

Implications of *Eikenella corrodens* in adverse pregnancy outcomes: The role of dental professionals – A narrative review

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ABSTRACT

This review elaborates on the mechanisms by which *E. corrodens* leads to APOs with a special emphasis on the role of dental professionals in their prevention. The analysis is based on open-access articles from PubMed, SCOPUS, Web of Science, and Google Scholar published in the English language without any restriction for the time of publication. A search was performed using the keywords 'Eikenella corrodens' and 'Pregnancy' to identify relevant open-access articles in PubMed, SCOPUS, Web of Science, and Google Scholar databases with full text available in the English language without any restriction for the time of publication. *Eikenella corrodens* is a commensal bacterium usually found in the upper respiratory tract, mucosal surfaces like gastrointestinal and genitourinary tract as well as in the human dental plaque. The physiological alterations in pregnancy or lesions such as pregnancy-related gingivitis and pyogenic granuloma render the body susceptible to transient bacteremia. The hematogenous spread of *E. corrodens* is associated with several adverse pregnancy outcomes that lead to high morbidity and mortality rates for mothers as well as neonates.

Keywords: *Eikenella Corrodens*; Pregnancy; Gingivitis; Periodontitis; Bacteremia

1. INTRODUCTION

The human body experiences rapid transient alterations during pregnancy as a consequence of abrupt hormonal surges.^[1] These alterations may dynamically affect various physiological systems and organs. The orofacial region witnesses a myriad of problems commonly including gingivitis, gingival hyperplasia, pyogenic granuloma, and salivary changes along with increased facial pigmentation.^[2,3] Pyogenic granuloma, also termed "pregnancy tumors" or granuloma gravidarum, is one of

the most common oral manifestations of hormonal alterations in pregnancy with prevalence rates reported to be as high as ranging from 40 to 75%.^[4,5]

Pregnancy tumors can cause bleeding gums, and the exposed blood vessels can serve as an entry point for bacteria to invade the body fluid and enter the hosts' systemic circulation. Coupled with the lowered body immunity during pregnancy, these events lead to a surge in the number of rapidly dividing bacteria in the bloodstream.^[6] The resultant bacteremia may give rise to various adverse pregnancy outcomes (APOs) by virtue of the ability of certain species of bacteria to cross the placental barrier and harm the developing fetus.^[7] These APOs include neonatal septicemia, chorioamnionitis, amniotic fluid infection syndrome, neonatal mortality, preterm labor, perinatal infection and congenital sepsis.^[8,9]

Various pathogenic bacterial species present in the oral cavity may contribute to this phenomenon including *Capnocytophaga*, *Fusobacterium nucleatum*, *Tennerella forsythia*, *Eikenella corrodens*, *Treponema denticola*, *Prevotella intermedia*, *Porphyromonas gingivalis*, *Aggregatibacter Actinomycetemcomitans* (Figure 1).^[10] While majority of these species belong to the orange and red complex and are thus, noted in advanced stages of periodontal diseases, the green complex species, *Capnocytophaga* and *Eikenella*, are predominant in the initial stages of gingivitis.^[11-13] The species contribute to inflammation-mediated damage at a much early stage. The emphasis of researchers has mostly been on the more destructive orange and red complex bacteria rather than the green complex. The fact that the latter can lead to APOs at initial or milder levels of gingival diseases cannot be overlooked.^[14] Thus, active vigilance against the initiator species is to be maintained to enable the progression of disease or development of APOs.

Figures Legends:

