



PERIODONTAL DISEASE AND PREGNANCY OUTCOMES: A GROWING CONCERN IN MODERN OBSTETRICS

**Kasukurthi Komali¹, Suryakanth Malgikar^{2*}, Reshma Parchuri³, Rohit Gampala⁴, Jagadish Reddy Gooty⁵ and
Raja Babu Palaparthi⁶**

¹Post Graduate Student, Department of Periodontology, Kamineni Institute of Dental Sciences, Narketpally, Nalgonda (Dist.), Telangana, India.

²Professor, Department of Periodontology, Kamineni Institute of Dental Sciences, Narketpally, Nalgonda (Dist.), Telangana, India.

³Tutor, Department of Conservative and Endodontics, Mamatha institute of Dental Sciences Bachupally, Hyderabad, Telangana, India.

⁴Senior Lecturer, Department of Periodontology, Kamineni Institute of Dental Sciences, Narketpally, Nalgonda (Dist.), Telangana, India.

⁵Professor, Department of Periodontology, Kamineni Institute of Dental Sciences, Narketpally, Nalgonda (Dist.), Telangana, India.

⁶Professor and Head, Department of Periodontology, Kamineni Institute of Dental Sciences, Narketpally, Nalgonda (Dist.), Telangana, India.



***Corresponding Author: Suryakanth Malgikar**

Professor, Department of Periodontology, Kamineni Institute of Dental Sciences, Narketpally, Nalgonda (Dist.), Telangana, India.

Article Received on 24/03/2025

Article Revised on 14/04/2025

Article Accepted on 03/05/2025

ABSTRACT

Pregnant women may face a higher risk of developing dental conditions like periodontal disease, which is an inflammatory and damaging condition affecting the tissues that support the teeth. Bacteria and their byproducts from periodontal disease can negatively affect pregnancy outcomes, including the potential for tooth loss in the mother by the spread of bacteria from the mouth into the bloodstream, production of cytokines and immunoglobulins which may also pose a risk to the fetus if an infection is already present during pregnancy. The present review will highlight recent findings focusing on how lifestyle-related diseases contribute to periodontal issues and how these can affect pregnancy outcomes.

KEYWORDS: Periodontal Disease, Pregnancy Gingivitis, Female Infertility, Poly Cystic Ovarian Disease, Endometriosis, Bacterial Vaginosis.

INTRODUCTION

Periodontal diseases are one of the most common infectious diseases in origin. Periodontitis is a chronic multifactorial inflammatory disease associated with dysbiosis plaque biofilms and characterized by progressive destruction of the tooth-supporting apparatus. Its primary features include the loss of periodontal tissue support, manifested through clinical attachment loss (CAL) and radiographically assessed alveolar bone loss, presence of periodontal pocketing and gingival bleeding.^[1] The belief that a woman's dental health is likely to deteriorate through having children remains common. In many cultures, there is an old adage for every child a tooth, meaning that the mother can expect to lose a tooth with each pregnancy.^[2] The most common maternal oral diseases that potentially could impact pregnancy outcome include dental caries, gingivitis, and periodontitis.^[3]

Estrogen-classified hormones have varying biological activity; for example, estriol, a weak form of estrogen, is the primary estrogen during pregnancy, whereas estradiol-17b, or estradiol, is the primary estrogen during the menstrual cycle. Apart from the hormone type in circulation, the tissue concentration of the hormones and the ratio of estrogen to progesterone are also crucial for the tissue response. During pregnancy, estrogens and progesterone serve a number of vital purposes. Maintaining pregnancy is progesterone's primary function. Over the past 20 years, numerous researchers have looked at the connection between different adverse pregnancy outcomes (APO) and periodontal disorders. There are two possible explanations for the possible impact of periodontal diseases: either the feto-placental unit is affected by inflammatory mediators like prostaglandin E2 (PGE2), interleukin-1 (IL-1), IL-6, IL-8, or tumor necrosis factor- α (TNF- α), or periodontal

pathogens translocation to the feto-placental unit.^[4] Periodontal disease is both preventable and curable, thus confirming it as an independent risk factor for adverse pregnancy outcomes would be extremely important for public health purposes.^[5]

According to emerging research, women with periodontal illnesses may be more likely to give birth to preterm, low-birthweight kids. For this reason, the American Academy of Periodontology recommends that women who are pregnant or contemplating a pregnancy receive periodontal check-ups.

