed periodontal disease as a risk factor for prematurely born babies, as well as understanding the characterization of the conditions of premature and low birth weight babies, as a serious public health problem, and analyzing the resulting risks of death of periodontal infection in premature and low birth weight babies.

Methods

For the development of this article, a literature review was chosen, based on bibliographical research in intellectual production related to the proposed theme. After defining the theoretical framework, there was the filing, citation, and identification of the consulted sources. The article was then produced, based on analytical reading, apprehension of content, and interpretation. The confrontation of ideas made it possible to confirm or refute initial hypotheses. Science is understood as a constant search for explanations and solutions, to promote an approximation of the truth through methods that provide control, systematization, and security regarding the information presented.

Comprehensive Review and Discussion

Characterization of the health condition of premature and low-weight babies

Low birth weight can be defined as weighing less than 2,500 g and remains a significant public health problem in both developed and developing countries [5]. Premature birth (PTB) is the leading cause of neonatal mortality and nearly half of all serious long-term neurological morbidity. Premature and low birth weight (LBW) babies are still 40 times more likely to die during the neonatal period. LBW who survive the neonatal period face an increased risk of various neurodevelopmental disorders, health problems (such as asthma, upper and lower respiratory infections, and ear infections), and congenital anomalies. Some risk factors associated with LBW include high (>34 years) and low (<17 years) maternal age, low socioeconomic status, inadequate prenatal care, substance abuse, alcohol, and tobacco use, hypertension, diabetes, and multiple pregnancies. Despite increasing efforts to reduce the effects of these risk factors through preventive interventions during prenatal care, there was only a small reduction in the number of PTB [6].

There is reason to believe that other unrecognized risk factors may contribute to the continued prevalence of LBW babies. A possible contributing factor to this phenomenon is the effect of an infection on LBW. Subclinical genitourinary and periodontal infections may adversely affect pregnancy outcomes. Women with premature labor do not always have a positive amniotic fluid culture, suggesting that subclinical infections, resulting in the translocation of bacteria, bacterial metabolites, and lipopolysaccharides (LPS), may be responsible for some of the inflammatory processes associated with LBW [7].

It should be noted that there are different subgroups of PTB, that is, delivery can occur due to premature rupture of membranes, it can be indicated for medical reasons or due to an unknown 15 etiology, with evidence showing that there are 22,25 etiologies multifactorial factors in cases of PTB [3]. Concerning prevention, they should not be based only on preventing the onset of premature labor or inhibiting it when it is detected, but on discussing issues related to risk factors [8].

Effectively, the etiological role of maternal infection in the occurrence of PTB (in the genital tract or elsewhere in the anatomy) is uncertain, but PTB may be an indirect consequence of the production of high levels of inflammatory mediators, such as cytokines (interleukin 1 beta and interleukin 6), prostaglandin E and tumor necrosis factor 2 alpha 3,15), which end up reducing the gestation period [9].

The possibility that remote infection arising from the fetus-placental unit may contribute to PTB has raised a more significant concern regarding the role of chronic bacterial infections in other parts of the body. Periodontal disease (PD) is one of the most common chronic infectious diseases in humans, with a reported prevalence ranging from 10% to 60% in adults, 30 depending on the diagnostic criteria used. This type of infection is mainly caused by Gram-negative anaerobic microaerophilic bacteria that colonize the subgingival area and produce significant amounts of pro-inflammatory cytokines that can have systemic effects on their host [9].

Periodontal Infection in Premature and Low Weight Children

It should be noted that the continuous production of cytokines in inflamed periodontal tissues is responsible for the progress of periodontitis and the destruction of periodontal tissue. In particular, inflammatory cytokines such as IL-1α, IL-1β, IL-6, and IL-8 are present in diseased periodontal tissues, and their unrestricted production appears to play a role in chronic leukocyte recruitment and tissue destruction [10].
Acute periodontal disease primarily involves a local innate immune response to oral biofilm microflora. Gingival epithelial cells recognize bacterial cell components through toll-like receptors and respond by producing IL-1 and TNF-α. Bacteria and bacterial products also penetrate underlying tissues. There they interact with fibroblasts and dendritic cells. These cells also produce pro-inflammatory cytokines. Additional immunological signals are generated by alternative complement activation. These bacterial products and pro-inflammatory cytokines also affect vascular endothelial cells [10].

