Periodontal disease: Understanding oral-systemic connections

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Abstract

Periodontal diseases are collection of several pathological conditions characterized by degeneration of gums, periodontal ligaments, alveolar bone, dental cementum, and migration of epithelium leading to the formation of periodontal pockets. Metastatic spread, metastatic injury, and metastatic inflammation are the three basic pathways linking oral infections to secondary systemic diseases. *Metastatic spread* of infection may occur from oral cavity to systemic circulation due to transient bacteremia. The study emphasizes on discussion about potential risk factors. Therefore, it is important to understand all possible risk-factors if morbidity and mortality due to this disease are to be reduced. Oral infection may represent a significant risk factor for systemic diseases, and hence the control of oral disease is essential for the prevention and management of these systemic conditions.

Keywords: bacteremia, inflammation, metastatic spread, periodontal ligaments

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Introduction

As per WHO (2012) oral health is essential to general health and quality of life. "*It is state of being free from the mouth and facial pain, oral and throat cancer, oral infection and sores, periodontal (gum) disease, tooth decay, tooth loss, and other diseases and disorders that limit an individual's capacity in biting, chewing, smiling, speaking and psychosocial well-being*" (WHO, 2012).

Periodontal diseases are characterized by chronic inflammation and are among the most prevalent chronic infections in humans worldwide. Periodontal diseases are collection of several pathological conditions characterized by degeneration of gums, periodontal ligaments, alveolar bone, dental cementum, and migration of epithelium leading to the formation of periodontal pockets. Activation of the host defense system against infectious microbes, releases inflammatory cell mediators which causes degeneration of supporting collagen, followed by loss of attachments, supportive connective tissue and bone leading to pocket formation 'a characteristic feature of periodontitis' (Armitage, 1999). Furthermore, tooth loss may occur affecting psychological and physiological functions of a person (Mishra and Yadav, 2015).

Loss of teeth is not only the problem with periodontitis but its linkage to systemic condition creates more severity. The pockets become a favorable residence for anaerobic microbes and transformation of the local environment of pockets from "an endogen poly-microbial opportunistic flora" to "gram-negative proteolytic and predominantly anaerobic" microorganisms occurs (Caton and Ryan, 2011; Oh et al., 2002).

Most importantly, lipopolysaccharide (LPS) component of the outer membrane of bacteria evokes the liberation of inflammatory mediators such as Interleukins (IL-β and IL-6), tumor necrosis factor (TNFα), and cytokines *via*. activation of p38 mitogen-activated protein kinase pathways (Kirkwood and Rossa Jr, 2009). However, only specific bacterial products are responsible for evoking the host inflammatory response (Havemose-Poulsen and Holmstrup, 1997). Thus, it has been observed that bacteria are necessary to drive inflammatory response for the occurrence of periodontitis, but they alone cannot cause disease. Presence of a susceptible host is another parameter as periodontal breakdown (bone loss, attachment loss) is predominantly caused by host-derived destructive enzymes including osteoclasts, proteolytic enzymes and MMPs, and inflammatory mediators such as cytokinins (C-reactive protein (CRP), TNF-α), prostaglandin E2 (PE2), and interleukins (IL-1 and IL-6) secreted during inflammatory cascade. Moreover, old age people (>45 years) having weakened immune system are most susceptible host. Besides, neutrophil dysfunction in children may lead to the development of periodontitis (Pihlstrom et al., 2005). Paradoxically, host immune

response which is for the protection against microbes, here is responsible for the breakdown of the soft and hard periodontal tissues (Caton and Ryan, 2011; Ryan, 2002).

As per the several reports available periodontitis is not only associated with irreversible bone and tooth loss but it introduces complications in various systemic diseases including cardiovascular diseases, stroke, atherosclerosis, overt nephropathy, end-stage renal disease, diabetes, arthritis, adverse pregnancy outcomes, obesity, and Alzheimer's disease (Fig. 1.).