Periodontal diseases during pregnancy

Although the research suggests that pregnancy is not a risk factor for periodontal disease, gingival problems are extensively documented in the mother throughout the second and third trimesters of pregnancy. Periodontal diseases are caused and maintained by variables connected to the subgingival bacteria. Periodontal disease is primarily caused by host inflammatory and immunological responses.^[6] There are different types of periodontal disease which are aggravated by pregnancy out of which the commonest are:

- I. Pregnancy gingivitis
- II. Oral lesions
- III. Periodontitis

I. Pregnancy gingivitis

Pregnancy gingivitis is characterized as gingival inflammation caused by plaque and worsened by endogenous sex steroid hormones. As a standalone condition, pregnancy gingivitis is clinically and histologically identical to gingivitis in non-pregnant individuals. The clinical signs of gingivitis are the same: gingiva with a smooth or glossy look, bleed easily, and have red, swollen, and thickened margins. Bacterial plaque is the most important contributor in the initiation and maintenance of gingival inflammation in pregnant women, and the exacerbation of the inflammatory response of the gingiva often seen during pregnancy is caused by altered tissue metabolism.^[7] Because gingivitis is caused by bacterial plaque, there may be no significant changes in gingival health between pregnant and non-pregnant women who maintain very good plaque control.^[8] Pregnancy gingivitis usually starts at the second month of gestation and reaches the highest level at the eighth month, and heals spontaneously after birth.⁹ Gingivitis is the most common oral disease in pregnancy, accounting for 60-75% of cases. The vulnerability of gingival tissues to inflammation in pregnancy appears to be tied to pregnancy-related hormonal changes; however, the exact mechanism by which these hormones enhance gingival inflammation is unknown.^[10]

Clinical and Microbial changes in the periodontal tissues during pregnancy

Increased periodontal probing depths, gingival inflammation, gingival crevicular fluid flow, bleeding upon probing, tooth mobility, incidences of pyogenic

granulomas and increase in numbers of periodontopathogens especially *P. gingivalis* and *P. intermedia*.

II. Oral lesion

Pyogenic granuloma (PG) also known as epulis of pregnancy, granuloma gravidarum, or pregnancy tumor, is a benign oral lesion. Pyogenic granuloma is a non-specific inflammatory lesion of the skin and mucous membranes that can occur in both men and women, but is most frequent during pregnancy. When gingival lesions appear during pregnancy, they are referred to as pregnancy tumors or granuloma gravidarum. Pyogenic gingival granuloma develops in upto 5% of pregnancies. Hullihen published the first report of PG in English literature in 1844.

The hormonal imbalance associated with pregnancy increases the organism's response to irritation; nevertheless, bacterial plaque and gingival inflammation are required for subclinical hormone abnormalities that lead to gingivitis. This vascular lesion is caused by elevated progesterone in conjunction with local irritants and microorganisms. Lesions are often erythematous, smooth, and lobulated, and they are seen mostly on the gingiva. The tongue, palate, and buccal mucosa may also be affected. Pregnancy tumors are most common after the first trimester, grow quickly, and usually disappear after birth.

Clinical complaints related with pregnancy-associated pyogenic granulomas are usually modest and include gingival bleeding, discomfort, and esthetic problems. The lesion typically appears as a quickly expanding gingival lump that bleeds abundantly when touched. Histologically, it is a highly proliferative vascular lesion that looks like granulation tissue. Estrogen stimulates vascular endothelial growth factor (VEGF) synthesis in macrophages, which is inhibited by androgens and may contribute to the development of pregnancy tumours.^[11]

These regulating effects of sex hormones can be used as therapeutic or preventive treatments in pregnancy tumors. Progesterone acts as an immunosuppressant in pregnant women's gingival tissues, preventing a rapid acute inflammatory response against plaque while allowing for an increased chronic tissue reaction, resulting in an exaggerated appearance of inflammation. Angiostatin expression in PG was significantly lower than in healthy and periodontally involved gingiva. The molecular mechanism underlying the regression of pregnancy tumors following parturition is unknown. It has been claimed that, in the absence of VEGF, Angiopoietin-2 (Ang-2) causes blood vessels to shrink. The highest protein level of Ang-2 was found in pregnant tumors, followed by postpartum and normal gingiva. VEGF levels were elevated in the granulomas.^[12]

III. Periodontitis

During pregnancy, women undergo physiological,

immunological, and hormonal changes that increase their susceptibility to infections, including oral and periodontal diseases. Changes in estrogen and progesterone levels also have an effect on the composition of the oral microbiota, compatible with the development of periodontitis.^[13] Periodontal diseases are also considered established or potential risk factors in numerous systemic diseases and conditions, such as cardiovascular disease, diabetes metabolic control, and a number of adverse pregnancy outcomes.^[14] Periodontitis can raise the risk of adverse pregnancy outcomes (APO), such as preterm birth, hypertension, gestational diabetes, low birthweight, and intrauterine development retardation. Furthermore, maternal periodontal disease appears to be related with stillbirth and infant death.^[15]

Two biological mechanisms supporting this association between periodontal diseases and APO have been proposed^[16]

- i. One through systemic dissemination of periodontal pathogens that could cross the placenta into the amniotic fluid and fetal circulation,
- ii. Other through inflammatory mediators such as interleukin-6 (IL-6), IL-8 and tumor necrosis factor alpha (TNF- α) produced during periodontal inflammation that could, by entering the systemic circulation, induce an acute inflammatory response affecting the foetus and placenta.

