Original Article

Detection of HbA1c Level in Type-2 Diabetes Mellitus Patients with Chronic Generalized Periodontitis

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Abstract

Introduction: Diabetes mellitus has been suggested as a risk factor for periodontal disease and periodontal disease is supposed to increase the severity of diabetes mellitus and complicated metabolic control. Thus, it is proposed to be a dual pathway. Research has been conducted on the relationship between diabetes and periodontal disease, since the 1960s; these studies reported that there was at least 2-fold increase in the risk of periodontal disease in diabetics, when compared with healthy controls. **Aim:** The aim of the study was to compare the response to non-surgical periodontal therapy in patients with Type-2 diabetes mellitus from clinical and metabolic stand point. **Materials and Methods:** A comparative clinical study was performed between Type 2 diabetic patients with chronic generalized periodontitis. The study period was 6 months. Conventional periodontal scaling and root planning were performed, and the response to this treatment was compared at baseline, 3 and 6 months, measuring the plaque index, gingival index, and community periodontal index. In diabetic patients, the clinical response was related to measurements of HbA1c in blood at baseline, 3 and 6 months. **Results:** Improvement in all clinical variables was observed. The improvement observed in blood HbA1c levels in diabetic patients confirmed a positive metabolic response to non-surgical periodontal treatment. **Conclusion:** With this study, we conclude that there is a definite reduction in HbA1c level in diabetic patients after conventional non-surgical periodontal treatment.

Keywords: HBA1c, type 2 diabetes mellites, chronic generalized periodontitis

Introduction

Periodontal disease is the periodontal inflammatory process in which the primary etiologic factor may be microbiologic, systemic, or physical injury. It is a condition that affects and destroys the attachment apparatus.[1] Periodontal disease is best considered as the outcome of an ongoing host-parasite interaction between pathogenic microorganisms that have colonized the periodontal pocket and host tissues that resist such bacteria or their products.[2] Many systemic disease and disorders have been impacted as risk indicator or risk factor in periodontal disease. One such example is diabetes mellitus.[3]

Diabetes mellitus is complex and globally evolving chronic health problem faced by the world today. The Indian task force on diabetes care have reported a crude prevalence rate of 9% in urban and 3% in rural population. The studies reported at least 2-fold increase in the risk of periodontal disease in diabetic when compared with healthy controls.[4-6] The systemic manifestation of diabetes includes artherosclerosis, microangiopathy, oculoretinopathy, and artherosclerotic heart disease. However, recently periodontal disease declared as the "sixth" complication of diabetes mellitus. The periodontal manifestations of maternal diabetes are: Frequently multiple abscess formation, gingival edema, sessile or pedunculated gingival polyps, loosened teeth etc. The extensive studies point to the fact that there is no consistent pattern of periodontal disease in diabetics. This led to the different researchers to find out the correlation between the oral features and diabetes mellitus.[7]

The association between diabetes mellitus and oral health has been the subject of study for both the medical and dental streams. A plethora of research reports have produced

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conflicting results. Most of them have observed an existence of two-way relationship between diabetes mellitus and periodontal disease. Diabetes mellitus has been suggested as a risk factor for periodontal disease and periodontal disease is supposed to increase the severity of diabetes mellitus and complicate metabolic control. Thus, it is proposed to be a dual pathway.[7]

Aims and objectives

The objectives of the study are as follows:

- To compare clinical changes (by Plaque index [PI], Gingival index, Community periodontal index) in response to conventional periodontal treatment – scaling and root planning, of Type 2 diabetic population with moderate chronic generalized periodontitis at baseline, 3, and 6 months
- With control of periodontal infection, to evaluate metabolic control of diabetes by means of improvement in blood HbA1c level in Type 2 diabetic population at baseline, 3, and 6 months.

