International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

*Original Research Article*

# Assessment of Atherogenic Index of Plasma in Periodontitis as a Risk Factor for Cardiovascular Disease

Pradnya Shree Dhotre[1], Abdul Kayyum Shaikh[2]

[1]Assistant Professor, [2]Professor & Head, Department of Biochemistry, Ashwini Rural Medical College, Hospital & Research Centre, Solapur, Maharashtra.

Corresponding Author: Pradnya Shree Dhotre

*Received: 26/08//2014* *Revised: 17/09/2014* *Accepted: 18/09/2014*

## ABSTRACT

Periodontitis is one of the most common oral infections induced by bacteria and bacterial products of dental plaque and is characterized by inflammatory destruction of tooth supporting connective tissues and alveolar bone. Recently, an association between periodontitis and cardiovascular disease has received considerable attention. The present study was carried out to assess the alteration of blood lipids & atherogenic index of plasma in the pathogenesis of periodontitis and cardiovascular disease. 100 periodontitis patients and 100 healthy controls were screened for periodontal pocket depth and clinical attachment loss as a measure of periodontal status. They were also assessed with total lipid profile and atherogenic index of plasma which is an established risk marker of cardiovascular disease.
Highly significant increase in periodontal pocket depth and clinical attachment loss was seen in periodontitis patients as compared to healthy controls. A significant increase in plasma total cholesterol, LDL cholesterol, triglyceride and non-HDL cholesterol along with a concomitant decrease in HDL cholesterol was observed in periodontitis patients when compared with healthy controls. All the ratios of atherogenic index of plasma were also increased in periodontitis patients when compared with healthy controls. These changes of altered lipid profile and atherogenic index of plasma in periodontitis patients could contribute towards the development of cardiovascular disease in them.

***Key words:*** periodontitis, atherogenic index of plasma, cardiovascular disease

## INTRODUCTION

Periodontitis is an infectious condition caused predominantly by a small group of anaerobic Gram negative bacteria present on the tooth surface as microbial bio-film that results in inflammatory destruction of the investing and tooth supporting periodontal tissues (gingivae, periodontal ligament and alveolar bone).

It is well established that bacterial irritation from the dento-gingival plaque is essential for the development and maintenance of periodontal disease. Dental plaque is a highly complex structured microbial mass in which more than four hundred bacterial types have been identified. Calcification of this dental plaque seen as calculus occurs above and within the gingival sulcus hence, the periodontium is

commonly exposed to it for almost the whole of adult life. [1]

Periodontitis affects a large number of individuals, especially adults and promotes continuous exposure to bacteria, endotoxins (lipopolysaccharides) and other bacterial products in both the periodontal tissue and the blood stream. This can induce local and systemic inflammatory reactions in the host affecting lipid metabolism through a mechanism involving pro-inflammatory cytokines.

It is well known that there is a causal relationship between serum lipid levels and systemic health particularly cardiovascular disease (CVD). [2]

Interest has recently increased in the relationship between periodontitis and cardiovascular disease. Periodontitis and cardiovascular disease have complex etiologies. The factors that place individuals at risk for periodontitis may also place them at risk for CVD and this means periodontitis and CVD may share common risk factors such as smoking, dietary habits, socio-economic status as well as diabetes. [3] Ardita Aliko and Joshipura K J et al. [3,4] referred to the possibility of an association between periodontitis and risk of CVD. Hujoel P.P. [5] suggested that chronic periodontitis increases the risk of CVD by 15%. However, some of the researchers such as Kinane, [6] Seymour [7] and Armitage [8] found no significant association between periodontitis and CVD. Thus insufficient evidence is available to confirm the association between periodontitis and CVD.

Therefore, we thought it worthwhile to study the role of atherogenic lipid parameters in periodontitis patients.

## MATERIALS AND METHODS

A total of 200 subjects were recruited in the study and out of these, 100 were healthy controls and 100 were periodontitis patients. Periodontitis group included 60 male & 40 female patients.

***Inclusion criteria:***

1. Healthy controls: 100 healthy volunteers were selected and matched for age and sex. None of them was suffering from any chronic disease/s.
2. Study group subjects: 100 periodontitis patients were included who had –

i. Clinical attachment loss of ≥ 4mm measured by using Williams's Periodontal probe.

ii. Periodontal pocket depth ≥ 4mm.

iii. Bleeding on gentle probing.

iv. Not undergone any periodontal treatment for at least six months prior to sampling.

All the examinations were done by a single trained dentist.

