Original Article

Association between chronic generalized periodontitis and hyperlipidemia – a case control study

A Ramesh[1], Shaju Jacob P[2], Zade RM[3]

Abstract

Introduction: Hyperlipidemia is a major risk factor for cardiovascular disease. Periodontal disease is caused by predominantly anaerobic gram negative bacteria. Microbial substances initiate and perpetuate the inflammation resulting in the production of high levels of proinflammatory cytokines and hyperactivity of white blood cells and of blood platelets, thus promoting the development of hyperlipidemia. ***Objective:*** To evaluate the plasma lipids (Total cholesterol, Low Density Lipoproteins and Triglycerides) as well as Fasting blood glucose levels in non diabetic, non-obese periodontal disease patients and controls. ***Materials and methods:*** 18 subjects with chronic periodontal disease (aged 38 to 50 years) were matched for age, sex and BMI (Body Mass Index) with 18 healthy subjects. Total cholesterol, low density lipoprotein, triglycerides and fasting blood glucose levels were measured using routine enzymatic biochemical methods. ***Results:*** Total cholesterol, LDL cholesterol and triglycerides was significantly higher in chronic periodontitis patients by 12 %($p<0.02$), 14 %($p<0.03$) and 22 %($p<0.03$) respectively as compared to controls. Fasting blood glucose levels was higher by 7% ($p<0.04$) in chronic periodontitis patients than controls. ***Conclusion:*** Hyperlipidemia and prediabetic state may be associated with chronic periodontitis.

Key words: chronic periodontitis; plasma lipids; body mass index; fasting blood glucose.

Introduction

Periodontal diseases are infections. They have a number of properties in common with infections in other parts of the body, but have unique features resulting from the passage of the tooth through the soft tissue integument into the oral cavity. The tooth provides a solid, non-shedding surface for the colonization of potentially pathogenic bacterial species as well as a wide range of host-compatible species. Periodontal pathogens frequently colonize the periodontal area for prolonged periods of time prior to disease initiation. Disease is caused by a finite set of bacterial species leading to the development of multiple periodontal diseases. Lipopolysaccharides (endotoxins) and other microbial substances gain access to the gingival tissues, initiate and perpetuate inflammation resulting in production of high levels of proinflammatory cytokines (especially TxA2, IL-1 beta, PGE2, and TNF-alpha), which lead to the destruction of the periodontal ligament and bone.

Several studies have indicated that subjects with periodontal disease may have a higher risk for cardiovascular diseases[1-6] when compared to subjects with a healthy periodontium. Factors that place individuals at risk for periodontitis may also place them at risk for cardiovascular

4. *Dr Ramesh **Amirisetty,** Reader, Department of Periodontics & Oral Implantology, Chhattisgarh Dental College & Research Institute, Rajnandgaon.
5. Dr Shaju **Jacob P,** Associate Professor, Department of Periodontics & Oral Implantology, Chhattisgarh Dental College & Research Institute, Rajnandgaon.
6. Dr Zade **RM,** Dean & HOD, Department of Periodontics & Oral Implantology, Chhattisgarh Dental College & Research Institute, Rajnandgaon.

Corresponds to: Dr Ramesh Amirisetty, Reader, Department of Periodontics & Oral Implantology, Chhattisgarh Dental College & Research Institute, Sundara, Rajnandgaon – 491441. ***Mobile:*** +91 9589895808. ***Tel:*** 0091-7744 281930. ***E-mail:*** rameshperio@yahoo.co.in.

disease as periodontitis and cardiovascular disease share common risk factors including smoking, diabetes, behavioral factors, ageing, and male gender. In a number of case-control or cohort studies[1-6] even after adjusting for these factors in multivariate analysis, the association remained statistically significant. Subjects with hypercholesterolemia and cardiovascular disease have a significantly worse periodontal condition than healthy subjects. Periodontal disease through infection related mediators and hyperactivity of white blood cells and platelets promotes the development of atherosclerosis and hence can be associated with cardiovascular disease.[7,8]

In the present study, we measured plasma lipids and fasting blood glucose levels in non diabetetic, non obese periodontal disease patients and healthy control subjects.

