Dyslipidemia In Chronic Periodontitis With And Without Type 2 Diabetes– A Cross Sectional Study.

Running title: Dyslipidemia in chronic periodontitis with and withoutT2DM

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Abstract:

Objective: The present study was conducted to assess the dyslipidemic status in periodontitis with or without type 2 diabetes.

Materials and Methods: This study is designed as hospital based cross sectional study.100 chronic periodontitis participants were included in this study. 50 were systemically healthy and 50 participants were type 2 diabetics. Demographic variables, clinical parameters of periodontal health, glycemic control and serum lipid profile were assessed. Statistical expressions were made using Students T test and Chi square test.

Results: Dyslipidemia is evident in chronic periodontitis with Type2 diabetes and subjects with chronic periodontitis also showed aberrant serum lipid profile.

Conclusion: Dyslipidemia is the key risk factor for cardiovascular diseases .It is apparent that both chronic periodontitis and type2 diabetes predispose individuals to cardiovascular disease by exerting their influence in serum lipid profile.

Key words: Dyslipidemia,HbA1c,Periodontitis,Type2 diabetes.

INTRODUCTION

Periodontitis is a chronic inflammatory disease of multifactorial etiology. Periodontitis is a heterogeneous disease that affects 10 to 15% of the world population[1].Gram negative bacteria such as P.gingivalis and Fusibacterium nucleatum are the major plaque bacteria that are responsible for periodontal pathogenisis[2].The prevalence of periodontitis in India is predicted to be up to 95%[3].

Type2 Diabetes(T2D) accounts to 90%of diabetes in the world.T2D has emerged as major non communicable disease in low and middle income countries especially in both rural and urban areas[4]
South Asians have increased predisposition of insulin resistance and type2 diabetes [5]
In India 41 million are diabetic and one in five diabetic in the world is Indian.[6]Especially India is described as the diabetic capital of the world. Poor glycemic control, with respect of HbA1c% are reported in India [7].
Dyslipidemia is characterized by elevated serum levels of triglycerides, total cholesterol, Very Low density lipoprotein(VLDL) and decreased levels of High Density Lipoprotein (HDL).Dyslipidemia is a major risk for cardio vascular disease(CVD)[8].Smoking,Diabetes and dyslipidemia are identified as known risk factors for CVD. However, the major contributor is inflammatory response which could be associated with periodontal pathogenisis as well as T2D.

The two way relationship between T2D and periodontitis is established in several cross sectional, case control and longitudinal studies[9.10,11,12].T2D increasing the severity of periodontitis and periodontitis influencing glycemic control is well established. Diabetes increases the risk of periodontitis three to four fold than non diabetics[13,14].

Hyperglycemia is also associated with hyperlipidemia. People with T2D have two to four fold increase in developing cardiovascular disease than non diabetics[15].Increased serum levels of LDL,Triglycerides and total cholesterol levels and decreased HDL levels were found in T2D[16]. T2D is a an established risk factor for dyslipidemia and CVD.However it is not only poor metabolic control of glucose that is the key factor for dyslipidemia.Persistent chronic sub clinical inflammation such as periodontitis also play a significant role in dyslipidemia. Association between periodontitis and hyperlipidemia is shown in human studies[17]Periodontitis influencing hyperlipidemia is also reported[18].

The critical factor for arthrogenisis is inflammation[19].Both T2D and periodontitis are chronic inflammatory diseases. Periodontitis is a natural concomitant that adds up to the inflammatory burden already existing in T2D. In addition,T2D mellitus is also associated with increased production of advanced glycation end products which in turn lead to many micro and macrovascular complications[20].

Periodontitis increases the risk of first myocardial infarction and subjects with periodontitis and T2D showing myocardial dysfunction is reported [21].

