Review Article

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PERIODONTITIS- SYSTEMIC DISEASES INTERRELATIONSHIP : AN UPDATE

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ABSTRACT:

It is now becoming widely recognized that certain systemic diseases may increase the risk for periodontal disease. The hypothesis that oral conditions, such as periodontal infections, may be a risk factors or indicators for important medical outcome represents a paradigm shift in thinking about causality and the two-way directionality of oral and systemic associations. The term Periodontal Medicine, as first suggested by Offenbacher (1996), can be viewed as a broad term that defines a rapidly emerging branch of Periodontology focusing on the wealth of new data establishing a strong relationship between periodontal health or disease and systemic health or disease. The current evidence also supports that prevention and treatment of periodontal disease may reduce chronic systemic disease risk at both the individual level and community level and the possibility that morbidity and mortality from systemic diseases may be reduced by improving periodontal health. Therefore, Proper use of the knowledge of potential relationships between periodontal disease and systemic health requires the dental professional to expand his or her horizons, to step back from the technically demanding aspects of the dental art, and to recognize the oral cavity as one of the many interrelated organ systems.

Keywords: Periodontitis, Systemic Diseases, Inflammation

INTRODUCTION

The term Periodontal Medicine, as first suggested by Offenbacher (1996), can be viewed as a broad term that defines a rapidly emerging branch of Periodontology focusing on the wealth of new data establishing a strong relationship between periodontal health or disease and systemic health or disease. This means a two-way relationship in which periodontal disease in an individual may be a powerful influence on an individual's systemic health or disease as well as the more customarily understood role that systemic disease may have in influencing an individual's periodontal health or disease. Logically included in this definition would be new diagnostic and treatment strategies that recognize the relationship between periodontal disease and systemic disease.[1]

It is now becoming widely recognized that certain systemic diseases, such as osteoporosis, diabetes and immune disorders, etc., may increase the risk for periodontal disease. The hypothesis that oral conditions, such as periodontal infections, may be also a risk factors or indicators for important medical outcome represents a paradigm shift in thinking about causality and the directionality of oral and systemic associations.[2]

The possibility that morbidity and mortality from systemic diseases may be

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reduced by improving periodontal health makes it imperative that this relationship be examined more closely. When one considers that periodontal disease is a chronic infection that produces a local and systemic host response, as well as a source of bacteremia, it is not surprising that there is increasing evidence to support this hypothesis. Proper use of the knowledge of potential relationships between periodontal disease and systemic health requires the dental professional to expand his or her horizons, to step back from the technically demanding aspects of the dental art, and to recognize the oral cavity as one of the many interrelated organ systems. [1]

WHAT DOES THE EVIDENCE SAY ?

A significant recent advance in health care has been moved toward a model of evidence-based practice, which is also gaining attention in dentistry. An important component of the evidence-based approach is risk assessment, involving the classification of an individual's probability of acquiring a disease based on scientifically determined risk factors. Currently, the most commonly used methods of assessing periodontal disease in populations typically involve measures of clinical attachment loss or radiographic alveolar bone loss. However, due to the chronic and episodic and multifactorial nature of periodontal disease, such assessments necessarily measure the cumulative effects of the disease process over time rather than the current disease activity. Since there is currently no generally accepted assessment tool to reliably measure active periodontal disease, the value of longitudinal studies become apparent as they permit assessments of change over time. Such longitudinal studies are of particular value in evaluating potential causal relationships, in large part as they allow examination of the temporal sequence of the appearance of risk factors and the subsequent occurrence of disease and its progression. However, the strongest evidence for evaluating the role of potential risk factors most often comes from experimental studies, such as a randomized controlled trial in which modification of the risk factor is randomly assigned to a test group as compared to a control group that receives a placebo intervention, for example. [2]

ORGAN SYSTEMS AND CONDITIONS POSSIBLY INFLUENCED BY PERIODONTAL INFECTIONS:

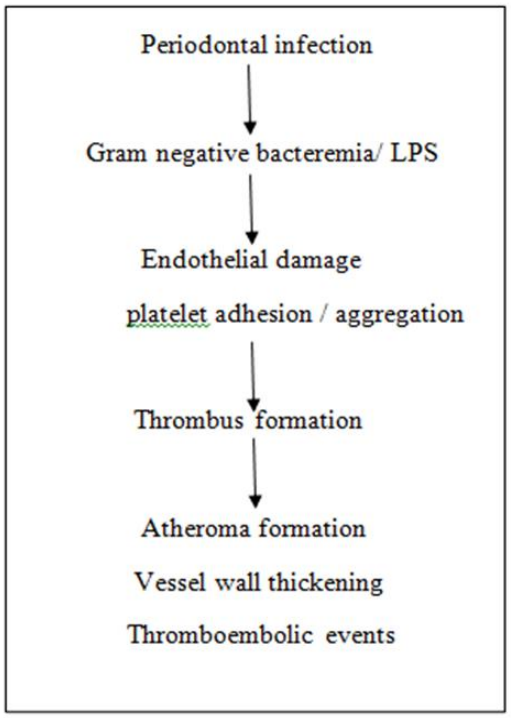
CARDIOVASCULAR/ CEREBROVASCULAR SYSTEM	• ARTERIOSCLEROSIS • CORONARY HEART DISEASES • ANGINA PECTORIS • MYOCARDIAL INFARCTION • CARDIOVASCULAR ACCIDENT(STROKE)
ENDOCRINE SYSTEM	• DIABETES MELLITUS • OBESITY
REPRODUCTIVE SYSTEM	• PRE TERM LOW BIRTH WEIGHT BABIES (PLBW) • ERECTILE DYSFUNCTION • POLYCYSTIC OVARY SYNDROME

RESPIRATORY SYSTEM	• CHRONIC OBSTRUCTIVE PULMONARY DISEASES • ACUTE BACTERIAL PNEUMONIA
BONE DISORDERS	• RHEUMATOID ARTHRITIS • OSTEOPOROSIS
CENTRAL NERVOUS SYSTEM	• DEMENTIA • ALZEIMER'S DISEASE • OBSTRUCTIVE SLEEP APNEA
RENAL SYSTEM	• CHRONIC RENAL DISEASE, END STAGE RENAL DISEASE
BLOOD DISORDER	• ANEMIA
GASTRO INTESTINAL SYSTEM	• HELICOBACTER PYLORI INFECTION
SKIN DISORDER	• PSORIASIS
NEOPLASMS	

CARDIOVASCULAR DISEASES

Cardiovascular diseases comprise a variety of heart and vascular conditions including: ischemia, atherosclerosis, peripheral artery disease, infective endocarditis and acute myocardial infarction. There is also increasing evidence that one of the potential risk factors may be periodontal disease. Cardiovascular disease and periodontal disease have a number of characteristics in common. These commonalities suggest that periodontal disease and heart disease may also share a similar causative pathway. [3]

Gram negative bacteria and the associated lipopolysaccharides cause infiltration of inflammatory cells into the arterial wall, proliferation of arterial smooth muscle, and intravascular coagulation. These changes are identified to those seen in naturally occurring atheramatosis. Patients with periodontitis are at a increased risk for thickening the walls of major coronary arteries. Periodontal diseases results in chronic systemic exposure to products of these organisms. Low level bacteremia may initiate host responses that alter coagulability, endothelial and vessel wall integrity, and platelet function resulting in atherogenic changes and possible thromboembolic events. [1]