Materials and methods

Subjects

18 subjects with periodontitis (13 males and 5 females) and 18 controls (13 males and 5 females) participated in the study. The age group of the patients ranged between 38 to 50 years (mean age 44.5).Both patients and controls were recruited from the OPD in the department of Periodontics in Saveetha Dental College, Chennai. Institutional ethical committee gave approval for the study. After getting informed consent forms, patients and controls were asked to answer a questionnaire regarding their social and general medical status. Exclusion criteria were any dental treatment during the past 6 months, diabetes mellitus or any endocrinal disease, myocardial infarction, stroke and cancer, smokers and BMI above 27 were excluded from the study. No subject took any therapy for hypercholesterolemia .All the subjects in the study group had at least 8 teeth having periodontal pockets with depths ranging from 5-7mm.

Measured Variables

All subjects were examined by the same dentist. All dental variables were assessed at 6 different sites around each tooth.

Presence of plaque: Presence or absence of plaque was registered quantitatively.

Bleeding on probing: If bleeding occurred immediately after probing for pocket depth, it was recorded positive.

Probing pocket depth was measured with Williams's periodontal probe. Periodontal pockets were categorized as healthy (within 3mm), moderate disease (4 to 5 mm), and advanced disease (more than 6 mm).

Measurement of Plasma lipids and fasting blood glucose levels

Table 1: Total cholesterol, HDL& LDL cholesterol, Triglycerides and Fasting blood glucose level in chronic periodontitis and healthy subjects

VARIABLE	Controls (Mean±SD)	Patients (Mean±SD)	p-value
Total cholesterol (mg/dl)	208.5±26.3	235.9±29.0	.02*
LDL cholesterol (mg/dl)	129.4±33.3	151.3±27.1	.03*
HDL cholesterol (mg/dl)	49.3±8.5	51.5±8.6	Not significant
Triglycerides (mg/dl)	137.7±21.6	177.3±47.8	.03*
Fasting blood glucose (mg/dl)	80.3±4.8	86.5±7.1	.04*

*Significant ($p \leq 0.05$)

After enrolling into the study the patients and the controls were sent to the department of Biochemistry for measuring Plasma lipids and fasting blood glucose

levels using routine enzymatic methods (Table.1). The following cut off points were used total cholesterol > 230mg/dl, LDL cholesterol > 160mg/dl, HDL cholesterol < 45mg/dl, triglycerides > 200mg/dl. These values were applicable to individual with a normal risk for cardiovascular disease.[9]

Statistical analysis

All the values are expressed on a patient basis.

Values are presented as mean and standard deviation.

Differences in means are proved for significance using student's *t*-test for unpaired samples.

Results

There was not much difference in the social status of periodontal disease patients and control subjects. Based on the extent of periodontal pockets most of the patients suffered from moderate periodontitis: 37.4±18.2% of sites had a probing depth of 4-5 mm. and 12.3±10.3% sites had a probing depth of more than 5 mm. In controls there were few moderate deep pockets (6.3±7.5% of sites) but no deep pockets were present (>7mm). Bleeding on probing was more frequent in periodontitis patients than healthy controls. Plaque accumulation did not reveal significant difference between periodontitis (54.2±13%) and healthy controls (46.6±12.3%).

Mean plasma cholesterol and LDL cholesterol levels in periodontitis subjects were significantly higher by 12 and 14% as compared to controls. Plasma triglycerides were higher in patients than controls. There was no significant difference in the HDL cholesterol. Triglycerides were higher in patients than in controls subjects (22%).

Subjects with Diabetes Mellitus were excluded from the study. We measured the fasting blood glucose levels in all the subjects and there was a significant difference between the periodontitis and healthy controls. Mean blood glucose levels were 7% higher in patients compared to controls.

The age range in our study was 38 to 50 years was indeed small to further subdivide them. We matched the age and BMI for selecting the patients and controls in the present study to check the association.

