Journal of
Periodontology
&
Implant Dentistry

Research Article

Correlation between Metabolic Control and Periodontal Parameters in Diabetic Patients

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Received: 28 October 2011; Accepted: 6 February 2012
J Periodontol Implant Dent 2012;4(1):19–23 | doi: 10.5681/jpid.2012.005
This article is available from: http://dentistry.tbzmed.ac.ir/jpid

Abstract

Background and aims. Recent reports suggest that some of the risk factors for periodontal disease are similar to those of certain systemic diseases, and that periodontal disease itself may be a risk factor for some systemic diseases. Therefore, the present study investigated the association of markers of metabolic control and systemic inflammation in diabetics with the extent and severity of periodontal disease; in addition, the relative cardiovascular risk was evaluated in such patients.

Materials and methods. A total of 50 known diabetic subjects participated in the study. Periodontal examination included a full-mouth assessment for bleeding on probing using sulcus bleeding index (SBI) and probing depths (PD). Blood analyses were carried out for glycosylated hemoglobin, (HbA1c), C-reactive protein (CRP) and lipid profile.

Results. Periodontal disease severity, in terms of SBI scores and PD, was found to be associated with inadequate glycemic control as measured by HbA1c. Similarly, increased probing depths were associated with increased CRP levels, total cholesterol, low-density lipoproteins, and triglycerides ($P<0.05$).

Conclusion. The results suggest that patients with poorer glycemic control are at increased risk for periodontitis with an associated risk for cardiovascular disease.

Key words: **C-reactive protein, cholesterol, glycosylated hemoglobin, HDL.**

Introduction

The association of periodontal infection with serious systemic conditions represents a "rediscovery" of a relationship that has a rich anecdotal history but has eluded scientific validation. As more is learned about the human body, a definite relationship between the diseases of the oral cavity, especially periodontal infections, and systemic diseases is emerging. In addition, it has been shown that some of the risk factors for periodontal disease are similar to those of certain systemic diseases, and that perio-

dontal disease itself may be a risk factor for some systemic diseases. With ever-increasing evidence during the last decade about the connection between oral and systemic conditions, the dividing line between medicine and dentistry is slowly disappearing. Inflammatory periodontal diseases affect 10−15% of the world's population and are major cause of tooth loss in adults. Epidemiologic studies support association between periodontal inflammation and systemic diseases, including atherogenic vascular disease and Type II diabetes and other conditions in which chronic inflammation underlies pathogenic processes or disease outcomes.[1] The relationship between diabetes mellitus and periodontal disease has been extensively studied. Increased prevalence and severity of periodontitis typically seen in patients with diabetes, especially those with poor metabolic control, led to the designation of periodontitis as the sixth complication of diabetes.[2]

According to Diabetes Atlas published by the International Diabetes Federation (IDF), an estimated 40 million people suffer from diabetes in India (until 2007) and this number is predicted to rise to almost 70 million by 2025 and the countries with the largest number of diabetic people will be India, China and USA by 2030.[3]

In the wake of alarmingly increasing incidence of diabetes among the world population, the present study was undertaken to investigate the impact of common laboratory markers of metabolic control and inflammation in diabetics, which may be associated with the extent and severity of periodontal disease and to evaluate the relative cardiovascular risk in such patients. To monitor metabolic control in diabetics glycosylated hemoglobin (HbA1c) was used and laboratory markers like CRP and lipid levels were used to identify systemic related factors.

Materials and Methods

This cross-sectional study was carried out in the Department of Periodontics, P.M.N.M Dental College & Hospital, Bagalkot, Karnataka, in association with Tulasigirish Diabetic Hospital and Research Centre, Bagalkot. Fifty known diabetic subjects in the 21−65-year age group, referring to the above-mentioned centers, were randomly selected. The inclusion criteria consisted of subjects with Type I or Type II diabetes and those who had not received any periodontal therapy during the preceding six months. Subjects with any known major medical complications, such as coronary heart disease and other systemic diseases like hypertension and respiratory disorders, smokers and subjects with acute infections or traumas, were excluded.

