



# Unifying Etiopathologic Association Between

# Periodontal Disease

and

# Pregnancy Hypertension

## Summary

Gestational hypertension or hypertension during pregnancy (Preeclampsia) is a yet to be understood significant obstetric problem which is responsible for poor perinatal and maternal outcome. It is hypothesized that presence of inflammatory disease as remote as the one like periodontal disease could contribute to the etiopathogenesis of pregnancy hypertension through proinflammatory vasoactive mediators. In the present article, the available published evidences are chronicled in logical manner and unifying pathogenesis is outlined.

**Keywords:** Periodontal disease, preeclampsia, hypertension in pregnancy, inflammatory mediators



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**D**espite the advances in prenatal care and increased public awareness, the adverse pregnancy outcomes continue to haunt the caring obstetricians and present a major public health problem worldwide. Complicated pregnancies impose a risk both to the mother and to the offspring. Of late, there has been a growing interest in exploring the association between periodontal disease and pregnancy complications. The ability of periodontal pathogens and their virulence factors to disseminate and induce both local and systemic inflammatory responses in the host has led to the hypothesis that periodontal disease may have consequences beyond the periodontal tissues themselves.

#### **Periodontal disease**

Periodontal disease is a common chronic disorder of infectious origin leading to progressive destruction of supportive tissues of the teeth. It is initiated by infection predominantly with gram negative, anaerobic organisms.<sup>1</sup>

In the absence of adequate oral hygiene, periodontal pathogenic bacteria accumulate in the gingival crevice and form an organized "bacterial biofilm." In mature biofilms, the bacteria possess variety of virulence factors, including lipopolysaccharide (LPS) which may cause direct destruction to the periodontal tissues or stimulate the host to activate a local inflammatory response intended to eliminate the infection.<sup>2</sup> Bacteria

and/or their virulence factors may disseminate throughout the body through blood stream and trigger the induction of systemic inflammatory responses. Though this concept was mooted initially by Miller in 1891, it is only in the last two decades that the increasing research and therapeutic interest is evinced.

#### **Periodontal disease and Systemic Diseases**

There is growing evidence that suggests an association between periodontal disease and various systemic diseases.<sup>3</sup> Different studies and analyses have added further evidence to the association between periodontal diseases and cardiovascular, cerebrovascular diseases and diabetes mellitus.<sup>4,5</sup>



### Periodontal Disease and Pregnancy

Periodontal disease represents an infectious disease affecting more than 23 percent of women between the ages of 30 and 54 years.<sup>6</sup> Commonly identified in pregnant women, periodontal disease has also been implicated in the etiopathologic process of second trimester miscarriage, preterm births and low birth weight babies and in preeclampsia. The interest in the associations is so keen that increased research and publications to study it has resulted in spate of meta-analyses and systematic reviews.<sup>7,12</sup>

### Periodontal Disease and Pregnancy Hypertension

Preeclampsia is a pregnancy specific form of hypertension that develops after 20 weeks of pregnancy, and presents a major health problem worldwide. The disorder has several names: preeclampsia or preeclamptic toxemia (pregnancy hypertension with significant proteinuria), pregnancy induced hypertension or gestational hypertension (hypertension-only developing in pregnancy and not

lasting beyond 12 weeks of delivery), pregnancy aggravated or superimposed hypertension (in a woman with pre-existing hypertension), and so on. The severe form may manifest with derangement of liver enzymes, reduction in platelets, features of hemolysis or even seizures. Vasospasm is considered as the central pathology. Preeclampsia is but one aspect of the disease process where there is hypertension developing in pregnancy with significant proteinuria. Most of the reports have referred to the disease as 'preeclampsia', which we feel is not representative. Since manifestation of hypertension in pregnancy is essential for the clinical diagnosis and other presentations could be considered as its effects, in the present communication it is preferred to refer as 'pregnancy hypertension' to encompass the whole spectrum of the disease.

