Association between Chronic Generalized Periodontitis and Hyperlipidemia

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Abstract:
OBJECTIVES: The objectives of the study were (1)To assess serum lipid levels among healthy subjects. (2) To assess serum lipid levels among subjects with chronic generalized periodontitis. (3) To compare the serum lipid profile among healthy subjects with that of patients having periodontitis.
METHODS: A cross sectional study comprising of 50 subjects, 25 subjects with chronic periodontitis and 25 healthy subjects (30-50 years). Serum lipid level (HDL,LDL,VLDL,TGL,TC) of all subjects were measured and compared.
RESULTS: The mean difference between total cholesterol, triglyceride, HDL, VLDL and LDL values of test and control groups are 14.5 (p<0.02) 11.1 (p<0.038) , 2.2 (p<0.784), 2.23 (p<0038.), and 7.96(p<0.046) respectively as compared to the controls. Results obtained in this study showed significant association between pronounced alterations in lipid profile of patients with generalized chronic periodontitis as compared to the healthy control groups.
CONCLUSION: The present study suggests that Plasma lipid levels significantly correlates with chronic periodontitis and hyperlipidemia.
Key Words: Periodontal disease, Plasma lipid, hyperlipidemia.

I. Introduction

Periodontal disease is a group of inflammatory disease in which Gram-negative microorganisms and their products are the principle etiological agents. These microorganisms produce endotoxins in the form of lipopolysaccharides (LPS) that are instrumental in generating a host-mediated response and perpetuate an inflammatory reaction, which leads to the destruction of periodontal ligament and alveolar bone and finally to tooth loss[1].

Periodontal disease affects 10% to 15% of the world's population, representing the greatest cause of tooth loss. Although mild and moderate forms of chronic periodontitis are rather common, severe form of periodontitis with advanced tissue destruction are rare worldwide. Periodontitis has even higher prevalence in developing countries and considerable global variation; although the prevalence of the severe generalized disease appears to be similar in most populations[2].

Several studies have shown that, a response of a periodontal infection includes production of several enzyme families and inflammation markers, which are released from stromal, epithelial, inflammatory or bacterial cells. The analysis of these enzymes in salivary secretion and inflammation markers in serum of periodontitis patients can contribute to clarification of pathogenesis and improvement of making a prompt diagnosis of periodontal disease [3]. Recently a casual relation has been demonstrated between high serum lipid levels and periodontal disease. Recent studies illustrate the existence of a relation between periodontal disorders and hyperlipidemia, which power the probable effect of periodontal disease as an underlying factor for hyperlipidemia. This theory is presented in Losche et al study, which demonstrated higher level of TGL and lower HDL among the patient suffering periodontitis than control group significantly [4], which was approved by some other studies [5].

Studies in humans and animals have shown that a number of cytokines such as tumor necrosis factor alpha and interlukin-1 beta are produced in response to systemic Gram-negative LPS exposure. It is believed that these cytokines exert effects on lipid metabolism by influencing production of other cytokines, altering

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hemodynamic/amino acid utilization of various tissues involved in lipid metabolism, or modifying the hypothalamic-pituitary-adrenal axis increasing plasma concentrations of adrenocorticotropic hormone, cortisol, adrenaline, noradrenalin and glucagon. Thus through action of TNF α and IL-1β, exposure to microorganisms/endotoxin results in elevated levels of free fatty acids, LDL and triglyceride. These elevations in serum lipids are thought to arise from enhanced hepatic lipogenesis, increased adipose tissue lipolysis/blood flow, increased synthesis or reduced clearance of triglycerides, and reduced clearance of LDL due to reductions in lipoprotein lipase activity. Thus, any condition producing elevations in serum TNF-α and IL-1β has potential to cause hyperlipidemia[6,7].

Several studies have indicated that subjects with periodontal disease may have a higher risk for hyperlipidemia, when compared to subjects with healthy periodontium. Factors that place individual at risk for periodontitis may also place them at risk for hyperlipidemia and cardiovascular disease.[8-10] 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.[11,12] So, the aim of the present study was to compare the periodontal condition and serum lipid levels in healthy individuals, subjects with periodontitis.

II.   Materials And Methods

Source of data:
A total of 50 subjects were selected based on convenient sampling method. Subjects were selected from Department of Periodontics of A.B. Shetty Memorial Institute of Dental Sciences, Mangalore after obtaining Ethical clearance from institutional ethical board. All the samples were collected with an informed consent from each of the patient and the procedure was explained in the language which subjects can understand.