Inclusion criteria

The following criteria were included in the study:

1. Patient age between 30 and 60 years,
2. Presence of Type 2 diabetes, criteria for diagnosis of diabetes mellitus would be – symptoms of diabetes and HbA1c ≥6.0%
3. Clinical diagnosis of moderate generalized chronic periodontitis (CP) defined by loss of clinical attachment of 3–4 mm in >30% sites
4. Presence of ≥20 teeth excluding III molar
5. No history of previous periodontal treatment for the past 6 months
6. No modification in diabetic medication for 2 months, before or during the study.

Exclusion criteria

The following criteria were excluded from the study:

1. Presence of systemic disease that could influence the course of periodontal disease or hemoglobin levels in blood
2. Consumption of NSAID's and antibiotics for 6 months before the study
3. Tobacco use in any form
4. Pregnancy or intent to conceive during the 6 months of the study.

Materials and Methods

Based on inclusion and exclusion criteria, participants were selected and written informed consent was obtained for the study

Clinical assessment

PI (Silness and Loe, 1967)

Amount of plaque was assessed using PI given by Silness and Loe. The surfaces examined were the four gingival areas of tooth – the distofacial, mesiofacial, facial, and lingual. The plaque on the cervical third of the tooth was evaluated with no attention to the plaque that has extended to the middle or incisal thirds.

Each of the four gingival areas of the tooth was given a score from 0 to 3; this was recorded as the PI for the area. The scores from the four surfaces were added and divided by four to give the PI for that tooth. All the teeth were scored and divided by the total number of teeth to estimate the PI of an individual.

Gingival index (Loe and Silness, 1963)

Gingival status was assessed using the gingival index given by Loe and Silness in 1963. Gingival inflammation was determined with the help of Gingival index given by Loe and Silness (1963). The tissue surrounding each tooth was divided into four gingival scoring units, distofacial papilla, mesiofacial papilla, facial margin, and lingual margin.

Community periodontal index

A specially designed light weight CPI probe with a 0.5 mm ball tip is used, with a black band between 3.5 and 5.5 mm and ring at 8.5 and 11.5 mm from ball tip is used. The mouth is divided into 6 sextants similar to CPITN. A sextant is examined only if there are two or more teeth present which are not indicated for extraction based on the scoring criteria specified. Scores were given from 0 to 4, X if sextent was excluded and 9 if the scores were not recorded.

Blood investigations

Estimation of HbA1c

Venous blood samples were collected and assessed for HbA1c, at baseline, 3, and 6 months of completion of non-surgical periodontal therapy treatment. Estimation of HbA1c was done by turbidimetric inhibition immunoassay (TINIA) method by Cobas auto analyzer. Blood investigations were done in Biochemistry Laboratory of Sawai Man Singh Hospital, Jaipur.

Treatment regimen

Conventional non-surgical periodontal treatment (scaling and root planning) under local anesthesia (if necessary) was performed in four sessions. Maximum time interval between each session was 1 week.

Follow-up examination was done at 3 and 6 months including all elements of initial examination and determination of HbA1c levels.

Results

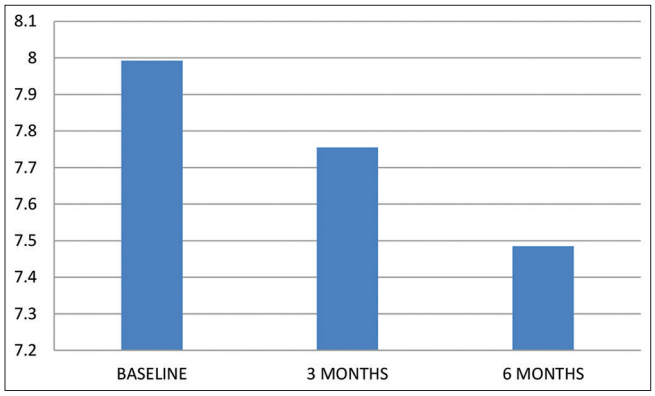
A total of 40 subjects in the age range of 30–60 years who had Type 2 diabetes mellitus with chronic generalized periodontitis who were eligible and willing to participate were included in the study. Glycated hemoglobin levels, PI, gingival index, and community periodontal index were measured and evaluated at baseline, 3 months, and 6 months.

