Inflammatory Markers and Association between Periodontics and Cardiovascular Disease

Preeti Sharma[1,*], Pradeep Kumar[2], Geeta Sharma[3], M. Itagappa[4]

Department of Biochemistry, Department of Oral Pathology, Santosh Dental College, Santosh University, Ghaziabad

***Corresponding Author:**
Email: prcdri2003@yahoo.co.in

ABSTRACT

Oral health and cardiovascular disease have been proposed to link for more than a century. Recently, concern about possible links between periodontal disease (PD) and Atherosclerotic vascular disease (ASVD) has intensified and become an active field of investigation into possible association and causality. Great attention of the world researchers has been focused on to explore a possible association between oral health and systemic diseases.

Key Words: *Inflammatory Markers, Periodontitis, ASVD*

INTRODUCTION

Millions and billions of bacteria and microbes that lie in the mouth unquestionably influence the health of the teeth and the gums. Whether they cause problem for the heart and blood vessels, and improving the oral health will prevent the cardiovascular problem? Periodontitis is a set of inflammatory diseases affecting the periodontium i.e., the tissues that surround and support the teeth. Periodontitis involves progressive loss of the alveolar bone around the teeth[1], and if left untreated, can lead to the loosening and subsequent loss of teeth[2].The disease is caused by microorganisms that adhere to and grow on the tooth's surfaces, along with an overly aggressive immune response against these microorganisms[3]. Coronary artery disease and periodontitis are the common chronic inflammatory diseases[4]. Scientists are exploring several mechanisms that may connect the two processes. In people suffering from periodontal diseases, have been found to have atherosclerotic plaques in the arteries heart and elsewhere. These plaques can lead to heart attack[5]. Several researchers have proposed that mechanism behind the dental infection and coronary diseases could be because of the bacteria on the cells contributing to the pathogenesis of the cardiovascular diseases[6]. One *in vitro* study showed the aggregation of the human platelets by *streptococcus sanguis*[7]. Oral bacteria take their entry in the systemic circulation and cause blood clots by releasing toxins that resemble the proteins found in the arterial wall of the blood stream. The immune system responses to these toxins, which in turn elevate the level of various inflammatory markers in the serum[8]. The elevation of the CRP(C- reactive protein), Interleukins, TNF-α and fibrinogen have also been recently linked to atherosclerosis and heart diseases[9]. The atherosclerosis, or plaquing of the arteries is known to have an inflammatory component. That is also thought to cause a rise in CRP level in the blood[10]. The plaque typically contains the blood cells of the inflammation, cholesterol deposits & cell debris from the injured cells in the blood vessels lining. The accumulation of these elements leads to narrowing of the wall of the blood vessels. This narrowing can hinder the blood flow and plaque can rupture and flakes off the vessel wall causing blockade and leading to strokes and heart attack[11].

REVIEW OF LITERATURE

Recognizing active phase of the periodontal disease through various inflammatory biomarkers and assessing the associated risks, still represents a great challenge for both clinicians as well as clinical investigators. Though advances in oral and periodontal disease are moving with fast pace through extensive research studies conductance on biomarkers.

Various researchers have suggested that oral infection may raise inflammatory markers in blood and biological fluids, which could contribute to the pathology of the coronary artery disease[12]. Studies indicate that serum inflammatory markers such as C-reactive proteins, ESR, and fibrinogen level are significantly higher in the individuals[13]. In fact conclusion of the various studies indicates that severity of the periodontal diseases is directly proportional to the severity of coronary artery disease. 5 additional researches showed that in individuals suffering from CAD, 84% had the periodontal disease compared to only 22.5%, in individuals without periodontal disease[14]. Periodontitis has been associated with elevated inflammatory markers and is higher risk factor for coronary artery diseases, than the elevated LDL or pulse pressure[15]. Though various other studies apparently give conflicting message suggesting cardiovascular disease and periodontitis are not related[16]. One more study suggested elevation of circulating level of some inflammatory markers, including monocytes, macrophages a no of cytokines and inflammatory cytokines especially tumor necrosis factor (TNF)-α, prostaglandin (PGE-2), interleukins (IL-1β and IL-). These inflammatory cytokines and prostaglandin have been associated with bacterial infections in periodontitis. Raised level of interleukins

