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# Correlation between maternal gingivitis/periodontitis and preterm delivery: fact or fancy?

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## ABSTRACT

Considering that periodontal diseases increase secretion of several pro-inflammatory cytokines and that also amniotic fluid analysis during preterm delivery (PTD) shows elevated levels of inflammatory mediators, it is possible to argue that periodontal inflammation could play a role in the triggering of this condition. In this view, the aim of this narrative short review is to evaluate the possible relationship between maternal periodontitis and PTD.

**Keywords**: obstetrics; gynaecology; pregnancy; preterm delivery; periodontitis; gingivitis.

## SOMMARIO

Considerando che le malattie parodontali aumentano la secrezione di diverse citochine pro-infiammatorie e che anche l'analisi del liquido amniotico durante il parto pretermine (PTD) mostra livelli elevati di mediatori infiammatori, è possibile sostenere che l'infiammazione parodontale potrebbe svolgere un ruolo nell'innesco di questa condizione. In questa prospettiva, lo scopo di questa breve revisione narrativa è di valutare la possibile relazione tra parodontite materna e PTD.

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## INTRODUCTION

Preterm delivery (PTD) is defined when it occurs before 37 gestational weeks. This condition has a global incidence of 9.6%[1–4] and complicates 5% of pregnancy: 15% occurs within 28, 20% between 28 and 31, 65% between 34 and 36 gestational weeks[5,6].

PTD is considered a syndrome caused by a number of factors which often have interaction with each other. Its causes may include individual-level behavioral and social-health factors, neighborhood characteristics, environmental exposures, medical conditions, infertility treatments, infectious episodes, biological factors and genetics. Many of these factors occur in combination, particularly in those who are socioeconomically disadvantaged or who are members of racial and ethnic minority groups[7–11]. Major causes of PTD are spontaneous preterm labor with intact membranes (50%), labor induction or caesarean delivery for maternal or fetal indications (30%), and preterm premature rupture of membranes or PPROM (20%)[2,7,10,12].

Nevertheless, PTD is nowadays the first cause (75%) of neonatal mortality[13,14]. Well-known risk factors for this condition are previous PTD, low maternal body mass index (BMI), infections and cigarette smoking. In particular, genital tract infections are strictly associated with risk of PTD[15–25] as well as intrauterine ones during early pregnancy[26].

### Association between gingivitis/periodontitis and pregnancy

Several dental infections are very common during pregnancy[27,28]: according to a report of 2002 by Laine, gingivitis occurs in more than 30% and periodontitis in 5-20% of pregnancies[29]. Gingivitis and periodontitis develop more easily during pregnancy as a consequence of variations in hormonal levels that promote systemic pro-inflammatory response. Even with good plaque control, 50%-70% of all women will develop gingivitis during their pregnancy, commonly referred to as pregnancy gingivitis. The increased levels of progesterone and estrogens can affect small blood vessels of the gingiva, making it more permeable and favoring the occurrence of gingivitis which is manifested during the second and eighth months of pregnancy[9].

It is widely accepted that pathogens of dental plaque are capable to invade periodontal tissues, to provoke recurrent bacteremia, to disseminate to distant foci and to activate systemic inflammatory response[30].

When gingivitis or periodontitis occurs during pregnancy, pathogens can pass through the placenta barrier and reach the amniotic fluid[31–33].

Several methodologically rigorous studies evidenced that acute maternal gingivitis or periodontitis may represent concurrent causes of pregnancy complications such as PTD[34–38], intrauterine growth restriction[39–42] and preeclampsia[43–47].

Microbiological analysis on amniotic fluid in case of acute maternal gingivitis or periodontitis evidenced the presence of Fusobacterium nucleatum, Peptostreptococcus, Porphyromonas[48,49], Prevotella, Eubacterium and Eichenella corrodens[50,51]. During labour, level of prostaglandins PGE2 increases[52]. Considering that in case of acute maternal gingivitis or periodontitis there is an increase of pro-inflammatory mediators[53,54], such as PGE2 and Tumor Necrosis Factor-α (TNF-α)[55], it is possible that they could trigger the cascade of events which lead to PTD or PROM[15,56,57]. During PTD is typical to find high levels of IL(Interleukin)-6, IL-1a, IL-1b, TNF-a, IL-10 e PGE2 in the amniotic fluid[58,59]. A prospective study on a large cohort already showed that acute periodontitis has an Odds Ratio (OR) of 5.28 of PTD before 37 weeks, and of 7.07 before 32 weeks[35]. Older case-control studies evidenced an overall 3-8-folds higher risk of PTD in case of maternal periodontitis[60].

Maternal gingivitis/periodontitis seems to affect also neonatal weight: a study of a cohort of 639 pregnant women with gingivitis/periodontitis, 406 pharmacologically treated and 233 untreated showed that they had 8.6% of low birth weight (LBW) newborns respect to controls[61]. Although to date many diagnostic tests for PTD are used, such as fFN (Fetal Fibronectin), the management of this condition is still far to reach the final shape[62]. A promising approach seems to be represented by the dosage of IL-10[59]. Moreover, it was hypothesized that hormonal modifications may affect and exacerbate gingival inflammation, modify the composition of oral biofilm and trigger a selective growth of periodontal pathogens such as Porphyromonas gingivalis, Prevotella intermedia[63] or Campylobacter rectus[64].

### Possible biological mechanism linking periodontal disease to adverse pregnancy outcomes

Considering that periodontal diseases increase secretion of several pro-inflammatory cytokines

(PGE-2, TNF-α, IL-6 and IL-1)[65,66] and that also amniotic fluid analysis during PTD shows elevated levels of inflammatory mediators[67], it is possible to argue that periodontal inflammation could play a role in the triggering of PTD[68].

Similar to cardiovascular diseases or diabetes, the pro-inflammatory status during periodontal disease may influence the course of pregnancy[69].

Periodontal diseases could cause a breakdown of the dynamic immunological homeostasis between mother and fetus: indeed, numerous studies tried to shed light on fetal and maternal antibodies directed against oral pathogens during pregnancy[70]. Boggess et al., for example, evidenced that 35.2% of serum samples of mothers with PTD were Ig-M positive for at least one oral pathogen, and 26.6% were positive for more than one[71].

The immune response typical of PTD could be triggered and exacerbated also in case of polymorphisms of genes coding for pro-inflammatory cytokines such as TNF-α, IL-1 or IL-6, which are associated to a hyperinflammatory response[2,72].

## CONCLUSION

Several reviews have investigated the relationship between periodontal disease and adverse pregnancy outcomes[73–76] and many authors report a positive correlation between periodontal disease and PTD or low birth weight[34,77].

However, some meta-analysis report contradictory result on the association between maternal periodontal disease and the risk of PTD and/or LBW[78,79].

The mechanisms linking periodontal diseases and PTD are not well defined. Further studies are needed to clarify the correlation between the two clinical conditions. Nevertheless, we could hypothesize that maternal periodontal disease may play a role in the triggering of PTD, causing an increase of the pro-inflammatory response.

## DECLARATION OF INTEREST

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper. No specific funding was obtained.

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