Research Article

Lipid profile and homocysteine levels in patients with chronic periodontitis with and without cardiovascular disease

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Abstract

Introduction: Common risk factors such as smoking, diabetes, hyperlipidemia, aging and male gender place an individual at risk for both periodontitis as well as cardiovascular disease. A Case control study was carried out in 50 subjects with chronic periodontitis aged 30-65 years (group II) and age matched with 50 control subjects (group I) .Group III (n=30) patients included patients of periodontitis with cardiovascular disease (CVD) and group IV(n=40) included patients with cardiovascular disease. Blood samples collected was assessed for lipid profile and homocysteine levels. Total cholesterol, LDL-cholesterol, triglycerides and homocysteine are significantly increased ($p<0.001$) in periodontitis patients with and without CVD and patients with CVD when compared with normal healthy controls. Significant positive correlation was found when total cholesterol and triglycerides are compared with homocysteine in periodontitis with and without CVD and patients with CVD alone. Hence, homocysteine assessment is useful in predicting the future risk of cardiovascular disease in chronic periodontitis patients

Keywords: lipid profile, homocysteine, periodontitis

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INTRODUCTION

Periodontitis regarded as the second most common disease world-wide, after dental decay is characterized by a destructive inflammatory process affecting tooth supporting tissues eventually leading to exfoliation of tooth. Periodontitis is often associated with endotoxemia from gram negative organisms. Common risk factors such as smoking, diabetes, hyperlipidemia, aging and male gender place an individual at risk for both periodontitis as well as cardiovascular disease (CVD). Inflammation plays an important role in the pathogenesis of atherosclerosis and markers of low grade inflammation are associated with a higher risk of CVD.[1] Though weight of epidemiological evidence supports the co-presence of periodontitis and CVD,[2] little is known regarding their association. The putative relationship may be related to some of the similarities in the underlying pathophysiological and physiological regulatory systems in periodontitis and CVD. The mechanism linking oral health and CVD could be due to systemic inflammation Periodontitis might exacerbate a process like inflammation which is similar to that of atherosclerosis as suggested by increased levels of inflammatory makers like C-reactive protein, interleukin -1 (IL-1), tumour necrosis factor – alpha (TNF-alpha) and matrix metalloproteinases (MMP).[3] Research over the last decade have focused on elevated levels of amino acid homocysteine (Hcy) as an independent risk factor for vascular disease.[4] Hcy, a sulfur containing amino acid, is an immediate product of methionine metabolism. It results from the demethylation of the essential amino acid methionine consumed in our diet. Genetically determined enzymes and environmental factors determine the concentration of plasma Hcy. Hcy mediated enhanced lipid peroxidation and generation of free radicals result in endothelial dysfunction Thus to assess the mechanisms behind the relationship between periodontitis and CVD the present study was carried out to estimate the concentration and correlate the levels of lipids and homocysteine in chronic periodontic patients with and without CVD.

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MATERIAL AND METHOD

A case control study approved by the institutional ethics committee was carried out in 50 subjects with chronic periodontitis aged 30-65 years (group II) diagnosed on the basis of existence of calculus and plaques, with an attachment loss of≥ 2mm, in at least 3 different sites and systemically healthy with no relevant medical history. They were age matched with 50 control subjects (group I) with good general health and with no history of systemic disease. Group III(n=30) patients included patients of periodontitis with cardiovascular disease and group IV(n=40) included patients suffering from cardiovascular disease alone. The patients suffering from other diseases such as diabetes, inflammatory diseases, hepatic impairment, and respiratory diseases or other systemic diseases, women who are pregnant, receiving hormone or vitamin therapy as well as smokers and alcoholics, were excluded from the study. Informed consent was obtained from each participant in the study. 5 ml of venous blood samples was collected in plain bulb from patients with periodontitis and normal healthy individuals. Blood samples were centrifuged at 3000g for 10 minutes. Clear serum was transferred in a plastic vial and stored in the refrigerator until analysis. Serum collected was estimated for lipid profile and homocysteine. Homocysteine was measured by microplate enzyme immunoassay kit method of Biorad laboratories.

Serum total cholesterol, triglyceride and HDL-cholesterol were measured by an enzymatic kit. LDL-C was calculated according to Friedwald`s formulae: VLDL-C=Triglyceride/5 and LDL-C= Total cholesterol-(VLDL-C + HDL-C). Statistical analysis of difference was estimated using students `t` test and correlation between variables was studied using pearson`s correlation coefficient test.

RESULTS

As depicted in table I the levels of Total cholesterol, LDL-cholesterol, triglycerides and homocysteine are significantly increased ($p<0.001$) in patients periodontitis with and without CVD and CVD patients alone when compared with normal healthy controls. Correlation analysis in patients with periodontitis reveals that there is a significant positive correlation when total cholesterol 0.78($p<0.001$) and triglycerides 0.47($p<0.001$) are compared with homocysteine. There is also a significant positive correlation when total cholesterol and triglycerides are compared with homocysteine in patients of periodontitis with CVD (0.69, $p<0.001$; 0.55, $p<0.001$) and patients with CVD alone (0.67, $p<0.001$; 0.57, $p<0.001$).