Pregnancy-associated periodontal disease is similar, but oestrogen and progesterone can aggravate gingival edema and vasculature. Carrillo de albornoz et al. (2010) discovered alterations in suspected periodontal disease (PD) pathogens throughout pregnancy. Periodontal pockets serve as a reservoir for oral microorganisms. Modifications in the oral microbiome may be considered a potential cause for the development of PD during pregnancy. A recent study found that deteriorating Parkinson's disease was connected with an increase in "red complex" bacteria such as *Porphyromonas gingivalis* and *Prevotella*. However, the proportions of the "red complex" bacteria did not change throughout pregnancy, although significant variations were discovered for all pathogens after childbirth.

A recent study found that bacterial loading of *Porphyromonas gingivalis* and *Tannerella forsythia* in the third month of pregnancy was associated with worsened PD as determined by bleeding on probing. Another recent study examined the bacteria load of pregnant women and the relationship to estradiol levels. The results revealed that *Campylobacter rectus* was higher in pregnant women than non-pregnant women.^[17]

Periodontitis and Female Infertility

The relationship between periodontitis and female infertility is not well understood. The scientific community has made numerous attempts to determine whether there is a link between these two conditions. Hart proposed in 2012, after analyzing the clinical

parameters of 3416 women, that the presence of periodontitis could be a risk factor for female conception (particularly in non-Caucasian women, given the high prevalence of periodontitis in 41.4% of the sample).

In a randomized controlled multicentre trial (Smile trial) done in Australia, women with oral inflammation (mainly non-Caucasian) had an average conception time of 7.1 months, compared to 5 months for women with normal oral health. Furthermore, they discovered a more than 2-month increase in the average female conception time among non-Caucasian women compared to the other groups.^[18]

The relationship between periodontal condition and the female reproductive system appears to be complex. Nonetheless, the secondary function of periodontitis in other disorders may help to explain why it can impair female fertility. Periodontitis has been associated to polycystic ovarian syndrome (PCOS), endometriosis (EM), obesity, bacterial vaginosis (BV), chronic kidney disease (CKD), and aging, all of which are risk factors for spontaneous pregnancy.

Poly Cystic Ovarian Disease and Periodontitis

Inflammation has a critical role in the pathophysiology of polycystic ovarian disease and periodontitis. As a result, the link between PCOS and PD was initially established on their shared correlation with Metabolic syndrome (MetS).^[19] Dursun et al.^[20] found that PCOS women exhibited higher levels of periodontal inflammation and destruction than non-PCOS women, with clear signs of oxidative stress and glycaemic dysregulation on GCF. Indeed, diabetes mellitus and oxidative stress are well-established risk factors for Periodontal Diseases and may play a substantial role in the PCOS-PD relationship. Furthermore, metabolic syndrome may play an important role by causing systemic inflammation and insulin resistance.^[21]

PCOS is associated with low-grade systemic inflammation, as evidenced by elevated levels of C reactive protein (CRP), proinflammatory cytokines and chemokines such as interleukin 18 (IL 18), monocyte chemoattractant protein 1 and macrophage inflammatory protein 1, as well as white blood cell count. Furthermore, elevated oxidative stress and its indicators indicate PCOS as an inflammatory condition.^[22] Periodontitis is a chronic inflammatory condition that is linked to a variety of systemic ailments. Later, the cascade of proinflammatory events was hypothesized as a potential link between PD and PCOS.^[23] Both disorders tend to function synergistically to promote proinflammatory cytokine expression, and the severity of Parkinson's disease may be related with PCOS exacerbation.^[24] Overall, the potential relationship between PD and PCOS is founded in chronic subclinical inflammation in both disorders.^[25] Chronic subclinical inflammation increases proinflammatory markers like C-Reactive Protein (CRP), tumor necrosis factor- α (TNF- α), interleukin (IL)-6, IL-

17, and matrix metalloproteinase-9, as well as local oxidative stress (e.g. myeloperoxidase and nitric oxide).

As a result, PCOS-induced subclinical inflammation may exacerbate periodontal damage, whereas PD-induced subclinical inflammation via direct invasion of periodontal microbiota may support PCOS etiology.^[26] Furthermore, PD management has been linked to insulin level control, as periodontal treatment reduced high glycemic levels; hence, unmanaged PD may have an indirect impact on PCOS clinical status (Figure 1).

Obesity and Periodontal Disease

The first report on the link between obesity and periodontal disease emerged in 1977, when Perlstein et al.^[27] discovered histopathologic alterations in the periodontium in genetically obese Zucker rats. Using ligature-induced periodontitis, they discovered that obese animals had higher alveolar bone resorption than non-obese rats. Furthermore, obesity did not appear to induce pathologic periodontal modifications in healthy oral settings; instead, in response to bacterial plaque accumulation, periodontal inflammation and destruction were more severe in obese mice. Later, epidemiological research validated the concept that obesity is a risk factor for periodontal disease.

In 1998, Saito et al.^[28] examined 241 healthy Japanese people and discovered for the first time a link between obesity and periodontal disease in humans. Furthermore, research have shown that the fat distribution pattern plays an important role in the connection with periodontitis. In 2005, Genco et al.^[29] examined National Health and Nutrition Examination Survey (NHANES III) data and found that BMI was positively connected with the degree of periodontal attachment loss; they discovered that this association is modified by insulin resistance.

