Periodontitis: A risk for delivery of premature labor and low-birth-weight infants

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Abstract

Periodontitis is a destructive inflammatory disease of the supporting tissues of the teeth and is caused by specific microorganisms or group of specific microorganisms. The association of periodontal infection with organ systems like cardiovascular system, endocrine system, reproductive system, and respiratory system makes periodontal infection a complex multiphase disease. Inflamed periodontal tissues produce significant amounts of proinflammatory cytokines, mainly interleukin 1-beta (IL-1β), IL-6, prostaglandin E2, and tumor necrosis factor-alpha (TNF-α), which may have systemic effects on the host. Low birth weight, defined as birth weight less than 2,500 g, continues to be a significant public health issue in both developed and developing countries. Research suggests that the bacteria that cause inflammation in the gums can actually get into the bloodstream and target the fetus, potentially leading to premature labor and low-birth-weight (PLBW) babies. One reasonable mechanism begins with deleterious effects of endotoxins released from Gram-negative bacteria responsible for periodontal disease. Hence periodontal disease appears to be an independent risk factor for PLBW and there is a need to expand preventive measures for pregnant women in harmonization with the gynecological and dental professions.

Key words: Cytokines, dental, periodontitis, premature labor and low-birth-weight

INTRODUCTION

Periodontitis is a destructive inflammatory disease of the supporting tissues of the teeth and is caused by specific microorganisms or group of specific microorganisms [Table 1] resulting in a progressive destruction of the periodontal ligament and alveolar bone with periodontal pocket formation, gingival recession, or both.[1,2] Periodontal diseases are recognized as infectious processes that require bacterial presence and a host response and are further affected and modified by other local, environmental, and genetic factors. The association of periodontal infection with organ systems like cardiovascular system, endocrine system, reproductive system, and respiratory system makes periodontal infection a complex multiphase disease. Bacteria are the primary etiological agents in periodontal disease, and it is estimated that more than 500 different bacterial species are capable of colonizing the adult mouth.[3] Inflamed periodontal tissues produce significant amounts of proinflammatory cytokines, mainly interleukin 1-beta (IL-1β), IL-6, prostaglandin E2, and tumor necrosis factor-alpha (TNF-α), which may have systemic effects on the host. Periodontitis initiates systemic inflammation and can be monitored by inflammatory markers like C-reactive protein or fibrinogen levels.

Table 1: Microorganisms commonly associated with periodontitis

Aggregatibacter actinomycetemcomitans
Porphyromonas gingivalis
Prevotella intermedia
Tannerella forsythia
Fusobacterium nucleatum
Peptostreptococcus micros
Campylobacter rectus

PHARMACOLOGY OF PROINFLAMMATORY CYTOKINES ASSOCIATED WITH PERIODONTITIS

The continuous production of cytokines in inflamed periodontal tissues is responsible for the progress of periodontitis and periodontal tissue destruction. Particularly, inflammatory cytokines, such as IL-lα, IL-1β,

IL-6, and IL-8, are present in the diseased periodontal tissues, and their unrestricted production seems to play a role in chronic leukocyte recruitment and tissue destruction. Acute periodontal disease primarily involves a local innate immune response to the microflora of the oral biofilm. Gingival epithelial cells recognize bacterial cell components via toll-like receptors and respond by producing IL-1 and TNF-α. Bacteria and bacterial products also penetrate into the underlying tissues. There they interact with fibroblasts and dendrite cells. These cells also produce proinflammatory cytokines. Additional immune signals are generated by alternative complement activation. These bacterial products and proinflammatory cytokines affect vascular endothelial cells as well. Endothelial cells express cellular adhesion molecules (ICAM and VCAM) that recruit circulating immune cells. Vascular permeability is also increased – allowing the influx of phagocyte cells and serum 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). Overall, these processes result in gingival inflammation, and are responsible for the clinical manifestations of gingivitis further leading to periodontitis. It is possible that monitoring cytokine production or its profile may allow us to diagnose an individual's periodontal disease status and/or susceptibility to the disease.

PREMATURE AND LOW-BIRTH-WEIGHT INFANTS

Low birth weight, defined as birth weight less than 2,500 g, continues to be a significant public health issue in both developed and developing countries.[4] Preterm delivery, or PTD, is the major cause of neonatal mortality and of nearly one-half of all serious long-term neurological morbidity.[5] Premature and low-birth-weight (PLBW) infants are still 40 times more likely to die during the neonatal period. PLBW infants who survive the neonatal period face a higher risk of several neurodevelopment disturbances, health problems (such as asthma, upper and lower respiratory infections, and ear infections), and congenital anomalies.[4] Some risk factors that have been associated with a PLBW include a high (>34 years) and low (<17 years) maternal age, a low socioeconomic status, inadequate prenatal care, drug abuse, alcohol and tobacco use, hypertension, diabetes, and multiple pregnancies. Despite increasing efforts to diminish the effects of these risk factors through preventive interventions during prenatal care, there has been an only a small decrease in the number of PLBW infants. There is a reason to believe that other unrecognized risk factors may contribute to the continuing prevalence of PLBW infants. One possible contributing factor to this phenomenon is the effect of an infection on PLBW. It is possible that subclinical genitourinary and periodontal infections can adversely affect the pregnancy outcomes. Women with preterm labor do not invariably present with positive amniotic fluid culture, suggesting that subclinical infections, resulting in the translocation of bacteria, bacterial metabolites, and lipopolysaccharide (LPS), may account for some of the inflammatory processes associated with PLBW.