T2D,Periodontitis and hyperlipidemia share a tripartite relationship[22,23]. Dyslipidemia associated with periodontitis and T2D is the connecting link between the two diseases and cvd.Hyperlipidemia plays a significant role in two way relationship between T2D and periodontitis. It is also important to study the relationship between periodontitis, T2D and hyperlipidemia,as hyerlipidemia interferes with T2D and Periodontitis and increases the risk of both the diseases.

Dyslipidemia and diabetes are co morbid conditions seen in general population. Especially in India, which is declared the diabetic capital of the world. This study evaluated the dyslipidemic status in chronic periodontitis with or without T2D, to understand the risk of aberrant lipid profile in both chronic periodontitis and T2D

MATERIALS AND METHOD

Study Design And Participants

This study is designed as cross sectional study. The study was approved by institutional ethical committee of Sree Balaji Dental College,BIHER,Chennai, India.(No.SBDCECM104/01/15/04) and written consent were obtained from the participating subjects. The study samples were recruited from patients seeking dental care from the Department of Periodontology,SBDCH,BIHER,and Chennai,India. A total of 100 subjects were included in this study and categorized in to two groups.

1. Group I (n=50) – Subjects without T2D and with severe chronic periodontitis (CP)
2. Group II (n=50) -Subjects with type 2 diabetes and chronic periodontitis.(T2D+CP)

Inclusion And Exclusion Criteria

Subjects in the age group between 40 to 60 years were included in the study. The diabetic status was confirmed by measuring Fasting Blood Sugar(FBS),Post prandial blood sugar(PPBS) &HbA1c%.Subjects with FBS ≥100mg%,HbA1c% ≥6%,were considered diabetic. The status of Periodontitis was assessed using Periodontal Probe Depth (PPD) .Subjects with PPD ≥6mm were included in the study. Pregnant women, smokers and subjects on bone remodeling drugs such as bisphosphonates, NSAIDs, antibiotic therapy in the past 3 months or any other periodontal therapy in the past 6 months were excluded from the study. Subjects with other systemic diseases which would have effect on progression of periodontitis were excluded from the study. Information related to medical and dental history was obtained through a questionnaire.

Screening For Periodontitis

All subjects were given a clinical periodontal examination to determine PPD and attachment level for each tooth (CAL), presence of calculus, Bleeding on Probing (BOP), assessment of plaque using the modified Loe and Silness gingival index [24]. PPD and CAL was determined using 1mmWilliams Probe (Pennsylvania, USA)

Biochemical Parameters For Glycemic Control And Lipid Profile

Biochemical measurements for glycemic control such as Fasting, postprandial glucose levels HbA1c and serum lipid profile was assessed using blood sample obtained from subjects. Venous blood samples were collected after an overnight fast.HbA1c was measured using HPLC method,FBS,PPBS,Total cholesterol,VLDL,HDL,TG were measured by enzymatic method. LDL was calculated using Friedewald formula. Dyslipidemia is defined as Serum cholesterol levels≥200mg/dL,Triglycerides≥150mg/dL,LDL≥130mg/dL,HDL≤40mg/dL according to NCEP guidelines[25].

Statistical Analysis

All statistical analysis was performed with the help of SPSS 20.0 (Chicago,IL:USA:IBM corp.). Statistical expressions were determined using Student's T test. Gender relationships between groups were analysed statistically using Chi-square test.P value <0.05 was considered to be significant statistically.

Results

This study included 50 individuals with chronic periodontitis and 50 individuals with chronic periodontitis and type2 diabetes.

Table1 represents the demographic values in the study groups. The mean age was 50.12±5.8 years in CP as compared to 57.31±6.48 years in T2D+CP. The mean age was much higher in CP+T2D and showed a greater statistical significance ($p<0.001$).The CP+T2D group showed longer duration of diabetes with an average of 57.28 months. Gender and income of the subjects did not show any statistical significance among groups.