Paired *t*-test to compare before and after values of HbA1c (Table 1, Graph 1)

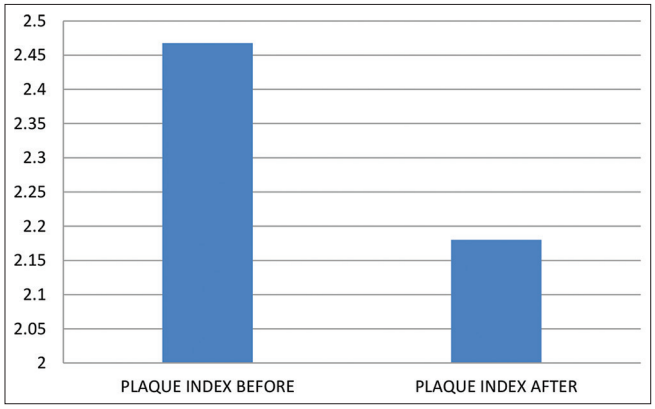
Table 1 depicts glycated hemoglobin levels at baseline to 3 months, baseline to 6 months, and 3–6 months after non-

Table 1: Metabolic parameters

Pair of comparision	Mean	*n*	Std. Deviation	Paired Differences		*t*	df	*P* value
				Mean difference	Std. deviation			
Pair 1								
Baseline	7.9925	40	0.187271	0.2375	0.086787	17.308	39	<0.001
3 months	7.755	40	0.193417					
Pair 2								
Baseline	7.9925	40	0.187271	0.5075	0.128876	24.905	39	<0.001
6 months	7.485	40	0.202					
Pair 3								
3 months	7.755	40	0.193417	0.27	0.093918	18.182	39	<0.001
6 months	7.485	40	0.202					



Graph 1: Shows comparision of baseline to 3 months and 6 months



Graph 2: Shows plaque index before and after treatment (NSPT)

surgical periodontal therapy using paired "T" test (Table 1, Graph 1).

In Table 1, when baseline HbA1c was compared to 3 months, the results were statistically significant with $P < 0.001$ using paired *t*-test. When baseline HbA1c levels were compared with 6 months of HbA1c levels show statistically significant $P < 0.001$. When the 3 months of glycated hemoglobin levels were compared with 6 months HbA1c levels, the results were statistically significant with $P < 0.001$.

Graph 1 depicts mean HbA1c values at baseline = 7.99, at 3 months = 7.75, and at 6 months = 7.49 with a standard deviation of 0.18–0.19 which shows a reduction in HbA1c levels with time period.

Paired *t*-test to compare before and after values of pi, gingival index, and community periodontal index (Table 2, Graphs 2-4)

- When the PI was compared before and after non-surgical periodontal therapy, the results were statistically significant with $P < 0.001$
- When the gingival index was compared before and after non-surgical periodontal therapy, the results were statistically significant with $P < 0.001$
- When the before and after community periodontal indices were compared, we got a statistically significant results with $P < 0.001$.

Graph 2 depicts PI levels before and after non-surgical periodontal therapy with a mean value of 2.46 before non-surgical periodontal therapy and 2.1 after non-surgical periodontal therapy with a standard deviation of 0.14.

Graph 3 depicts the value of gingival index before and after non-surgical periodontal therapy with a mean value of 2.5 before and 2.2 after the non-surgical treatment with a standard deviation of 0.16.

Graph 4 depicts the values of community periodontal index after non-surgical periodontal therapy with a mean value of before non-surgical therapy as 2.0 and after the therapy as 1.3 with a standard deviation of 0.46.

