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A study to evaluate the relationship between periodontitis, cardiovascular disease and serum lipid levels

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Raja S, Byakod G, Pudakalkatti P, Patil R. A study to evaluate the relationship between periodontitis, cardiovascular disease and serum lipid levels.

Abstract: *Background:* The search for cellular mechanisms linking periodontitis to changes in systemic health has resulted in the evolution of a new area of lipid research. So far the causality and possible pathways of the association between periodontal disease and cardiovascular disease is obscure. *Method:* A total of 120 subjects were included in the study with 30 subjects in each of the following groups: healthy group (A), chronic periodontitis group (B), coronary heart disease (CHD + periodontitis group) (C) and CHD – periodontitis group (D). All subjects underwent oral examination and their Gingival Index, Oral Hygiene Index, Periodontal Disease Index scores and attachment loss were recorded. Two millilitres of fasting venous blood sample was drawn and tested for the level of total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL) and triglyceride level. *Results and Conclusion:* The results revealed no significant difference with respect to the lipid profile levels between the four groups. Interpreting the results of the study, periodontal disease did not cause an increase in total CHL, LDL or triglyceride levels or a decrease in the HDL levels in an otherwise systemically healthy individual or in a CHD patient. Periodontitis in a CHD patient did not seem to exacerbate the destruction of periodontal tissue. Higher triglyceride levels did not have any correlation with the severity of attachment loss in a periodontitis subject.

Key words: calculus; periodontitis; systemic disease

Introduction

Oral sepsis was introduced in the medical literature in a report entitled 'oral sepsis as a cause of disease' by William Hunter in 1911. The evidence that periodontal pathogens seed arterial vasculature contributes to a disruptive paradigm for coronary heart disease (CHD). It is said that factors that place individuals at risk for periodontitis may also place them at risk for cardiovascular disease such as smoking, diabetes, behavioural factors, ageing, male gender, etc. There has been great interest in the systemic effects of serum pro-inflammatory cytokine levels potentially elevated by periodontitis. These elevated pro-inflammatory cytokines cause an elevated serum lipid levels. This alters immune cell function resulting in increased production of pro-inflammatory cytokines by Polymorpho nucleocyctes and decreased production of growth factors from tissue macrophages reducing tissue repair capacity and leading to further tissue breakdown, and a hyper-responsive monocytic state resulting in further elevations of serum pro-inflammatory cytokines and lipids. Thus, in otherwise healthy individuals, the potential linkage of the monocytic hyper-response trait and systemic disease can actually begin with periodontitis (1).

While numerous studies have demonstrated an association between CHD and periodontal disease, several recent studies have failed to identify an association between the two. A key question is whether periodontitis is a causal factor in the aetiology of CHD. Much epidemiological research is devoted to the estimation of causal effects using non-experimental data. Unfortunately, the results of epidemiological studies, typically yielding a measure of association are insufficient to conclude whether such associations are causal. The correct interpretation of statistical associations between periodontal disease and CHD depend on a variety of issues, including but not limited to confounding bias, other sources of bias and chance (2).

Methodology

This study was conducted in the Department of Periodontics, KLES Institute of Dental Sciences, Belgaum and Department of Cardiology of KLES Hospital and Medical Research Center, Belgaum, Karnataka. A total of 120 subjects were included in the study. The subjects were divided into four groups consisting of 30 subjects in each group.

1 Group A: periodontally healthy patients without cardiovascular disease or any other systemic disease formed the control group.
2 Group B: patients with chronic periodontitis and without any systemic disease.
3 Group C: CHD patients with chronic periodontitis.
4 Group D: CHD patients without periodontitis.

Inclusion criteria

1 Patients diagnosed as having CHD based on coronary angiogram showing evidence of atherosclerosis.
2 Age group between 40 and 60 years.
3 Patients should have at least 14 natural teeth present.
4 Periodontitis group patients should exhibit clinical attachment loss of >1 mm and/or probing depth of >4 mm in around 30% of the existing natural teeth.

Exclusion criteria

1 Non-ambulatory cardiovascular disease patients.
2 Patients with any other systemic diseases.
3 Patients on any drugs for hyperlipidaemia prior to the study.
4 Patients on any antibiotics 4 weeks prior to the study.
5 Patients who have undergone dental treatment 6 months prior to the study.
6 Patients having habits like smoking, tobacco chewing, etc.

