Evaluation of association between periodontitis and early carotid atherosclerosis – A clinico-biochemical study

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Abstract

Background & Objectives: A mechanism has been proposed whereby periodontitis contributes to the process of thermogenesis and thromboembolic events. The purpose of the present study is to evaluate the association between periodontitis and early carotid atherosclerosis in systemically healthy individuals.

Material and Method: Sixty patients aged between 18–50 years, with BMI ranging between 25-30 kg/m^2 and systemically healthy were included in the study. Based on the clinical parameters subjects were grouped into test group and control group. All the patients were subjected for blood investigations to assess lipid profile and ultrasonography of common carotid artery to assess the Intima Media Thickness. Descriptive statistical analysis has been carried out in the present study.

Results: Data analysis showed that subjects with periodontitis from test group had statistically significant increase in Carotid Intima Media Thickness when compared to the subjects without periodontitis from control group. It was found that in test group the values of Total Cholesterol, Triglycerides, LDL, and VLDL were higher than values found in control group. However significant differences were observed only with triglycerides and VLDL levels.

Conclusion: Periodontitis is associated with increased carotid IMT showing early carotid atherosclerosis.

Keywords: Carotid Intima Media Thickness, Lipid profile, Chronic Periodontitis, Sub Clinical Atherosclerosis.

Introduction

In the last ten years, several epidemiological studies have assessed the association between oral infection and systemic disease. Studies have provided support that oral infections, specifically periodontitis, may present independent risks for different systemic conditions like, diabetes mellitus, cardiovascular diseases, pulmonary infections, pre-term low-weight births and osteoporosis. Since cardiovascular diseases are the leading cause of death worldwide, greater attention has been focused on evidence that infections of the oral cavity might be associated with atherothrombosis: heart infarction, stroke, and peripheral vascular disease.(1)

The conservative risk factors for atherosclerosis are well understood, but they can account for only about 50% to 70% of atherosclerotic events in the general population.(2) Among the panel of novel risk factors, dental and periodontal disease are potential candidates.(3) Accumulating evidence suggests that dental and periodontal diseases are potentially associated with atherosclerosis.

There are several possible explanations for the association between periodontal disease and complications of atherosclerosis. First, it may merely reflect confounding by common risk factors such as smoking, obesity, and diabetes. Second, the association may reflect an individual propensity to develop an exuberant inflammatory response to intrinsic (age, sex, genes) or extrinsic stimuli (diet, smoking, etc).Third, an inflammatory focus in the oral cavity may stimulate humoral and cell-mediated inflammatory pathways. Fourth, the presence of periodontal infection may lead to brief episodes of bacteremia with inoculation of atherosclerotic plaques by periodontal pathogens.(3)

Atherosclerosis, unless in a severe form, is often asymptomatic, so that a direct examination of the vessel wall is necessary to detect affected individuals in the early stages. Measurement of the intima-media thickness (IMT) of the common carotid artery (CCA) by B-mode ultrasound was found to be a suitable non-invasive method to visualize the arterial walls and to monitor the early stages of the atherosclerotic process. Carotid intima media thickness is considered as a surrogate marker of atherosclerosis. Increase in carotid intima media thickness is associated with an increased risk of Ischemic heart disease (IHD) and Cerebrovascular disease (CVD) in periodontitis patients.

Several studies have indicated that severe periodontitis is associated with a modest decrease in high density lipoprotein (HDL) cholesterol, increase in low density lipoprotein (LDL) cholesterol, and a more robust increase in plasma triglycerides. However, it is unclear whether periodontitis causes an increase in levels of serum lipids or hyperlipidemia is a risk factor for both periodontitis and cardiovascular disease.(4)

Thus to investigate the role of hyperlidemia in periodontitis and early atherosclerosis there is a need to correlate between serum lipid levels and carotid intima media thickness values. In this study the association between periodontitis and early atherosclerosis in systemically healthy individuals was evaluated. Aim of this study was to evaluate the association of

periodontitis with Carotid Intima- Media Thickness (IMT) and to compare the values in Lipid Profile and Body Mass Index (BMI) between test group and control group.

Methodology

This study included **Sixty** patients visiting to the Department of Periodontics.