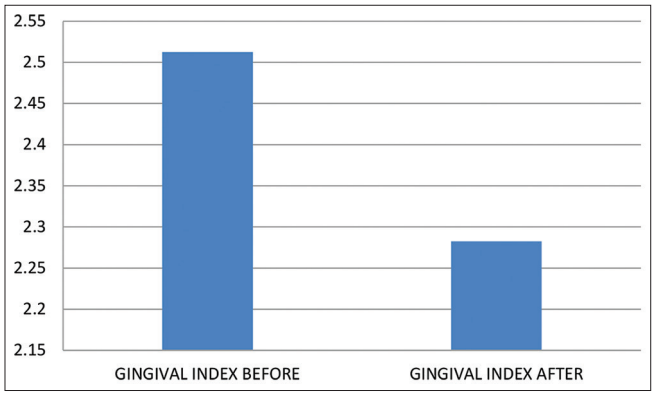
Comparison between HbA1c, PI, GI, and CPI in patients with chronic generalized periodontitis (Table 3, Graphs 5 and 6)

Table 3 depicts the HbA1c levels, GI, PI, and CPI levels in patients with chronic generalized periodontitis.

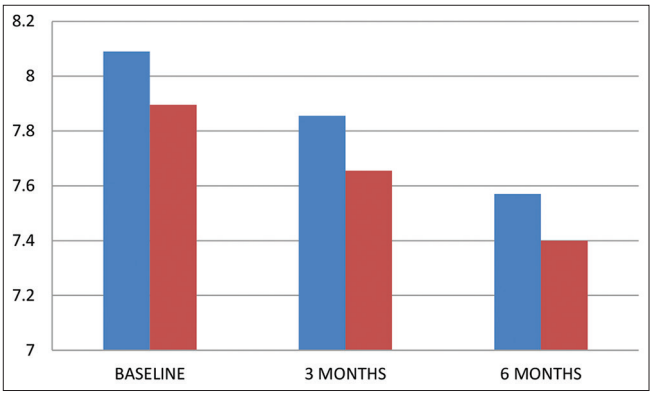
- There was a statistically significant difference in relation to glycated hemoglobin in chronic generalized periodontitis patients at baseline $P < 0.001$, at 3 months $P = 0.001$, and at 6 months also $P = 0.006$
- There was a statistical difference in before and after scores of PI, gingival index in patients with Type 2 diabetes in chronic generalized periodontitis patients with $P < 0.05$. Community periodontal index was not significant after non-surgical periodontal therapy.

Table 2: Clinical parameters

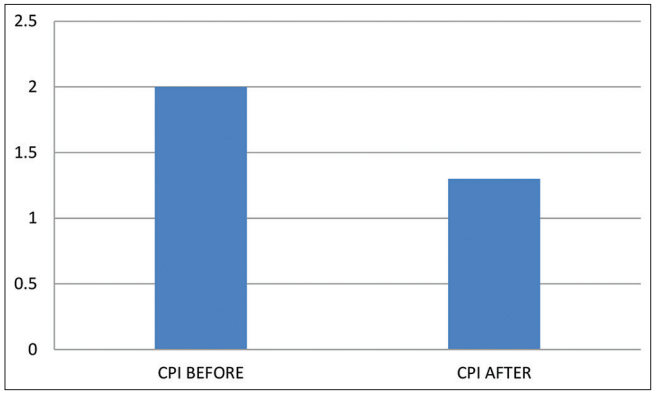
Parameters	Mean	*n*	Std. Deviation	Paired differences		*t*	df	*P*-value
				Mean difference	Std. deviation			
Pair 1								
Plaque index before	2.4675	40	0.220009	0.2875	0.14882	12.218	39	<0.001
Plaque index after	2.18	40	0.162038					
Pair 2								
Gingival index before	2.5125	40	0.165153	0.23	0.166718	8.725	39	<0.001
Gingival index after	2.2825	40	0.206171					
Pair 3								
CPI before	2	40	0	0.7	0.464	9.539	39	<0.001
CPI after	1.3	40	0.464					