Cardiovascular and periodontal infection interrelationship

DIABETES MELLITUS

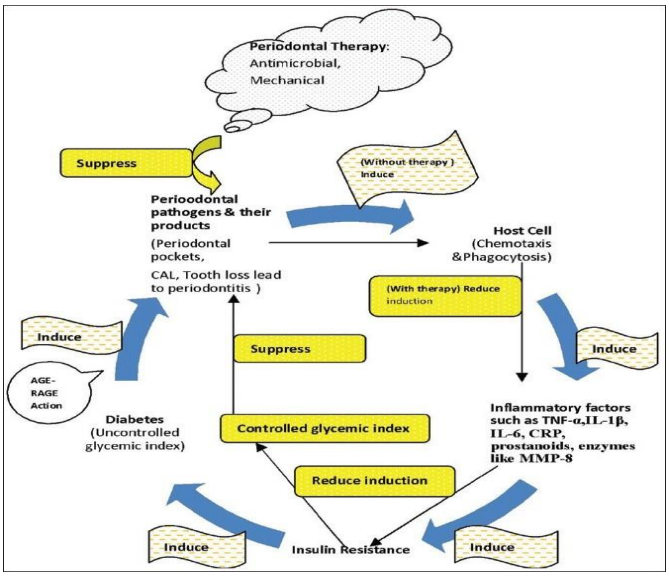
"Diabetes mellitus is a clinically and genetically heterogenous group of disorders affecting the metabolism of carbohydrates, lipids and proteins".

Mechanisms of interaction between diabetes mellitus and periodontium[5]	
Changes in subgingival environment	Altered microbiota Change in gingival crevicular fluid Composition
Altered tissue homeostasis and wound healing	Decreased collagen production Increased matrix metalloproteinase activity Accumulation of advanced glycation end products Decreased tissue turnover
Changes in host immunoinflammatory response	Decreased polymorphonuclear leukocyte chemotaxis, adherence, phagocytosis Elevated proinflammatory cytokine response from monocytes/macrophages Increased tissue oxidant stress

Diabetic influence on periodontium

Examination of the available data reveals strong evidence that diabetes is a risk factor for gingivitis and periodontitis, and the level of glycemic control appears to be an important determinant in this relationship. Loe in 1993 had stated that periodontal disease can be considered as sixth complication of diabetes. [4]

Effects of periodontal therapy on glycemic control



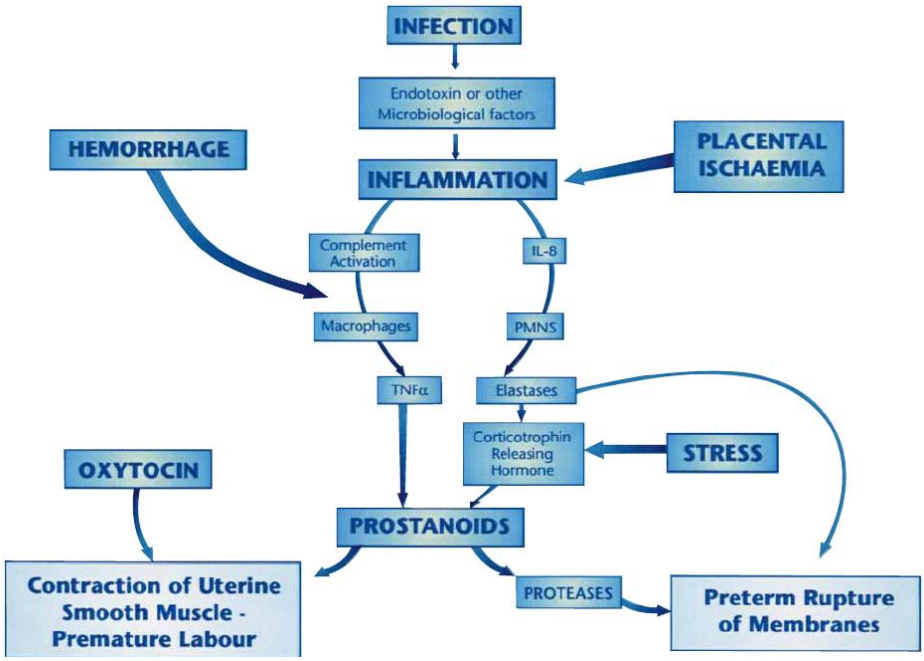
PREGNANCY COMPLICATIONS

Adverse pregnancy outcomes include Preterm Birth Low birth weight, Preeclampsia, Bacterial vaginosis, Pre mature rupture of membranes, Small for gestational baby.

Mechanisms involved in preterm labour [6]:

The possible mechanisms involved with preterm labor includes normal physiologic process happening early,

infection, inflammation, hemorrhage, placental ischemia.



