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Guest Editorial

PERIODONTAL PHYSIOLOGY DURING PREGNANCY

Reproductive biologist, endocrinologist, consultant and physician running antenatal clinics, inadvertently, ignore the examination of oral cavity in women where lot of interactions occur between different tissues, cells, microbes and vascularity. Current research implies periodontial disease may alter the systemic health of the patient and adversely affect the well being of the foetus by elevating the risk for low–birth–weight preterm babies.

Hormones exert significant influence in body physiology throughout life. Women in particular, experience hormonal variation under both physiologic (e.g. menstruation, pregnancy) and non physiologic (e.g. use of hormonal contraceptives) conditions. This variation significantly affects the female health, by influencing physiology of host–parasite interaction in the body, and the oral cavity in particular.

What is the periodontium?

The word periodontium refers to the investing and supporting structures of the tooth. Periodontal tissues comprise of two parts : gingiva (the part of the oral mucosa that covers the alveolar processes of the jaws and surrounds the necks of the teeth) and whose main function is protection of the underlying tissues, and the attachment apparatus, composed of the cementum (the calcified mesenchymal tissue that forms the outer covering of the anatomic root of the tooth), the periodontal ligament (the connective tissue that surrounds the tooth and connects it to the bone), and the alveolar process. The periodontium is subject to morphologic, vascular and functional variation due to hormones (including female sex hormones) as well as changes associated with age. Gingivitis is the commonest disease of the periodontium. Others include periodontitis, in which the inflammation from the gums spreads into alveolar bone and periodontal ligament, leading to alveolar bone loss.

Pregnancy and the periodontium

Periodontal inflammation and pregnancy have now been linked for many years; as early as 1978, Vermeeran discussed "toothpains" in pregnancy (1). In 1818, Pitcarin described gingival hyperplasia in pregnancy (2). In 1887, Pinard described pregnancy gingivitis (3). Pregnancy–related changes are most frequent and most marked in gingival tissue. Pregnancy does not cause gingivitis, but may aggravate pre–existing disease. The most marked changes are seen in gingival vasculature. The gingival changes usually resolve within a few months of delivery if local irritants are eliminated (4).

The concept that ovarian hormones may increase inflammation in the gingival tissues and exaggerate the response to local irritants has been postulated by several studies (5, 6). Gingival inflammation is aggravated by an imbalance and/ or increase in sex hormones. Numerous studies have demonstrated in vitro and in vivo, that sex hormonnes affect and modify the actions of the cells of the immune system (7). In addition, evidence suggests that the interaction between estrogen and cells of the immune system can have non immune regulatory effects (8). Receptors for estrogen and progesterone (9) have been demonstrated in the gingiva and the gingival tissues and subgingival microflora respond with a variety of changes due to raised hormonal levels in pregnancy.

Epidemiological studies show the prevalence of pregnancy gingivitis ranging from 35% to 100% (8, 10, 11). Clinically, pregnancy gingivitis may range from mild to severee gingival inflammation. It may be characterised by erythema, edema, hyperplasia and increased bleeding tendency. Increased tissue edema may lead to increased probing depth and transient tooth mobility (12). Anterior site inflammation may be exacerbated by increased mouth breathing, primarily in third trimester due to pregnancy rhinitis.

Pregnancy tumors, pyogenic granuloma or pregnancy epulides occur in 0.2% to 9.6% of pregnancies (13). The anterior region of the maxilla is most commonly affected and the tumor appears most commonly in 2nd and 3rd month of gestation. They bleed easily; and may become hyperplastic or nodular. Clinically and histologically, they are indistinguishable from the same occurring in non pregnant females and men.

Due to pioneering research by Offenbacher, evidence exists that untreated periodontal disease in pregnant women may be a significant risk factor for preterm (<37 weeks gestation), low birth weight (<2500 grams) babies (14). The current opinion is that the co–relation of periodontal disease to preterm low birth weight (PLBW) births occur as a result of infection, and is mediated indirectly mainly by the translocation of bacterial products such as endotoxin (lipopolysaccharides/ LPS) and the action of maternally produced inflammatory mediators (15). Biologically active molecules such as prostaglandin PGE_2 and tumor necrosis factor-alfa (TNF) which are normally involved in normal parturition, are raised to artificially high levels by the infection process, which may foster premature labor (16). Recently, gingival crevicular fluid levels of PGE_2 were positively associated with intra amniotic PGE_2 levels (P=0.018) suggesting that Gram negative periodontal infection may present a systemic challenge sufficient to initiate the onset of premature labor, as a source of LPS and/ or through stimulation of secondary mediators such as PGE_2, Interleukin 1 beta (IL-1β), (17). Ongoing research supports the association of periodontal disease and PLBW. (18).

Raised sex hormone level and its effects

Estrogen and progesterone can contribute to pregnancy gingivitis (19). The

hormonal changes that occur during pregnancy include an elevation of both estrogen and progesterone. Upon fertilization and implantation, the corpus luteum continues to produce increasing amount of estrogen and progesterone while the placenta develops. The placenta, aside from providing nutrition to the fetus, serves as an endocrine organ that regulates the progress of the pregnancy. By the end of the third trimester, progesterone, estrogen reach their peak levels of 100 ng/ml and 6 ng/ml respectively, which represents 10 and 30 times the levels observed during the menstrual cycle (20). Estrogen may regulate cellular proliferation, differenciation and keratinisation, where as progesterone influences the permeability of microvasculature, alters the rate and pattern of collagen production and increases the metabolic breakdown of folate (necessary for tissue maintenance) (21). High concentration of sex hormones in the gingival tissue, saliva, serum and crevicular fluid may also exaggerate the response.

