

Parodontopathy as a Risk Factor for Premature Birth

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Abstract

Despite the use of state-of-the-art medicines and devices, the number of premature births in the world is on the rise. One out of ten births is premature and is considered the main cause of over 75% of babies' deaths. Infection is the most significant etiological factor that disrupts local hemostasis of the delivery mediator by various mechanisms. Three hypotheses that can explain the relationship between periodontal infection and premature labor are: 1) periodontal pathogens causing direct contamination of the fetoplacental unit, 2) lipopolysaccharide, bacterial endotoxin, found in infected periodontium, is released and affects the fetoplacental unit through the blood, and 3) inflammatory mediators from the infected periodontal reservoir can cause problems in the fetoplacental unit. Patients with periodontal disease have been found to have elevated levels of PGE₂, IL-1 β , IL-6, TNF- α in gingival fluid compared to respondents with healthy periodontal tissue. Cytokines stimulate the production of prostaglandins that induce myometrial contractions, maturation of the uterine cervix, and fetal membrane rupture, resulting in premature birth. Based on numerous scientific studies conducted on the subject of correlation between periodontal disease and premature birth, it can be concluded that periodontitis, as a remote infectious focus, is a highly important factor that can cause premature birth of children.

Keywords: Periodontal disease; Inflammation mediators; Premature birth; PGE₂; TNF- α ; IL-1 β

Introduction

Premature delivery is the one that begins before the 37th week of pregnancy [1]. Low Birth Weight (LBW) babies, defined as babies having birth weights of less than 2,500 g, represented disproportionately large component of neonatal and infant mortality rates. Although LBW babies make up only about 6% to 7% of all births, they account for more than 70% of neonatal deaths [2]. Despite the use of state-of-the-art medicines and devices, the number of premature births in the world is on the rise [3]. One out of ten births is premature and is considered the main cause of over 75% of babies' deaths [4]. In our country, the incidence of premature births varies from 6% to 10% [5]. Today, over 40% of premature births are thought to be a consequence of an intrauterine infection [6,7].

Medical complications (preeclampsia, autoimmune diseases, fetal distress), socio-economic factors (smoking, alcohol, pregnant woman's age), previous surgical interventions, infection, vaginal bleeding is reported as etiological factors and risk factors for spontaneous premature delivery [8]. In addition to the indication of numerous etiological factors as well as risk factors, a large percentage of premature births are of unknown aetiology. Infection is the most significant etiological factor for many diseases, so the presence of a distant infection during pregnancy is a key precondition for the occurrence of premature birth as it disrupts the local haemostasis of the delivery mediator by different mechanisms [9,10]. The influence of oral cavity disease, primarily periodontium disease, on people's systemic health is a several decade-long subjects of many studies. The

results of numerous studies have shown the association of periodontal disease and many systemic diseases, including diabetes mellitus, cardiovascular diseases, respiratory diseases, cerebrovascular diseases, rheumatoid arthritis, and several types of cancer, allergic disorders the risk of premature delivery and other complications with pregnancy and childbirth [11-13].

In the early 20th century, oral apical focal infections were very current [14]. Little importance was given to the effect of periodontal infection on the general health of the organism. The latest studies of aetiology and pathogenesis of periodontitis have confirmed the actuality of this problem [15].

Periodontal disease is a chronic inflammatory disease of tooth tissue caused by dental plaque bacteria. The presence of bacteria alone is not sufficient for the development of periodontal disease.

The progression of the disease is determined by the immune response of the host to the presence of bacteria [16]. During the local inflammatory reaction, inflammatory mediators are produced. The most is prostaglandin E₂ (PGE₂), interleukin-1 β (IL-1 β), interleukin 6 (IL-6) and tumour necrosis factor alpha (TNF- α). These inflammatory mediators are also referred to as biochemical markers-predictors of birth, hence the correlation between periodontal disease and premature birth. The level of these inflammatory mediator increases gradually during pregnancy and the achievement of their critical values lead to the onset of delivery [12,17,18].

Patients with periodontal disease have been found to have elevated PGE₂, IL-1 β , IL-1, ICAM-1, IL-8, IL-6, TNF- α levels in the gingival fluid compared to respondents with healthy periodontal tissue [19].

The aim was to investigate interrelation between periodontal disease and premature birth on the basis of literary findings.

The Possible Role of PGE₂

Prostaglandins are arachidonic acid metabolites. PGE₂ is produced as a response to bacteroides LPS. PGE₂ is one of the most commonly studied mediators of periodontal disease activity [20].

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PGE2 stimulates alveolar bone resorption and is considered a tissue destruction mediator [13,21].

Offenbacher et al. [22] have confirmed a significant increase in PGE2 in the gingival fluid of patients with periodontal disease compared to a healthy periodontium control group. This study also suggests that increase in prostaglandin levels leads to the more pronounced destruction of the epithelial attachment and alveolar bone [23].

Prostaglandins play an important role in the basic stages of delivery: fetal membrane rupture, cervical dilatation, and myometrium contractions [24]. The role in initiating myometrium contraction is particularly emphasized and considered to be a birth trigger factor [25]. Many inflammatory processes, including periodontal disease, are accompanied by an increase in biological markers i.e. cytokine that will affect many mechanisms and increase the concentration of PGE2, which will result in premature contractions of the myometrium and therefore premature delivery [26,27].