Role of periodontitis

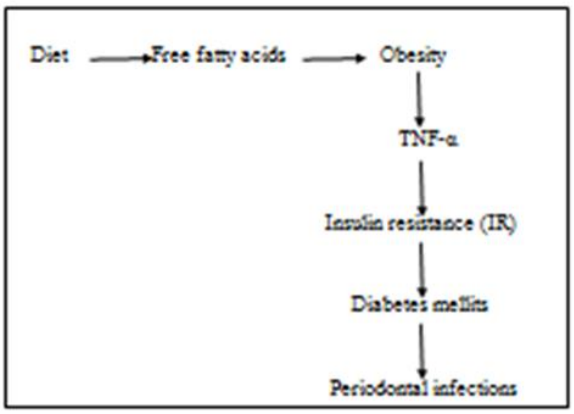
In the early 1990s, studies havehypothesized that oral infections, such as periodontitis, could represent a significant source of both infection and inflammation during pregnancy. Studies stated that periodontal disease is a Gram-negative anaerobic infection with the potential to cause Gram negative bacteremias in persons with periodontal disease. They hypothesized that periodontal infections, which serve as reservoirs for Gram negative anaerobic organisms, lipopolysaccharide (LPS, endotoxin) and inflammatory mediators including PGE2 and TNF-α may be a potential threat to the fetal-placental unit.[4]

Women having LBW infants have higher levels of Actinobacillus actinomycetemcomitans, Tannerella forsythia, Porphyromonas gingivalis and Treponema denticola in their subgingival plaque. Women having LBW infants have higher levels of gingival crevicular fluid (GCF) PGE2 and IL-1. GCF levels of IL-1 and PGE2 have been shown to correlate highly with intraamniotic IL-1 and PGE2 levels. Thus women having LBW infants have a higher prevalence and severity of periodontitis, more gingival inflammation, higher levels of putative periodontal pathogens and an elevated subgingival inflammatory response compared with women having normal birth weight infants.[4]

OBESITY

Obesity, defined as a body mass index (BMI) ≥ 30.0 kg/m2.

$$BMI = \frac{\text{Body weight(in Kg)}}{\text{Body height (in mt2)}}$$



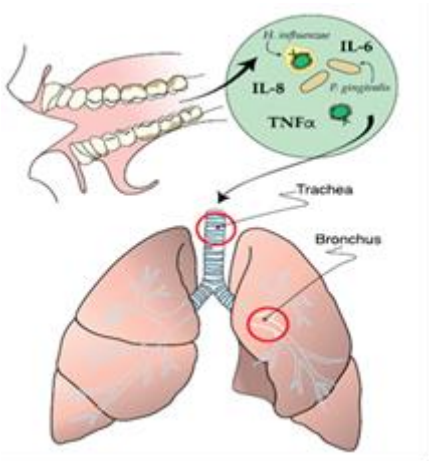
Association between obesity and periodontal disease

The underlying biological mechanisms for the association of obesity with periodontitis are not well-known. However, adipose tissue derived cytokines and hormones may play a key role. Fat tissue is not merely a passive triglyceride reservoir of the body, but also produces a vast amount of cytokines and hormones, collectively called adipokines or adipocytokines, which in turn may modulate periodontitis. [7] In 1998, for the first time Saito et al analyzed in healthy Japanese individuals an association between obesity and periodontal disease in humans. Studies have indicated that the fat distribution pattern plays a crucial role in the association with periodontitis.[8]

A proposed model linking inflammation to obesity, diabetes and periodontal disease [9]

RESPIRATORY DISEASE

Accumulating evidence suggests that oral dis¬orders, particularly periodontal disease, may influ¬ence the course of respiratory infection. Many studies have described the major respiratory diseases caused or influenced by bacteria, the epidemiologic evidence that supports a role for oral bacteria in the process of respiratory infection, and possible mechanisms that may explain the role of oral bac¬teria in the process of respiratory infection.