An informed consent was obtained from the subjects before further assessment. Ethical approval was obtained from the Institutional Review Board and Rajiv Gandhi University of Health Sciences, Karnataka, India.

The patients were classified as urban or rural according to the Census of India 1991. The following criteria were adopted for treating a place as urban: All statutory towns, i.e., all places with a municipality, corporation, cantonment board or notified town area committee; all the other places which met the following criteria of a minimum population of 5000, at least 75% of the male working population engaged in non-agricultural pursuits, and a population density of at least 400/km^2. All other areas not identified as urban were classified as rural. Periodontal status assessment for all the subjects was carried out by a full-mouth assessment for bleeding on probing using sulcus bleeding index (SBI) (Muhlemann H.R and Son S. 1971); probing depths (PD) were recorded to their nearest millimeter using a Williams graduated probe.

Two milliliters of fasting venous blood samples were taken from the anticubital fossa of the patients and subjected to further analyses. Quantitative CRP analysis of serum samples were carried out using turbidimetric immunoassay technique by "TURBILYTE-CRP" (Tulip Diagnostics, Goa, India), which had a detection limit of 0.5 mg/dL and a measuring range of 0–22 mg/dL. Nycocard HbA1c, a rapid in vitro test, was used for the measurement of glycated hemoglobin. It has a reference measuring range of 3–18% HbA1c. Serum total cholesterol (TC), triglycerides (TG), low density lipoproteins (LDL) and high density lipoproteins (HDL) were measured using Erbadiagnostic kit (Trans – Asia BioMedicals LTD., Solan, India: in technical collaboration with ERBA Diagnostics Mannheim, Germany)

Results

Among the total subjects 33 were males (mean age of 47.8182 ± 6.8668), and 17 females (mean age of 49.0588 ± 6.8142). Sixteen were under 45 years of age, of which males comprised 62.50% and females 37.50%. The remaining 34 subjects aged above 45 years were 67.65% males and 32.35% females.

Pair-wise comparison of periodontal disease parameters with the location showed statistical signifi-

Table 1. Comparison of urban and rural subjects with respect to periodontal disease (SBI and PD)

Variables	Location	Mean	SD	t-value	p-value
SBI	**Urban**	2.6500	1.0400	-4.1394	0.0001*
	Rural	3.7667	0.8584		
PD	**Urban**	3.8400	0.8375	-4.0907	0.0002*
	Rural	4.8833	0.9124		

*Significant at 5% level of significance (P<0.05)

cance. The mean SBI score and PD were higher among rural subjects compared to the urban group (Table 1). Comparison of gender, age groups and location with respect to mean HbA1c scores showed statistical significance with respect to age groups and location. Subjects ≤45 years exhibited a mean HbA1c value of 0.0733 and those >45 years exhibited a value of 0.0809, showing statistical significance (with a P=0.0064). Urban group had a mean HbA1c value of 0.0736 as compared to 0.0818 among rural group (P=0.0017) (Table 2).

Correlation between SBI scores and PD with HbA1c, total cholesterol, LDL, HDL, triglycerides and CRP scores by Pearson's correlation coefficient method showed a positive correlation, i.e. periodontal disease severity was increased with the values of HbA1c, TC, LDL, TG and CRP (Tables 3 and 4) (P<0.05). A negative correlation was found between CPI, SBI and PD scores and HDL values.