Table 2 represents the clinical periodontal parameters.CAL was found to be very highly statistically significant in CP ($p<0.001$).Differences in percentage of BOP % was much higher in

CP when compared to T2D+CP (p<0.001).However, PPD was also found to be increased in T2D+CP than CP, with Mean ±SD values of 7.13±1.50.The relationship was found to be very highly significant (p<0.001).

Table 3 represents the biochemical parameters of glycemic control. The mean±SD values of FBS, PPBS were much higher in T2D+CP than CP 93.50±6.458 and showed very high statistical significance. HbA1c levels were found to be significantly elevated (p<0.001) in T2D as compared to CP, indicating poor glycemic control in diabetics.

Table 4 represents serum lipid profile. The mean±SD levels of Total cholesterol, VLDL, LDL were higher in CP than HC.The p value for VLDL were found to be very highly increased and showed statistical significance in T2D+CP (p<0.001).The HDL levels were higher in CP (52±6.2) than T2D+CP (49.05±7.14).However the TC/HDL ratio also showed very high statistical significance between groups.

DISCUSSION

Chronic periodontitis and type2diabetes are most prevalent chronic inflammatory disease across the globe. The extent of dyslipidemia in chronic periodontitis with and without T2D is evaluated in this study.

This study assessed the basic demographic variables such as Age,gender,socio economic status of the study participants.Periodontitis and dyslipidemia are reportedly found in older adults and predominantly males. In this study the mean age of the study participants were above 50 years in CP and 57.3years in T2D+CP. Age is a risk factor for periodonitis,T2D and also dyslipidemia and it is reflected in this study.

The study participants are not gender matched. The number of male participants were higher in both the study groups but there was no statistical significance among gender in the present study. The socioeconomic status and monthly income of the study participants suggest that they were above the poverty line, however there was no significant difference with respect to monthly income.

The glycemic status of the study participants were assessed by evaluating the FBS,PPBS and glycemic control as determined by measuring HbA1c%.The FBS and PPBS levels in CP group were within normal limits .However the gold standard for glycemic control HbA1c levels were found to high indicating pre diabetes like condition in CP. The HbA1c levels in T2D+CP indicated controlled diabetes in the study group. However, the duration of diabetes was found to be much higher with respect to numbers of months suffering from the disease, which could play a profound role in dyslipidemia.

The clinical periodontal parameters such as BOP,CAL and PPD were increased and showed a statistically significant expression in T2D+CP,indicating increased periodontal inflammation and loss of tooth supporting structure in T2D.The BOP,CAL and PPD values in CP were also evident indicating the extent of periodontal tissue destruction.

Kapellas *etal* have reported Periodontal pocketing as a marker of CVD in Australians[26].

Positive relationship between periodontal pocket depth and LDL and cholesterol levels were reported by Katz *etal*[27].

The serum lipid profile in CP as well as T2D+CP is increased than normal. However the dyslipidemic status was much higher in T2D+CP.Dyslipidemia is a characteristic feature of diabetes mellitus [28] .In T2D dyslipidemia is characterized by increased levels of triglycerides and decreased HDL. Triglycerides and VLDL do not take part in arthrogenesis directly. However, they influence the level of LDL and decreases HDL level. [29].

In line with this, our study also shows increased serum levels of triglycerides, LDL and VLDL in T2D.Haffner et al has reported that these lipidemic changes are evident even before clinical onset of hyperglycemia[30].This could be the reason for dyslipidemic status in our study even though the T2D+CP patients are controlled diabetics with mean HbA1c values of 6.5%.