PERIODONTAL INFECTION IN PREMATURE AND LOW-BIRTH-WEIGHT

The concept that periodontal disease might influence systemic health is not new. Miller originally published his focal infection theory in 1891[6] suggesting that microorganisms or their waste products obtain entrance to parts of the body adjacent to or remote from the mouth. Infection is now considered one of the major causes of PLBW deliveries, responsible for somewhere between 30% and 50% of all cases, and periodontitis and periodontal diseases are true infections of the oral cavity.[1] The oral cavity works as a continuous source of infectious agents, and its condition often reflects progression of systemic pathologies. Periodontal infection happens to serve as a bacterial reservoir that may exacerbate systemic diseases. Research suggests that the bacteria that cause inflammation in the gums can actually get into the bloodstream and target the fetus, potentially leading to PLBW babies. One possible mechanism begins 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 quantities stimulate labor,[5] and proinflammatory mediators may cross the placenta barrier and cause fetal toxicity resulting in preterm delivery and low-birth-weight babies.[7] High concentrations of these cytokines, in pregnant women, are responsible for rupture of the uterine membranes causing premature birth and retardation. As periodontal medicine is still in its infancy here in Asia, there is a compelling need to determine the possible association between adverse pregnancy outcomes and periodontal infections. It has been well documented that periodontal disease is a treatable and preventable condition. In the event of a positive association of periodontal infection with PLBW, this would have potential applications in preventive oral health programs as an integral component of prenatal care for pregnant mothers. Indeed, as healthcare professionals working as a team, an understanding of the role of periodontal and systemic relationship and its implications will further enhance the quality of medical and dental care being provided to our

Table 2: Oral health guidelines

Oral health module	Key points
Oral health education	Counseling and early intervention by healthcare providers such as physicians, nurses, and dentists to provide expectant mothers with the tools and resources necessary to understand the importance of oral health care during pregnancy
Oral hygiene	Removing the bacterial plaque, which researchers have connected to preterm birth and low-birth-weight babies, is essential. Using the correct brushing and flossing methods greatly increase the amount of plaque that is removed from the teeth and gums
Fluoride	The American Dental Association recommends the use of toothpaste with fluoride by persons over the age of 6. Echoing their sentiment, the AAP oral health guidelines advise the continued use of fluoridated toothpaste during pregnancy, and recommends the use of an over-the-counter alcohol-free fluoride rinse to help reduce the amount of plaque in the mouth
Nutrition	Educating expectant mothers about proper diet and nutrition during pregnancy will limit unnecessary sugar intake and in turn, prevent plaque buildup
Treatment	Expectant mothers are encouraged to have existing tooth decay treated during their pregnancy, which experts believe is a completely safe practice during pregnancy. Restoring decayed teeth will help achieve oral health by removing the bacteria associated with tooth decay
Transmission of bacteria	Expectant mothers are discouraged from sharing food and utensils in order to prevent the transmission of the bacteria known to cause tooth decay
Chewing gum	Expectant mothers are encouraged to chew xylitol gum (four times a day) as research suggests that chewing this gum may decrease the rate of tooth decay in children
Consultation	For any doubt and consultations, approach the dentist at the earliest

patients in the community.[7] Several animal and clinical studies clearly indicate an association between periodontal infection and adverse pregnancy outcomes. Although no definitive causal relationship has been established, and other explanations for the correlation might be offered, a model can nevertheless be envisaged wherein chronic periodontal infection could mediate this systemic effect through one or more of the following mechanisms:[4]

- Translocation of periodontal pathogens to the fetoplacental unit
- Action of a periodontal reservoir of LPS on the fetoplacental unit
- Action of a periodontal reservoir of inflammatory mediators (IL-1, IL-6, TNF-α, PGE2) on the fetoplacental unit.

RECOMMENDED ORAL HYGIENE PRACTICES AND VISITS TO DENTIST DURING PREGNANCY

Oral health guidelines for pregnant women were accomplished to assist them in maintaining healthy teeth and gums during their pregnancy and into the early stages of motherhood. The American Academy of Pediatric Dentistry (AAP) announced new oral health guidelines for pregnant women in 2009, modified and illustrated in Table 2.

SUMMARY

Thus it can be concluded that periodontal disease appears to be an independent risk factor for PLBW and there is a need to expand preventive measures for pregnant women in harmonization with the gynecological and dental professions, and to provide professional oral hygiene measurements during pregnancy.

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