Inclusion Criteria

1. Both male and female patients aged 18-50 years participated in the study.
2. Patients having BMI ranging between 25-30 Kg/m2.
3. Systemically healthy subjects.

Exclusion Criteria

1. Pregnant or Lactating women and smokers.
2. Patients with history of any antibiotics therapy 3 months prior to study enrolled or any other regular medication.
3. Patients who underwent periodontal therapy for last six months.

Method of Collection of Data

Patients visiting the outpatient of Department of Periodontics were screened for their Body Mass Index (BMI). BMI was calculated by measuring height of the patient in meter and weight of the patient in Kilogram. BMI was calculated using WHO formula (Kg/m^2). Sixty patients whose BMI was ranging between 25-30 $Kg/m^{(2)}$ according to the WHO chart were included in the study. The nature and purpose of the study was explained to the patients and written consent was obtained. Oral health status examination was carried out for all the patients.

Periodontal status was assessed by following parameters

1. Plaque Index by Sillness and Loe (1964).[5] (PI)
2. Gingival Sulcus Bleeding Index by Muhlemann .H.R. and Son.S (1971).[6] (BI)
3. Mean probing pocket depth. (PPD)
4. Mean clinical attachment level. (CAL)

After screening, sixty patients were segregated into test group and control group consisting 30 patients in each. Criteria for test group and control group were as follows.

Test group

Generalized chronic Periodontitis.

1. With probing depth ≥ 5mm in > 30% of the sites
2. With clinical attachment loss > 30% of the sites.

Control group

Periodontally healthy individuals.

1. With probing depth < 3mm.
2. With no clinical attachment loss.

Both the groups were subjected for ultrasonography for the assessment of Carotid Intima-Media Thickness (IMT) and Lipid Profile.

Measurement of PPD

Probing Pocket depth measured was the distance from the free gingival margin to the base of the sulcus or pocket. 0-3 mm is normal gingival sulcus and >3mm probing depth was considered as periodontal pocket. The pocket depth was measured by using Williams's graduated periodontal probe at six sites i.e. Distobuccal, midbuccal, mesiobuccal, distolingual, midlingual and mesiolingual of each tooth. All six measurements were added and divided by the number of sites examined i.e. 6 to obtain the mean probing depth for an individual tooth.

Measurement of Carotid IMT

Carotid IMT was assessed by a single experienced MD Radiologist at Clumax Diagnostics in Bangalore. In each group, Carotid IMT was bilaterally assessed by using B mode ultrasonograghy at the common carotid artery in both the groups, using high frequency linear probe (4- 5.5 MHz), with the patient in supine position and the examiner seated near the patient's head. Tilting the patient's head away from the side being examined facilitates neck exposure. With this technique, two parallel echogenic lines separated by an anechoic space can be visualized at levels of the artery wall. These lines are generated by the blood-intima and media-adventitial interfaces. Carotid IMT was measured with an orthogonal incidence of the ultrasonic beam to the axial course of the artery, on a 10mm segment of the far wall of the common carotid artery using software. The average of both right and left IMT was considered for statistical analysis.

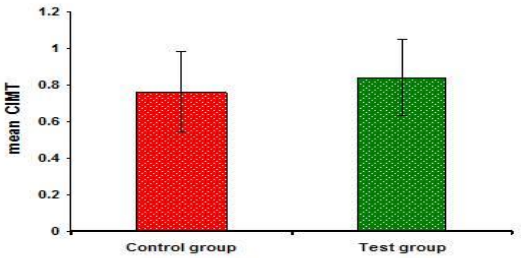

Fig. 1: Mean CIMT in different groups. Mean CIMT value is greater in the test group compared to th control group.

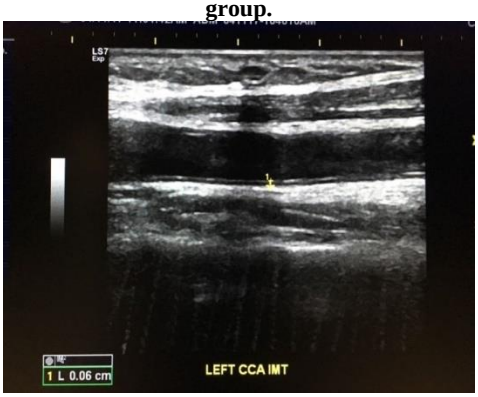

Fig. 2: Ultrasonogram image of LEFT CIMT

Fig. 2: Ultrasonogram image of LEFT CIMT

Collection of blood sample for lipid profile

Under aseptic measures, venous blood samples were drawn by venipuncture in antecubital fossa using 5ml syringe and collected in a plain vacuum tubes and transported to clinical laboratory for lipid profile analysis.