Potential mechanisms of action of oral bacteria in the pathogenesis of respiratory infection [10]

Several mechanisms can be envisioned to help explain how oral bacteria can participate in the pathogenesis of respiratory infection:

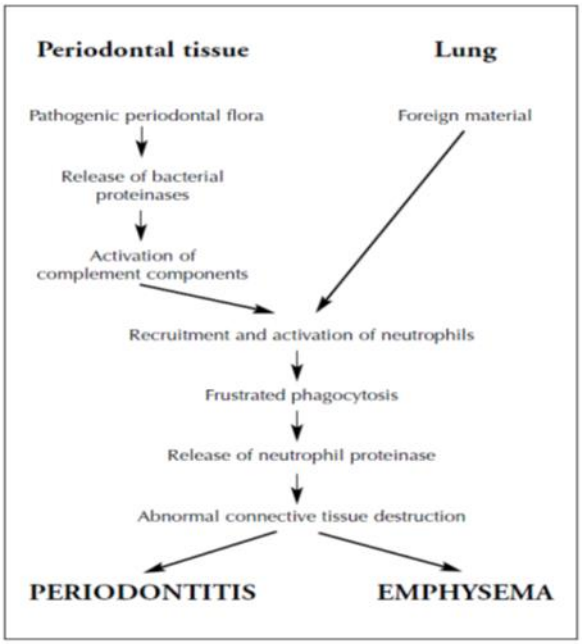
a)Aspiration of oral pathogens (such as P. gingivalis, A. actinomycetemcomitans) into the lung to cause infection.

b)Periodontal disease associated enzymes in saliva may modify mucosal surfaces to promote adhesion and colonization by respiratory pathogens.

c)Periodontal disease associated enzymes may destroy salivary pellicles on patho¬genic bacteria.

d)Cytokines originating from periodonral tissues may alter respiratory epitheli¬um

to promote infection by respiratory pathogens.



Mechanism of tissue destruction in periodontal disease and respiratory diseases. [11]

OSTEOPOROSIS

Osteoporosis can be defined as "a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration with a consequent increase in bone fragility and susceptibility to fracture." According to Third National Health and Nutrition Examination survey (NHANES III) osteopenia of hip was significantly associated with severity of periodontal disease in females and males, independently of the confounding effect of age, gender, smoking or intake of dietary calcium. Osteoporosis and periodontal disease are chronic, multifactorial diseases. Risk factors common to both osteoporosis and periodontal disease are genetic, dietary, environmental, and systemic factors. Common treatment strategies for osteoporosis and periodontal disease includes hormone replacement therapy, bisphosphonates, calcitonin, selective estrogen receptor modulator, parathyroid hormones etc.

RENAL DISEASES

Chronic kidney disease (CKD) is a catchall term for a variety of chronic conditions that result in compromised kidney function, which is measured as the glomerular filtration rate (GFR).

Chronic periodontal inflammation may also contribute to the chronic systemic inflammatory burden associated with CKD. Recent data suggest that high periodontal pathogen antibody titers, periodontal disease incorporating bleeding as a indicator of active inflammation and markers of chronic inflammatory burden contribute to chronic kidney disease. Systemic dissemination of bacterial pathogens, antigens, endotoxins, and inflammatory cytokines is related to the chronic inflammatory burden of periodontal disease. As a source of systemic inflammatory burden, it is biologically plausible to consider periodontal disease as a putative risk factor for chronic kidney disease.

CRP a marker of inflammation in blood has been shown to be elevated in both periodontal and CKD patients. In an ESRD patient population on hemodialysis, serum IgG antibody to P. gingivalis was reported to be correlated with CRP values, suggesting that destructive periodontal diseases may elevate CRP in

this population. Elevated CRP values with periodontal infections would seem likely that periodontal infections may significantly contribute to the increased incidence of atherosclerotic complications faced by ESRD patients on hemodialysis. [12]

NEOPLASMS

Several studies have reported associations between periodontal disease or tooth loss and risk of oral, upper gastrointestinal, lung, and pancreatic cancer in different populations.