The molecular processes underlying the obesity-periodontitis relationship are unknown; however, cytokines and hormones generated from adipose tissue may play an important role. Fat tissue is more than just the body's passive triglyceride store; it also produces a large variety of cytokines and hormones known as adipokines or adipocytokines, which can affect periodontitis (Figure 2).^[30,31]

Endometriosis and Periodontitis

While endometriosis and periodontal disease appear to be unconnected since they affect distinct physiological systems, both are chronic inflammatory illnesses with altered immune responses. This similar trait, known as "global immune dysregulation," may account for the increased prevalence of other systemic autoimmune illnesses in people with both conditions. The idea of global immunological dysregulation implies that immune system changes in one part of the body might have widespread repercussions, potentially impacting the development of numerous autoimmune and

inflammatory disorders. Recognizing these linkages may provide useful insights into diagnosis and treatment techniques.

Furthermore, both endometriosis and periodontal disease are associated with changes in immune modulators. Endometriotic lesions are associated with decreased NK cell activity and cytotoxicity against endometrial cells, as well as increased levels of sICAM-1, peripheral monocytes, peritoneal macrophages, and lymphocytes. Endometriosis patients have elevated levels of cytokines and factors in their peritoneal fluid, including IL-1 β , IL-6, IL-8, TNF- α , vascular endothelial growth factor, RANTES (regulated upon activation, normal T cell expressed and secreted), and monocyte chemoattractant protein-1.

Chronic periodontitis is associated with a persistent systemic inflammatory burden caused by the spread of periodontal pathogenic bacteria, their products (e.g., lipopolysaccharides), and locally produced inflammatory mediators (e.g., IL-1 β , IL-6, TNF- α , prostaglandin E2, and thromboxane B2) (Figure 3).^[32,33]

Bacterial Vaginosis (BV) and Periodontitis

There are microbial similarities between the oral and vaginal environments in the presence of both PD and BV, respectively.^[34] This association may indicate shared pathophysiological mechanisms, such as a weakened host response to infection. However, periodontal disorders and bacterial vaginosis may be connected due to similarities in the microbiota, specifically *Prevotella* species, as well as *Prevotella*-mediated inflammation. *Prevotella* stimulates dendritic cells to release IL-1 β , IL-6, and IL-23 via Toll-like receptor 2 (TLR2), which then triggers IL-17 synthesis by Th17 cells and activates neutrophils. On the other hand, recently discovered peptide toxins released by *Prevotella* may play a crucial role in causing systemic inflammation. As a result, *Prevotella*-mediated chronic inflammation causes localized bone loss and tissue degradation in PD and endotoxemia through lipopolysaccharides. Local inflammation generated by these illnesses spreads and can compromise systemic health.^[35] Overall, the possibilities for contamination through haematogenous spread or oral-genital direct transfer;^[36] however, the link between these two diseases is still poorly known.

Periodontal Disease and Pregnancy Outcomes

Galloway originally proposed that maternal periodontal infection could contribute to pregnancy difficulties such as "miscarriage, pyelitis, mastitis, phlebitis, anaemia, and toxemia of pregnancy" in 1931.^[37] Since then, evidence has accumulated associating maternal periodontal disease with poor pregnancy outcomes. Aside from increasing gingival inflammation, female sex hormones, particularly progesterone, play an important role in regulating several critical processes during pregnancy, including embryo implantation, gravidity maintenance, gestational immune responses, parturition

induction, and cervical ripening. Maternal immune responses are important not only for protecting the mother and her fetus from external infections, but also for allowing the pregnant woman to accept the fetus, which carries external DNA from the father and so functions as an allograft.^[38,39]

It is obvious that any triggering mechanisms that may disturb these physiologically complex processes may contribute to adverse pregnancy outcomes, including

mainly preeclampsia (i.e., maternal hypertension with proteinuria or pulmonary edema, oliguria, or convulsions after the 20th week of pregnancy), intrauterine infections (caused by microorganisms originated from genital or nongenital sources), preterm birth (any live birth before the 37th week of gestation), low birth Preeclampsia and premature birth are among the most common causes of maternal and neonatal morbidity and mortality (Figure 4).^[40-41]