Ethical clearance

Ethical clearance was obtained from the institutional ethical committee.

Statistical analysis

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Analysis of covariance was carried out to adjust for the effect of significant age and gender difference among the groups. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Partial correlation of study variables with CIMT was performed after controlling for age.

Results

Total 60 patients aged between 18-50 years with BMI ranging between 25-30kg/m$^{(2)}$ were examined. Clinical parameters like PI, BI, PPD and CAL, Lipid profile and CIMT were compared between control and test group to find any association present between periodontitis and carotid atherosclerosis. Age was distributed into four groups for observation where in the control group 20(66.7%) patients were in the age group of 21-30 yrs and in the test group 18(60.0%) patients were in the age group of 41-50 yrs. It was found that in control group out of 30 subjects 22(73.3%) were females and 8(26.7%) were males. In the test group 19(63.3%) were males and 11(36.7%) were females. Even though Periodontal disease is age related, since the criteria for inclusion of subjects to this study was based on only BMI (overweight subjects), age and gender were not statistically matching. However, since the groups were different in age and gender distribution, Analysis of Covariance was employed for the comparison of groups, as it adjusts for the effects of age and gender.

Table 1: Age distribution

Age in years	Control group	Test group
18-20	6(20.0%)	0
21-30	20(66.7%)	2(6.7%)
31-40	4(13.3%)	10(33.3%)
41-50	0	18(60.0%)
Total	30(100.0%)	30(100.0%)
Mean ± SD	24.27±5.36	42.67±6.12

Table 2: Gender distribution

Gender	Control group	Test group
Male	8(26.7%)	19(63.3%)
Female	22(73.3%)	11(36.7%)
Total	30(100.0%)	30(100.0

Table 3: Clinical parameters of the subjects (Mean ± SD)

	Control group	Test group	p value	F value
BMI (kg/m^2)	27.02±1.35	27.46 ±1.87	0.202	1.59
PI	0.88±0.42	1.03±0.28	0.020*	3.54
GI	0.30±0.22	0.67±0.34	< 0.001**	8.3
PPD(mm)	1.25±0.37	2.69±0.87	< 0.001**	25
CAL(mm)	0.000	1.67±1.3	< 0.001**	16.8

Table no 3 shows the mean BMI, Plaque Index, Gingival Sulcus Bleeding Index (BI), Probing Pocket Depth (PPD), Clinical Attachment Level (CAL) of control group and test group. Mean BMI of control and study group was 27.02±1.35kgm^2 and27.46 ±1.87kg/m^2 respectively showing p value 0.202 and F value

1.59.Clinical parameters like PI, BI, PPD and CAL were assessed in both the groups. Results showed that mean Plaque index (PI) in the test group was 1.03±0.28 which was moderately significant with the p value 0.020 and F value 3.54 when compared with control group in which mean PI was 0.88±0.42. Mean Gingival Sulcus Bleeding Index (BI) in the test group was 0.67±0.34 which was highly significant with the p value < 0.001 and F value 8.3 when compared with control group in which mean GI was 0.30 ±0.22.The mean PPD in the test group is 2.67±0.87mm which was highly significant with the p value < 0.001 and F value 25 when compared to the control group in which the mean PPD score is 1.27±0.37mm. The mean CAL in the test group is 1.67±1.3mm which is statistically highly significant with the p value < 0.001 and F value 16.8 when compared to the control group showing mean CAL score 0. All 60 subjects were investigated for the lipid profile.