Similarly, multiple regression analysis of SBI scores by HbA1c, TC, LDL, HDL, TG, CRP, sex, age and location as independent variables was found to be statistically significant for HbA1c and location (Table 5). Multiple regression analysis of PD scores by HbA1c, TC, LDL, HDL, TG, CRP, sex, age and location as independent variables was found to be statistically significant for HbA1c and LDL (Table 6)

Discussion

The present study showed that CRP levels increased with an increase in periodontal disease severity, which is consistent with the results of studies carried out by Slade GD et al,[4] Saito et al,[5] D'Auito et al[6] and Loos et al.[7]

Periodontitis is a mixed infection of supporting tissues of the teeth caused by dental plaque which harbors many putative pathogens. Once the disease sets in, the subgingival tissues become inflamed and ulcerated, providing a pathway for bacteria and bacterial products such as lipopolysaccharide (LPS) as well as locally produced pro-inflammatory cytokines to enter the systemic circulation. Subsequently, the systemically dispersed bacteria and LPS, as well as cytokines from periodontal lesion, may stimulate hepatocytes to produce elevated CRP levels.[8] CRP hepatic production is usually elicited by an inflammatory stimulus and mediated through a complex network of cytokines, mainly Interlukin-6 (IL-6) (Ablij and Meinders).[9] Therefore, the current investigation indicates that CRP could be a potential risk factor in periodontal tissue destruction.

In this study poor glycemic control was seen in older patients and among rural subjects. One probable reason for this might be unawareness among rural people and lack of proper treatment facilities at their disposal as compared to people residing in urban areas. Due to scarce literature available further studies should be carried out to establish a definitive relationship between poor glycemic control and rural population.

Table 2. Comparison of gender, age and location with respect to mean HbA1c scores

Variable	Factor	Mean	SD	t-value	p-value
HbA1c	**Male**	0.0778	0.0091	-0.6895	0.4938
	Female	0.0798	0.0102		
HbA1c	**≤45 years**	0.0733	0.0049	-2.8526	0.0064*
	>45 years	0.0809	0.0101		
HbA1c	**Urban**	0.0736	0.0059	-3.3218	0.0017*
	Rural	0.0818	0.0099		

*Significant at 5% level of significance (p<0.05)

Table 3. Correlation between SBI scores and HbA1c, total cholesterol, LDL, HDL, triglycerides and CRP scores by Pearson's correlation coefficient

	Correlation between BOP scores	
Variables	**Correlation coefficient (r-value)**	**t-value**
HbA1c	0.7700	8.3605*
Total cholesterol	0.7272	7.3397*
LDL	0.7094	6.9743*
HDL	-0.5368	-4.4081*
Triglycerides	0.5730	4.8441*
CRP	0.7677	8.3009*

*Significant at 5% level of significance (p<0.05)

Table 4. Correlation between probing depth scores and HbA1c, total cholesterol, LDL, HDL, triglycerides and CRP scores by Pearson's correlation coefficient

	Correlation between probing depth scores	
Variables	**Correlation coefficient (r-value)**	**t-value**
HbA1c	0.8795	12.8044*
Total cholesterol	0.7183	7.1525*
LDL	0.8022	9.3099*
HDL	-0.4849	-3.8416*
Triglycerides	0.6444	5.8390*
CRP	0.8903	13.5447*

*Significant at 5% level of significance ($p<0.05$)

Table 5. Multiple regression model with dependent variable of SBI scores

Independent variables	Regression coefficient	Standard error of coefficient	t-value	p-level
HbA1c	100.5180	43.1455	2.3297	0.0250*
Total cholesterol	0.0087	0.0050	1.7354	0.0904
LDL	0.0014	0.0055	0.2504	0.8036
HDL	-0.0058	0.0097	-0.5951	0.5551
Triglycerides	-0.0058	0.0036	-1.5892	0.1199
CRP	-0.2458	0.2732	-0.8994	0.3738
Sex	0.1598	0.1995	0.8014	0.4276
Age	-0.0075	0.2366	-0.0315	0.9750
Location	0.4139	0.1927	2.1479	0.0415*

*Significant at 5% level of significance ($p<0.05$)

Poor glycemic control was associated with increases in SBI and PD scores. These findings concurred with previously reported studies by Bridges et al and Taylor et al. This could be explained by the hyperglycemic state resulting in accumulation of glycated end products, which then initiate a cascade of inflammatory reactions leading to release of mediators like IL-1, IL-6, tumor necrosis factor-α (TNF-α) and CRPs, thereby enhancing the periodontal breakdown process (Iacopino,[10] Bretz et al,[11] Takeda et al[12]). TNF-α is known to induce insulin resistance, thus suggesting a possible mutual relationship between periodontal disease and diabetes. Therefore, achieving good glycemic control appears to be a realistic approach to improve systemic health as well as periodontal health in diabetics.