The dental variables that were measured were as follows:

1 Gingival Index (Loe and Silness)
2 Oral Hygiene Index (Greene and Vermillion)
3 Periodontal Disease Index (PDI)
4 Clinical attachment loss

Laboratory estimation of serum lipid profile

Informed consent was obtained from all subjects. Estimation of serum lipid was carried out using (Coral Clinical Systems, Goa, India). Estimation of serum cholesterol, high density lipoprotein (HDL) cholesterol was carried out by Cholesterol oxidase/Phenol-amino-4-antipyrine peroxidase method and Poly-Ethylene-Glycerol precipitation method, respectively, using an Coral Clinical Systems, Goa, India (Fig. 1). Calculation of low density lipoprotein (LDL) cholesterol in mg dl^{-1} was carried out using Freldewald's formula:

$$\text{LDL} = \text{Total cholesterol} - \left[\frac{\text{Triglycerides}}{5}\right] - \text{HDL cholesterol}$$

Estimation of triglyceride was carried out by Glycerol-3-phosphate-oxidase/PAP method and cut-off levels of serum lipid levels in Indian population were taken according to the

Fig. 1. Autoanalyser for estimation of lipid profile.

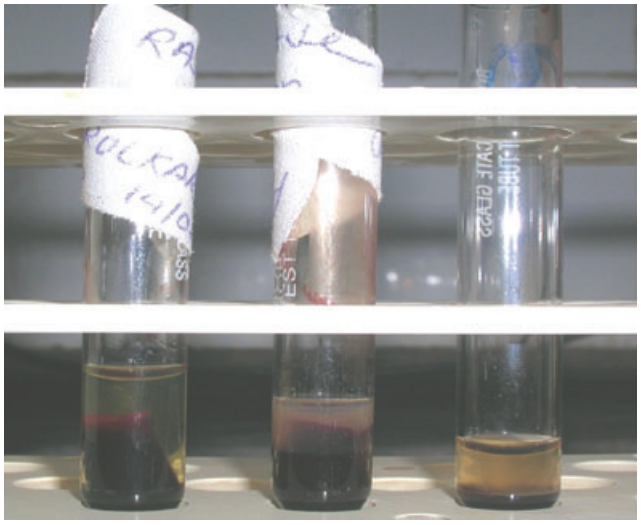

Fig. 2. Serum sample in test tubes for estimation of serum lipid levels.

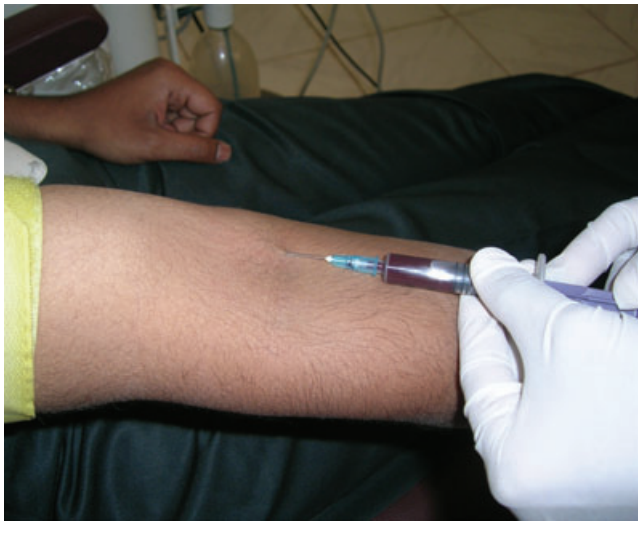

Fig. 3. Collection of venous blood sample.