The criteria for inclusion in the study were Subjects with minimum complement of 20 natural teeth and the subjects were between the age group of 30-50 years. The criteria for exclusion in the study were patients with any systemic diseases such as Diabetes Mellitus,myocardial infarction, stroke and cancer, smokers, on Antibiotics, Anti-inflammatory drugs, and subjects with BMI above 27 and patients who had undergone periodontal treatment in last 6 months and not under any therapy for hypercholesterolemia.

Study participants were divided into 2 groups. Group I comprising of healthy subjects without any periodontal and/or systemic disease. Group II comprising of subjects having moderate to severe chronic periodontitis with clinical attachment loss ≥ 4mm in more than 30% of sites and all measurements and samples were taken before starting any periodontal therapy.

Screening examination:
Medical and dental history of the subjects was determined. All subjects were examined by the same dentist. 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).

Method of collection of blood
Under all aseptic conditions, approximately 2ml of venous blood collected from anticubital vein at the morning hours between 10-12am was sent for lipid profile estimation. A sterile disposable syringe and 24 gauge needle was used for this purpose.The serum lipid estimation of each sample was performed by using a semi-automatic analyzer "TRANSASIA ERBA CHEM 5 plus" at the biochemical laboratory of A.B. Shetty Memorial Institute of Dental Sciences, Mangalore. Estimation of total cholesterol was done by CHOD-POD method, estimation of HDL-Cholesterol by precipitation end point method. 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.

Statistical analysis
Descriptive statistics for cholesterol levels among the study groups was expressed as mean and standard deviation. Student's t-test was used to compare the statistical significance between two groups. Analysis was done with 95% confident interval and a p value less than 0.05 was considered as statistically significant. Data was analysed using SPSS software.

III. Results

TABLES

Table (1): Distribution of study subjects based on gender

Groups	Gender		Total
	Male	Females	
Group I	16	9	25
Group II	14	11	25
Total	30	20	50

Table (2) Mean age among study subjects

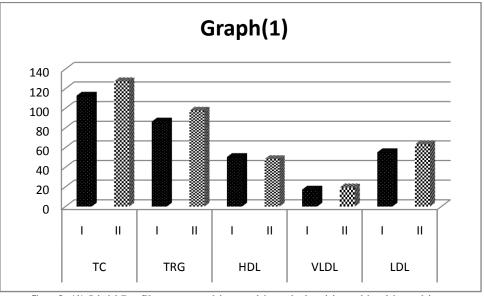| Groups	Mean	SD
Group I	37	+6.5
Group II	40	+5.2

Table(3) shows Mean and Standard Deviation values of of TC, TGL,HDL,VLDL and LDL of both the Groups.

CHARACTERISTICS	GROUP	MEAN	STANDERED DEVIATION	MEAN DIFFERENCE	't' VALUE	P-VALUE
TOTAL CHOLESTROL	Group I	113.0	13.79	14.5	3.62	0.02*
	Group II	127.5	15.6			
TRIGLYCERIDE	Group I	86.57	20.31	11.1	2.13	0.038*
	Group II	97.67	16.59			
HDL	Group I	50.5	8.5	2.2	2.05	0.784
	Group II	48.3	8.6			
VLDL	Group I	17.30	4.06	2.23	2.13	0.038*
	Group II	19.53	3.31			
LDL	Group I	55.36	9.71	7.96	2.05	0.046*
	Group II	63.32	16.78			

*Significant (p>0.05)

Graph (1) Lipid Profile among subjects with periodontitis and healthy subjects

Table (1) shows the distribution of study subjects based on gender where 30 subjects where males and 20 were females. Group I consisted of 16 males and 9 females. Table (2) represents the distribution of study subjects based on age. Group I consisted of subjects with mean age 37+6.5 years and group II consisted of subjects with mean age 40+5.2 years.

Table (3) represents the Mean and Standard Deviation values of TC, TGL, HDL, VLDL and LDL of both the Groups. The mean difference of Total Cholesterol between Group I and Group II was 14.5 and the p value was found to be highly significant. Triglycerides also showed a significant difference between the study and the control groups. The mean difference between HDL levels was 2.2 which also showed a non significant p value. The mean difference of VLDL and LDL between Group I and Group II were 2.23 and 7.9 respectively. VLDL and LDL also showed a highly significant difference between the groups.

IV.   Discussion

Periodontitis begins with a microbial infection, followed by a host-mediated destruction of soft tissue caused by hyper activated or primed leukocytes and the generation of cytokines eicosanoids and matrix metalloproteinase that cause clinically significant connective tissue and bone destruction. Clinical and basic science researches over past several decades have led to an improved understanding and appreciation for complexity and pathogenesis of periodontal disease. There is an essential bacterial etiology and there are specific periodontal pathogens associated with destructive periodontal disease. However, these pathogens do not invariably cause disease simply by their presence alone[13].