Endothelial cells express cell adhesion molecules (ICAM and VCAM) that recruit circulating immune cells. Vascular permeability is also increased – allowing the influx of phagocytes and serum cells into the gingival tissue. Neutrophils and macrophages are attracted to the site of infection by chemotaxis following gradients of complement proteins, cytokines, and bacterial products. Activated macrophages produce IL-12 and interferon-gamma (IFN-γ). In general, these processes result in gingival inflammation and are responsible for the clinical manifestations of gingivitis leading to periodontitis [7].

It is possible that monitoring cytokine production or its profile may allow the diagnosis of an individual's periodontal disease status and/or disease susceptibility. Infection is now considered one of the main causes of LBW deliveries, accounting for somewhere between 30% and 50% of all cases, and periodontitis and periodontal diseases are true infections of the oral cavity. The oral cavity functions as a continuous source of infectious agents, and its condition often reflects the progression of systemic pathologies. Periodontal infection serves as a bacterial reservoir that can exacerbate systemic diseases. Research suggests that the bacteria that cause gum inflammation can get into the bloodstream and reach the fetus, potentially leading to premature LBW babies. A possible mechanism starts with endotoxins resulting from Gram-negative bacterial infections (such as periodontal disease). These endotoxins stimulate the production of cytokines and prostaglandins (IL-1β, IL-6, and TNF-α) and in appropriate amounts stimulate labor and delivery, and pro-inflammatory mediators can cross the placental barrier and cause fetal toxicity resulting in delivery premature and low birth weight infants. High concentrations of these cytokines, in pregnant women, are responsible for the rupture of the uterine membranes, causing premature delivery and delay [11].

Periodontal disease is a treatable and preventable condition. In the case of a positive association of periodontal infection with LBW, this would have potential applications in preventive oral health programs as an integral component of prenatal care for pregnant women. Indeed, as health professionals working as a team, understanding the role of the periodontal and systemic relationship and its implications will further enhance the quality of medical and dental care provided to patients [12].

Although no definitive causal relationship has been established and other explanations for the correlation can be offered, a model can nevertheless be considered in which chronic periodontal infection could mediate this systemic effect through translocation of periodontal pathogens to the fetoplacental unit, action of a periodontal reservoir of LPS in the fetoplacental unit or through the action of a periodontal reservoir of inflammatory mediators (IL-1, IL-6, TNF-α, PGE2) in the fetoplacental unit [13].

Effectively, an association between periodontal disease and premature birth is evidenced by a series of studies, but also presents, for some authors, conflicting conclusions. Most authors, based on studies carried out in different countries by specialists, attribute to periodontal disease the risk of premature delivery and low birth weight. Periodontal disease is a serious infection of the gums that is responsible for a chronic inflammatory response in the body and is mainly a result of infection and inflammation of the gums, which can lead to activation of the immune-inflammatory response [14].

In line with the diagnostic criteria, the prevalence of periodontal disease in adults is around 10 to 60%. The clinical manifestation of the disease occurs through the host's immune response to periodontal pathogens, persistent inflammation, and destruction of the connective tissue supporting the tooth and bone [15].

Said systemic inflammation is associated with adverse pregnancy outcomes, such as low birth weight. The pathophysiological mechanism of a potential association between periodontal disease and low birth weight may be based on increased systemic inflammation caused by oral flora, which influences the onset and course of premature birth, including preeclampsia, and low birth weight. During pregnancy, approximately 40% of pregnant women have periodontal disease. Considering that the association between periodontal disease and premature birth has become a public health problem, the adoption of preventive and therapeutic interventions is essential to reduce the occurrence of premature birth and infant deaths in pregnant women with periodontal disease [8].

Several studies suggest that women with periodontal disease may be more likely to give birth to
premature babies than mothers with healthy gums. Low-birth-weight newborns may be at risk for long-term health problems, including intellectual and developmental disabilities, delayed motor skills, obesity, diabetes, high blood pressure, and heart disease [8]. There are also similar complications for babies born before 37 weeks of pregnancy. It is necessary to consider the existence of other problems, such as respiratory problems, vision, and hearing loss, as well as eating and digestive problems [10].

Conclusion
This study suggests that periodontal disease may have varying associations with the risk of premature delivery in different ethnicities and populations. Scaling and polishing remove deposits such as plaque and tartar from tooth surfaces. In addition, it is necessary to ensure that the pregnant woman has a balanced diet, in addition to strengthening oral hygiene care through daily brushing and flossing after meals. The professional in dentistry plays a fundamental role in prevention, considering that consultations held every three months can avoid any dental setback that interferes with the health of the pregnant woman and the baby.

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