The mean total cholesterol, LDL and TG values showed positive correlation with respect to location, i.e., rural subjects showed much higher values. This could be attributed to unhealthy dietary patterns among rural people with insufficient micronutrients and excessive sugar and fat content in their normal diet.

A positive correlation between periodontal infection and unfavorable lipid composition was observed in the present investigation, consistent with the results of studies carried out by Cutler et al,[13] Katz et al,[14],Morita et al,[15]and Nibali et al.[16]

Subjects with poor glyemic control were found to have higher LDL and triglyceride levels than those with better control. The association of elevated cholesterol level with periodontal inflammation could be explained by the local production of cytokines and endotoxins from bacteria leading to changes in lipid metabolism (increased LDL, reduced HDL). Of special interest is the report which found a significant

Table 6. Multiple regression model with dependent variable probing depth (PD) scores

Independent variables	Regression coefficient	Standard error of coefficient	t-value	p-level
HbA1c	53.2458	23.1768	2.2974	0.0461*
Total cholesterol	-0.0017	0.0033	-0.5364	0.5946
LDL	0.0073	0.0036	2.0161	0.0500*
HDL	-0.0027	0.0063	-0.4226	0.6749
Triglycerides	-0.0031	0.0024	-1.3259	0.1924
CRP	0.2782	0.1784	1.5588	0.1269
Sex	0.0967	0.1303	0.7427	0.4620
Age	0.0944	0.1545	0.6111	0.5446
Location	0.1917	0.1389	1.3799	0.1753

*Significant at 5% level of significance ($p<0.05$)

relationship between periodontitis, hyperlipidemia, and serum antibodies against *P. gingivalis* lipopolysaccharide. This study indicated that elevated triglyceride levels are able to modulate IL-1β production by polymorphonuclear leukocytes stimulated by *P. gingivalis*.[13] A possible explanation for changes in lipid profile is the clearance of cytokines from the blood by HDL particles resulting in atherogenic ratio of HDL to total cholesterol.[17] Total cholesterol, CRP and fibrinogen have been identified as possible intermediate factors that may link periodontal disease to elevated cardiovascular risk.[18]

This investigation demonstrated a significant relationship between glycemic control and periodontal health. There is also an indication that CRP is associated with periodontal disease progression in terms of increased probing depths. Elevated CRP levels and dyslipidemia can possibly contribute, at least in part, to the increased risk for cardiovascular disease among the study subjects.

The effects of periodontal infections on the oral cavity are well known; however, periodontal disease is associated with systemic effects in the body, such as cardiovascular disease. The evidence of a periodontal/systemic risk warrants serious considerations. As we increase our knowledge between periodontal disease and other systemic diseases, we will be able to prevent periodontal disease in more patients as well as develop better treatments for the disease. It is important for physicians and dentists to improve their collaboration to provide better patient care. Physician's awareness of the increased risk for dental complications in certain patients will benefit their patients' overall well-being.

Therefore, periodontal disease assessment and its treatment should be instituted in current health programs to improve overall health status of an individual. The findings of this study highlight a need to promote oral health in patients with diabetes as an integral component of total patient care. In the light of findings of the present study, a special emphasis should be placed on educating and providing timely treatment for the rural people suffering from diabetes as they are at an increased risk for CVD and other associated complications. However, more controlled interventional studies are required to investigate possible causal relationships between metabolic control and periodontal health.

Acknowledgments

The authors would like to acknowledge the kind support given by Dr. Rajendra B Naik, Diabetologist, Tulasigirish Diabetes Hospital and Research Foundation, Bagalkot, Karnataka, India.

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