The Possible Role of Cytokines

Cytokines are protein-nature molecules that bind to cell surface receptors activating cell proliferation and/or differentiation, activation and apoptosis mechanisms. The cells that secrete the largest amounts of cytokines are called leukocytes. Cytokines secreted by lymphocytes are called lymphokines; monocyte and macrophage cytokines are called monokines, while many lymphokines are known as interleukins [28].

Pro-inflammatory cytokines (IL-1 β , IL-6 and TNF- α) have been distinguished as inflammatory mediators whose production intensity is an indicator of the periodontium tissue destruction activity. Patients with periodontal disease have been shown to have elevated values of these pro-inflammatory cytokines in the gingival fluid compared to respondents with healthy periodontal tissue [29,30].

Due to the increased permeability of periodontium blood vessels, which occurs as a result of inflammation, pro-inflammatory cytokines have the ability to penetrate the systemic circulation.

Their increased presence in circulation may be a premature labour trigger [17]. Cytokines stimulate the production of prostaglandins that in turn induce myometrial contractions, uterine cervix maturation and fetal membranes rupture [31]. IL-1 β and TNF- α stimulate prostaglandin biosynthesis in amnion, chorion, decidua and myometrial cells through the increase in the synthesis and activity of cyclooxygenase-2 (COX-2) [32]. The cascade of COX-2 activation and increased prostaglandin synthesis is associated with a cytokine response to newly-formed, chronic or exacerbating infectious agent. Romero have confirmed that the enhanced synthesis and secretion of decidual prostaglandins is mediated by increased activity of IL-1 and IL-6, although TNF- α , in this case, can play a major role [33].

When it comes to the relationship between pregnancy and TNF, the role of TNF in the mechanisms of miscarriage, resorption of placenta and embryos and other clinical entities related to pregnancy pathology could be discussed first. Since it belongs to cytokines with pronounced apoptotic mediator properties, any increased TNF activity in pregnancy leads to severe compromising of immunoregulation in pregnancy and questions the further fate of pregnancy [34].

The adverse effect of TNF on pregnancy is related to the fact that TNF is particularly active in terms of activation of apoptotic

mechanisms on proliferative tissues, including trophoblast tissue. Probably for these reasons, the synthesis and secretion of TNF in normal pregnancy is very low [35].

Cytokines increase the expression and activity of Matrix-MetalloProteinase (MMP). The activity of MMP may be responsible for cervical ripening and premature fetal membrane rupture [22]. Intrauterine infections are associated with higher MMP values in amniotic fluid.

Discussion

Three hypotheses that can explain the relationship between periodontal infection and premature labor are: 1) periodontal pathogens causing direct contamination of the fetoplacental unit [36], 2) lipopolysaccharide, bacterial endotoxin, which is found in infected periodontium, is released and affects the fetoplacental unit through blood [37], and 3) inflammatory mediators from the infected periodontal reservoir can cause problems in the fetoplacental unit [38,39].

Offenbacher et al. [22] was suggested link between the infection in periodontium and adverse outcomes of pregnancy-premature birth and the birth of low birth weight children. In a study published in 1996, Offenbacher et al. [22] defined, for the first time, periodontal disease as a risk factor for the occurrence of premature birth. Their study concludes that the risk of premature labour is 7 times higher in respondents with periodontal disease than in those respondents without.

In 2005, Jarjoura et al. [34] conducted a survey involving 203 pregnant women. The conclusion of their study was that periodontitis was significantly represented in prematurely delivered women compared to those delivered within the term.

Le et al. [40], Siqueira et al. [41], Santos-Pereira et al. [42], Giannella et al. [30], Piscoya et al. [43] have found similar results.

In a prospective study including a sample of 1,313 pregnant women, Jeffcoat et al. [44] found an approximately four times higher risk of early delivery in respondents with severe periodontitis.

Numerous studies are studying the factors of inflammation, prostaglandin and cytokines, as the main triggers for premature delivery. In the study Menon et al. [1], IL-1 β , IL-6, TNF- α and PGE2 are labelled as biochemical markers-the triggers of premature delivery.

The results of the study by Sanz et al. [45] indicate that periodontal status may have an impact on the circulating levels of the delivery mediator and participate in the onset of delivery. In pilot study by Tarannum et al. [46], which included 22 respondents, the level of PGE2 in the serum was evaluated, taken immediately after the onset of delivery and one month after the delivery. The results of this study have shown that, at the very beginning of the delivery process, significantly higher PGE2 values are present in the serum of pregnant women who gave birth prematurely compared to the pregnant women who gave birth within the term.

In addition to numerous studies on the relationship between periodontal disease and premature delivery, there remains a whole series of unexplained mechanisms that would confirm the complete importance of periodontitis as an important factor for premature delivery. Dentists play a very important role in detecting the connection and the potential danger of periodontal infections on systemic health. Recommendations for dental professionals include

performing the necessary periodontal therapy for the stabilization of periodontium of women planning pregnancy as well as adequate education on the importance of regular maintenance of the oral cavity health.

Conclusion

Based on numerous scientific studies conducted on the topic of correlation between periodontal disease and premature labour, it can be concluded that periodontitis, as a distant infectious focus, is a very important factor that can cause premature birth of children.

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