The main risk factors for the development of oral cancer are tobacco and alcohol consumption, both of which are associated with dental hygiene and therefore likely to be confounders of an association with tooth loss. Similarly, as H.pylori is only associated with non cardia gastric cancer, the observed increase in risk with tooth loss suggests that certain oral bacteria could play a role in this subtype of cancer through similar inflammatory mechanisms. [13]

ANEMIA

Periodontitis is an inflammatory disease of the supporting tissues of tooth caused by specific microorganisms in the susceptible host. Gram negative anerobic bacteria are most commonly associated with initiation of periodontitis. The bacteria and their products evoke an immunoinflammatory reaction in the host tissue. Although this process is intended to eliminate the microbial challenge it often results in damage to the host tissue. The sulcular epithelium acts as a protective barrier and prevents entry of microorganisms and other irritants into the systemic circulation. The host microbial interaction in periodontitis leads to ulceration of the sulcular epithelium. The ulcerated epithelium acts as portal of entry for the bacteria to enter the connective tissue and thus into systemic circulation. Bacteremia has been observed in the patients with periodontitis and has been directly related to severity of inflammation and release of proinflammatory cytokines. The proinflammatory cytokines are thought to act as mediators in suppressing erythropoesis from bone marrow leading to anemia. The cytokines IL-1α, IL-6, TNF α have been related to suppression of erythropoiesis ,leading to anemia. [14]

HELICOBACTER PYLORI INFECTION

H. pylori is one of the most common bacterial infections of humans and has been closely linked to chronic gastritis, peptic ulcer, gastric cancer, and mucosa associated lymphoid tissue (MALT) lymphoma. Periodontal pocket has been considered as a very rich environment for colonization of H.pylori. Several studies support the presence of H.pylori in subgingival biofilm of subjects with chronic periodontitis and poor oral hygiene and thus leading to the reinfection and gastritis. Members of orange complex such as campylobacter spp. wich are closely related to H. pylori increase in frequency and numbers in

sites with deep pockets, loss of attachment and bleeding on probing. Fusobacterium spp. which is also on eof the member of orange complex has been found to be coaggregated with H. pylori. [15]

ERECTILE DYSFUNCTION

Several studies revealed that among all selected vasculogenic ED subjects, subjects with severe ED had highest prevalence of chronic periodontitis (CP). From the findings of those studies it can be hypothesized that an association exists between vasculogenic ED in young men and CP. However, the mechanism is still not known. [16]

PSORIATIC SKIN LESION

Preus et al had studied to investigate the prevalence of periodontal disease in psoriasis patients. Psoriasis patients in the study had significantly fewer teeth, significantly larger distance from CEJ to the alveolar crest that is lower radiographic bone level. One mechanism they thought was the innate immune system that isdirecting the subsequent adaptive immune response (T- and B-cell response) is important in the pathogenesis of both psoriasis and periodontitis. [17]

OBSTRUCTIVE SLEEP APNEA

Gururatnem et al investigated wether there may be any association between OSA and periodontitis as these two disorders are associated with systemic inflammation and cardiovascular morbidity. When sleep related variables were compared against periodontal variables significant correlations were found between periodontal clinical attachment level and total sleep time. [18]

POLYCYSTIC OVARY SYNDROME (PCOS)

Erhan et al for the fisrt time investigated periodontal status in women with PCOS and evaluated potential interrelationship between periodontal clinical and oxidant status in the syndrome. This study suggests an increased susceptibility for periodontitis and a local/periodontal prooxidative state in lean and normal glucose-tolerant women with PCOS compared with healthy women. This study stated that the women with PCOS had increased MPO and NO levels in GCF along with unaltered serum NO levels, suggesting a local/periodontal oxidative stress in these patients. [19]

CONCLUSION:

The current evidence supports that prevention and treatment of periodontal disease may reduce chronic systemic disease risk at both the individual level and community level. Recent consensus recommended that education to encourage improved oral health should be part of efforts to improve general health and this will reduce the burden of systemic diseases. The jury is watching on the role of oral health in systemic disease but the quantity of indirect evidence is increasing so additional research is required to understand the value of oral interventions in prevention of systemic disease.

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