

Does Periodontal Disease Exacerbate Systemic Conditions? A review of existing evidence

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INTRODUCTION

Systemic health is often closely linked to the state of oral cavity. Many systemic diseases and conditions have oral manifestations; likewise, oral microbial infections may also affect one's general health status¹. Animal and population based studies now suggest that periodontal diseases may be linked with systemic diseases.² This concept is not new; it was in 1891 when "focal infection theory" by Miller was documented to suggest that "microorganisms or their waste products obtain entrance of parts of the body adjacent to or remote from the mouth".³

In the late 1990s an organized effort was launched to disseminate information on new findings which support what dental professionals had long suspected: infections in the mouth can cause damage elsewhere in the body.⁴

Periodontal infection is associated with a complex micro biota of approximately 500 microbial taxa and various human viruses with significant virulence potential.⁵ Recently several mechanisms of metastatic spread of infections from oral cavity through their toxins and inflammatory cytokines have been proposed which open the way for a more realistic assessment and better understanding of the systemic importance of periodontal disease.⁵⁻⁸

This paper reviews evidence from published literature that correlates periodontal infections and systemic disorders. It also attempts to indicate periodontal disease as potential risk factors in various diseases.

Periodontal Infections

Dental plaque is a natural biofilm that forms on the tooth surface and consists of a diverse microbial community embedded in a polymer matrix of bacterial and salivary origin⁹. There is about 500 species of bacteria in the oral cavity, 415

of these are part of sub gingival plaque¹⁰. Dental plaque adheres to the tooth surface and if not removed by regular tooth brushing would cause gingival irritation and lead to inflammation of periodontium.

Periodontitis is a chronic inflammatory disease of the supporting tissue of teeth, the cause of which is infection by oral microflora¹¹. It is a condition that can result in the inflammatory destruction of periodontal ligament and alveolar bone. Bacteria from these diseases in the oral cavity can enter the blood stream, travel to major organs, begin new infections and pose a serious threat to people whose health is compromised.

Several observational studies indicate periodontal infection as a risk factor for systemic condition like cardio-vascular disease, cerebro-vascular accidents, bacterial pneumonia, diabetes mellitus and pre-term delivery of low birth weight babies.⁵⁻⁸

Correlation between Periodontal Disease and Coronary Artery Disease

Coronary heart disease is caused by thickening of the inside walls of the coronary arteries, called atherosclerosis, is by far the commonest cause of coronary artery blockage. Recent studies indicate that dental infection such as periodontal disease as a potential risk factor for Cardio-Vascular Diseases (CVD)¹².

Oral bacteria such as streptococcus sanguis and Pseudomonas gingivalis induce aggregation of platelets¹³. These platelets aggravating the bacteria on entering the blood stream may increase the risk for thrombogenic events including myocardial infarction and stroke.

It has also been reported that inflammation caused by periodontitis increases plaque build up in the arteries, which creates a greater risk of CVD¹³. Studies have found that people with periodontal

disease are almost twice as likely to suffer from coronary disease as those without periodontal disease. Periodontal diseases can also exacerbate existing heart conditions¹⁴.

Periodontal Disease and Cerebro-vascular Disease or Stroke

Stroke is damage to brain tissue either due to cerebral infarction or hemorrhage. The most common underlying cause of stroke is atherosclerosis in the vessels. Risk Factors for this phenomenon are Hypertension, Diabetes Mellitus, Smoking, Hyperlipidemia and chronic inflammation.^{15,16}

In chronic periodontitis it has been found that there is increased levels of systemic markers of inflammation¹⁷ e.g., C-reactive Proteins (CRP) and interleukin 6 (*IL6*). It also causes activation of WBCs, leading to pro inflammatory cytokines release, which causes arterial inflammation, hepatic synthesis of clotting factors and platelet aggregation, all resulting in thrombus formation^{18,19}

High Tumor Necrosis Factor (TNF) levels and high TNF receptor levels are documented in atherosclerosis and each unit increase in TNF receptor levels increases the odds of maximal carotid plaque thickness $\geq 1.5\text{mm}$.¹⁹ TNF and IL-6 are cytokines, produced by Macrophages and are acute phase reactants and are marker of chronic infection and inflammation.