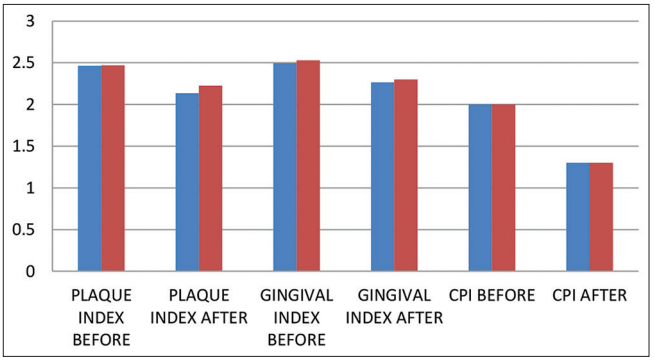
Graph 3: Shows gingival index before and after NSPT



Graph 5: Comparision of baseline, 3 months and 6 months after NSPT



Graph 4: Shows CPI score before and after NSPT



Graph 6: Comparision of indices before and after NSPT

Discussion

Periodontitis is a complex multifactorial disease. Similarly, diabetes mellitus is a complex metabolic syndrome. It is the complexity of both of these processes which has contributed to the controversies and their probable interrelationship in the literature.[8] It is generally perceived that subjects with diabetes mellitus are at a great risk of having periodontitis. In addition, periodontitis has also been found to modify the effect of diabetes mellitus.[9]

In individuals with Type-2 diabetes, who already have insulin resistance, further tissue resistance to insulin induced by infection like periodontitis may considerably exacerbate poor glycemic control. Periodontal treatment designed to decrease the inflammation might restore insulin sensitivity overtime, resulting in improved metabolic control.

The present study was a prospective, comparative, longitudinal, and clinical study, in which 40 subjects with Type 2 diabetes mellitus and chronic generalized periodontitis were selected from the out-patient department of periodontics NIMS Dental college Jaipur. Very strict inclusion and exclusion criteria were applied to minimize confounding factors. The clinical periodontal examination was performed by the same examiner to eliminate interexaminer variability. The calibration of the examiner was done to minimize intraexaminer variability.

Table 3: Indices before after treatment

Parameters	Disease	*n*	Mean	Std. deviation	*t*	Df	*P*-value
Baseline	CGP	40	8.09	0.180351	3.825	38	<0.001
	CGP	40	7.895	0.139454			
3 months	CGP	40	7.855	0.190498	3.789	38	0.001
	CGP	40	7.655	0.139454			
6 months	CGP	40	7.57	0.1949	2.904	38	0.006
	CGP	40	7.4	0.1747			
Plaque index before	CGP	40	2.465	0.253969	−0.071	38	0.944
	CGP	40	2.47	0.18666			
Plaque index after	CGP	40	2.135	0.138697	−1.807	38	0.049
	CGP	40	2.225	0.174341			
Gingival index before	CGP	40	2.495	0.143178	−0.665	38	0.51
	CGP	40	2.53	0.18666			
Gingival index after	CGP	40	2.265	0.2059	−0.532	38	0.048
	CGP	40	2.3	0.210263			
CPI after	CGP	40	1.3	0.47	0	38	1
	CGP	40	1.3	0.47			

The aim of present study was to evaluate the HbA1c level at baseline, 3 months, and 6 months after non-surgical periodontal therapy and also to compare the clinical variables (PI, gingival index and community periodontal index). Primary method used to diagnose diabetes mellitus and monitor blood glucose level was HbA1c assay which does not require fasting, does not rely on patient compliance, and gives indication of blood glucose level over an extended period of the previous 3–4 months.