Pregnancy hypertension complicates 5% to 8% of all pregnancies and increases both maternal and neonatal morbidity and mortality.<sup>11</sup> The mainstay of therapy for it remains clinical recognition through prenatal care and termination of the disease process with delivery. In countries where prenatal care is not adequate, pregnancy hypertension accounts for 40% to 80% of maternal deaths, an estimated 50000 per year. Many of these deaths may be preventable with prenatal care, evidence-based pharmacologic therapy and timely termination of pregnancy.

Infants of women with pregnancy hypertension have a 5-fold increase in mortality compared with infants of

mothers without the disorder. Much of the neonatal mortality is attributable to iatrogenic prematurity. In developing countries, perinatal mortality is further increased.

Advances in the understanding of preeclampsia are essential to guide preventive and therapeutic strategies to decrease the worldwide impact of this disease. In spite of active research for many years, how pregnancy incites or aggravates hypertension remains unsolved.<sup>14</sup> Current theories include abnormal placentation, cardiovascular maladaptation to pregnancy, genetic and immune mechanisms, an enhanced systemic inflammatory response, and nutritional, hormonal, and angiogenic factors contributing as affectors or effectors.<sup>15, 16</sup> It seems probable, however, that multiple factors are involved. It is suggested that inflammation mediators may



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have a role in causing preeclampsia or its manifestations.

Normal pregnancy evokes a mild increase in the systemic inflammatory response that becomes considerably greater in pregnancy hypertension (preeclampsia).<sup>16</sup> Based on this concept, some authors have hypothesized that inflammation mediators might be involved in the etiology and pathogenesis of preeclampsia, both in terms of its initiation by increasing the risk of acute uteroplacental atherosclerosis and/or its potentiation by amplifying the maternal systemic inflammatory response.<sup>17, 18</sup> Cytokines including TNF- $\alpha$  and some interleukins may contribute to the associated oxidative stress. According to this hypothesis, oxygen-free radicals may lead to the formation of self-propagating lipid peroxides that propagate highly toxic radicals, which in turn, injure endothelial cells. Such injury modifies endothelial cell production of nitric

oxide and interferes with prostaglandin balance. Other consequences of oxidative stress include activation of microvascular coagulation, increased capillary permeability, and the production of lipid-laden macrophage foam cells, which are the characteristic features of atherosclerosis. Acute atherosclerosis, the characteristic placental lesion of pregnancy hypertension (preeclampsia), shares with atherosclerosis a similar pathology, pathogenesis (inflammation), and clinical settings (endothelial cell damage). It is also characterized by focal endothelial disruption, fibrinoid necrosis of the arterial wall, infiltration of perivascular spaces by mononuclear cells, and lipoprotein deposition.<sup>19</sup>

There are efforts to etiopathologically related periodontal disease and hypertension developing in pregnancy. Periodontal disease during pregnancy is shown to markedly increase a woman's risk of developing



pregnancy hypertension. In addition, those women in whom periodontal disease progressed were more likely to get preeclampsia.<sup>20, 21</sup> Significant associations between a recent history of early-onset preeclampsia and severe periodontal disease has been reported.<sup>22</sup>

It has been suggested that the mechanisms described in the development of atherosclerosis resemble the pathophysiological mechanisms described in preeclampsia, and are associated with infectious agents. There is evidence

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that chronic infection can be an important cofactor in initiating atherogenesis, and these epidemiological data support the premise that chronic infection could link pre-eclampsia (pregnancy hypertension) with atherosclerosis, especially given the increased susceptibility to chronic infection because of reduced cell-mediated immunity in pregnancy.<sup>23</sup> Studies conducted on different populations have suggested that atherosclerosis could be linked with chronic oral infections.<sup>24</sup>