Periodontitis is also associated with cardiovascular diseases[31].The CP group also show increase in serum levels of TG, VLDL and LDL. Earlier studies have proven that aberrant lipid profiles are seen in adverse periodontal conditions. A similar study by us relating the lipid profile

between healthy controls and CP also proved the periodontitis abberates serum lipid profiles [32].
Periodontitis is associated with elevation of biomarkers of dyslipidemia [33] In addition to lack of glycemic control, periodontitis also plays a significant role in elevation of serum lipids. Periodontal conditions of patients with dyslipidemia were found to be severe than normolipidemics. A study by Fentoglu *et al*[34] shown that mild and moderate hyperlipidemia increase severity of periodontitis. However the influence of T2D in periodontal severity is more in this study.
Inflammatory mechanism in periodontitis linking to cardiovascular system is reported by Schenkein and Loos[35].This study also reports how periodontitis is casually linked to CVD. Futhermore,Nepomucena *et al* has reported that dyslipidemia influences systemic inflammatory markers than type 2 diabetes in chronic periodontitis[36]. In periodontitis there is release of inflammatory cytokines such as TNF alpha and IL6.These cytokines increase the release of lipids from adipose tissue and liver[37].This could be the reason behind increased lipid profile in CP.

Individuals with T2D and chronic Periodontitis show significant increase in thickness of medial wall and higher incidence of coronary artery disease when compared with individuals without diabetes or periodontal disease[38].A longitudinal study by Saremi *etal* in pima Indians has predicted increased coronary heart disease associated mortality in chronic periodontitis with type 2 diabetes[39]

Although there are several studies correlating the severity of periodontal parameters with T2D there is paucity of literature regarding dyslipidemic status in periodontitis and T2D,as both increases the risk of CVD.
There are also several studies that contradict the relationship between CP, CVD and serum lipid levels. [40,41].Such studies attribute CVD to other confounding variables such as smoking,socio economic status,life style,stress, physical inactivity etc.Smokers and patients with other systemic complications are excluded from the study which is a key strength of this study.
Future studies, with a larger sample size and with key determinants of cardio vascular health including anthropometric and life style patterns other than serum lipid profile should be done to enable better understanding of dyslipidemia in periodontitis with or without type 2 diabetes.

CONCLUSION

Deranged serum lipid profile is seen in periodontitis and also in diabetes and this aspect should be carefully monitored in periodontitis patients with or without type2 diabetes. Treating dyslipidemia should be considered an important aspect of managing periodontitis and T2D, as in most conditions impaired lipid profile remains undiagnosed. Treating periodontal disease could prove effective in treating dyslipidemia as well as improving glycemic control in type2 diabetes.

Table1: Demographic variables.

Base line characteristics	**CP**		**T2D+CP**		**P value**
Age (years)	50.12±5.83		57.31±6.48		0.001**
Income(Rs/month)	11500±3750		12200±4350		NS
Duration of Diabetes(months)	00		57.28±49		0.000***
Gender (%)	Male	Female	Male	Female	NS
	69	30.8	51	48.3	

	.2		.1		

Values represented as Mean±SD;**- represents p value < 0.001; NS -p value not significant; CP-chronic periodontitis.T2D+CP-Type2diabetes with chronic periodontitis.

Table2: Clinical Periodontal Parameters

Parameter	CP	CP+T2D	p Value
PPD(mm)	5.90±0.71	5.01±1.44***	<0.001
CAL(mm)	5.75±1.04	7.13±1.50***	<0.001
BOP (%)	65.42±8.21	61.01±23.36***	<0.001

Values represented as mean±SD ;***- represents p value < 0.001;CP-chronic periodontitis,T2D+CP-Type2 diabetes +chronic periodontitis.

Table 4.3: Biochemical Parameters of Glycemic control.

Biochemical Parameters	CP	CP+T2D	p Value
FBS(mg/dL)	93.50±6.458	128.76±42.476	0.001***
PP (mg/dL)	115.81±8.154	183.28±64.07	0.001***
HbA1c (%)	5.61±0.27	6.5±0.5	0.001***

Values represented as Mean±SD; ***- represents p value < 0.001; CP-chronic periodontitis. T2D+CP-Type2 diabetes +chronic periodontitis.