Regulation via hormones of most cellular processes occurs by interaction of these products with intracellular receptors. The resulting effects are dependent on the concentration of unbound hormone, diffused through the cell membrance. Receptors for estrogen and progesterone (9) have been demonstrated in the gingiva, providing direct biochemical evidence that this can be a target organ for both sex hormones. Also evidence of sex hormone concentration in the crevicular fluid exists, providing a growth medium for periodontal pathogens.

Sex hormone levels and maternal immune response

The maternal immune response is thought to be supressed in pregnancy. This may allow the fetus to survive as an allograft. Sera of pregnant women show marked increase of monocytes, which in large numbers inhibit in vitro, proliferative response to mitogens, allogenic cells & soluble antigens (22) and pregnancy specific B–1–glycoproteins contribute to diminished lymphocyte responsiveness to mitogens and antigens. Also, a decrease in the ratio of peripheral T helper cells to T supressor cells (CD4/CD8) has been reported to occur throughout pregnancy (23).

These changes in maternal immune response suggest an increase susceptibility to develop gingival inflammation. Studies have also shown decrease in neutrophil chemotaxis, depression of cell mediated immunity and phagocytosis and decreased T cell response with elevated ovarian hormones, especially progesterone (24). Decrease in vitro response of peripheral blood lymphocytes to several mitogens and a preparation of *Prevotella Intermedia* has been reported (25, 7). Evidence formulates a decrease in absolute numbers of CD4 positive cells in peripheral blood during pregnancy as compared with the number of same cells post partum (26, 23). Lapp et al suggest that high level of progesterone during pregnancy affects the development of localized inflammation by down regulation of interleukin 6 production, rendering the gingiva less efficient at resisting the inflammatory challenges produced by the bacteria (27).

Progesterone stimulates the production of prostaglandins PGE_2 and PGE_2 in particular, which are protent mediators of the inflammatory response. With PG acting as immunosuppressants, gingival inflammation may increase, when PGE_2 and PGE_2 (mediators) levels are high (28, 29).

Kinnby et al found that high progesterone levels during pregnancy influenced plasminogen activator–inhibitor type 2 (PAI–2) and disturbed the balance of fibrinolytic system. As PAI–2 serves as an inhibitor of tissue proteolysis, the above research implies that the components of the fibrinolytic system may be involved in the development of pregnancy gingivitis (30).

Sex hormone levels and subgingival plaque composition

Dental plaque can be defined as the soft deposits that form a biofilm adhering to the tooth surface or other hard surfaces in the oral cavity. It is composed primarily of microorganisms, which exist within an intercellular matrix of host cells like epithelial cells, macrophages and leukocytes. Subgingival plaque is found below the gingival margin.

An alteration in the composition of subgingival plaque occurs during pregnancy due to the change in subgingival microenvironment, caused by an increased accumulation of active progesterone, whose metabolism is reduced during pregnancy (29) and the ability of *Prevotella Intermedia* to substitute an essential growth factor, Vitamins K with progesterone and estrogen (31). Kornman and Loesche found that during the second trimester, gingivitis and gingival bleeding increased without an increase in plaque levels (32). These authors suggested that estrogen or progesterone could act as substitute growth factors in place of menadlone (vitamin K) for *P. Intermedia* (33).

Despite similar scores for plaque levels in both pregnant and nonpregnant women, the Gingival index (GI) of pregnant women was significantly increased, during 1st and 2nd trimeters as compared to controls (34).

Bacterial anaerobic to aerobic ratios increased in addition to *Bacteroides Melaninogenicus and Prevotella Intermedia* proportions (2.2% to 10%). Jansen et al demonstrated a 55–fold increase in the proportion of P. Intermedia in pregnant women compared with non–pregnant controls (35). This suggests that progesterone plays a major role in the shift of microorganisms. There was also an increase in *Porphymonas gingivalls* during the 21st to 27th weeks of gestation, but this was not statistically significant.

Conclusions

Both estrogen and progesterone affect the oral cavity significantly. Fortunately, healthy women experience minimal and transient side effects from variation in hormone levels. Although a significant proportion of pregnant women suffers from pregnancy gingivitis, this condition is both self limiting and transient. Gingival tissues return to their original healthy state post partum when estrogen and progesterone levels reach baseline values.

In the clinical situation, aside a transient increase in gingivitis, bleeding and a subgingival microbial shift, pregnant women in good health are unlikely to experience any significant gingival response that would have serious clinical implication. However, women who are susceptible or have a pre–existing gingival condition should seek treatment to prevent extension of the inflammatory process into the deeper structures of the periodontium that may cause bacteremia. In general, pregnant women should note that preventive measures consisting of dental prophylaxis and meticulous plaque control help to prevent any periodontal condition from developing. Hence routine peridontial examination should be included as one of the antenatal check up during pregnancy and any dysfunction should be thoroughly investigated and treated for the sake of health of the mother and baby.

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