Table 4: Comparison of mean value of Lipid parameters in control and test groups

	Control group	Test group	p value	F value
Total Cholesterol (mg/dl)	182.83±23.40	201.43±34.79	0.085	2.32
Triglycerides (mg/dl)	130.33±43.56	216.67±111.25	< 0.001**	7.6
HDL(mg/dl)	39.70±4.53	40.67±3.57	0.397	1.005
LDL (mg/dl)	117.46±21.06	120.77±31.58	0.310	1.22
VLDL(mg/dl)	25.20±9.22	42.97±22.35	<0.001**	8.4

Table 5: Comparison of CIMT (normal thickness 0.5 to 0.8 mm) between test and control group

CIMT	Control group	Test group	p value	F value
Mean CIMT(mm)	0.76±0.22	0.84±0.21	0.035*	3.1

Following observations were made from the Table no 4.

Total Cholesterol (TC)

Mean Total Cholesterol (TC) level in controls and test group was 182.83±23.40 and 201.43±34.79 respectively. No significant difference was observed between both the groups.

Triglycerides (TG)

We found that mean Triglycerides level in the test group was 216.67±111.25 which was highly significant with the p value <0.001when compared with control group in which mean TG value was 130.3±43.56.

High Density Lipoprotein (HDL)

Results showed that mean HDL level in controls and test was 39.70 ±4.53 and 40.67±3.57 respectively. No significant difference was observed between both the groups.

Low Density Lipoprotein (LDL)

Results showed that mean LDL level in controls and test was 117.46±21.06 and 120.77±31.58 respectively. No significant difference was observed between both the groups.

Very Low Density Lipoprotein (VLDL)

Results showed that mean VLDL level in the test group was 25.20±9.22 which was highly significant with the p value < 0.001 when compared with control group having mean VLDL value 42.97±22.35.

Table 5 shows the comparison of Carotid Intima Media Thickness (CIMT) between both the groups .The mean CIMT in the test group was 0.84±0.21 which was moderately significant with the p value of 0.035 when compared with control group showing mean CIMT value 0.76±0.22.

Correlation of CIMT with BMI, clinical parameters and lipid parameters was of no significance.

Discussion

Atherosclerosis is a process that significantly involves the coronary, cerebral, and peripheral arteries which are of clinical importance.[7]Clinical manifestations tend to coexist, and the presence of one manifestation increases the likelihood of developing others because, major risk factors tend to affect all arterial territories. Also, clinical atherosclerosis in one area may directly predispose the patient to occurrence of atherosclerosis in another vascular territory. In spite of significant medical advances, atherosclerotic coronary artery disease such as myocardial infarction and atherosclerotic cerebrovascular disease such as stroke are responsible for more deaths than all other causes combined.[8,9] The risk factors for CVD that are unique to Asian Indians are low HDL cholesterol, high LDL cholesterol ,high triglycerides, central obesity-Insulin resistance syndrome.[10,11]

Recent reports point towards a possible association between periodontal disease and increased risk for cardiovascular disease. Periodontitis and cardiovascular disease share common risk factors, and association between periodontitis and coronary heart disease may be due to the elevated levels of plasma lipids. Epidemiological and clinical studies have also suggested that there is a relationship between periodontal disease and impaired lipid metabolism. Although there are several studies regarding the association between periodontal disease and systemic lipid levels, the results are extremely controversial. Some reports[12,13] suggested that there is a relationship between cholesterol levels and periodontitis, while other studies showed[14,15] a relationship between triglyceride levels and periodontitis; however, it also

was reported that there is a relationship between periodontal disease and cholesterol and triglyceride levels.[16] This discrepancy may arise from the methodological difficulties associated with the complexity of lipid metabolism and variety in the metabolic lipid parameters.

So, the challenge for all health care professionals is to implement comprehensive method for identification of initial atherosclerotic events in high risk patients and also in general public so that more vigorous preventive measures can be taken. For this, various non-invasive markers of early arterial wall alteration are currently available such as arterial wall thickening and stiffening, endothelial dysfunction and coronary artery calcification.[17] Intima media thickness (IMT) of large artery walls, especially carotid, can be assessed by B-Mode ultrasound in a relatively simple way and represents a safe, inexpensive, precise and reproducible measure.[1] This study was designed to evaluate the IMT of common carotid arteries in subjects with healthy periodontium and in periodontitis subjects. Physical parameters like BMI, and biochemical parameters like lipid profile were determined and their effects on IMT was studied.

