

## Cardiovascular Diseases and Periodontal diseases: Exploring the Connection: A Review

Sumit Bhateja, Geetika Arora

Sumit Bhateja, Senior Lecturer (MDS), Department of Oral Medicine Diagnosis and Radiology, Vyas Dental College and Hospital, Jodhpur (RAJASTHAN), India

Geetika Arora, Senior Lecturer (MDS), Department of Public Health Dentistry, Vyas Dental College and Hospital, Jodhpur (RAJASTHAN), India

Correspondence to: Geetika Arora, Senior Lecturer (MDS), Department of Public Health Dentistry, Vyas Dental College and Hospital, Jodhpur (RAJASTHAN), India.

Email: [drgeetuarora@gmail.com](mailto:drgeetuarora@gmail.com)

Telephone: +9660829204

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### ABSTRACT

Cardiovascular diseases (CVDs) are a leading cause of death and disability across the developed world and impose a vast burden on healthcare resources. Periodontitis, although not a cause of mortality, is also a major public health concern because of its high prevalence in the population and its negative impact on oral health, ability to chew, appearance, quality of life, dental care costs and tooth loss. In addition, as a progressive, chronic inflammatory disease, untreated periodontitis has the potential to undermine overall health and even exacerbate other inflammatory conditions, such as CVDs. This review discusses about association between cardiovascular diseases & periodontal diseases.

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**Key words:** Cardiovascular disease (CVD); Periodontal disease; Periodontitis; Inflammation; Coronary heart disease (CHD)

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### INTRODUCTION

Cardiovascular disease (CVD) is a broad term used to categorize any abnormal condition characterized by dysfunction of the heart and blood vessel and includes: (1) Coronary heart disease, which presents as angina or heart attack (myocardial infarction); (2) Ischaemic cerebrovascular disease, which may manifest as stroke or mini-stroke (transient ischaemic attack or TIA); (3) Peripheral vascular disease.

CVD is the leading cause of mortality in the United States and other industrialized countries and is among the major causes of death worldwide. In the US, CVD accounts for 40% of all deaths each year; over three-quarters of a million people die each year from CVD<sup>[1]</sup>.

Periodontitis is defined as an infectious and inflammatory intraoral disease that results from sustained failure to properly cleanse the mouth and gums. 5 to 10% of any population suffers from severe, generalized periodontitis, although mild to moderate periodontitis affects a majority of adults<sup>[1,2]</sup>.

Epidemiological Studies have presented periodontal diseases as a risk factor for development of cardiovascular diseases. A chronic oral infection such as periodontitis is a constant potential source of infection and has now been considered as a separate risk factor for cardiovascular diseases. This article will focus on evidence published for the association between periodontal disease and CVD<sup>[2]</sup>.

### CONCEPT OF FOCAL INFECTION THEORY<sup>[3,4]</sup>

"Focal infection theory" was published in 1891 suggesting that microorganisms or their waste products gain entrance to parts of the body adjacent to or remote from the point of entry. Other proponents of this theory blamed oral foci of infection for a number of regional and systemic diseases, ranging from tonsillitis and middle ear infections to pneumonia, tuberculosis, syphilis, osteomyelitis, endocarditis, meningitis, and septicemia. The "Focal infection theory" was not given any attention until recent progress in identification and characterization of periodontal pathogens, as well as elucidation of potential systemic mechanisms of action of bacterial products and inflammatory cytokines. This has opened the way for a more realistic assessment of the systemic importance of periodontal disease.

## MECHANISMS PROPOSED FOR PERIODONTAL INFECTION AND CVD ASSOCIATION<sup>[5-17]</sup>

Infection has been recognized as a risk factor for atherogenesis and thromboembolic events. Gram-negative bacteria or the associated lipopolysacchride (endotoxin), when presented as a systemic challenge in animal models, can induce inflammatory cell infiltration into major blood vessels, vascular smooth muscle proliferation, vascular fatty degeneration and intravascular coagulation. The remarkable similarities of bacterially induced vascular pathology, natural history of atherogenesis has led certain investigators to suggest that, in addition to genetic, lifestyle and dietary influences, infections of unknown origin may contribute to the observed cardiovascular pathology.

The chronic inflammatory burden of periodontal infection and the host response provide the bases for hypothetical model of the observed associations between periodontal disease and atherosclerosis, coronary heart disease and stroke. This model emphasizes that among certain individuals there may be an underlying hyperinflammatory trait in response to stimuli that is manifests by an excessive production of pro-inflammatory cytokine and lipid mediators by monocytes and other cell types.

Four potential mechanisms by which periodontal infections might contribute to the pathogenesis of CVD are: (1) Effects of Endotoxins in the circulation; (2) Role of heat shock proteins; (3) Infection induced alterations in lipid profiles; (4) Formation of acute-phase reactants.

### Effects of endotoxins in the circulation

The microflora associated with periodontal infections is a rich source of endotoxins, which are lipopolysacchride (LPS) components of the cell walls of all gram-negative bacteria. Entry of endotoxins into the circulation can occur from many sources including respiratory infections (*C. Pneumoniae*), gastric ulcers (*H. Pylori*), and periodontitis (*P. gingivalis*, *A. actinomycetemcomitans*, *B. forsythus*, etc).