A recent study found periodontal bacterial species in the samples of carotid plaques removed during surgeries.²⁰ Another study suggested the role of a role for periodontitis in atherosclerosis by the interaction of *Porphyromonas gingivalis* with low-density lipoproteins²¹. It has been reported that in patients with periodontal inflammation, a *Streptococcus sanguis* protein associated with platelet aggregation and bacteremia associated with *Porphyromonas gingivalis* may contribute to some acute thromboembolic events²².

These studies suggest a strong cause and effect relationship between periodontal disease and stroke.

Periodontal Disease and Diabetes Mellitus

Diabetes mellitus develops either as deficiency in insulin production or an impaired

utilization of insulin. It is a major health problem characterized by metabolic abnormalities and long-term complications involving eyes, kidneys, nerves, vasculature²³.

Recent studies have provided suggestive evidence for a bi-directional adverse inter relationship between diabetes mellitus and periodontal disease^{24,25}. Several reports describing periodontal treatment of diabetic patients have provided direct evidence that periodontal infection has an adverse, yet modifiable, effect on glycemic control²⁶.

At least one study has suggested that effective control of periodontal infection in diabetic patients reduces the level of AGE'S (Advanced Glycation End Products) in the serum. These AGE'S are formed due to hyperglycemia. They act with the endothelial cells and monocytes making them more susceptible to stimuli that induce the cells to produce inflammatory mediators²⁷. Studies have shown that periodontal anti microbial treatment has the potential to reduce the level of glycated hemoglobin in diabetic patients^{24,25,28}.

Periodontal Disease and Pre-Term Delivery of Low Birth Weight Babies

Pre term delivery of low birth weight (PLBW) is considered major problem in many countries²⁹⁻³². PLWB is defined as birth rate $< 2.5\text{ kg}$ before the gestational age of 37 weeks³³. PLWB remains a significant public health issue, as it is a leading cause of neo-natal death before their first birthday³⁴.

It has been suggested that during normal pregnancy, maternal hormones and locally acting intra amniotic cytokines play a key role in regulating the onset of labor, uterine contractions and delivery. Abnormal production of these mediators and cytokines in the setting of infection triggers pre-term labor and low birth weight^{35,36}.

A recent study suggests that periodontal disease during pregnancy could have a casual relationship with low birth weight babies (LBWB). Microbiological data indicate that four microorganisms associated with mature plaque and progression of periodontitis (*Bacteroides forsythus*, *Porphyromonas gingivalis*, *Actinobacillus actinomycetemcomitans* and *Treponema denticola*)

were detected at higher levels in PLWB mothers as compared to normal birth weight (NBW) controls³⁶.

Another study shows that some pro inflammatory mediators such as Prostaglandin E2 and Interleukin 1 beta levels in women with PLWB were found to be higher in their gingival crevicular fluid and blood serum after the bacterial lipopolysaccharide stimulations^{34,38}, such as localized non-disseminating substantaneous infection with *Porphyromonas gingivalis* (a common periodontal pathogen) which can significantly reduce the fetal weight by up to 25%³⁷.

In 1996, a scientific team composed by Periodontists, Gynecologists and Epidemiologists found that 18% of pre-term low birth weights in 250,000 cases studied were due to periodontal infections³⁸. Poor periodontal health of the mother is considered as a potential independent risk factor for PLWB with a greater influence rate compared to other risk factors. Periodontal disease was concluded to be seven times more likely to be associated with a pre-term delivery of a low birth weight infant than mother's age, race, number of births and use of tobacco or alcohol³⁹.