Recently, it has been demonstrated that several candidate periodontal pathogens, including *Porphyromonas gingivalis*, can be detected in atheromatous plaque and not only the presence of antigens of five cell types in the placental tissues have been demonstrated, statistically higher bacterial counts of all six periodontopathic bacterial species are found in the placenta of women with preeclampsia.<sup>25, 26, 27</sup> These findings suggest that *P. gingivalis* and other periodontal pathogens may commonly colonize placental tissue, leading to an inflammatory response. It is possible that these pathogens can promote and modify pre-eclampsia sharing the mechanisms described in the development of atherosclerosis. The report claiming association between exposure to oral pathogens and increased plasma levels in women with preeclampsia and in their placenta of sFlt-1, an antiangiogenic factor that induces endothelial dysfunction, adds to the causal hypothesis theory for the disease.<sup>28</sup> It can be suggested that periodontal disease, which causes chronic inflammation, could thus be linked with pregnancy hypertension. These relationships leading to the disease of hypertension in pregnancy could be summarized as in Fig 1.

Although, most of the above details point to the etiopathogenic relationship between these two

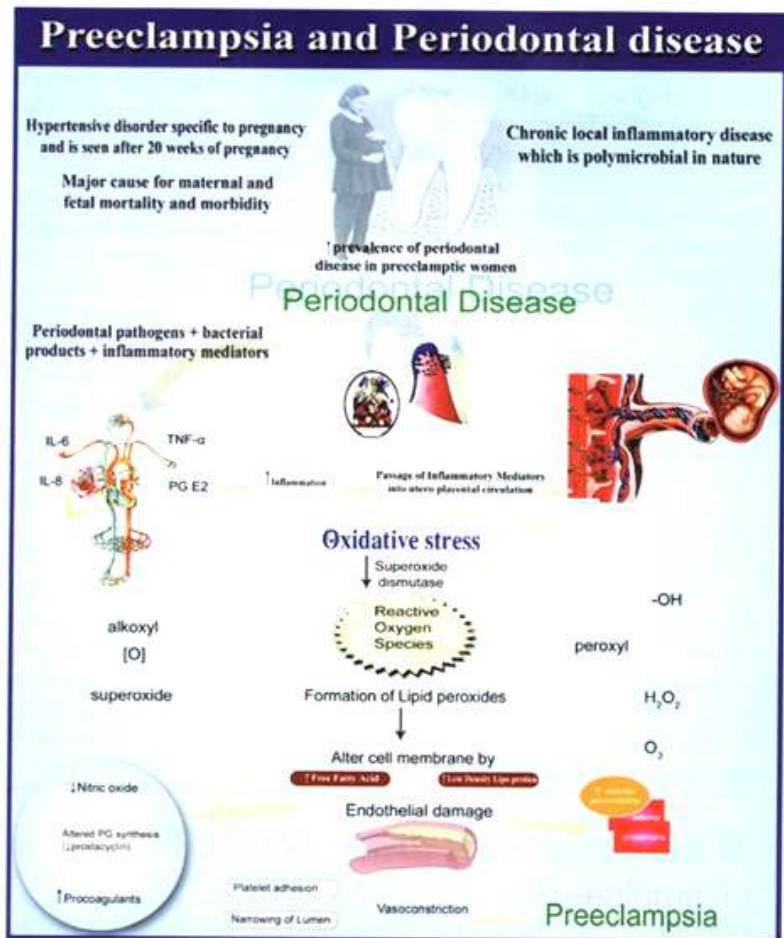


Fig 1: Unifying pathogenesis

entities, one cannot ignore the findings of the studies that failed to find evidence of an association between periodontal disease and preeclampsia.<sup>29</sup>

### Conclusions

Although periodontal organisms are implicated, it is not known whether a particular bacterial species or group of bacteria is involved in the disease process initiating pregnancy hypertension. To relate periodontal disease with pregnancy hypertension it is necessary to know effect of prevention or treatment of periodontal disease to reduce the incidence and severity of pregnancy hypertension. However, periodontal disease treatment in pregnant



woman carried out in second trimester is safe for both mother and the unborn child. There is a biological plausibility that untreated periodontal disease may increase the risk of development of hypertension in pregnancy that may affect the wellbeing of offspring.

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