The metabolic assessment was based on the blood HbA1c levels. Blood glucose measurements show the level of glucose in blood at a given point of time. In contrast, HbA1c measurements predict the level of glucose in blood over a period of time (30–90 days). The glycosylated hemoglobin assay is a relatively new test used in the diagnosis and monitoring of the diabetic patient.[10] Numerous proteins in the body are capable of being glycated. Glycated hemoglobin is formed continuously in erythrocytes as a product of the non-enzymatic reaction between the hemoglobin proteins which carrr oxygen molecules and glucose. Binding of glucose to hemoglobin is highly stable thus hemoglobin remains glycated for the life-span of erythrocyte approximately 123 ± 23 days.[11]

One of the hemoglobin fractions resulting from the glycosylation reaction is hemoglobin A1c. It is this fraction which is elevated in the diabetic and which is measured by the assay.[12] There are principally three methods of HbA1c examination. They are flow cytometry, high performance liquid chromatography (HPLC), and TINIA. The method used in this study was TINIA by COBAS® auto analyzer. This method used Tetradecyltrimethylammonium bromide as the detergent in the hemolyzing reagent to eliminate interference from leukocytes (TTAB does not lyse leukocytes). All hemoglobin variants which were glycated at the β-chain N-terminus and which had antibody-recognizable regions identical to that of HbA1c are determined by this assay. This method is easily accessible and widely applied in routine practice of medicine.[13]

Gurdol (2014)[14] analyzed and evaluated the performances of the Sebia capillary electrophoresis (CE), Roche TINIA, Tosoh G8 cation-exchange HPLC, and Premier boronate affinity chromatography methods and concluded that TINIA and boronate affinity chromatography methods showed good agreement and correlation with the comparative method (CE), whereas a significant difference was obtained between the mean levels of HPLC and CE.

The influence of diabetes on periodontal health and vice versa has been discussed widely in the dental literature.[15,16] There is an evidence to support periodontal infection having adverse effect on glycemic control.[8,17,18] More direct evidence regarding the effects of periodontal infection on glycemic control in diabetes comes from treatment studies.

In the present study, reduction in HbA1c level in diabetic group (Tables 1 and 2) from baseline to 3 month was 12%, from 3 to 6 months was 6.5%, and from baseline to 6 months was 18.5%. These results were statistically significant with $P < 0.001$ and suggested that non-surgical periodontal therapy led to a reduction in HbA1c levels, especially in patients with severe diabetes mellitus and periodontal disease. The present study also showed a reduction in PI, gingival index, and community periodontal index (Table 1) from baseline to 3 months and from baseline to 6 months with a highly significant $P < 0.001$. Thus, it is possible that the treatment of CP can improve glycemic status of diabetic. Moreover, this status is measured by HbA1c levels, which is an accurate, specific (specificity of HbA1c assay is 83–89%), and sensitive (sensitivity of HbA1c assay is 45–90%) marker of long-term metabolic control (30–60 days) in diabetic population. Reduction in HbA1c level seen in the present study is in accordance with the results of following studies: Stewart *et al.* (2001)[6] in a retrospective study, evaluated patients who received scaling and root planning without antibiotics. After 10 months, glycated hemoglobin examinations were performed and revealed an average reduction of 17% in HbA1c levels

from baseline levels. HbA1c level in non-diabetic control group was at baseline 5.33 ± 0.45, after the treatment at 3 months was 5.21 ± 0.37, after the treatment at 6 months was 5.26 ± 0.39, which were statistically significant with $P < 0.05$. Debora *et al.* (2003)[19] evaluated the effects of the periodontal treatment on the reduction of HbA1c in two groups and concluded that the periodontal therapy improved glycemic control in patients with Type 2 diabetes mellitus in both groups; however, the use of antibiotics significantly reduced HbA1c values below that achieved by root planning alone.

Dag *et al.* (2009)[20] determined the effect of non-surgical periodontal therapy on serum tumor necrosis factor-alpha (TNF-α) and HbA1c levels in poorly and well-controlled Type 2 diabetic patients. Moreover, they found that all periodontal parameters and serum TNF-α levels to be significantly decreased 3 months after the non-surgical periodontal therapy compared to the baseline values in all groups. The HbA1c values were significantly decreased only in well-controlled diabetic patients. Corresponding to the results of the present study, Teeuw (2010)[21] stated that there is a growing evidence that periodontitis may affect general health. The meta-analysis demonstrated a weighted mean difference of HbA1c before and after therapy of 0.40% (95% CI 0.77–0.04%, $P = 0.03$) favoring periodontal intervention in Type 2 diabetic patients. Nevertheless, this improvement in %A1C must be interpreted with care due to limited robustness as evidenced by heterogeneity among studies (59.5%, $P = 0.04$). Thus, the meta-analysis suggests that periodontal treatment leads to an improvement of glycemic control in Type 2 diabetic patients for at least 3 months.