***Exclusion criteria:***

v. Subjects who required antibiotic or anti-inflammatory drug therapy.

vi. Having history of alcoholism, smoking, diabetes mellitus, cardiovascular disease etc.

vii. Subjects who regularly use mouth washes like Chlorhexidine mouth wash etc.

The study was approved by institutional ethical committee. The purpose of our study was explained to all subjects and their consent was taken. 3 ml fasting venous blood was collected in sterile heparinised bulb under aseptic condition. Plasma was separated by centrifugation at 3000 rpm for 10 minutes at room temperature. All the samples were analysed on the same day of collection.

***Clinical Examination:***

Body mass index (BMI) and waist circumference (WC) was used to assess overall adiposity and abdominal adiposity respectively. To obtain BMI, heights of all individuals were measured and they were accurately weighed with digital balance.

BMI is defined as the individuals body weight divided by the square of their height and measured in Kg/m2. (BMI=weight (kg) / height (m2)). Waist circumference was measured in centimetres at the level of umbilicus. The measurements were taken after participants exhaled.

***Methods:***

Plasma lipoproteins were measured by using kits of Span Diagnostics Limited, India.

The principle of the method for measuring total cholesterol involves the use of three enzymes: Cholesterol Esterase (CE), Cholesterol Oxidase (CO) and Peroxidase (POD). In the presence of the former the mixture of phenol and 4- aminoantipyrine (4-AA) are condensed by hydrogen peroxide to form a quinoneimine dye the intensity of which is proportional to the concentration of cholesterol in the sample. The HDL measuring technique uses a separation method based on the selective precipitation of apoliprotein B- containing lipoproteins, namely, (VLDL, LDL and (a) Lpa) by the use of phosphotungstic acid/MgCl2, then the sedimentation of the precipitant by centrifugation and subsequent enzymatic analysis of HDL, as it will be the only residual cholesterol remaining in the clear supernatant. The principle of the method for measurement of triglyceride is that triglycerides incubated with lipoprotein lipase (LPL), liberate glycerol and free fatty acids. Glycerol is converted to glycerol-3-phosphate (G3P) and adenosine-5-diphosphate (ADP) by glycerol kinase and ATP Glycerol-3- phosphate is then converted by glycerol phosphate dehydrogenase (GPO) to dihydroxyacetone phosphate (DAP) and hydrogen peroxide (H2O2). In the last reaction, hydrogen peroxide reacts with 4- aminophenazone (4-AP) and p- Chlorophenol in the presence of peroxidase (POD) to give red colored dye the intensity of which is proportional to the triglycerides concentration in the sample. The LDL concentration was estimated using the equation of Friedewald et al.

***Statistics:***

Statistical analysis was done by using students 't' test and the data were expressed as mean ± standard deviation. Probability values of $< 0.05$ were considered to be statistically significant.

## RESULTS

Table 1 shows the levels of body mass index, waist circumference, clinical attachment loss and periodontal pocket depth in healthy controls and periodontitis patients. Body mass index and waist circumference were significantly higher in periodontitis patients when compared to healthy controls ($p<0.001$). Periodontitis patients also demonstrated significantly higher clinical attachment loss and periodontal pocket depth when compared to healthy controls ($p<0.001$).

Table1. Shows the levels of body mass index (BMI), waist circumference (WC), clinical attachment loss (CAL) & periodontal pocket depth (PD) in healthy controls and periodontitis patients

| Sr. No | Parameters | Healthy Controls | Periodontitis patients |
|---|---|---|---|
| 1. | Body mass index (Kg/m2) | 24.1 ± 3.88 | 27.7 ± 2.38* |
| 2. | Waist circumference (cm) | 83 ± 1.19 | 108 ± 2.28* |
| 3. | Clinical attachment loss (mm) | 2.24 ± 0.1 | 4.70 ± 0.14* |
| 4. | Periodontal pocket depth (mm) | 1.40 ± 0.11 | 4.27 ± 0.11* |

Compared to healthy controls * P < 0.001

Table 2 depicts the levels of total cholesterol (TC), LDL-cholesterol, HDL-cholesterol, triglyceride & non-HDL cholesterol in healthy controls and periodontitis patients. Levels of total cholesterol, LDL-cholesterol, triglyceride and non-HDL cholesterol were significantly higher in periodontitis patients ($p<0.001$) when compared to healthy controls; whereas a significant decrease was observed in HDL-

cholesterol in periodontitis patients than healthy controls ($p<0.001$).

Table 3 shows the atherogenic index of plasma represented by various risk ratios in healthy controls and periodontitis patients. All the ratios were significantly elevated in periodontitis patients ($p<0.001$) when compared to healthy controls.