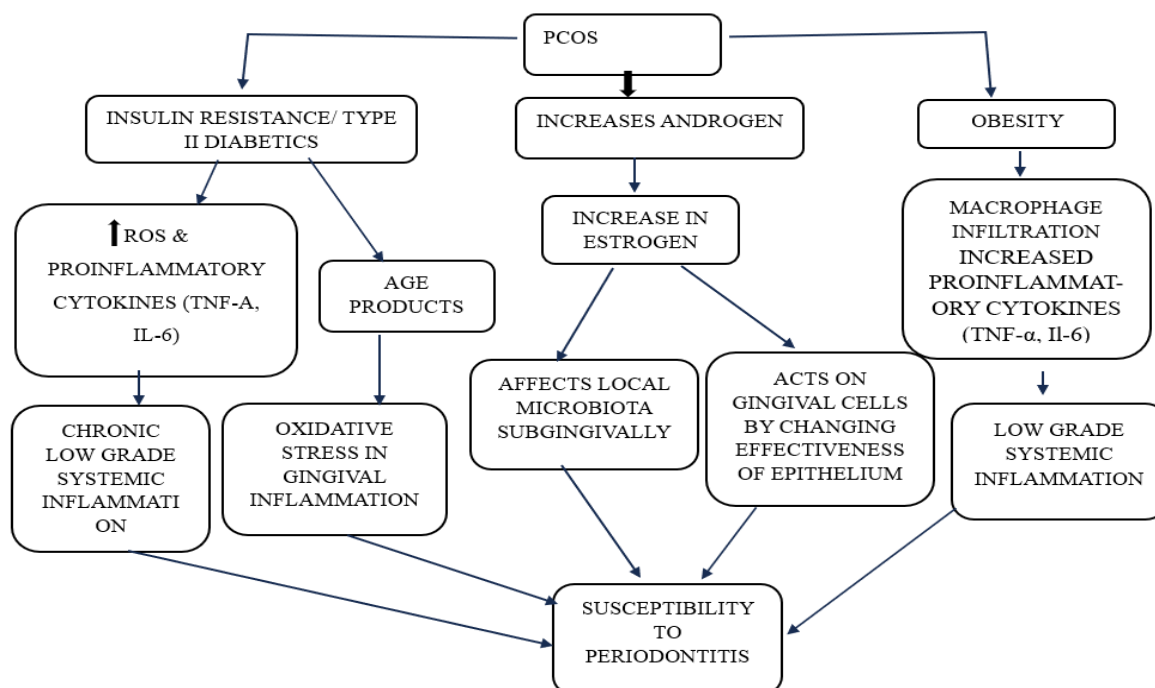


Figure 1: Type-II D.M. Type-II Diabetes Mellitus. ROS - Reactive Oxygen Species. AGE - Advanced Glycation End products. TNF α - Tumor Necrosis Factor α , IL-6 – Interleukin-6 (adapted from Tanguturi & Nagarakanti).^[26]

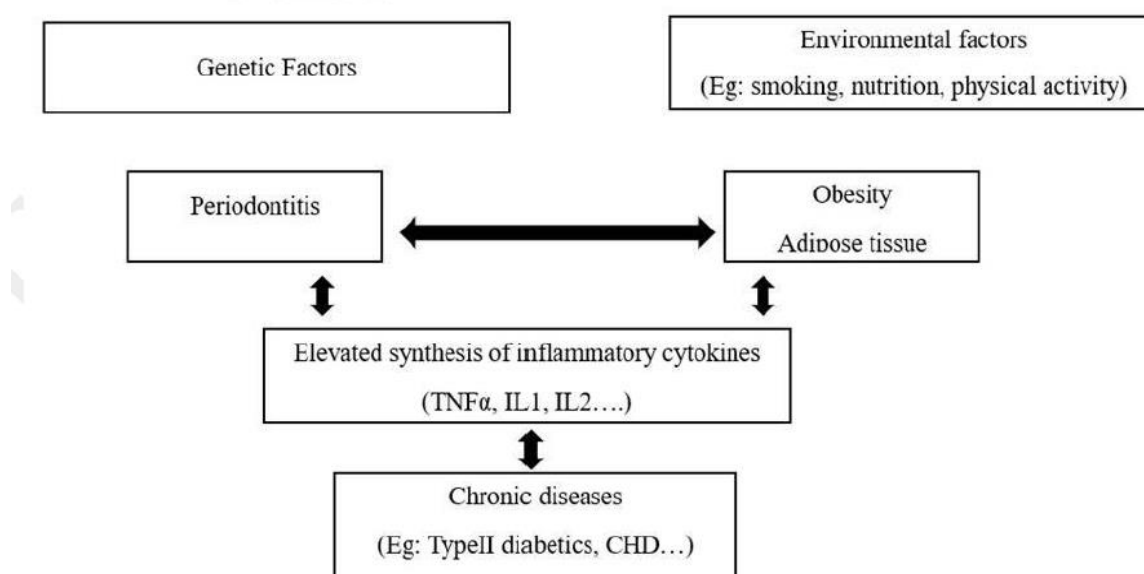


Figure 2: Model linking Periodontitis and Obesity with inflammation related chronic diseases (adapted from Jagannathachary & Kamaraj).^[31]