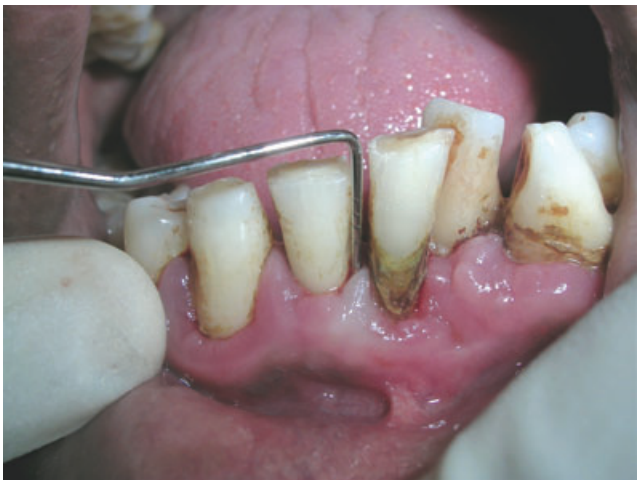

Fig. 4. Periodontitis case.

Indian Council of Medical Research (ICMR) 1995 and Indian consensus 1997 (3). Venous blood (3 ml) was collected from each subject after an overnight fasting period of 8–12 h for estimation of serum lipid profile (Figs 2 and 3). A case of periodontitis is shown in Fig. 4. The study was statistically analysed using ANOVA, Student's unpaired '*t*'-test, chi-squared test and Karl-Pearson's co-efficient of correlation.

Results and interpretation

Mean values of gender, age and clinical parameters among the four groups

The mean age all the four groups is between 40 and 56 years. Though the Gingival Index (GI) scores were more for the periodontitis subjects (Group B) than subjects with CHD + periodontitis (Group C), Oral Hygiene Index-Simplified scores for Group C were relatively more when compared with Group B. While subjects with CHD only (Group D) revealed mild gingival inflammation and a fair oral hygiene, healthy subjects (Group A) exhibited the least GI, OHI-S and PDI scores. PDI scores for Group B subjects were highest with a score of 4.74, exhibiting a poorer periodontal condition when even compared with Group C subjects (Table 1).

Intercomparision of attachment loss between Group B and Group C subjects

In addition to the high GI and OHI-S scores exhibited by subjects with only periodontitis (Group B), they also revealed an increased attachment loss when compared with subjects with periodontitis and CHD (Group C) which was statistically significant (Table 2).

Table 1. **Mean values of gender, age and clinical parameters among the four groups**

Group	M:F ratio	Age	GI	OHI-S	AL (mm)	PDI
Healthy (A)	12:18	42.87	1.22	1.64	0.03	1.32
Chronic periodontitis (B)	14:16	46.67	1.75	3.95	4.22	4.74
CHD + periodontitis (C)	25:5	56.17	1.51	3.61	3.58	4.35
CHD – periodontitis (D)	25:5	50.13	1.36	2.35	0.13	1.58

AL, attachment loss; CHD, coronary heart disease; PDI, Periodontal Disease Index; OHI-S, Oral Hygiene Index-Simplified; M, male; F, female; GI, Gingival Index.

Table 2. **Intercomparison of attachment loss between group B and C (Student's unpaired '*t*'-test)**

Group	Mean (mm)	SD	*P*
Chronic periodontitis (B)	4.22	1.04	0.014 S
CHD + periodontitis (C)	3.58	0.9	

S, significant; CHD, coronary heart disease.

Comparision of mean serum lipid levels between the four groups

Statistical significance was achieved for only HDL and triglyceride among the four groups. Subjects with CHD (Group C and D) exhibited lower levels of the cardioprotective HDL levels while healthy subjects (Group A) revealed the highest score for HDL levels (Table 3). Periodontitis in Group B subjects did not seem to lower the cardioprotective HDL levels as they exhibited a higher level of HDL when compared with Group C. High triglyceride levels were exhibited by subjects with CHD (Group C and D) while the healthy subjects (Group A) had the least triglyceride levels. Though periodontitis group (Group B) triglyceride levels were less, compared with CHD groups, they were still higher than the healthy subjects.

Correlation of attachment loss between Group B and C subjects

When HDL was correlated with attachment loss, a moderate negative correlation was obtained. When attachment loss was correlated with triglyceride levels, the values obtained were statistically insignificant (Table 4).

Table 4. **Correlation of attachment loss (AL) with HDL and triglyceride (TRG) levels (Karl Pearson's coefficient correlation)**

Group	AL + HDL	AL + TRG
Periodontitis (B)	0.035	0.0853
CHD + periodontitis (C)	–0.3811	–0.096

CHD, coronary heart disease; HDL, high density lipoproteins.