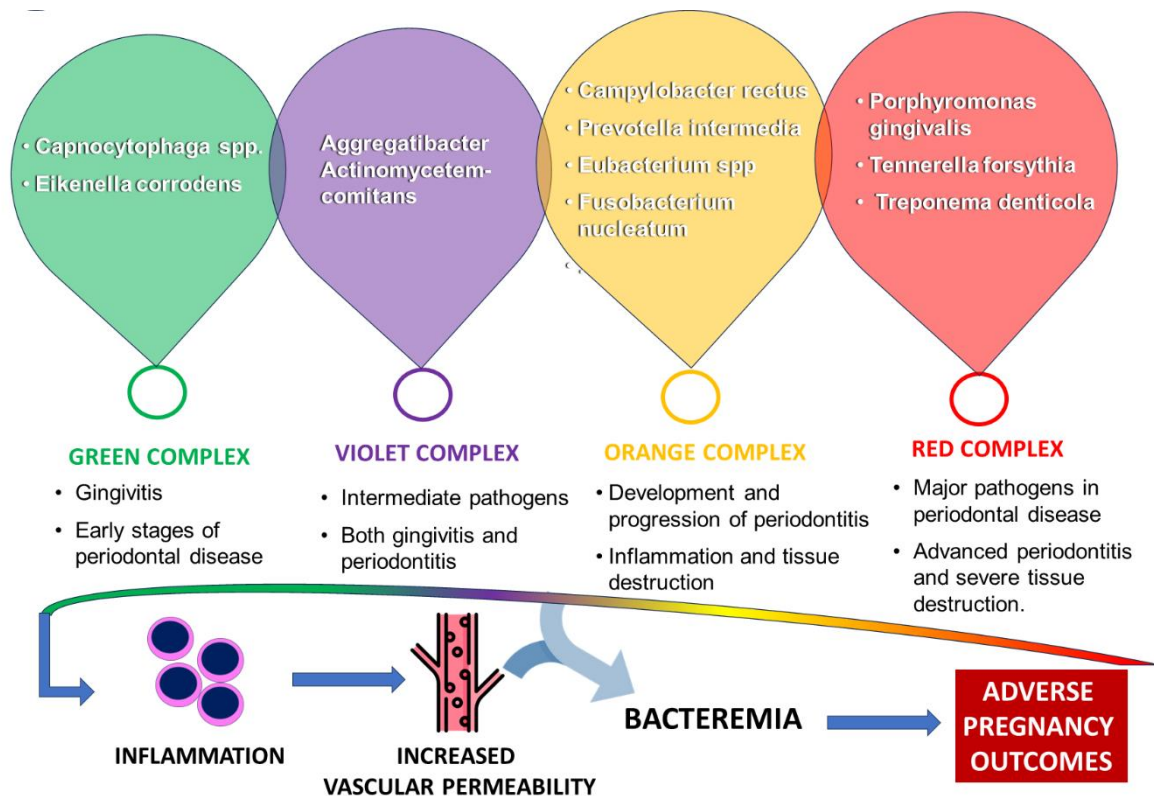


Figure 1: Different pathogens in dental plaque leading to adverse pregnancy outcomes

Even so, only scant data is available about these microorganisms and their relation to APOs.^[7] Medical professionals should have adequate knowledge about the microorganisms that may cause harm to the developing fetus so that they can provide necessary medical care to pregnant women. Similarly, dentists can provide timely dental care to pregnant women to prevent the harmful effects of the early-stage plaque bacteria like *E. corrodens*. Dental professionals play a key role in this regard, as they are at the forefront when the individual's oral hygiene is concerned and thus, they need to have a sound understanding of this aspect of APOs. In this context, the present article focuses on elaborating the complex interplay between *E. corrodens* and APOs aiming to bridge the gap between existing data on *E. corrodens*-related APOs and the information available to prevent the harm that may come to the mother or fetus.

2. METHODOLOGY

A literature search was performed using the keywords 'Eikenella corrodens' and 'Pregnancy' to identify relevant open-access articles in PubMed, SCOPUS, Web of Science, and Google Scholar databases with full text available in the English language without any restriction for the time of publication. Relevant cross-references of interest were also identified from the full texts. The literature available in these articles was reviewed by three authors and the essential information was recorded as bullet points in an MS Word document. The data was structured and re-arranged according to different sub-topics and then drafted in the form of a manuscript text by the three authors, the particulars of which were then reviewed by two subject experts.

3. PREGNANCY-RELATED PHYSIOLOGICAL AND MICROFLORA ALTERATIONS

Pregnancy is a dynamic state marked by numerous physiological and hematological changes. Various lesions occur during pregnancy due to changes in the levels of estrogen and progesterone, changes in the oral microbiome, and pregnancy-related physiologic immunodeficiency, all of which lead to a significant exacerbation of the pre-existing gingivitis.^[2,3] Evolutionarily, it is preferable for inflammatory immune responses to be suppressed during pregnancy in order to prevent the possibility of fetal rejection.^[15,16] The production of inflammatory cytokines and the activity of natural killer cells, inflammatory macrophages, and T-helper cells decrease during pregnancy.^[17]

Leukocytosis is a common feature seen during pregnancy, which occurs as a response to microbial infections.^[18] A pregnant woman's differential count frequently shows neutrophils as the commonest leukocyte present. There is impaired neutrophil apoptosis and toxic granulation in the pregnant female's neutrophil cytoplasm.^[19] This causes a decrease in neutrophil chemotaxis and phagocytic activity, which is aided by inhibitory factors found in pregnant women's serum, which results in a reduction in neutrophil count and phagocytosis. This leads to a decline in the defence mechanisms of the body of a pregnant female and a concomitant increase in the virulence of the bacteria.