Montoya-Carralero *et al.* (2010)[22] studied the effect of non-surgical periodontal treatment on blood glucose control in Type 2 diabetics with periodontal disease. They found an improvement in glycosylated hemoglobin (HbA1c) after non-surgical periodontal treatment which was statistically significant ($P = 0.042$). Thus, the results of the above study were similar to the present study.

Raman *et al.* (2014)[23] evaluated periodontal parameters, glycosylated hemoglobin (HbA1c), and high-sensitivity C-reactive protein at baseline, 2-, and 3-month intervals in two groups, one receiving non-surgical periodontal therapy and other oral hypoglycemics. HbA1c levels decreased in both groups with NSPT group recording statistically significant reduction ($P = 0.038$).

Kara *et al.* (2015)[24] evaluated the influence of periodontal therapy on glycosylated hemoglobin and fasting blood glucose and serum levels of interleukin (IL)-4, IL-6, IL-8, IL-10, and TNF-α in CP patients with Type 2 diabetes mellitus (T2DM) and in controls. PI, gingival index, bleeding on probing, periodontal probing depth, and clinical attachment level were assessed and recorded at baseline, 1, and 3 months after non-surgical periodontal therapy. All clinical parameters were significantly improved after the periodontal therapy in both groups ($P < 0.001$). Glycosylated hemoglobin levels were decreased; however, the difference was not significant ($P > 0.05$). Fasting blood glucose levels were decreased 1 month after therapy, and increased at 3 months. Patients with T2DM had significantly higher levels of circulating IL-8 at each time point and TNF-α ($P < 0.05$) at baseline. The IL-4 and IL-10 levels were decreased at 1 month after therapy ($P > 0.05$).

A number of different surgical and non-surgical therapies have been successful in achieving this goal. The primary non-surgical approach involves mechanical scaling and root planning. If a patient suffering from periodontitis is able to establish and maintain effective individual oral hygiene, subgingival scaling, and root planning may result in resolution of inflammation, reduced probing pocket depth and clinical attachment gain.[25] The present study, utilizing non-surgical periodontal therapy, showed a significant reduction in infection and periodontal inflammation as well as reduced HbA1c levels after 3 and 6 months in diabetic patients. Significant changes ($P < 0.05$) in PI, gingival index and community periodontal index were also evident in the present study (Table 1).

Hence, there is a two-way relationship between diabetes mellitus and periodontitis, with the former producing a greater severity of periodontal disease and the latter compromising blood glucose control in diabetic patients. Treatment of periodontitis in diabetic patients would lead to a reduction in the soluble mediators responsible for periodontal tissue destruction and would lessen the insulin resistance of the tissues. The findings of this study showed that effective periodontal treatment resulted in lower glycemic levels, which can be measured with the help of HbA1c assay and in the reduction of clinical parameters of periodontal infection, confirming the existing interrelationship between diabetes mellitus Type-2 and periodontitis. Therefore, periodontal treatment should be included in diabetes preventive measures.

Conclusion

Hence, there is a two-way relationship between diabetes mellitus and periodontitis, with the former producing a greater severity of periodontal disease and the latter compromising blood glucose control in diabetic patients. Treatment of periodontitis in diabetic patients would lead to a reduction in the soluble mediators responsible for periodontal tissue destruction and would lessen the insulin resistance of the tissues. The findings of this study showed that effective periodontal treatment resulted in lower glycemic levels, which can be measured with the help of HbA1c assay and in the reduction of clinical parameters of periodontal infection, confirming the existing interrelationship between diabetes mellitus Type-2 and periodontitis. Therefore, periodontal treatment should be included in diabetes preventive measures.

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