Table 1: Levels of lipid profile and homocysteine in patients with periodontitis with and without CVD

	Controls(n=50)	Group II (n=50)	Group III(n=30)	Group IV(n=40)
Total cholesterol (mg%)	162.42 ± 12.61	186.78 ± 20.08*	230.63± 23.19*	219.47 ± 27.61*
Triglycerides (mg%)	48.04 ±6.87	67.34 ± 10.48*	51.23 ± 12.07*	62.62 ± 9.3*
HDL (mg%)	50.18 ± 6.89	47.64 ± 8.83	43.06 ± 8.12	51.17 ± 11.17
VLDL (mg%)	9.00 ±1.37	13.46 ± 2.09	10.24 ± 2.41	12.52 ± 1.86
LDL	64.2 ± 16.1	71.8 ± 20.14	169.15 ± 16.64*	144.32 ± 25.69*
Homocysteine (µmol/L)	6.65 ± 0.89	11.12 ± 4.2*	51.13 ± 13.35*	46.8 ± 14.13*

*p<0.001when group II, III and Iv compared with controls.

DISCUSSION

Periodontitis develops in response to the release of toxic substances and enzymes from the subalveolar bacteria group. Periodontal disease being associated with microbial plagues, local and systemic immunological response affects the overall health of the patient. Our study demonstrates that periodontic patients have hyperlipidemia.(increased cholesterol, triglyceride levels). This is in concordance with the study of Losche *et al*[5] and Katz J[6]. However, Hamissi J[7] and Machodo AC[8] showed confounding reports. Ours being a case control study to determine whether hyperlipidemia is a risk factor or outcome of periodontitis is difficult. Inflammation can operate in all stages of periodontitis from initiation through progression and ultimately the thrombotic complications of atherosclerosis, thus emerging as an integrative cardiovascular factor. Gram negative periodontal pathogen porphyromonas gingivalis and gram positive bacteria streptococcus sanguis are known to express collagen like platelet like aggregation and platelet activation thus having a role in atheroma formation and thrombosis.[9] IL-1, TNF-alpha and MMP, inflammatory mediators stimulate the adhesion of molecule and chemokine expression, and production of other inflammatory mediator such as prostaglandin E2. Stimulation of the apoptosis matrix producing cells and induction of the MMP expression limit the repair of the periodontium and myocardium.[10] Thus this inflammation may be responsible for the greater risk of cardiovascular disease in patients with periodontitis. Our study also reveals an increase in the levels of homocysteine in patients of periodontitis. These findings are similar to that of Agnihotram G[11]. The levels are also in correlation with cholesterol and triglycerides in patients with periodontitis. The increase in the levels of homocysteine, a marker for cardiovascular disease suggests periodontitis and cardiovascular disease might share complex etiologies, pathogenic mechanisms as well as common risk factors

like hyperlipidemia.[12] Homocysteine mediated enhanced lipid peroxidation and generation of free radicals such as superoxide anion, hydrogen peroxide, hydroxyl, and thiol free radicals result in inflammation could be related to the acute endothelial dysfunction. The anti-atherothrombotic function of endothelium derived nitric oxide is also reduced due to the autooxidation of Hcy. Increased Hcy also stimulates the LDL oxidase property which potentially promotes atherogenesis. Thus homocysteine either by causing impairment of blood flow and stimulation of the vascular smooth muscle proliferation may be one of the signals for the inducing apoptosis by activating an unfolded protein response.[13] Moderate hyperhomocysteinemia has been identified as a new independent risk factor for cardiovascular disease.[14] Also, homocysteine is capable of increasing the activity of HMG-CoA reductase, which results in increased cholesterol synthesis.[15] All the patients from periodontitis in our study were in good general health and not anemic hence homocysteine levels being influenced by vitamin B status was excluded from the study. The commonest cause of elevated Hcy levels is the C677T polymorphism in the methyltetrahydrofolate reductase (MTHFR) gene. This genotype encodes a thermolabile enzyme with reduced MTHFR activity and may cause moderate hyperhomocysteinemia particularly in impaired folate status.[16] MTHFR enzyme status as a cause of hHcy in our patients is also an unlikely cause as the frequency of this mutation is 1.4-10% of an unselected population. Thus hyperlipidemia along with impaired metabolism of homocysteine occurs in periodontitis. Hyperhomocysteinemia is a known independent factor risk for cardiovascular disease because it exerts a negative role on the endothelial membrane. We suggest that the additional complicating factor of hyperlipidemia, hyperhomocysteinemia and cardiovascular disease risk assessment has important diagnostic and treatment implications and warrant further clinical and laboratory investigations in patients with periodontitis. It would be unwise to ignore determination of homocysteine levels in patients with periodontitis. As treatment with vitamin B12, folic acid is extremely successful in the majority of the patients, supplementation with these vitamins as options for lowering homocysteine levels and decreasing risk for the development of cardiovascular events can be taken into consideration.

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