Periodontitis presage pre-diabetes – A comparative study of glycemic control in non-diabetic population with and without periodontal disease

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ABSTRACT

Introduction and Aim: The understanding of the etiology and pathogenesis of periodontal diseases and their chronic, inflammatory and infectious nature suggests that these infections may influence events elsewhere in the body. Poorly controlled diabetes is a well-recognized risk factor for developing periodontal disease. There is also ample evidence that periodontal disease can worsen a patient's glycemic control and proper management of periodontal disease can improve the same. However, very few have determined effect of periodontitis on glycemic control, of non-diabetic population and concluded that untreated periodontitis pose a risk of pre -diabetes in systemically healthy individuals. The purpose of this study is to estimate and compare the HbA1c levels in non-diabetic subjects with periodontitis and periodontally healthy controls.

Materials and Methods: A total of 639 non-diabetic subjects were selected for the study and were divided into 2 groups based on the periodontal status: Group A (n = 324) Periodontally Healthy controls months and Group B (n = 315) subjects with Chronic periodontitis. Clinical parameters like Plaque index (PI), Modified sulcular bleeding index (mSBI), Probing depth (PD), and Clinical attachment level (CAL) were measured. Glycemic control was measured by assessing HbA1c.

Results: The mean PI for Group A was 0.99 ± 0.38 and Group B was 1.9 ± 0.59. mSBI score for the test group was 2.9 ± 0.87 and it was 1.79 ± 0.57 in the control group. The mean PD in the Group A was 2.73 ± 0.9 and in Group B was 7.16 ± 0.93. The mean CAL for Group A was 2.24 ± 0.65 and in Group B was 5.86 ± 0.75. The values for all the clinical parameters were statistically significant. The mean HbA1c% for control group was 2.94 ± 0.29 and for the test group was 5.95 ± 0.36. This value was statistically significant between the two groups.

Conclusion: In a non-diabetic systemically healthy population, the glycated hemoglobin level of the subjects with severe periodontitis is significantly greater than the subjects without periodontitis. Non- diabetic subjects with severe periodontal disease presented a pre-diabetic state reflecting that periodontal disease has created a state of insulin resistance.

Keywords: Diabetes mellitus; HbA1c levels; glycemic control; periodontitis; pre-diabetes.

INTRODUCTION

Diabetes mellitus and periodontitis are chronic diseases that affect a large number of populations worldwide. Periodontitis is a chronic inflammatory response to the subgingival bacteria, producing irreversible periodontal tissue destruction and tooth loss. Diabetes mellitus is a group of metabolic disorders characterized by chronic hyperglycemia with disturbances of carbohydrates, fat and protein metabolism resulting from the defects in insulin secretion, insulin action or both (1).

Years of research have established a number of mechanisms by which diabetes can influence the periodontium (2, 3). In case of diabetic patients, concentrations of oral microflora are increased due to high concentrations of glucose in saliva and gingival crevicular fluid. Diabetic patients have higher than normal levels of perio-pathogenic bacteria. Diabetic state also results in a state of exaggerated immune response to these bacteria, resulting in more rapid and severe periodontal destruction (4). There is also abundant evidence that periodontal disease can worsen a patient's control of diabetes mellitus and that proper management of periodontal disease can improve control of diabetes mellitus (5, 6).

Several studies revealed that the degree of glycemic control is an important variable in relationship between

diabetes and periodontitis. Studies have reported that individuals with type 1 diabetes manifested advanced periodontal diseases with a higher prevalence and severity of gingival inflammation and periodontal destruction being seen in those with a higher glycemic index (7,8). Significantly, more periodontal attachment and alveolar bone was lost in type 1 diabetic patients who had poor glycemic control than those who were well controlled or non-diabetic patients (9).

Recent research is directed towards the effect on untreated severe periodontitis on the glycemic control of non-diabetic population. It has been noted in a pilot study that non-didactic population with severe periodontitis exhibited increased levels of glycemic index than normal controls (10). Another study found chronic periodontitis to be associated with a significant increase in glycosylated hemoglobin levels in non-diabetic periodontitis subjects. Furthermore, with improvement of periodontal status by treatment, the glycemic levels return to near normal values (11). On the contrary, another study compared the glycohemoglobin levels with severity of periodontitis in non-diabetic population and concluded that there was no significant difference in fasting plasma glucose and postprandial plasma glucose in non-diabetic periodontitis (12). In lieu with the above, the purpose of this study is to estimate and compare the HbA1c levels in non- diabetic subjects with periodontitis and periodontally healthy controls.