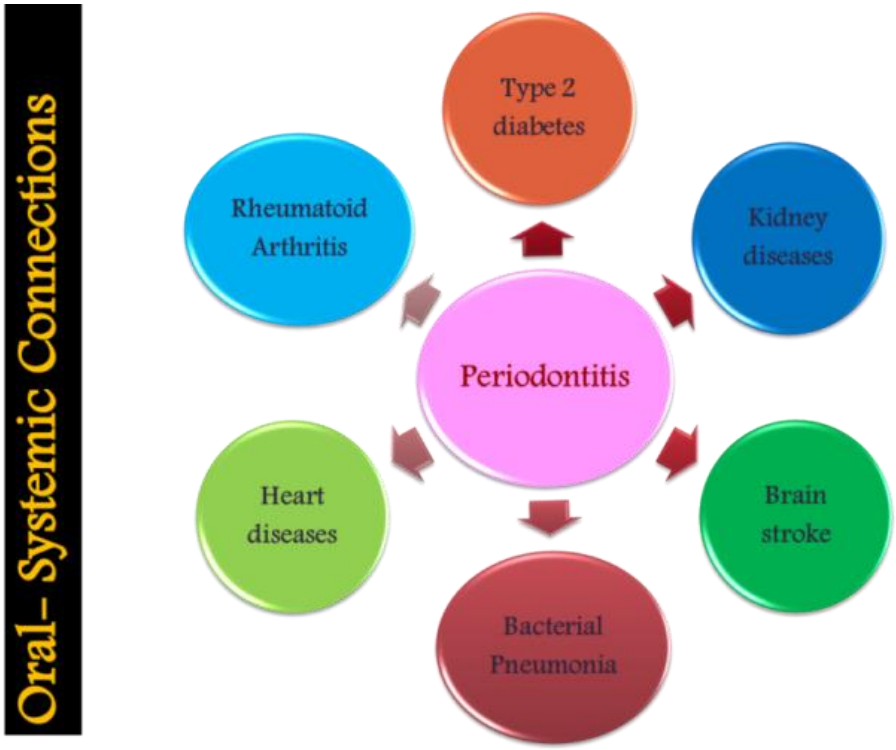

Fig1.: Schematic diagram illustrating oral-systemic connections

Previous reports suggest periodontitis and systemic diseases are interconnected *via*. circulation of cytokines and other inflammatory mediators in blood, due to spread of infection to other tissue and systemic circulation when the disease is untreated. Nevertheless, patients suffering from periodontitis often appear asymptomatic but these patients have a high risk of development of cardiovascular diseases including atherosclerosis, stroke, and myocardial infarction (Cotti et al., 2011; Katz et al., 2001).

Further, infective endocarditis has been found to be linked with periodontitis, as per the reports of World biomedical literature during 1930 to 1996, infective endocarditis has been found to be associated with periodontal infection. The incidence of infective endocarditis was about 0.70 to 6.8 per 100,000 people. Of all cases, 8% cases were related with the periodontal disease without any dental procedure and the risk of infective periodontitis after the dental procedure was about 1 per 3,000 to 5,000 procedures (Drangsholt, 1992; Li et al., 2000).

Additionally, systemic inflammation produced by periodontal infection lead to overt nephropathy and end-stage renal disease (ESRD) in individuals with type II diabetes. the inflammatory markers such as C-reactive protein and chronic low-level inflammation causes endothelial dysfunction, which is further responsible for the pathogenesis of kidney diseases (Craig et al., 2002; Shultis et al., 2007).

More and more studies point towards a possible association between periodontal disease and increased risk of cardiovascular disease. Higher incidence of poor oral hygiene and periodontal disease was found in patients with cerebrovascular, coronary and peripheral vascular atherosclerotic disease (Katz et al., 2001).

Pathways linking periodontitis to systemic disease

Periodontium acts as a reservoir for inflammatory mediators. The most common circulating cytokines include: CRP, IL-1, IL-6, TNF-α and PE2 were found in high concentration in periodontium (Kuo et al., 2008; Seymour et al., 2007). The spillover concentrations of mediators make them enter blood circulation to perpetuate systemic effects. For instance, IL-1β augments coagulation and thrombosis and retards fibrinolysis, whereas IL-1, TNF-α, and thromboxane can cause platelet aggregation and adhesion, the formation of lipid-laden foam cells, and deposition of cholesterol (Li et al., 2000). Studies indicated high levels of CRP were present in patients with cardiovascular diseases and advanced periodontitis (Seymour et al., 2007). They further account for preterm labor and low birth weight of infants (Page, 1998).

Metastatic spread, metastatic injury, and metastatic inflammation are the three basic pathways linking oral infections to secondary systemic diseases. *Metastatic spread* of infection may occur from oral cavity to systemic circulation due to transient bacteremia (caused by the presence of bacteria in the blood), *metastatic injury* occurs from the effects of circulating oral microbial toxins which may enter other organs, and *metastatic inflammation* is caused by immunological injury provoked by oral microorganisms. (Li et al., 2000)

Additionally, two susceptibility models had been proposed to explain these connections; (i) in common susceptibility model hypothesis, the presence of periodontal microbes, a susceptible person will develop periodontitis and atherosclerosis due to involvement of genetically determined phenotype which has greater risk for both diseases. (ii) The hypothesis of systemic inflammation model states that there is increased circulation of cytokines and other inflammatory mediators emanating from diseased periodontium, which in turn could damage the vascular endothelium and result in atherosclerosis (Seymour et al., 2007).

Conclusion

A common phrase says 'A healthy mouth is a gateway to a healthy body'. Thus, good oral health contributes towards good overall health. From the several reported studies it is clear that oral infection may represent a significant risk factor for systemic diseases, and hence the control of oral disease is essential for the prevention and management of these systemic conditions. Therefore, it is important to understand all possible risk-factors if morbidity and mortality due to this disease are to be reduced.

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