Discussion

Coronary heart disease remains one of the leading causes of death and morbidity despite the remarkable progress in our understanding of the pathogenesis and treatment of the disease. Notwithstanding their importance, the classic coronary risk factors do not explain all clinical and epidemiological features of CHD. Several studies have suggested that development of CHD is influenced by infections (4, 5). The scope of infections associated with CHD also includes dental infections, especially periodontitis (3). In the present study data were collected using a detailed performa. The body mass index (BMI) (6) of each individual was calculated using the formula, weight (in kg)/height (m^2), to exclude any obese individuals from the study and subjects having BMI >25 were not included in the study.

Severity of inflammation was relatively higher in subjects with periodontitis, i.e. in Group B and C, displaying a higher GI and OHI-S scores. Ramfjord's PDI scores in periodontitits groups, i.e. Group B and C, were higher, depicting an increase in the periodontal destruction. PDI score for an individual may range from 0 to 6 with higher scores displaying poorer periodontal status (7). Attachment loss in chronic periodontitis group (B) subjects displayed statistically significant higher attachment loss than CHD + periodontitis group (C) subjects. This data may infer that the presence of CHD in a periodontitis subject may not necessarily exacerbate the destruction of

Table 3. **Comparison of mean serum lipid levels between the four groups – ANOVA**

Lipid profile	Group	*n*	Mean	SD	F	*P*
HDL	Healthy (A)	30	41.07	9.52	4.01	0.00929 VS
	Periodontitis (B)	30	39.20	7.19		
	CHD + periodontitis (C)	30	34.80	7.01		
	CHD – periodontitis (D)	30	35.17	9.54		
TRG	Healthy (A)	30	90.30	32.70	11.80	8.4×10^{-7} HS
	Periodontitis (B)	30	100.57	35.05		
	CHD + periodontitis (C)	30	164.93	76.64		
	CHD – periodontitis (D)	30	137.80	62.13		

VS, very significant; HS, highly significant; F, female; CHD, coronary heart disease; HDL, high density lipoprotein; TRG, triglycerides.

periodontal tissue. Bazile *et al.* (8) showed no significant association between probing depth, attachment level and CHD. A negligible loss of attachment was noted in the healthy (A) and CHD-periodontitis (D) groups.

Serum lipid profile for the Indian population has been assessed by councils like the ICMR, programs like the National Cholesterol Education Program (1998) and by authors like Reddy and Tendon (3) and Goswami and Bandyopadhyay (9). The values of serum lipid levels obtained in our study for the healthy group (A) corroborate well with the normal values obtained by the aforementioned authors. The lipid profile values obtained in chronic periodontitis group (B) too were within the normal limits though relatively higher than the healthy group (A). In the CHD groups (C and D), though a relatively higher serum lipid levels were seen, they did not exhibit levels over the normal cut off values which could be explained as follows. Studies in the past have shown that high rates of CHD in Asian Indians are accompanied by a paradoxically low prevalence of conventional risk factors, such as hypertension, hypercholesterolaemia, smoking, etc. The newly emerging risk factors responsible for early onset and increased prevalence of CHD in Indians may be elevated lipoprotein-a, insulin resistance syndrome, hypertriglyceridaemia, small dense LDL, apolipoprotein-B and -A, thrombogenic factors, hyperhomocysteinaemia and infections and inflammatory factors (3).

Significant differences were achieved only with HDL and triglyceride levels between the four groups which explains the heterogenous nature between the groups while there was no significance achieved with total cholesterol or LDL levels, depicting homogeneity within the groups. This data support the study by Loesche *et al.* (10) and Morita *et al.* (11) who did not find any significant difference with regard to total cholesterol and serum LDL levels between the diseased and the control groups.

Intercomparison of mean HDL and triglyceride levels among the four groups was carried out to ensure whether the significance observed revealed any difference when each group was compared with the other. HDL is cardioprotective in nature and its normal level in a healthy individual as obtained by the National Cholesterol Education program (1998) is $\geq$35 mg dl^{-1} (3). Healthy group (A) and the chronic periodontitis group (B) subjects did not reveal any statistical significant difference in their levels of HDL or triglycerides implying that both the groups were at equal intermediary risk of developing CHD. Hence periodontitis did not seem to lower the cardioprotective HDL levels nor cause an increase in the triglyceride levels in an otherwise systemically healthy subject. This is in accordance with the study conducted by Ebersole *et al.* (12) who did not find any correlation with HDL levels and periodontitis. Losche *et al.* (13, 14) too did not find any positive correlation with HDL and triglyceride levels and clinical parameters of inflammation and periodontal disease.