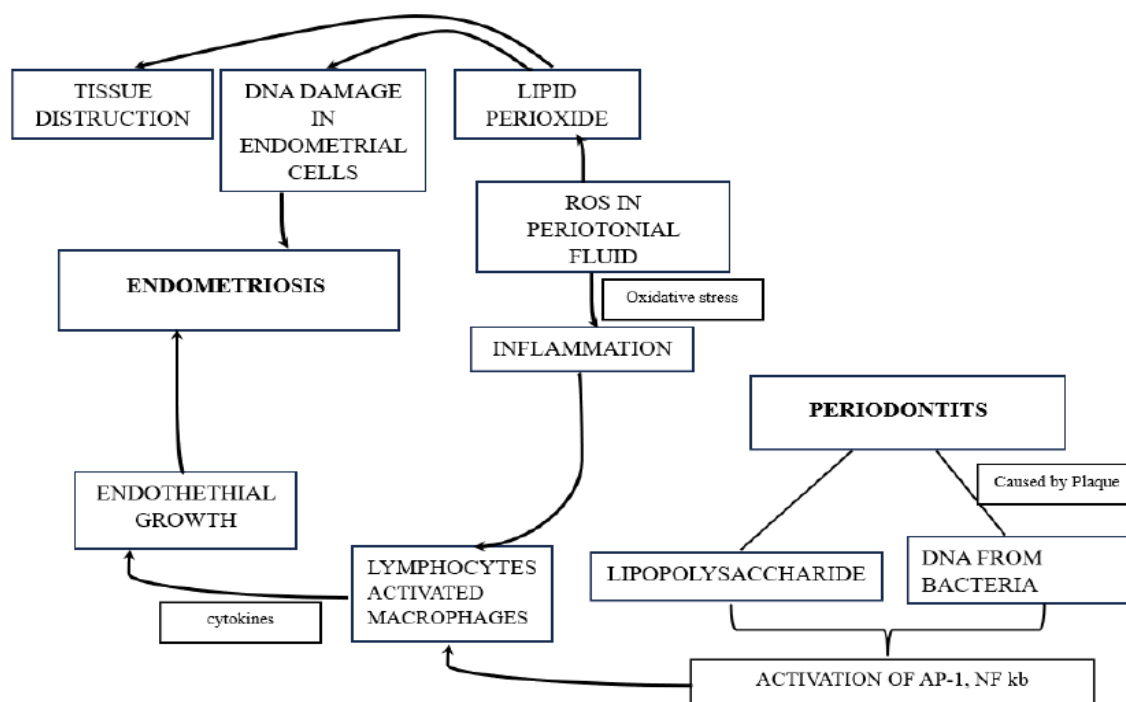


Figure 3: Towards a common etiopathogenesis: Periodontal disease and endometriosis (adapted from Thomas et al.,)^[33] (NF-κB – Nuclear factor kappa-light chain enhancer of activated B cells, AP-1 – Activator Protein 1).

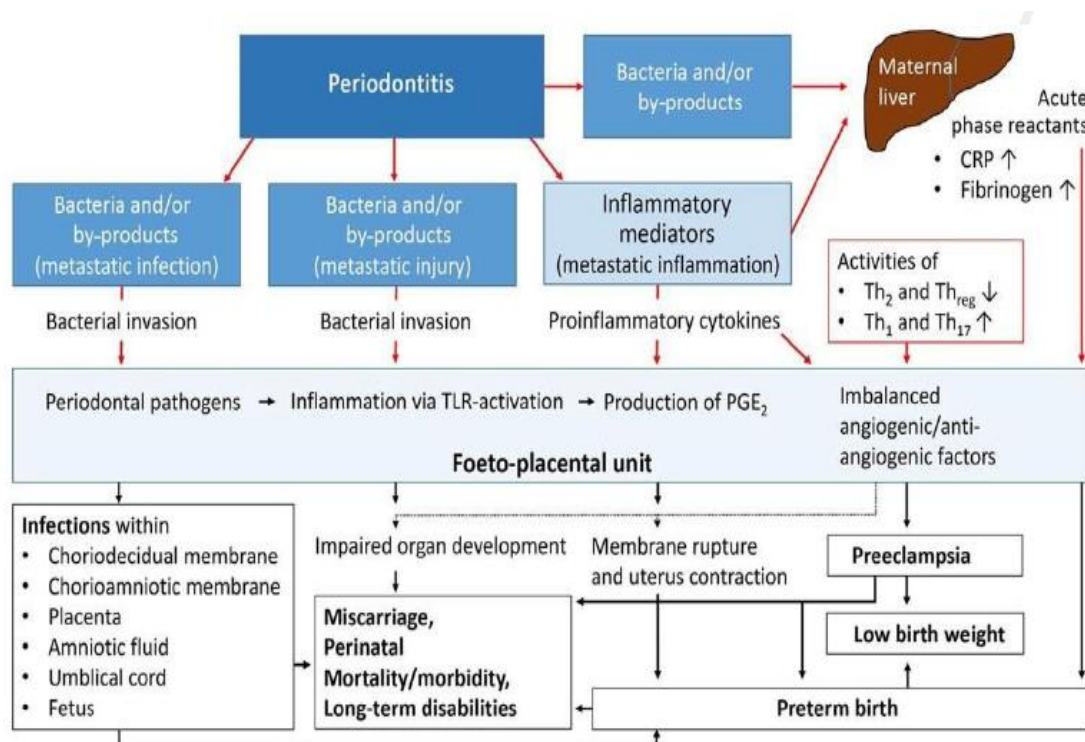


Figure 4: Proposed mechanisms/ pathways linking periodontal diseases to adverse pregnancy outcomes. CRP, C Reactive protein; PGE2, prostaglandin E2; Th, T helper cells; TLR, toll-like receptor (adapted from Bobetsis et al.).^[41]

CONCLUSION

In conclusion, the interplay between pregnancy and periodontal diseases highlights a critical area of concern in maternal health. Pregnancy-induced hormonal fluctuations, particularly increased levels of estrogen and

progesterone, contribute to an elevated risk of developing periodontal diseases such as gingivitis and periodontitis. These conditions can result in adverse pregnancy outcomes, including preterm birth, low birth weight, and potentially gestational diabetes. Emerging

evidence suggests that periodontal pathogens may influence systemic inflammation and immune responses, thereby exacerbating pregnancy-related complications.