Discussion

Periodontitis and cardiovascular diseases share some common risk factors like diabetes and smoking. Although patients with known diabetes were excluded from the study, we still found slight increase in the mean fasting blood glucose levels in chronic periodontitis patients as compared to controls, indicating poor glycaemic control and a prediabetic condition. Poor glycaemic condition is known as an established risk factor of periodontitis.[10, 11] Severe periodontitis may deteriorate glycaemic control.[12-14] Monocyte-derived cytokines such as TNF α, IL-1β or interferon-γ produced in response to infection with gram-ve bacteria may be responsible for an insulin resistance and subsequent poor glycaemic control in periodontitis patients.[15-17] TNF-α has been suggested as the mediator of insulin resistance in infection by suppressing insulin-induced tyrosine phosphorylation of insulin receptor substrate-1 (IRS-1), thus impairing insulin action.[18]

Acute-phase proteins, such as C-reactive protein, or CRP, and fibrinogen, affect coagulation, platelet activation and aggregation. The LPS and inflammatory cytokines that are present in periodontal disease may also increase the expression of leukocyte adhesion molecules such as intercellular adhesion molecules, or ICAM, or vascular cell adhesion molecules, or VCAM, by endothelial cells. ICAM and VCAM, in turn, are associated with atheroma formation. Another potential linking mechanism includes immune

responses that result in production of antibodies to periodontal bacteria, including antibodies to bacterial heat-shock proteins that cross-react with heat-shock proteins of the heart. These autoreactive antibodies to heat-shock proteins are found in patients with periodontal disease and may contribute to atheroma formation.

Compared to controls the periodontitis patients had higher plasma cholesterol and triglycerides. Endothelial dysfunction, an early step in atherosclerosis has been shown to occur in individuals with periodontitis.[19]Periodontitis is believed to cause a low, but long-lasting, systemic inflammatory reaction, which in turn contributes to the development of atherosclerosis.[20] Elevation of plasma triglycerides has been observed in infection with gram-ve bacteria.[21] P. gingivalis DNA and viable pathogens have been found in human atherosclerotic lesions.[22,23]. The oral gram-positive bacteria Streptococcus sanguis and the gram-negative periodontal pathogen P. gingivalis have been shown to induce platelet activation and aggregation through the expression of collagen like platelet aggregation–associated proteins. The aggregated platelets may then play a role in atheroma formation and thrombosis.

Cutler *et al.*[2] showed a significant association between periodontitis and hyperlipidemia, in relation to the triglycerides and total cholesterol levels. However, the groups were not age-matched, and the mean age of the group with disease was 50.5 years, statistically higher than that of the control group, 41.6 years.

Similar methodology was used in the study of Lösche *et al.*[4] in which the authors observed significantly higher total cholesterol levels (8%), LDL (13%) and triglycerides (39%) in the group with periodontal disease in comparison to the group without the disease. In this study, the groups were not sex matched, but only age-matched and BMI was not considered in selecting the subjects. Body Mass Index (BMI) is a reliable indicator of hyperlipidemia [24] and this factor needs to be considered when correlating the association between hyperlipidemia and periodontitis. In the present study we considered body mass index and excluded obese individuals to know if there is any direct association between periodontitis and lipid levels in otherwise systemically healthy subjects. Our results are consistent with this study with respect to total cholesterol and LDL levels and we found triglycerides rise by 22% only in chronic periodontitis patients than controls. This may be due to the exclusion of obese individuals in our study.

Hyper-reactive Mononuclear Phagocytes may be induced in patients with infections such as periodontal disease. These may be induced if leukocytes are passing through lesions in vessels traversing close to areas of high proinflammatory cytokine release, LPS presence, matrix metalloproteinase activity, or prostaglandin or protease release. These leukocytes may, by virtue of their induced hyperresponsiveness, be effectual in creating atheromas at distant sites, particularly in areas of turbulence or where the vasculature is already damaged. There is also the possibility that cells such as macrophages or Langerhans' cells, which recirculate under normal circumstances, may themselves be activated and enter the circulation or may activate other peripheral circulation cells. These indirectly activated cells may have an effect at distant sites. [25]

Conclusion

The proatherogenic changes in plasma lipids and blood glucose that were observed in our study in periodontitis patients may provide some evidence for the association between periodontitis and cardiovascular disease. Periodontal pockets by favoring adherence of plaque microbes cause a cytokine release by the various

host immune cells thereby causing a systemic effect It is not clear whether the observed changes in the lipid profiles and fasting glucose levels is the cause or consequence of periodontitis. Further longitudinal studies are needed to see the effect of periodontal pocket elimination therapy on the changes in the lipid profile in chronic periodontitis patients.

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