MATERIALS AND METHODS

The study subjects were selected from the patient pool of Department of Periodontology, Meenakshi Ammal Dental College and Hospital, Chennai and the "Meenakshi institutional review board" approved. the study. The participants were recruited for the study according the following inclusion and exclusion criteria: Patients within the age group of 35 to 65 years, who are non-diabetic and who had ≥ 15 remaining natural teeth were included in the study. Subjects with history of antibiotic usage in the previous 6 months, Patients with conditions that shorten erythrocyte survival (hemolytic anemia, pregnancy or recent significant blood loss), Smokers, Patients who had undergone periodontal therapy within the previous 6 months and pregnant and feeding mothers were excluded.

Study design

Out of all the patients who reported to the outpatient department, a total of 639 non diabetic subjects were selected for the study and were divided into 2 groups based on the periodontal status: Group A (n = 324), Healthy controls with no probing depth (PD) greater than 4 mm, bleeding on probing (BOP) at ≤ 15% of tooth sides and no periodontal treatment (scaling and root planing or surgery) within the previous six months; Group B (n = 315), Chronic periodontitis cases were defined as those having 5 or more teeth with PD ≥ 5mm and clinical attachment loss (CAL) >3mm or radiographic bone loss.

All the clinical periodontal parameters were measured by a trained periodontist. The following periodontal parameters were measured: Plaque index (PI), Modified sulcular bleeding index (mSBI), Probing depth (PD), and Clinical attachment level (CAL). Glycemic control was measured by assessing HbA1c using commercially available kit (Quantia HbA1c – Tulip laboratories, India. The kit works under the immunoturbidometric principle). Reference ranges: Non-diabetic – 4.0% - 5.6 %; Pre-diabetic – 5.7% - 6.4% and Diabetic - > 6.4% (13).

Statistical analysis

Mean and standard deviation were estimated for all the clinical parameters and the Hba1c values. Mean changes were compared against the null hypothesis. Student's independent t test was used to compare the two mean values in the control and the test group.

RESULTS

On comparing the clinical parameters between the two groups, all the periodontal parameters were increases for the test group than the control group. The mean PI for Group A was 0.99 ± 0.38 and Group B was 1.9 ± 0.59. mSBI score for the test group was 2.9 ± 0.87 and it was 1.79 ± 0.57 in the control group. The mean PD in the Group A was 2.73 ± 0.9 and in Group B was 7.16 ± 0.93. The mean CAL for Group A was 2.24 ± 0.65 and in Group B was 5.86 ± 0.75. All the parameters were statistically significant between the two groups. The mean HbA1cpercentage for control group was 2.94 ± 0.29 and for the test group was 5.95 ± 0.36. When both the groups were compared a statistically significant difference in the glycosylated hemoglobin levels was noted ($p < 0.001$). The case group showed higher HbA1c levels than control group.

Table 1: Comparison of periodontal and glycemic parameters between two groups

	Group		t test value	p value
Plaque index	A	0.99 ± 0.38	7.79	< 0.001
	B	1.9 ± 0.59		

mSBI	A	2.9 ± 0.87	9.12	< 0.001
	B	1.79 ± 0.57		
PPD	A	2.73 ± 0.9	18.91	< 0.001
	B	7.16 ± 0.93		
CAL	A	2.24 ± 0.65	9.72	< 0.001
	B	5.86 ± 0.75.		
HbA1c%	A	2.94 ± 0.29	7.38	< 0.001
	B	5.95 ± 0.36.		

Level of significance set at < 0.05. Plaque index (PI); Modified sulcular bleeding index (mSBI); Probing depth (PD); and Clinical attachment level (CAL)

DISCUSSION

The understanding of the etiology and pathogenesis of periodontal diseases and their chronic, inflammatory and infectious nature suggests that these infections may influence events elsewhere in the body (14). Poorly controlled diabetes is a well-recognized risk factor for developing periodontal disease. There is also ample evidence that periodontal disease can worsen a patient's glycemic control and proper management of periodontal disease can improve the same (15). However, very few have determined effect of periodontitis on glycemic control, of non-diabetic population and concluded that untreated periodontitis pose a risk of pre-diabetes in systemically healthy individuals (11, 12).