Consequently, various infections or inflammatory lesions may develop, with pregnancy gingivitis and pyogenic granuloma being the commonest ones among the oral lesions.^[3] Studies have found the presence of gingivitis invariably in all women between the third and the eighth month of their pregnancy, with a steady decline after delivery.^[20-22] Current literature states that most clinical symptoms associated with pregnancy gingivitis comprising gingival bleeding, tenderness and aesthetic problems are usually mild.^[23] At times, lesions rich in vascularity such as pyogenic granuloma can cause profuse bleeding for prolonged periods or aggravation of symptoms which may, in turn, even force early induction of labor.^[24,25] While the bleeding and symptoms may resolve after the delivery, the pre-term termination of pregnancy may have several other adverse effects on the child as well as the mother.^[26,27]

Persistent gingivitis may lead to periodontitis characterized by aggressive destruction of the bone and soft tissues surrounding the teeth. Probing depths increase as the gingival inflammation increases in pregnancy. This is due to the movement of the gingival margin in a coronal direction because of inflammation-induced swelling of the gingiva.^[28] The problem gets further aggravated by the buildup of subgingival calculus which is inaccessible to regular cleaning aids. The subsequent section describes *E. corrodens*, which is a green complex bacterium, seen in early stages of gingivitis, and its relation to APOs.

4. EIKENELLA CORRODENS

E. corrodens is a commensal bacterium of the oral cavity; however, its counts are significantly elevated in gingivitis and pregnancy due to the mechanisms described above.^[29] It is a fastidious, facultative, anaerobic, gram-negative bacillus that is endogenous to the upper respiratory tract, mucosal surfaces of the gastrointestinal and genitourinary tracts, and human dental plaque.^[30,31] *E. corrodens* grows slowly in blood agar or chocolate agar under aerobic conditions requiring a temperature of 35-37°C and 5% carbon dioxide for optimum growth.^[31] The colonies are small and greyish (older colonies may turn light yellow), and they emit a bleach-like odour. A characteristic phenomenon of formation of pits on the agar plates when the bacteria is cultured has notoriously earned its name "corroding" bacteria.^[32]

The organism is susceptible to fluoroquinolones, azithromycin, ampicillin, ureidopenicillins, second and third-generation cephalosporins, and tetracyclines.^[33,34] On the other hand, resistance to clindamycin, erythromycin, metronidazole and aminoglycosides has been observed.^[35] Infections caused due to *E. corrodens* have a slow or a languid course, usually taking more than a week from the time of injury to show any clinical manifestations of disease. The bacteria is also associated with meningitis, endocarditis, head and neck infections, intra-abdominal infections and gynecological infections.^[36-38] Apart from causing upper respiratory tract infections and other head, face, and neck infections, it has been linked to a number of gynecological and pregnancy-related conditions.^[39]

Spread of *E. corrodens* is primarily through the genitourinary tract, although another likely mode of spread is through the blood.^[40] This aspect of its spread is relevant to the oral cavity, especially when the vascular permeability is increased due to pregnancy and gingivitis. Most important clinical manifestation in gingivitis is bleeding from gums, and this can serve as an entry point for bacteria into systemic circulation. Such dissemination of bacteria from the oral cavity to other organ systems usually leads to bacteremia. Bacteremia frequently occurs following dental procedures such as extractions, scaling and root planing as well as periodontal surgeries.^[41] *E. corrodens* is amongst the microflorae that have the ability to cross the

placental barrier and harm developing fetuses, as well as result in a variety of APOs.^[39]

5. THE RUINOUS ROLE OF *E. CORRODENS* IN PREGNANCY

E. corrodens has been implicated as the causative agent in chorioamnionitis of the placenta resulting in preterm labour.^[42] The presence of oral pathogens in the placenta may be normal, although the quantity of some oral pathogens is greatly influenced by the periodontal health of the mother.^[43] Early-stage periodontitis caused by *E. corrodens* evokes the release of inflammatory mediator Prostaglandin E₂ (PGE₂), which is a potential mediator in the pathogenesis of periodontitis (Figure 2). It has been demonstrated that the levels of PGE₂ are elevated in patients with periodontitis as compared to healthy individuals.^[44] A possible link between women with preterm low birth weight pregnancy outcomes with higher levels of PGE₂ has been established owing to the tendency of latter to cause smooth muscle contractions.^[41,45] Thus, it can be hypothesized that elevated levels of PGE₂ owing to the gingival and periodontal diseases caused by *E. corrodens* during pregnancy can induce preterm labor thereby resulting in preterm low birth weight pregnancy outcomes.