Table 2. Shows the levels of plasma total cholesterol (TC), LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), triglyceride (TG) & non-HDL cholesterol in healthy controls and periodontitis patients

| Sr. No | Parameters | Healthy Controls | Periodontitis patients |
|---|---|---|---|
| 1. | Total cholesterol (mg/dl) | 190 ± 19.10 | 222.7 ± 35.46* |
| 2. | LDL-cholesterol (mg/dl) | 119.8 ± 11.66 | 152.5 ± 23.15* |
| 3. | HDL-cholesterol (mg/dl) | 46 ± 7.82 | 40 ± 7.28* |
| 4. | Triglyceride (mg/dl) | 111 ± 17.81 | 145 ± 29.23* |
| 5. | Non-HDL cholesterol (mg/dl) | 144 ± 20.81 | 182.7 ± 29.62 * |

Compared to healthy controls * P < 0.001

Table 3 depicts 'Atherogenic index of plasma' in healthy controls and periodontitis patients

| Sr. No | Parameters | Healthy controls | Periodontitis Patients |
|---|---|---|---|
| 1. | TC/HDL cholesterol ratio | 4.27±0.92 | 5.74±1.36* |
| 2. | LDL/HDL cholesterol ratio | 2.7 ±0.62 | 3.93± 0.92 * |
| 3. | Non-HDL/HDL cholesterol ratio | 3.27±0.92 | 4.7± 1.23* |

Compared to healthy controls * P < 0.001

## DISCUSSION

The focus of the relationship between periodontitis and cardiovascular disease is shifting from a purely epidemiological association towards biological understanding of the underlying mechanisms. Recent evidences consider obesity as an independent risk factor for CVD. Studying the relationship between obesity and periodontal disease is, therefore, important since this association could further contribute to increased morbidity of these diseases in overweight or obese individuals. [(9)]

The present findings of increased BMI & WC in periodontitis patients are in accordance with previous findings supporting a positive correlation between obesity and periodontal damage. [(10,11)]

Obesity has been found to be significantly associated with alveolar bone loss among adults, with a stronger association in females. [(12)] Obesity has been postulated to reduce blood flow to the periodontal tissues, promoting the development of periodontal disease. [(13)] Furthermore, obesity may enhance immunological or inflammatory disorders, which might be the reason why the obese subjects, tend to exhibit escalating poor periodontal status relative to non-obese individuals. [(14)]

The present study revealed an increase in total cholesterol, LDL-cholesterol, triglyceride & non-HDL cholesterol in periodontitis patients. One possible explanation for these findings could be that pro-inflammatory cytokines such as interleukin-1β & tumour necrosis factor-α leaking from periodontal lesion into the circulation inhibits the lipoprotein lipase activity, causing disturbance in lipid metabolism. [(15)] These elevations in serum lipids are thought to arise from enhanced hepatic lipogenesis and increased adipose tissue lipolysis/blood flow. [(16-18)]

Recently, elevated levels of non-HDL-cholesterol have also been found to be related with CVD risk. Non HDL-cholesterol is defined as the difference between total cholesterol (TC) and HDL-cholesterol and contains all known and potentially atherogenic lipid particles including LDL cholesterol, lipoprotein (a), intermediate density lipoprotein cholesterol and very low density lipoprotein cholesterol remnants, therefore a good and potential predictor of risk of CVD.

In addition, defective cholesterol removal is attributable to inflammation -induced changes in HDL which may provide one of the mechanisms underlying the relationship between periodontitis and CVD.

Periodontitis induced changes in HDL compositions may impair its efflux capacity. Thus periodontitis diminishes the anti-atherogenic potency of HDL and may thus increase the risk for CVD. [19]

Thus, inflammation is strongly associated with dyslipidemia which is one of the dominant risk factors for cardiovascular disorders. [20]

The study also showed increased atherogenic index of plasma (AIP) represented by various risk ratios in periodontitis patients. Several epidemiological studies have shown that the ratio of total cholesterol/ HDL-cholesterol is a better predictor of future coronary heart disease than total cholesterol, LDL-cholesterol, HDL-cholesterol or triglycerides alone. [21-23] TC/HDL-c ratio estimates the net effect of two way traffic of cholesterol in and out of tissues.

Periodontal infection has been found to increase the concentration of triglyceride and lower the concentration of HDL-cholesterol. These changes were found to contribute towards the atherogenic potential of periodontitis.

Reduction in HDL-cholesterol also has a consequence in increased LDL/HDL cholesterol ratio. This ratio also represents an atherogenic index which is an important prognostic marker for CVD. The association of TG, TC, HDL and LDL-cholesterol along with non-HDL cholesterol reflects the balance between risks and protective lipoprotein forces. Periodontitis induced changes in lipoproteins suggest a potential role of inflammation in atherogenic profile and the higher cardiovascular risk in these patients.