The present study assessed the glycemic control of systemically healthy, non-diabetic subjects with and without periodontitis. Non-diabetic subjects without periodontal disease was enrolled into Group B and subjects with severe periodontitis were enrolled into Group B. Glycemic status of the subjects were assessed using HbA1c as the biochemical parameter. HbA1c was chosen as it provides evidence about an individual's average blood glucose levels during the previous two to three months, which is the predicted half-life of red blood cells. The same is the recommended standard of care for testing and monitoring diabetes, specifically the type 2 diabetes (16).

The results of this study reveal that in non-diabetic systemically healthy subjects, the glycated hemoglobin level of the subjects with severe periodontitis is significantly greater than the subjects without periodontitis. (5.95 ± 0.36 Vs. 2.94 ± 0.29). Similarly, Wolffe *et al.,* reported that adjusted HbA1c values were statistically higher in periodontitis cases than in healthy controls (10). Murrah *et al.,* compared blood glucose levels between subjects with, without advanced periodontal, and reported significant higher glucose levels in subjects with advanced periodontal disease (17). Jananni *et al.,* had compared the HbA1c levels in subjects with and without periodontitis and found higher levels of glycated hemoglobin in healthy subjects with periodontitis (11). Galhauth *et al.,* compared the glycated hemoglobin levels with severity of periodontitis and reported that glycated hemoglobin levels were not significantly different with severity of the periodontal disease (12).

The mechanism how periodontitis affects glycemic control is largely studied. Periodontitis is primarily a Gram-negative bacterial infection that initiates a cascade of host inflammatory response. The systemic infection by increasing tissue resistance to insulin, prevents glucose entry into the target cells thereby in turn increasing the blood glucose levels. This triggers pancreas to secrete more insulin as an attempt to maintain normoglycemia. In diabetic subjects, who are already resistant to insulin, further tissue resistance to insulin induced by periodontal pathogens significantly exacerbates the blood glucose levels (18).

Our study also found that non-diabetic subjects with severe periodontal disease presented a pre diabetic state reflecting that periodontal disease has created a state of insulin resistance in such cases. Insulin resistance is now considered as a chronic and low-level inflammatory condition. Insulin functions by binding to the hetero tetrameric membrane receptor leading to IRS-1 phosphorylation and IRS-1-associated phosphatidylinositol 3 phosphate kinase (PI3 kinase) activation (19). This event in turn affects effectors like Akt/protein kinase B (PKB), which triggers the glucose transporter GLUT4. GLUT4 is further translocate into the membrane and induces glucose import into the cell (20). But chronic inflammation like periodontitis leads to increased expression of pro inflammatory mediators like TNF alpha that in turn results in serine phosphorylation of IRS 1. This in turn inactivates PI3 kinase and results in insulin resistance (21).

Many studies have studied the effect of periodontal therapy in controlling the glucose levels on diabetic patients and found that periodontal therapy has beneficial effect on glycemic control (22, 23). The magnitude of reported HbA1C reductions ranges from 0.27% to 0.48% at 3-4 months following periodontal therapy (24). It has also been found that non-surgical periodontal therapy reduced slight elevation in HbA1c

levels in non-diabetic population back to normal levels (12). This reflects the importance of periodontal therapy on the maintenance of glycemic control both in diabetic as well as non-diabetic group.

Within the limitation of the study, a significant relationship between periodontal disease and glycemic control of non-diabetic population is well evident. The study did not attempt to establish any dose dependent relationship between the periodontal disease extent and the glycemic levels.

CONCLUSION

The study results reveal that HbA1c levels in non-diabetic subjects with severe periodontitis was significantly greater than non-diabetic subjects without periodontitis. Moreover, the subjects with periodontitis seem to exhibit a pre diabetic state as result of insulin resistance induced by periodontal inflammation. Though this study did not attempt to establish a causal relationship between the two disease entities, a strong association between periodontal disease and pre-diabetes is observed.

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