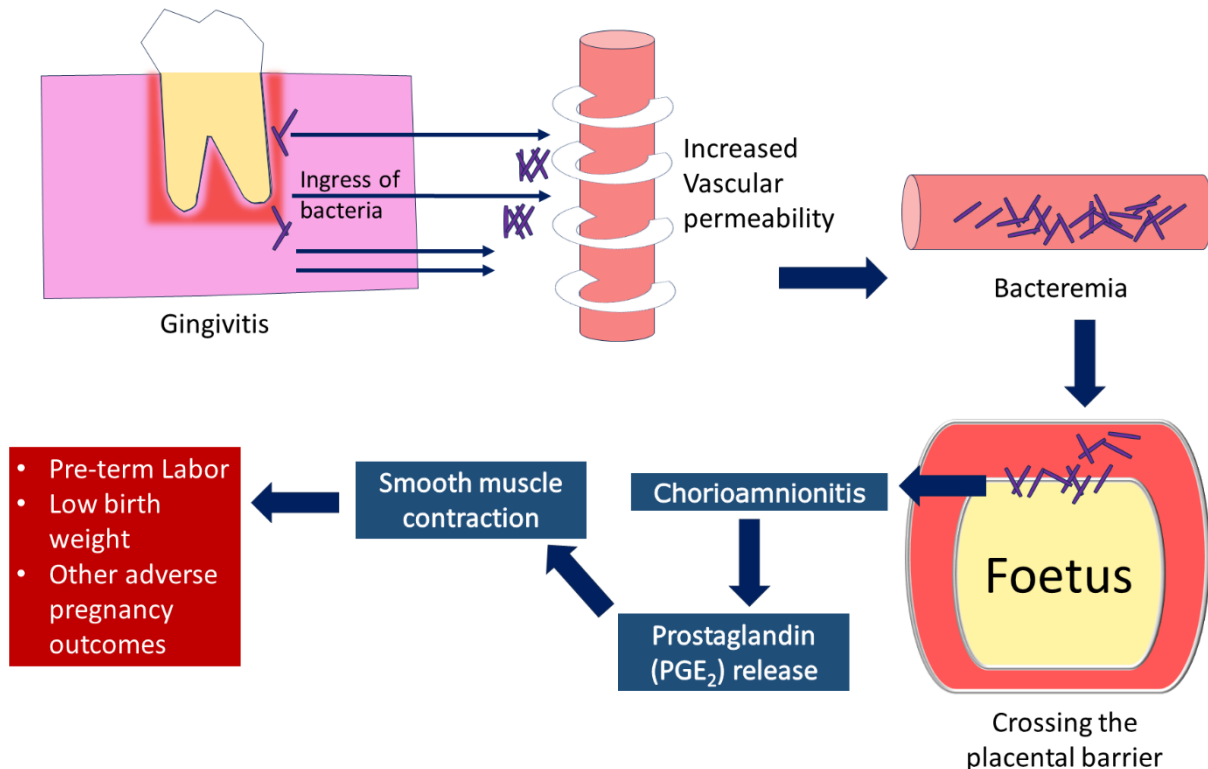


Figure 2: Probable Mechanism of Action of *E. corrodens* Associated Pregnancy Outcomes

Antibiotics such as ampicillin are generally administered after the rupture of chorioamniotic sac and the onset of premature labor.^[46] There is a drastic drop in the bacterial count leading to negative culturing results of the sample collected, owing to its susceptibility to the drugs.^[47] Therefore, detecting the organism in the neonates or the mother, and implicating its causative role in the APO becomes unlikely. This complicates the diagnostic process and is a cause of grave concern for clinicians.