Results of assessment of Plaque Index, Gingival Sulcus Bleeding Index (BI), Probing pocket depth and Clinical attachment level(Ref .Table no 3) in the present study indicated that mean PI, BI, PPD and CAL were significantly high in the test group subjects when compared to the control subjects. The association between altered lipid profile and periodontitis has been investigated in several studies.[4, 12, 13,14,16,18,19,20,21] The results of these studies, however, are somewhat inconsistent. Machado et al. (2005)[18] reported no significant differences between the serum lipid levels of periodontitis cases and controls. Hyperlipidemia has been suggested to be one possible mechanism explaining the association between obesity and periodontitis, which has been found in several cross-sectional studies in recent years.[22,23]

CIMT >8mm is considered abnormal and associated with a greater cardiovascular risk for myocardial infarction and stroke. [32] In our study mean CIMT in the test group was moderately significant with p value (0.035) when compared with mean CIMT in control group. Similar results were found in many other studies.[26, 27, 28,29,30,31]

Infections with Chlamydia pneumonia and with Helicobacter pylori which are believed to be associated with an increased risk of cardiovascular disease has been recently shown to be associated with increased plasma cholesterol and triglyceride levels.[33]These findings support the hypothesis that chronic infections including periodontitis may modify the serum lipid profile and increases the risk of atherosclerosis.

When compared with healthy individuals without periodontitis, the periodontal patients showed carotid IMT 0.84±0.21 in our study which is assumed as critical index of increased cardiovascular risk as per the study conducted by Cairo et al.[26]

In the present study we found that there was strongly significant increase in the Triglycerides values and VLDL values with P value <0.001 in the test group (Ref. Table no 2). There was an increased level of LDL and TC in the test group as compared to the levels found in control group, but the difference was not statistically significant. Similar results were found with previous studies conducted by Morita et al (2004)[15] and Taleghani F, Shamaei M (2010).[24]

Although we found higher total cholesterol and LDL levels in the test group, and also more frequent pathological values of serum lipids, the results were not statistically significant. On the contrary significant association was found between periodontitis and hyperlipidemia, specifically in relation to the triglycerides and total cholesterol levels (Cutler et al.1999,Losche et al.2000).[13,16]

Similarly significant association was seen between hyperlipidemia and periodontal disease in systemically healthy subjects,[20] showing LDL and HDL serum levels not significantly higher in test group than in control group, which was similar to our study. But in contrast, test and control groups were matched by sex and age in this study.[19]

Although the difference in HDL levels from test and control group were not significant, increased triglyceride levels in test group was highly significant as compared to the levels in control group in the study conducted by Morita et al (2004).[15]These results were matching with the results we got from our study.

Acute infections are known to interfere with lipid metabolism, and elevation of plasma triglycerides has been observed especially in infection with gram-negative bacteria (Alvarez et al. 1986).[25] These changes are thought to be mediated by cytokines, which may be produced at the inflamed periodontal tissue in high quantities.

Many studies showed the association between periodontal disease and increased carotid IMT.[26, 27, 28,29,30,31]

The results of this study showed an association between periodontal disease and early carotid atherosclerosis exists in systemically healthy patients which was moderately significant (P= 0.035). Many studies showed that periodontal disease is a predictor variable causing increased carotid IMT. [26, 27,28,29,30,31]

When CIMT was correlated with all lipid parameters in test and control groups, no significant association was found in both the groups. Similar results were seen in studies conducted by Cairo et al[26] and Beck et al.[27]

Obesity is a common risk factor for both periodontitis and atherosclerosis. Various reports found a stronger association between obesity, cardiovascular and chronic adult diseases in younger age groups.[34,35] Thus exclusion of subjects with BMI > 30kgm may have tend to dilute the association.

The limitations of the present study were:

1. Smaller sample size.

2. Differences in age between test and the control group: test group patients were older than control group subjects. However, in the present study the association was seen after adjusting the age using ANCOVA test.

Conclusion

The results obtained in this study, provides evidence that periodontal disease has association with early carotid atherosclerosis which is a risk factor for cardiovascular diseases .Thus oral health and systemic health are closely related and overall systemic health of an individual can be improved by maintaining a proper oral health regimen.

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