Given the potential risks, it is imperative to incorporate routine periodontal screenings and early intervention strategies within prenatal care. This approach not only promotes maternal oral health but also mitigates the risk of adverse obstetric outcomes, ultimately improving both maternal and neonatal health.

REFERENCES

- Papapanou, P. N., Sanz, M., Buduneli, N., Dietrich, T., Feres, M., Fine, D. H., Flemmig, T. F., Garcia, R., Giannobile, W. V., Graziani, F., Greenwell, H., Herrera, D., Kao, R. T., Kebschull, M., Kinane, D. F., Kirkwood, K. L., Kocher, T., Kornman, K. S., Kumar, P. S., Loos, B. G., ... Tonetti, M. S. Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Clin Periodontol*, 2018; 45(Suppl 20): S162–S170.
- Bond TE. Pregnancy. In: A practical treatise on dental medicine, 2nd edn. Philadelphia, PA: Lindsay & Blakiston, 1852; 163–164.
- Srinivas, S. K., & Parry, S. Periodontal disease and pregnancy outcomes: time to move on? *J of Women's Health*, 2012; 21(2): 121–125.
- Komine-Aizawa, S., Aizawa, S., & Hayakawa, S. Periodontal diseases and adverse pregnancy outcomes. *The J of Obst and Gynaec Res.*, 2019; 45(1): 5–12.
- Xiong, X., Buekens, P., Fraser, W. D., Beck, J., & Offenbacher, S. Periodontal disease and adverse pregnancy outcomes: A Systematic Review. *BJOG: An Int J of Obstetrics and Gynaec.*, 2006; 113(2): 135–143.
- Gonzalez-Jaranay, M., Tellez, L., Roa-Lopez, A., Gomez-Moreno, G., & Moreu, G. Periodontal status during pregnancy and postpartum. *PloS one*, 2017; 12(5): e0178234.
- Silness, J., & Loe, H. Periodontal disease in pregnancy. 3. Response to local treatment. *Acta Odontol Scand*, 1966; 24(6): 747–759.
- Morelli, E. L., Broadbent, J. M., Leichter, J. W., & Thomson, W. M. Pregnancy, parity and periodontal on the subgingival microbiota? *J Periodontol.*, 2009; 80(1): 72–81.
- Hart R. Periodontal disease: could this be a further factor leading to subfertility and is there a case for a pre-pregnancy dental check-up? *Women's health (London, England)*, 2012; 8(3): 229–230.
- Dursun, E., Akalın, F. A., Guncu, G. N., Çınar, N., Aksoy, D. Y., Tozum, T. F., Kılınç, K., & Yıldız, B. O. Periodontal disease in polycystic ovary syndrome. *Fertility and Sterility*, 2011; 95(1): 320–323.
- Chen, M., Cai, W., Zhao, S., Shi, L., Chen, Y., Li, X., Sun, X., Mao, Y., He, B., Hou, Y., Zhou, Y., Zhou, Q., Ma, J., & Huang, S. Oxidative stress-related biomarkers in saliva and gingival crevicular fluid associated with chronic periodontitis: A systematic review and meta-analysis. *J of Clin Periodontol*, 2019; 46(6): 608–622.
- Nibali, L., Tatarakis, N., Needleman, I., Tu, Y. K., D'Aiuto, F., Rizzo, M., & Donos, N. Clinical review: Association between metabolic syndrome and periodontitis: a systematic review and meta-analysis. *The Journal of Clinical Endocrinology and Metabolism*, 2013; 98(3): 913–920.
- Kelly, C. C., Lyall, H., Petrie, J. R., Gould, G. W., Connell, J. M., & Sattar, N. Low grade chronic inflammation in women with polycystic ovarian syndrome. *The Journal of Clinical Endocrinology and Metabolism*, 2001; 86(6): 2453–2455.
- disease. *Aust Dent J.*, 2018. Yenen, Z., & Atacag, T. Oral care in pregnancy. *Journal of the Turkish German Gynecological Association*, 2019; 20(4): 264–268.
- Laine M. A. Effect of pregnancy on periodontal and dental health. *Acta Odontologica Scandinavica*, 2002; 60(5): 257–264.
- Armitage G. C. Bi-directional relationship between pregnancy and periodontal disease. *Periodontology* 2000 2013; 61(1): 160–176.
- Gondivkar SM, Gadail A, Chole R. Oral pregnancy tumor. *Contemp Clin Dent.*, 2010; 1(3): 190-2.
- Teles, F., Wang, Y., Hajishengallis, G., Hasturk, H., & Marchesan, J. T. Impact of systemic factors in shaping the periodontal microbiome. *Periodontol.*, 2000 2021; 85(1): 126–160.
- Beck, J. D., Papapanou, P. N., Philips, K. H., & Offenbacher, S. Periodontal Medicine: 100 Years of Progress. *J Dent Res.*, 2019; 98(10): 1053–1062.
- Han, Y. W., Fardini, Y., Chen, C., Iacampo, K. G., Peraino, V. A., Shamonki, J. M., & Redline, R. W. Term stillbirth caused by oral *Fusobacterium nucleatum*. *Obstetrics and Gynecology*, 2010; 115(2 Pt 2): 442–445.
- Ozaka, O., Ceyhan, B. O., Akcali, A., Bicakci, N., Lappin, D. F., & Buduneli, N. Is there an interaction between polycystic ovary syndrome and gingival inflammation? *J Periodontol.*, 2012; 83(12): 1529–1537.
- Porwal, S., Tewari, S., Sharma, R. K., Singhal, S. R., & Narula, S. C. Periodontal status and high-sensitivity C-reactive protein levels in polycystic ovary syndrome with and without medical treatment. *J Periodontol.*, 2014; 85(10): 1380–1389.
- Tong, C., Wang, Y. H., Yu, H. C., & Chang, Y. C. Increased Risk of Polycystic Ovary Syndrome in Taiwanese Women with Chronic Periodontitis: A Nationwide Population-Based Retrospective Cohort Study. *Journal of Women's Health*, 2019; 28(10): 1436–1441.
- Tanguturi, S. C., & Nagarakanti, S. Polycystic Ovary Syndrome and Periodontal disease: Underlying Links- A Review. *Indian Journal of Endocrinology and Metabolism*, 2018; 22(2):