Thus, an uncontrolled, over-exuberant inflammatory response in periodontitis may serve as an intermediate variable linking these two diseases.

## CONCLUSION

In the present study, we observed an altered lipid profile as well as increased atherogenic index of plasma in periodontitis patients. When we consider these data together, with the results of the study, we hypothesize that periodontal disease may be a potential risk factor for the severity, progression and even the initiation of cardiovascular disease. However studies of larger groups with the clinical endpoint are required to address this hypothesis.

## REFERENCES


1. Burt BA. 1993 The role of epidemiology in the study of periodontal disease. Periodontol 2000.2: 26-33.
2. Machado A, Quirino M, Nascimento L. 2005 Relation between chronic periodontal disease and plasmatic levels of triglycerides and total cholesterol and fractions. Braz Oral Res.19(4):284-289.
3. Aliko A, Alushi A, Refatllari E. 2007 Physio-pathological relationship between periodontal and cardiovascular diseases. Balk J Stom; 11:96-99.
4. Joshipura K, Wand H. Merchant A et al. 2004 Periodontal Disease and Biomarkers Related to Cardiovascular Disease. J Dent Res. 83(2): 151-155.
5. Hujoel PP.2002 Does chronic periodontitis cause coronary heart disease? : A review of the literature. J Am Dent Assoc. 133: 31S-36S.
6. Kinane D. 1998 Increasing evidence of a link between dental health and coronary heart disease. Br Dent J.184:39-41.
7. Seymour R.2001 Heart of the matter. Br Dent J. 190: 106-106.
8. Armitage G.2000 Periodontal disease and cardiovascular disease- how strong is the association. Oral diseases 2000.6: 335-350.
9. Tessari P.2000 Changes in protein, carbohydrate, and fat metabolism with aging: possible role of insulin. Nutrition reviews. 58:11–19.

10. Edgar WM.1992 Saliva—it's secretion, composition & functions. British Dental Journal. 72:305-312.
11. Rehman MM, Salaam RI. 2004 Association between Periodontal Disease and Cardiovascular Disease. Pak J Med Sci.20(2):151-156.
12. Al abdul karim M et al. 2005 Alveolar bone loss in obese subjects. Journal of the International Academy of Periodontology. 7(2):34–38.
13. Shuldiner A, Yang R, Gong D.2001 Resistin. Obesity and insulin resistance-the emerging role of the adipocytes as an endocrine organ. New England journal of medicine.345:1345–1346.
14. Nishida N, Tanaka M, Hayashi N.2005 Determination of smoking and obesity as periodontitis risks using the classification and regression tree method. Journal of Periodontology.76:923–928.
15. Tiejian W. 2000 Examination of Relation between Periodontal health status and Cardiovascular risk factors: Serum Total and High density Lipoprotein Cholesterol, C-reactive Protein and Plasma fibrinogen. Am J Epidemiol. 151(3):273-282.
16. Ozlem Fentoglu,F. Yesim Bozkurt. April 2008 The bi-directional relationship between periodontal disease and hyperlipidemia. European journal of Dentistry.2:142-149.
17. Feingold KR, Grunfeld C.1987 Tumour necrosis factor –α stimulates hepatic lipogenesis in the rat in vivo. J clin Invest. 80: 184-190.
18. Kurpad A, Khan K, Calder AG.1992 Effect of noradrenalin on glycerol turnover and lipolysis in the whole body and subcutaneous adipose tissue. Am J Physiol.263:850-855.
19. Pirkko J. Pussinen et al.2004 Periodontitis decreases the antiatherogenic potency of high density lipoprotein. Journal of Lipid Research.45:139-147.
20. H. El-Sayed Amin.2010 Relationship between overall and abdominal obesity and periodontal disease among young adults. EMHJ. 16(4):429-433.
21. Wilson PWF, Kannel WB. 1993 Hypercholesterolemia and coronary risk in the elderly. Am J Geriatr Cardiol. 2:52.
22. Grover SA, Coupal L, Hu X-P. 1995 Identifying adults at increased risk of coronary disease. J Am Med Assoc.274:801.
23. Kinosian B, Glick H, Garland G.1994 Cholesterol and coronary heart disease. Ann Intern Med. 121:641.

How to cite this article: Dhotre PS, Shaikh AK. Assessment of atherogenic index of plasma in periodontitis as a risk factor for cardiovascular disease. Int J Health Sci Res. 2014;4(10):117-122.

**********