Many systemic disease and disorders have been implicated as risk indicators in periodontal disease.Periodontitis and cardiovascular diseases share some common risk factors like diabetes and smoking. Certain systemic diseases and conditions alter host tissue and physiology, which may impair host barrier integrity and host defense to periodontal infection, resulting in more destructive disease. Although the potential impact of many systemic diseases on periodontium is well documented, recent evidence suggests that periodontal infection may significantly enhance the risk for certain systemic diseases or alter natural course of systemic diseases[14]. Conditions in which periodontal infection are documented include coronary heart disease and coronary heart disease related events such as angina and infraction, atherosclerosis, stroke, diabetes mellitus, preterm labor, low birth weight delivery, and chronic respiratory conditions[15].

The results of the present study shows the elevation in total cholesterol, triglycerides and low density lipoprotein(LDL) which can be due to the reason that serum lipid alterations were related to the underlying pathological conditions rather than the infectious process. However study conducted by OzlemFentoglu et.al have demonstrated that lipid metabolism may be altered by chronic local and acute systemic infections which are involved in plasma concentrations of unregulated cytokines and hormones. The main features of this catabolic state are lipid oxidation and elevated free fatty acids, triglycerides and low density lipoprotein(LDL) cholesterol[13] and these results are in accordance with the present study.

As the results obtained in the present study the elevations in serum lipids are thought to arise from enhanced hepatic lipogenesis, increased adipose tissue lipolysis/blood flow, increased synthesis or reduced clearance of triglycerides, and reduced clearance of LDL due to reductions in lipoprotein lipase activity. Studies in humans and animals have shown that a number of cytokines such as tumor necrosis factor alpha and interlukin-1 beta are produced in response to systemic Gram-negative LPS exposure. It is believed that these cytokines exert effects on lipid metabolism by influencing production of other cytokines, altering hemodynamic/amino acid utilization of various tissues involved in lipid metabolism, or modifying the hypothalamic-pituitary-adrenal axis increasing plasma concentrations of adrenocorticotropic hormone, cortisol, adrenaline, noradrenalin and glucagon. Thus through action of TNF α and IL-1β, exposure to microorganisms/endotoxin results in elevated levels of free fatty acids, LDL and triglyceride. Thus, any condition producing elevations in serum TNF-α and IL-1β has potential to cause hyperlipidemia[6,7.]

In this study, we analyzed the level of HDL and LDL that seem to play an important role in lipid metabolism and alteration in the level may result in hyperlipidemia. The study was performed on simultaneously collected serum samples from documented subjects with periodontitis and periodontal healthy subjects. The results obtained clearly show the significant increase in the mean TC, TGL, and LDL levels between Group 1(healthy) and Group 2 (Chronic Periodontitis) at 5% level of significance. The results obtained in the present study was in accordance with the study conducted by Losche et al in 2005 assayed plasma TGL and total cholesterol levels and that study states there is a significant increase in TGL and LDL along with decreased HDL values in chronic periodontitis[4]. A study by Bullon P et al., was conducted to prove the relation between chronic periodontitis and atherosclerosis by measuring the lipid profile and inflammation markers. Study gives the conclusion showing simple, economical clinical parameters such as Total lipid profile (Cholesterol, TGL, HDL, LDL) can assess the damage of periodontal tissue and useful in prediction of future risk of atherosclerosis in chronic periodontal patients [15].

Body Mass Index (BMI) is a reliable indicator of hyperlipidemia[16] 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 only in chronic periodontitis patients than controls. This may be due to the exclusion of obese individuals in our study.

The subjects with periodontitis had higher plasma cholesterol and triglycerides. Endothelial dysfunction, an early step in atherosclerosis has been shown to occur in individuals with periodontitis.[17,18] Periodontitis is believed to cause a low, but long-lasting, systemic inflammatory reaction, which in turn contributes to the development of atherosclerosis.[19]

V. Conclusion

The present study suggests that the TC, TGL and LDL levels significantly correlates with chronic periodontitis and hyperlipidemia. Periodontal disease not only associated with severity of the deterioration of lipid metabolism, but also that the worsening hyperlipidemic state is associated with periodontal inflammation by increasing the serum and GCF pro-inflammatory cytokines. It is necessary to perform longitudinal evaluations in larger populations in order to provide more insight on relationship between periodontitis and hyperlipidemia, and also on future risk of cardiovascular diseases in chronic periodontitis patients.

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