in blood has been proposed to be associated with immunopathologies[17]. Elevated level of Interleukin-6hasbeen reported by many workers researching on periodontal lesions. IL-6 has been suggested to be a very useful indicator or diagnostic inflammatory marker for periodontal patients[17].Through various studies conducted on cytokins have shown relevance of these in periodontal destruction such as attachment loss in teeth, destruction of collagen and alveolar bone resorption[18].Masada et al demonstrated elevated concentration of IL-1β is closely associated to periodontitis[19]. The concentration of IL-1β was found to be decreased after scaling and root surface planning[19]. Preiss et al also found raised level of interleukins in gingival cervicular fluid[20]. Preponderance of available data supports the possible association between oral health and systemic diseases. Paraskevas *et al* concluded through his own review analysis that plasma CRP was elevated in periodontitis affected patients compared with controls[21]. And any association between periodontitis and CVD could lead the moderate increases in CRP reported in subjects with poor periodontal health[22]. Patients treated by nonsurgical periodontal therapy displayed a significant increase in plasma tumor necrosis factor-α, CRP, and IL-6 levels immediately after intervention, which suggests a systemic acute-phase response, possibly caused by massive bacterial inoculation in conjunction with instrumentation of periodontal tissues[23].The relation between PD and CVD is potentially of great public health importance because of their high prevalence. Extensive review of the literature indicates that PD is associated with atherosclerotic vascular diseases and this information comes mostly from observational studies. From literature survey, it becomes very obvious that various inflammatory diseases like rheumatoid arthritis, periodontitis are clearly implicated in the etiology of vascular diseases[24]. Hundreds of prospective epidemiological studies of individuals with no prior history of ASVD have demonstrated that a single non-fasting measure of CRP is a predictor of future vascular events, including MI, stroke, peripheral arterial disease, and sudden cardiac death. CRP is an independent predictor of future cardiovascular events[25]. Other inflammatory markers like interleukin-6, soluble intercellular adhesion molecule-1, macrophage inhibitory cytokine-1, and soluble CD40 ligand etc. have been shown to be elevated among those at increased vascular risk, albeit to a lesser magnitude than CRP[26-28].Periodontal inflammation is similarly associated with increased systemic inflammatory markers, including CRP, tumor necrosis factor-α, IL-1, IL-6, and IL-8.

Biochemical Basis of relation between PD and CVD

Systemic inflammation is concerned with cellular activation involving cellular adhesion molecules, toll-like receptors, matrix metalloproteinase, and nuclear factor-κB activation[29]. The coordinated impact of endothelium, monocytes, and platelets may play a role in proatherogenic events, contributing indirectly to atherogenesis or to adverse cardiovascular outcomes related to atheromatous plaque rupture in subjects with periodontitis[30].

Several pathways have been examined to explain this finding. They include those related to systemic inflammation and bacteremia/systemic infection by periodontal pathogens, among others. The one possible mechanism linking periodontal infection with atherosclerosis has been proposed to be the molecular mimicry and that is thought to occur when sequence similarities between foreign and self-peptides produce cross-activation of auto-reactive T or B cells leading to tissue pathology or autoimmunity[30]. Cross-reactive autoantibodies against periodontal bacterial lipopolysaccharides and heat shock proteins have now been recognized[32]. Generation of these autoantibodies is invoked as a potential explanation for the putative relationship between PD and ASVD[31]. Atherosclerotic vascular diseases is the formation of atheromatous plaques, manifested in the form of fatty deposits on the lining of arteries and rupture of such plaques activates thrombosis and leads to acute coronary syndrome, MI, or stroke[31-32]. Inflammation of the atheroma's fibrous cap increases the risk of rupture occurrence, followed by infiltration of monocytes &macrophages, T-cells, and neutrophils within cap tissues, as well as by increased circulating markers of inflammation in the blood. One such circulating marker is C-reactive protein (CRP). CRP has been shown to be a prognosticator for future cardiac events. A no. of observational studies have indicated raised level of CRP in Inflammation caused due to periodontitis[33-35].

CONCLUSION

Periodontitis, a very common chronic condition, predisposes affected patients to ASVD by increasing the levels of systemic markers of inflammation. It may contribute to the process of atherosclerosis. Therefore, disease deserves serious consideration as a risk factor for CVDs. Further confirmatory and mechanistic investigations are needed to be clear to assess this inflammatory burden. Proper understanding or pathophysiology of periodontal disease and atherosclerotic cardiovascular disease, and systemic inflammation's role in each, is required to better link this association between these diseases. General overall health including periodontal and cardiovascular health should be promoted by all health-care providers.

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