Coronary heart disease groups with or without periodontitis (Group C and D) were compared for their levels of HDL and triglyceride but no statistical significant difference could be achieved. Hence the data imply that a CHD patient with periodontitis was neither under the risk of the triglyceride levels being increased further nor the cardioprotective HDL levels being decreased further because of periodontitis. In the present study, Group (C) and Group (D) subjects did show a relatively higher triglyceride levels when compared with the chronic periodontitis group (B) achieving statistical significance and also lower levels of HDL, though significance for HDL was seen between Group B and C only. Nevertheless, this only strengthens the fact that it is only CHD and not periodontitis which is associated with higher levels of triglyceride and lower levels of cardioprotective HDL value. There is evidence suggesting a role for infectious agents in the pathogenesis of cardiovascular disease and cause an increase in the levels of these cytokines. Hence the decrease in HDL levels in Group C when compared with Group B could be because of the increase in the active cytokines because of CHD. When HDL levels were correlated with the attachment loss, a moderate degree of negative correlation was seen in CHD + periodontitis group (C) indicating that the larger values of HDL are associated with smaller levels of attachment loss.

Studies have shown a positive correlation between periodontitis and increased serum lipid profile (12–16). But most of the mentioned studies were unable to infer a positive correlation with all the parameters of lipid profile (i.e. total cholesterol, LDL, HDL and triglyceride) to arrive at a definitive conclusion vis-à-vis periodontitis and increased lipid profile. Losche *et al.* (14) found only LDL to be significantly associated with the clinical parameters of inflammation and periodontal tissue destruction in periodontitis subjects.

Iacapino and Cutler (1) reported that existence of an association between periodontitis and serum lipid levels does not establish whether periodontal disease causes elevations in lipid levels or whether elevations in serum lipids predispose to periodontitis. Hence these studies in actual fact do not depict a strong correlation between serum lipid profile levels and periodontal disease. In our study there was no correlation between periodontitis and serum lipid levels.

Studies have assessed the periodontal status in CHD patients (17–23) and have compared them with the control

group subjects unlike the present study with four groups whose lipid profiles were compared. Though this study was carried out on a modest sample size of 120 subjects, the results did not prove periodontitis to be an independent factor in causing an increase in the lipid levels nor did it provide any evidence to substantiate hyperlipidaemia to be a common risk factor in chronic periodontitis subjects and CHD patients. Thus the results of the present study failed to draw any convincing evidence to show any correlation between periodontal disease, CHD and serum lipid levels.

Summary and Conclusion

The aim of the present study was to assess the relationship between periodontal disease and CHD and serum lipid profile. Analysing the data of this study, the following conclusions can be drawn:

1 No statistically significant difference in mean serum total cholesterol and LDL levels among healthy chronic periodontitis, CHD + periodontitis and CHD − periodontitis group subjects were seen.

2 Periodontitis did not seem to cause a decrease in the cardioprotective HDL levels or an increase in the triglyceride levels in an otherwise systemically healthy individual or in CHD patients.

3 A CHD patient also suffering from periodontitis did not seem to have an exacerbated destruction of the periodontal tissues.

4 Higher triglyceride levels did not have any correlation with the severity of attachment loss in periodontitis subjects (Group B or C).

In this present study, there seems to be no correlation between periodontal disease and healthy subjects with respect to lipid profile. Also no correlation could be drawn when the lipid levels were tested in CHD groups with periodontal health and disease. Future investigations of the relationship need to emphasize the definition of CHD so that potential associations of periodontal disease with specific processes in the pathogenesis of CHD can be detected. Additional studies are necessary to better define the relationship between periodontal conditions and coronary artery disease. A larger sample, representative of the general population in terms of socio-economic factors and demographics along with alveolar bone level assessment would be necessary to determine the nature of the association. Hence future longitudinal studies need to be conducted on larger epidemiological group to delineate the relationship between periodontitis, cardiovascular disease and serum lipid level.

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