Periodontal Disease and Chronic Obstructive Pulmonary Disease (COPD)

COPD is a condition that arises due to chronic obstruction to airflow and excess production of mucous secretion. Main cause of this disease is smoking and bacterial infection. However, recent studies suggest that the mouth may play an important role in infections acquired in hospitals and nursing homes, especially infections of the respiratory tract⁴⁰.

Periodic exacerbations of COPD are due to infection typically by bacteria such as streptococcus pneumoniae, haemophiles influenza and branhamella catarrhalis. Aspiration of saliva into which oral bacterial antigens, lipopolysaccharide and enzymes have been released promotes inflammation and infection of lower airway⁴¹, it is also possible that host derived mediators such that cytokines and prostaglandins which are elevated in saliva of subject with periodontal disease, may modify oropharyngeal mucosal surfaces to promote growth of respiratory pathogens which are then aspirated into the lungs.

Several studies have demonstrated that daily mechanical oral hygiene with or without use of an oral antiseptic such as 0.12% chlorhexidine gluconate or 1% povidone iodine not only reduces the prevalence of colonization by oral pathogens but also reduces the rate of COPD and pneumonia by 50%⁴².

Periodontal Disease and failure of Orthopedic Implants

Studies have shown that staphylococcus aureus and staphylococcus epidermis are the main causative agents of orthopedic implants infection and failures^{43,44}.

Infections are usually caused by microorganisms which have remained latent since the time of operation or have metastasized from other infected site such as skin, respiratory tract, urinary bladder, nasal cavity or certain dental procedures which are known to cause transient or prolonged bacteremia thus causing infections around total joint replacement⁴⁵.

Staphylococcus aureus being normal commensal of oral cavity enter the periodontal pocket and subsequently the blood circulation through open blood vessels in the deep periodontal pocket causing bacteremia^{2,3,5}. This bacteria has hydrophobic strains which help them to adhere to the orthopedic implant⁴⁶. Microorganisms there make a biofilm around the implant⁴⁷. Bacteria are less exposed to host defense system and antibiotics thus causing infection around orthopedic implant and can only be cured by removing the implant⁴⁵.

Periodontal Disease and Osteoporosis

Osteoporosis is a progressive metabolic disorder characterized by decrease both in bone minerals and bone Matrix. A direct association between periodontal disease and osteoporosis has been postulated because there is likelihood of decreased oral bone density with it, which can contribute towards periodontitis progression. In addition it may affect treatment options⁴⁸.

The histological and radiographic evidence also support that osteoporosis affects alveolar bone density⁴⁹. Therefore, oral loss of bone can cast similar effect on weakening of tooth socket and eventually its loss as systemic osteoporosis might

result in vertebral and other fracture⁵⁰. Similarly bisphosphonates, which are used in osteoporosis to reduce osteoclastic activity in bone, have shown promise in outcome of periodontal diseases⁴⁹.

The prevalence of osteoporosis is high among the women especially those who post menopausal and are not taking hormone replacement therapy (HRT), interestingly in the same group of tooth loss is high⁵¹. Another indirect but seemingly convincing evidence which points towards a strong link between systemic osteoporosis and periodontal problems is emerging through studies in which the impact of systemic treatment of osteoporosis on periodontal conditions has been evaluated. It has been observed when HRT was given for osteoporosis it leads to reduce risk of being edentulous^{52,53}.

CONCLUSIONS

For a long time risk factors which contribute to certain diseases have been known. Measures are adopted to prevent disease and this includes elimination or control of the known risk factors. Now evidence is mounting that suggests a new risk factor – periodontal disease.

This review highlights studies that indicate periodontal infection as a risk factor for systemic condition like cardio-vascular disease, cerebro-vascular accidents, bacterial pneumonia, diabetes mellitus and pre-term delivery of low birth weight babies. It also emphasizes the role of periodontal infections in success of orthopedic implants and indicates that periodontal disease may be an early marker for osteoporosis.

While more research needs to be done to say definitively that people with oral disease are at higher risk for developing above mentioned diseases. We do know that diseases of the oral cavity are bacterial infections, and all infections are cause for concern.

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