Once endotoxins enter the circulation they present a considerable threat to the well-being of the host. They can directly injure endothelial cells, promote adhesion of monocytes to endothelium, induce macrophage foam cell formation and cause general endothelial dysfunction. All of these effects play a significant role in the initiation and development of atherosclerosis. One of the primary features of acute occlusion of vessels in CHD and stroke is the disruption of existing atherosclerotic plaques by macrophage-mediated inflammation.

### Role of heat shock proteins

Heat shock proteins (Hsp) are produced by a wide variety of bacteria and human cells under a variety of stressful or harsh conditions such as high temperature, infection, inflammation, and mechanical stress. It is well established that endothelial cells produce Hsp under stressful conditions such as exposure to endotoxins.

### Infection-induced alterations in lipid profiles

It known from some studies that hyperlipidemia frequently accompanies many bacterial infections. Low doses of endotoxins cause a rapid rise in serum triglycerides due to an increase in triglyceride-rich very-low-density lipoprotein (VLDL). Hyperlipidemia may have negative effects such as promoting the release of proinflammatory cytokines from neutrophils. It is

interesting to note that hyperlipidemia occurs during periodontal infections. Cytokines like IL-1, IL-6, and TNF- have been implicated as risk factors for CHD and prolonged hyperlipidemia is likely to have deleterious clinical effects.

### Formation of acute-phase reactants

Acute phase reactants appear in the circulation in response to infections and tissue injury. C-reactive protein (CRP) is of particular interest since at "high-normal" levels it has been shown to be an important risk factor for CHD and is also elevated in patients with extensive periodontal disease. It remains to be determined if CRP elevations occurring during periodontal infections play a role in atherosclerosis.

## EPIDEMIOLOGICAL STUDIES: LINK BETWEEN PERIODONTITIS AND CARDIOVASCULAR DISEASE<sup>[18-21]</sup>

A number of studies have shown an association between oral conditions and atherosclerosis and coronary heart disease. According to DeStefano *et al*, patients with periodontitis have a 25% increased risk of coronary heart disease relative to those without it (DeStefano *et al* 1993). Periodontal disease was shown to be a stronger risk factor in men younger than 50 years at baseline, with a relative risk of 1.72. In this particular study, the periodontal index was used to assess exposure to periodontitis and the main outcome evaluated was hospital admissions and deaths related to coronary heart disease. Beck *et al* conducted a cohort study using combined data from the Normative Aging Study and the Dental Longitudinal Study sponsored by the United States Department of Veterans Affairs. The study found that the incidence odds ratios for bone loss and total cardiovascular disease, fatal cardiovascular disease and stroke were 1.5, 1.9, and 2.8 respectively, after adjustment for established cardiovascular risk factors. For every 20% increase in bone loss, the incidence of total cardiovascular disease increased by 40% (Beck *et al* 1996).

After completing a case control study with 303 patients examined within seven days after acute ischemic stroke or transient ischemic attack (Grau *et al* 2004), it was further concluded that periodontitis is an independent risk factor for stroke. Subjects with severe periodontitis had 4.3 times higher risk for cerebral ischaemia than subjects with mild or without periodontal disease (Rosenberger *et al* 1996). The weight of epidemiological evidence, then, seems to support the concept that periodontitis and cardiovascular disease co-present and may predict one another's presence. The studies still do not indicate, however, that there are causal associations between the two diseases; or even if there are causal associations, whether they are bidirectional as has been demonstrated with diabetes. That said, the lack of bi-directional effects does not rule out the possibility that periodontitis might play a causal role in cardiovascular disease, or at least exacerbate cardiovascular disease processes such as inflammation.

Indeed, there is good evidence to indicate that atherosclerosis, and in particular, atherosclerotic lesions were once considered as bland lesions. However, at this time there is good evidence to suggest that atherosclerosis is in fact, an inflammatory disease with correlations to c-reactive protein levels as also shown in periodontitis. Hence, certain inflammatory mediators that are produced in periodontal lesions are found in the bloodstream, e.g. prostaglandins, and these could conceivably contribute to remote inflammatory lesions such

as atherosclerotic plaques. Thus, there is biological plausibility with regard to the notion that periodontal lesions could lead to exacerbation of atherosclerosis and hence coronary artery disease for example. Biological plausibility notwithstanding, one must also consider that the risk factors for periodontitis are, in many cases, similar to those reported for cardiovascular disease.

## CLOSING COMMENTS

Overall, reports contribute to strengthening the concept that periodontal disease may play a role in severe and often fatal cardiovascular events. Periodontitis is increasingly regarded as a risk factor for CVD. Eventually, good periodontal health may become accepted as an important goal that could contribute to reducing the risk for cardiovascular events. Most common forms of periodontal disease are conditions relatively easy to diagnose and treat. Based on evidence, the expected outcome of periodontal treatment is improved periodontal health with negligible side effects.

## CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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**Peer reviewers:** Aldona Bernadeta Kubica, Associate Professor at Health Promotion Department, Nicolaus Copernicus University in Torun, Collegium Medicum in Bydgoszcz, ul. Technikow 3; 85-801 Bydgoszcz, Poland; Michele Gesualdo, Department of Emergency and Organ Transplantation, Section of Cardiovascular Diseases, School of Medicine, University of Bari, Piazza G. Cesare 11, 70124, Bari, Italy.