- 267–273.
25. Perlstein, M. I., & Bissada, N. F. Influence of obesity and hypertension on the severity of periodontitis in rats. *Oral Surgery, Oral Medicine, and Oral Pathology*, 1977; 43(5): 707–719.
 26. Hajishengallis G. Periodontitis: from microbial immune subversion to systemic inflammation. *Nature Reviews. Immunology*, 2015; 15(1): 30–44.
 27. Adriaens, L. M., Alessandri, R., Sporri, S., Lang, N. P., & Persson, G. R. Does pregnancy have an impact Saito, T., Shimazaki, Y., Kiyohara, Y., Kato, I., Kubo, M., Iida, M., & Yamashita, Y. Relationship between obesity, glucose tolerance, and periodontal disease in Japanese women: the Hisayama study. *J Periodont Res.*, 2005; 40(4): 346–353.
 28. Genco, R. J., Grossi, S. G., Ho, A., Nishimura, F., & Murayama, Y. A proposed model linking inflammation to obesity, diabetes, and periodontal infections. *J Periodontol*, 2005; 76 (11 Suppl): 2075–2084.
 29. Kershaw, E. E., & Flier, J. S. Adipose tissue as an endocrine organ. *The Journal of Clinical Endocrinology and Metabolism.*, 2004; 89(6): 2548–2556.
 30. Jagannathachary, S., & Kamaraj, D. Obesity and periodontal disease. *Journal of Indian Society of Periodontology*, 2010; 14(2): 96–100.
 31. Offenbacher, S., & Beck, J. D. A perspective on the potential cardioprotective benefits of periodontal therapy. *American Heart Journal*, 2005; 149(6): 950–954.
 32. Thomas, V., Uppoor, A. S., Pralhad, S., Naik, D. G., & Kushtagi, P. Towards a Common Etiopathogenesis: Periodontal Disease and Endometriosis. *Journal of Human Reproductive Sciences*, 2018; 11(3): 269–273.
 33. Genco R. J. Host responses in periodontal diseases: current concepts. *Journal Of Periodontology*, 1992; 63(4 Suppl): 338–355.
 34. Larsen J. M. The immune response to *Prevotella* bacteria in chronic inflammatory disease. *Immunology*, 2017; 151(4): 363–374.
 35. Edwards, S., & Carne, C. Oral sex and transmission of non-viral STIs. *Sexually Transmitted Infections*, 1998; 74(2): 95–100.
 36. Galloway C. Focal infection *The American Journal of Surgery*, 1931; 14: 643–645.
 37. La Rocca, C., Carbone, F., Longobardi, S., & Matarese, G. The immunology of pregnancy: regulatory T cells control maternal immune tolerance toward the fetus. *Immunology Letters*, 2014; 162(1): 41–48.
 38. Bearfield, C., Davenport, E. S., Sivapathasundaram, V., & Allaker, R. P. Possible association between amniotic fluid micro-organism infection and microflora in the mouth. *BJOG: An International Journal of Obstetrics and Gynaecology*, 2002; 109(5): 527–533.
 39. Nature Chaiworapongsa, T., Chaemsathong, P., Yeo, L., & Romero, R. Pre-eclampsia part 1: current understanding of its pathophysiology. reviews. *Nephrology*, 2014; 10(8): 466–480.
 40. Bobetsis, Y. A., Graziani, F., Gursay, M., & Madianos, P. N. Periodontal disease and adverse pregnancy outcomes. *Periodontology* 2020, 2000; 83(1): 154–174.