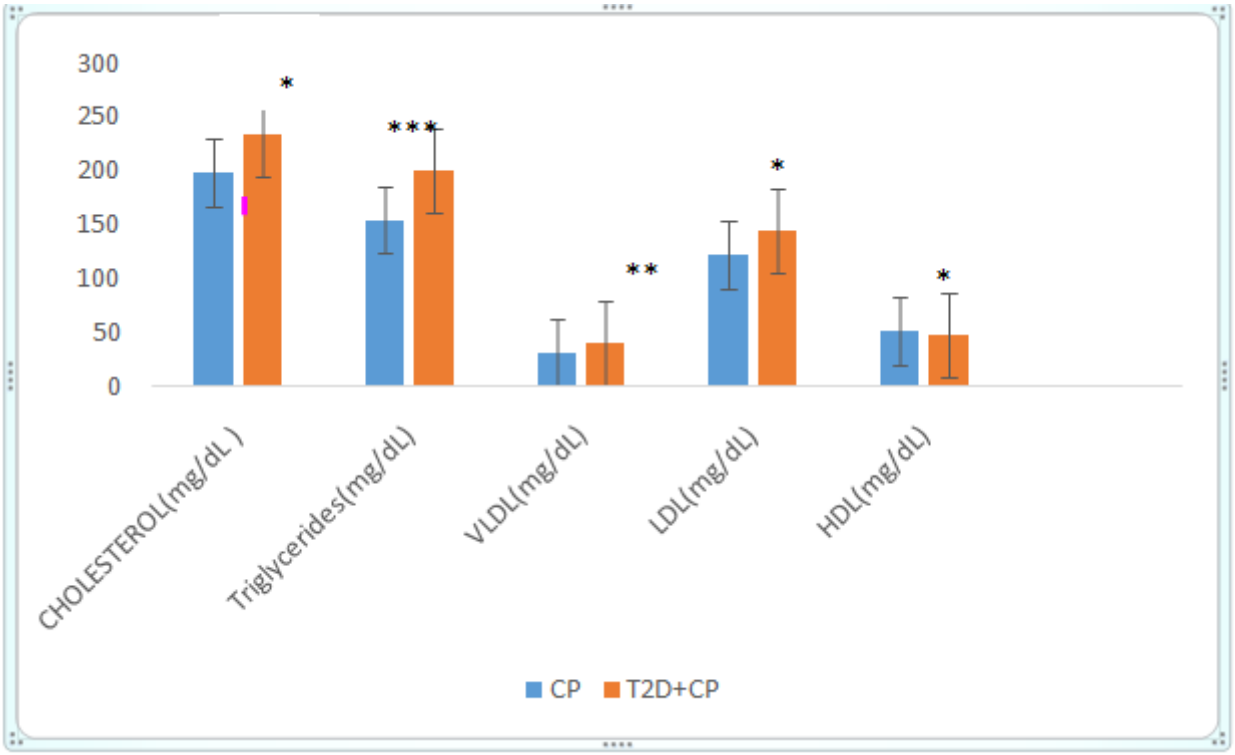
Table 4.4: Serum lipid profile

Lipid profile	CP	CP+T2D	p value
Cholesterol(mg/dL)	198.23±54	233.35±76.4	0.04*
Triglycerides(mg/dL)	155±23	200±70.7	0.001***
VLDL(mg/dL)	31±12.3	40±14.5	0.01**
LDL(mg/dL)	123±20.5	144.3±70	0.04*

HDL(mg/dL)	52±6.2	49.05±7.14	0.02*
Cholesterol/HDL Ratio	3.81±1.2	4.81±1.5	0.001***

Values represented as Mean±SD; ***- represents p value < 0.001;** represents p<0.01;*-p value<0.05; CP-chronic periodontitis. T2D+CP-Type2 diabetes +chronic periodontitis.

Graph



Graph 1:Lipid profile in chronic periodontitis in comparison with chronic periodontitis with type2diabetes;* p value<0.05, ** $P < 0.01$, *** $P < 0.001$.

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