6. ROLE OF HEALTHCARE PROFESSIONALS

It has been established that preterm births, low birth weights, and other APOs are linked to the poor dental health of pregnant women.^[48] It is important to understand the attitude of pregnant women towards dental care so that oral health promotion programs may be targeted in the right direction to avoid pregnancy-related gingivitis and periodontitis by early diagnosis and treatment. Women should undergo a dental checkup before their pregnancy so that dentists can assess their oral health conditions and inform the female patients about anticipated changes in their oral tissues, particularly gingiva. The dental practitioners can also instruct the patients on preventive measures to be taken and put into practice in order to avoid oral health-related issues during their pregnancy.^[49]

Pregnancy alone is not a reason to postpone routine dental therapy and treatments. To avoid the development of gingivitis, expectant mothers should be advised and educated by a dental expert on the importance of maintaining good oral health. Patients should also be informed about the precautions that must be followed before and after labor to avoid complications.

The California Dental Association Foundation in collaboration with The American College of Obstetrician and Gynaecologists have produced a guideline in 2010, stating “prevention, diagnosis and treatment of oral diseases, including, needing dental radiographs and use of local anesthesia, is highly beneficial and can be undertaken during pregnancy without additional fetal and maternal risk when compared to the risk of not providing care”.^[50]

Pregnant women are often warned, and are thus, equipped to handle bacterial infections stemming from the genitourinary or gastrointestinal tract, sites where *E. corrodens* is commonly detected. However, pregnant women are rarely informed about the risks associated with *E. corrodens* present in the dental plaque. Nutritional counseling as well as plaque-control measures should be incorporated and reinforced in a preventive periodontal health program for pregnant women. Increased tendency for gingival inflammation during pregnancy should be highlighted to the expectant parents, in hopes of incorporating healthy oral hygiene habits in the mother. Scaling and root planing should be performed whenever necessary during pregnancy.

Numerous non-modifiable factors like genetic predisposition, age or history of unassociated ailments can unfortunately be instrumental in APOs. Health care professionals can positively influence the outcome of a pregnancy by monitoring modifiable factors, such as the level of dental care provided and observed during pregnancy.^[51] According to a study that looked at seven eligible controlled randomized trials, scaling and/or root planing during pregnancy significantly reduced preterm birth rates.^[52] This solidifies the importance of advocating for dental care to improve pregnancy outcomes.

7. CHAIRSIDE TESTS AVAILABLE

MyPerioPath®

To identify the kind and quantity of important bacteria causing periodontal illnesses, MyPerioPath® examines saliva samples.^[53] It allows for the individualization of periodontal therapy by identifying mouth infections early. It measures the bacterial load to identify high risk pathogens like *A. actinomycetemcomitans*, *P. gingivalis*, *T. forsythia*, and *T. denticola*. Moderate risk pathogens like *Eubacterium nodatum*, *Fusobacterium nucleatum*, *P. intermedia*, *Campylobacter rectus*, *Parvimonas micros*, and low risk pathogens like *E. corrodens* and *Campylobacter sputigena* can also be detected.

OMNIGene

OMNIGene, a genetic nucleic acid probe, has created species-specific DNA probe assays for eight periodontal diseases using the concepts of genetic engineering (*P.gingivalis*, *P.intermedia*, *A.actinomycetemcomitans*, *F.nucleatum*, *E.corrodens*, *C.rectus*, *T.forsythia*, *T.denticola*).^[54,55] Samples of the subgingival plaque are taken from the patients and mailed for analysis. Results are delivered by phone, fax, or mail to the practitioner.

8. PATHWAY FOR FURTHER RESEARCH

There is a dearth of clinical studies to establish an accurate and significant pathogenesis behind the effects of *E. corrodens* on pregnancy and APOs. Spread of *E. corrodens* from oral sources such as dental plaque or gingival fluid has not been given its due importance and doing so is essential because dental plaque is a risk factor that can be modified and can be effectively controlled. There exists a multitude of opportunities for clinical research, to test and detect the strains associated with infection caused by *E. corrodens*, and whether the strains are antibiotic sensitive or resistant.

9. CONCLUSION

Pregnancy-related gingival and periodontal diseases can lead to elevated levels of *E. corrodens* in the bloodstream. The resultant APOs as a consequence of bacteremia is a matter of grave concern. While the APOs cannot be treated, tackling the oral diseases is definitely possible. Dentists can play an extremely vital role in controlling mortality associated with preterm low birth weight pregnancy outcomes. Dental and other health care professionals should consistently educate pregnant women about the significance of maintaining oral health.

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